UNIVERSITE CHEIKH ANTA DIOP DE DAKAR
FACULTE DE MEDECINE, DE PHARMACIE ET D'ODONTOLOGIE

15 – 17 May 2016
Radisson Blu,
Dakar, Sénégal.

9th Meeting of the African Society of Human Genetics (AfSHG)

9ème Congrès de la Société Africaine de Génétique Humaine (AfSHG)
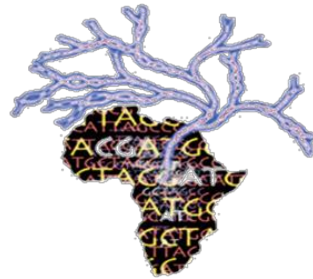
Scientific Program and Abstracts book

Programme Scientifique et Livre des Résumés

UNIVERSITE CHEIKH ANTA DIOP DE DAKAR

FACULTE DE MEDECINE, DE PHARMACIE ET D'ODONTOLOGIE

En partenariat avec

H3Africa (Human Heredity and Health in Africa) Consortium

Groupe d'Etude et de Recherche sur le Cancer

9ᵗʰMeeting of the African Society of Human Genetics

9ᵉᵐᵉ Congrès de la Société Africaine de Génétique Humaine

14- 17 Mai 2016, Radisson Blu, Dakar

THEME :

Strengthening Human Genetics Research in Africa
Renforcer les capacités de l'Afrique en Génétique Humaine

Young Researchers Forum : 14ᵗʰ May - UCAD
Forum des Jeunes Chercheurs le 14 Mai à l'UCAD

Faculté de Médecine, de Pharmacie

et d'Odontologie

Université Cheikh Anta Diop

Welcome to Senegal

Bienvenue au Sénégal

Dear guests,

On behalf of the Local and International Organizing committees, it is a great honor and pleasure to welcome you to the 9th conference of the African Society of Human Genetics (AfSHG) in Dakar, Senegal. This year's conference theme is 'Strengthening human genetics research in Africa'. This choice was dictated by the need to bring Africa up to speed with the development of human genetics outside the continent.

Consolidating and strengthening existing capacities, by improving current technical and human resources, would allow for a better and more efficient handling of genetic diseases that represent a non-negligible public health burden.

We believe that this unique international meeting, the first in a francophone context, will give all individuals involved in genetics and genomics around the world, a great opportunity to exchange, debates and discuss the latest scientific developments in the field. The Scientific committee has prepared a multidisciplinary and attractive program to meet the needs of all participants.

The Conference is hosted at the Radisson Blu hotel, where all plenary talks, posters and exhibitions will occur during May 15th – 17th 2016.

Présidente du Comité d'Organisation

Chers congressistes,

Nous avons l'honneur et le plaisir, au nom des membres des comités d'organisation local et international, de vous accueillir au 9ème congrès de la Société Africaine de Génétique Humaine (AfSHG). Le thème de la de cette année est «Renforcer les capacités de l'Afrique en génétique humaine». Les raisons qui ont motivé le choix de ce thème sont liées au retard accusé par l'Afrique dans le développement de la génétique humaine. Ce renforcement de capacités (amélioration du plateau technique, développement de compétences, …) permettra une prise en charge plus efficiente des pathologies à composante génétique qui posent de réels problèmes de Santé Publique.

Nous espérons que cette rencontre internationale, la première dans un contexte francophone, donnera à tous ceux qui sont impliqués dans la recherche médicale en génétique humaine, une excellente occasion d'échanger, de débattre et de discuter des derniers développements scientifiques relatifs à la thématique. Le comité scientifique a préparé pour cela, un programme multidisciplinaire et attrayant pour répondre aux attentes de tous les participants.

In a pre-conference agenda on May 14th, a Young Researcher Forum hosted by University Cheikh Anta Diop of Dakar, will gathered the next generation of researchers in Human Genetic, who will be presenting, exchanging and discussing through their different research topics.

Senegal also name "Pays de la Téranga", "Country of Hospitality", has a prestigious reputation of hospitality in Africa. Dakar city offers a variety of touristic sites which reflects the rich cultural heritage of the African continent. Much hope you will make time to visit among these cultural sites, the Goree Island, one of the UNESCO world heritages.

We are confident that you will enjoy your stay in Senegal, and wish you a very successful meeting.

Welcome, Bienvenue, "Dal leen Diam"

Warm regards,

Le congrès se tiendra du 15 au 17 Mai 2016 à l'hôtel Radisson Blu, où se dérouleront les conférences plénières, les communications orales et affichées et les expositions.

Un forum des jeunes chercheurs sera organisé en précongrès, le 14 Mai 2016 à l'Université Cheikh Anta Diop de Dakar. Ce forum sera un prétexte pour les jeunes chercheurs de partager les résultats de leurs travaux et de réfléchir sur les perspectives de la génétique en Afrique. Nous adressons nos chaleureux remerciements à tous les membres des comités d'organisation et scientifique qui ont travaillé sans relâche au cours de ces derniers mois pour la bonne réussite de cette manifestation, mais également à nos sponsors et invités.

Nous terminerons en vous souhaitant une rencontre très fructueuse, riche en enseignements.

Bienvenue au Sénégal, "Pays de la Téranga", à la prestigieuse réputation d'hospitalité en Afrique.

Welcome, Bienvenue, "Dal leen Diam"

R. Ndiaye

WELCOME ADDRESS OF THE CHAIRMAN OF THE LOCAL SCIENTIFIC COMMITTEE

MOT DE BIENVENUE DU PRESIDENT DU COMITE SCIENTIFIQUE LOCAL

Dear colleagues,

This is the first time in Senegal, a French speaking country, when the African Society of Human Genetics is going to organize it's Congress, which is the ninth one, from fifteenth to seventeenth of May 2016 (two thousand and sixteen), in a partnership with the H3Africa (Human Heredity and Health in Africa) which is to organize jointly one of its annual meetings.

It is a very great pleasure for the local Scientific Committee to welcome you to this country of ''Teranga'' these two internationally renowned events which will be, besides, an opportunity for young researchers to meet around a forum, on the one hand, and on the other hand, to the members of the Senegalese Group of Study and Research on Cancer (GSRC) to report their works.

The Scientific Committee is welcoming this international meeting so rich in scientific events as in accordance with its dimension, with an attracting program that will undoubtedly permit fruitful exchanges between participants with around fifty or so selected oral papers and a hundred of posted ones.

Chers collègues,

La société Africaine de Génétique Humaine (African Society of Human Genetics) va organiser son Congrès, le neuvième, pour la première fois au Sénégal, pays francophone, du 15 au 17 Mai 2016, avec comme partenaire le consortium H3Africa (Human Heredity and Health in Africa) qui, conjointement, organisera une de ses rencontres annuelles.

Le Comité Scientifique Local a l'immense et l'agréable plaisir d'accueillir au pays de la « téranga » ces deux évènements de renommée internationale, qui, de plus, donneront l'occasion d'une part aux jeunes chercheurs, à travers un Forum de Jeunes Chercheurs, et d'autre part, aux membres sénégalais du Groupe d'Etude et de Recherche sur le Cancer(GERC), d'exposer leurs travaux.

Le Comité Scientifique accueille cette rencontre internationale riche en évènements scientifiques à l'image de sa dimension, avec un programme alléchant qui va sans doute permettre des échanges fructueux entre les participants, autour d'une sélection finale d'une cinquantaine de communications orales et de plus d'une centaine de communications affichées.

Now is the time to appreciate the presence and the support of our colleagues and participants from Europe, from America and other far-off areas, who have come to contribute and ensure the scientific success of this event. We are extremely grateful to them all for their enthusiastic response to the call for papers, and wish you an excellent stay in Dakar and very fruitful discussions.

The Chairman of the Scientific Board.

Professor Oumar FAYE

C'est le moment de saluer la présence et le soutien de nos collègues conférenciers d'Europe, d'Amérique et d'autres contrées bien lointaines, pour contribuer à assurer la réussite scientifique de cet évènement. Nous leurs témoignons ici notre gratitude.

Nous souhaitons à tous les participants un excellent séjour à Dakar et des travaux enrichissants.

Le président du comité Scientifique Local

Professeur Agrégé Oumar FAYE

African Society of Human Genetics
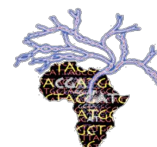
Professor Michèle Ramsay, President of
the African Society for Human Genetics

Dear Delegates,

A very warm welcome to the 9th Meeting of the African Society of Human Genetics in the city of Dakar in Senegal, the most westerly city in Africa!

The theme of the conference is *"Strengthening Human Genetics Research in Africa"*, a theme that is central to the mission of the African Society of Human Genetics. In the absence of extensive research on the genetic contribution to diseases in diverse African populations, it would not be possible to offer appropriate genetics services to our people or to offer the hope of a precision medicine approach on the continent.

We are delighted to jointly host the first day of our conference as a collaborative venture with the Human Heredity and Health in Africa (H3Africa) Consortium. This strengthens our already significant links and provides a great opportunity for engagement and networking. The panel discussion on "Funding sustainable genomic research in Africa" is particularly pertinent and we are looking forward to sharing diverse and innovative ideas.

This meeting serves to bring together members from country-specific Societies of Human Genetics in Cameroon, Democratic Republic of Congo, Egypt, Mali and Southern Africa and we hope to inspire those from other African countries to form societies to strengthen the discipline locally. It is our aim to actively build capacity by inspiring our young students, investigators, clinicians and genetic counsellors to train and to work in the field of Human Genetics. We need to be creative in nesting our discipline and activities in existing structures in our tertiary institutions, hospitals and health care sectors and to demonstrate its utility to patient care.

I wish to thank and commend all those involved in the organisation of the Conference for their hard work, dedication and commitment to making this a memorable meeting. My heartfelt appreciation to Professor Rokhaya Ndiaye Diallo (Chair of the Local Organising Committee), Professor Oumar Faye (Chair of the Local Scientific Committee) and Professor Ambroise Wonkam (Chair of the International Scientific Committee) and their teams – it is not an easy task!

We express our sincere appreciation to our sponsors for their generous contributions.

To all of you, young and not so young, enjoy, engage, participate and learn from your peers, mentors, colleagues and friends. Remember that we are united in our quest to explore the treasure trove of African genetic diversity and to promote an understanding of the genetic contribution to health and disease in African populations with a view to improving health on the continent.

With my best wishes for a highly successful meeting!

Summary / Sommaire

Aknowledgements / Remerciements

Comités d'Organisation et Scientifique - AfSHG ORGANISING COMMITTEES

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                          Pr Raphael Darboux
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Senegalese Society for Sickle-Cell
Senegalese Society for Albino
Senegalese League for fight against cancer

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Didier Lacombe	Raj Ramesar	Anatole Laleye	Henriette Poaty
RokhayaNdiaye Diallo	Mireille Tre-Yavo	Serigne Magueye Gueye	

Saturday 14 May 2016
Young Researchers Forum

8h15
Opening Ceremony
Professor Amadou Diouf : Doyen de la Facultéde Médecine, de Pharmacie et d'Odontologie, UCAD

Dean of the Faculty of Medicine, Pharmacy and Odontology of University Cheikh Anta Diop

Session 1 : 8h45-9h45
Cancer Genetics and Genomics

8h45-8h53	CF01	Beliefs and attitudes of Egyptian parents influencing participation in a pediatric cancer research genetic biorepository **(Rania M. Labib, Egypte)**
8h53-9h01	CF02	Replication of GWAS identified loci in the Tunisian population: Susceptibility and prognostic implications in Breast Cancer. **(Wijden Mahfoudh, Tunisie)**
9h01-9h08	CF03	Impact des mutations des gènes mitochondriaux dans le cancer du sein chez les femmes Sénégalaises **(Fatimata Mbaye, Sénégal)**
9h08-9h16	CF04	Evaluation de l'activation et de l'apoptose des lymphocytes T et B sanguins dans le cancer du col de l'utérus: impact de la chimiothérapie anticancéreuse **(Maimouna Diop, Sénégal)**
9h16-9h24	CF05	Brca1 and Brca2 mutations in hereditary breast cancer in Senegal **(Jean Pascal Diop Sénégal)**
9h24-9h32	CF06	Gut microbiome compositional characterization in colorectal cancer patients from Morocco, **(Imane Allali, H3A fellow, Morocco)**
9h32-9h40	CF07	Mise en place de techniques moléculaires de détection et de typage du Papillomavirus Humain. **(Ahmed Fakhfakh, Sénégal)**

Session 2 : 9h45-10h30
Medical Genetics

9h45-9h53	CF08	Predictive utility of a genetic risk score of common variants associated with type 2 diabetes in a black South African population **(Tinashe Chikowore, South Africa)**
9h53-10h01	CF09	Genetic heterogeneity of spastic paraplegia in Mali **(Salimata Diarra, Mali)**
10h01-10h09	CF10	Molecular diagnosis of Rwandan children with unexplained intellectual disability and neurodevelopmental delay by a-CGH and whole exome sequencing **(Annette Uwineza, Rwanda)**
10h09-10h18	CF11	Struggling to Breathe: Challenges and solutions to diagnosing cystic fibrosis in

		Africa (Cheryl Stewart, South Africa)
10h18-10h26	CF12	Prévalence de l'alpha-thalassémie au sein de la population drépanocytaire sénégalaise (Fatou Gueye Tall, Sénégal)

Session 3 : 10h30-11h30
Coffee break and Poster session

Session 4 : 11h30-12h30
Genetics of Infectious Diseases

12h30-12h38	CF13	The Association Between Drug Resistant Phenotype and Geno types of M. tuberculosis Isolated from pulmonary tuberculosis patients in central Ethiopia. (Zufan Bedewi, Ethiopie)
12h38-12h46	CF14	Application of MCODE algorithm to Plasmodium falciparum interactome (Trust Odia, Nigéria)
12h46-12h54	CF15	The pathway genome database of Anopheles gambiae agamp3 (Marion Adebiyi, Nigéria)
12h54-13h02	CF16	Le domaine basique de la protéine Tat(44-61) du VIH-1 : Etude par fluorescence de son interaction avec des oligonucléotides. (Mor Fall, Sénégal)
13h02-13h10	CFf17	Genome sequence of tsetse bracoviruses: insights into symbiotic virus evolution (Kelvin M. Kimenyi, H3Africa fellow, Kenya)
13h10-13h18	CF18	Genetic variants found in apolipoproteins gene loci and their association with HIV progression amongst HIV perinatally infected children in Botswana (Koketso Maplanka, Botswana)
13h18-13h26	CF19	The African Initiative for Multi-omics Education and Research: Focus on the Human Microbiome Research in Africa (Mamadou Kaba, South Africa)

12h30-14h
Lunch break

14h-14h15	Conférence 1	Funding opportunities, Srinivasan Sudha, NIH, NIAID
14h15-14h30	Conférence 2	Cancer in Africa : challenges and perspectives, Pr Serigne Maguèye Guèye, Senegal

Session 5 : 14h30-15h15
Human Genetic Diversity

14h30-14h38	CF20	Study of host genetics factors in the resistance / susceptibility to Trypanosoma brucei gambiense infection in Guinea. (Justine Kaboré, Burkina)
14h38-14h46	CF21	HLA class II allele polymorphisms in patients with pulmonary Tuberculosis at Mulago hospital in Kampala Uganda (Samuel Kirimunda, Ouganda)
14h46-14h54	CF22	Ancestral African Genomes Provide Insight into Human Evolution and Relationship with Neanderthal (Maha Osman, Soudan)
14h54-15h02	CF23	A Comparison of Retinal Gene Expression Levels in Human and Mouse (Edson Ishengoma, Tanzanie)
15h02-15h10	CF24	Y chromosome haplotype diversity for 17 STR further attests to the linguistic-genetic link and the large east African population size (Eyoab Gebremeskel, Eritrea)
15h10-15h18	CF25	Anomalie du développement sexuel 46,XY avec gynécomastie et orchi-épididymite : à propos d'un cas (Mame Vénus Gueye, Sénégal)
15h18-15h26	CF26	Relationship between socio-economic status and chronic kidney disease in a multi-ethnic cohort – The HELIUS study (DN. Adjei H3A fellows)

Session6 : 15h15-16h15
Coffee break and Poster session

Session 7 : 16h15-17h15 Genomic Medicine		
16h15-16h23	CF27	Implication de l'exon 2 du gène MED12 dans des cas de fibromes utérins chez les femmes Sénégalaises **(Binta Kénémé, Sénégal)**
16h23-16h31	CF28	Statin pharmacogenetics **(Nyarai Soko, Zimbabue)**
16h31-16h39	CF29	Genome-wide Search for Genetic Loci Influencing Circulating Visfatin Levels **(Sally Adebamowo, USA)**
16h39-16h47	CF30	Transcriptome analysis of human adipogenesis reveals novel patterns of gene expression **(Melvin Ambele, South Africa)**
16h47-16h53	CF31	Association of variants in APOL1 and MYH9 with micro-albuminuria among SCD patients from Cameroon **(Emi Geard, South Africa)**
16h53-17h01	CF32	A translational approach to elucidating disease mechanisms - A case study of GPx4 in cardiometabolic disease **(Lalage Katunga, USA)**
17h01-17h09	CF33	Pasteur_galaxy: An open and sustainable Galaxy instance for NGS data analysis **(Ousema Souiai, Tunisie)**
17h15-18h15 Jury Selection Closing Ceremony		

PROGRAMME SCIENTIFIQUE

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Day 1 (Sunday, 15th May 2016): Joint AfSHG/H3Africa Day
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07H30-08H30   REGISTRATION

08:30   **Nature Genetics Training workshop on Research Leadership**

Chairs: Souleymane Mboup (Senegal) and Raj Ramesar (South Africa)

8:30   A Perspective on the Context of Genetic Research in H3Africa (Barry Bloom, USA)
9:00   Managing a team and building capacity (Siana Nkya Mtatiro, Tanzania)
9:30   Communicating effectively with decision makers (Clement Adebamowo, Nigeria/USA)
9:50   Ethical leadership in research (Ruth Chadwick, UK)
10:10   Useful high impact publications (Myles Axton, Editor of Nature Genetics)

10: 30:   **Coffee break**

Session 1   **OPENING CEREMONY**

Chairs: Rokhaya Ndiaye (Senegal) / Ambroise Wonkam (AfSHG)

11:00   Welcome address by the President of the LOC (Rokhaya Ndiaye)
11:15   Opening remarks by H3Africa Steering Committee co-Chair (Enock Matovu)
11:30   Opening remarks by AfSHG President (Michèle Ramsay)
11:45   Allocution of the Ministry of Higher Education and Scientific Research, Senegal
          (SE Prof Mary Teuw Niane)

12: 00   **Keynote: Charles Rotimi (NIH, USA)**

The African Society of Human Genetics: Looking back to shape the future

13H00   **LUNCH BREAK AND POSTER SESSION 1**

Session 2   **Panel discussion: Funding sustainable genomic research in Africa**
          Chairs: Charles Rotimi (NIH, USA) / Audrey Duncanson (WT, UK)

14:00   Position statement panellists:
          Serigne Magueye Gueye - UCAD (Senegal),
          Gavin Churchyard - Aurum Institute (South Africa)
          Thomas Kariuki - AESA (Kenya)
          Rizwana Mia - MRC SHIP (South Africa)
          Maki Kajiwara - WHO (Geneva)
          Ereck Chakauya - SANBio (South Africa)

Session 3   **H3Africa SNP Array: Updates and Opportunities**
          Chair: Adebowale Adeyemo (USA)
15:30   Nicola Mulder (South Africa)
15:50   Zané Lombard (South Africa)

16:10   **Coffee break**

Session 4	**Human-non-human system studies Symposium: TB genomics**
	Chair: Scott Williams (USA) / Branwen Hennig (UK)
16: 40	Invited Speaker 1: Sebastien Gagneux (Switzerland): Evolution of Mycobacterium tuberculosis
	Invited Speaker 2: Scott Williams (USA): A TB resistance locus in highly susceptible individuals
17: 30	**Special Communication:** Bernie Jones (STI4D, UK): Genetics research across Africa – improving outreach and collaboration
18:00	**Annual General Meeting of the AfSHG**
19:00	**Reception cocktail**

8

Day 2 (Monday, 16th May 2016)

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Session 5
08:00

Early bird session Training Workshop

Next generation sequence data analysis in complex traits: principles and examples
Chairs: Fasil Ayele (NIH) / Amadou Gaye (NIH)

Session 6

Cancer Genetics/Genomics with the Cancer Research Group (GERC), Senegal

Chairs: Ahmadou Dem (Senegal) / Raj Ramesar (South Africa)

09:00   Guest speaker 1: Clement Adebamowo (Nigeria/USA): Cervical cancer and genomics

09:25   Guest speaker 2: Macoura Gadji (Senegal): Nuclear Remodelling and Genomic Instability in Cancer

9:50 – 10:40   **Free communications**

9:50 – 10:00   **C01** - Utility of a microarray diagnostic for AML in the South African setting (**Marco Alessandrini, South Africa**)

10:00 – 10:10   **C02** - Aspects moléculaires des patients opérés de cancer colorectal à TOURS, (**Fatou Diallo, Senegal**)

10:10 – 10:20   **C03** - Genetics and Pharmacogenetics Aspects of Chronic Myeloid Leukemia in Morocco (**Kassogue, Morocco**)

10:20 – 10:30   **C04** - L'allèle arginine du codon 72 du gène p53 serait un facteur de risque de cancer du sein au Sénégal (**Yacouba Dia, Senegal**)

10:30 – 10:40   **C05** - Place de la cytogénétique et de la biologie moléculaire dans le diagnostic et le suivi des patients atteints de leucémie myéloïde chronique (**Nata Dieng, Senegal**)

10:40   **Coffee break**

Session 7   **Medical Genetic Services**

Chairs: Oumar Faye (Senegal) / Ambroise Wonkam (South Africa)

11:00
Congo: Guest Speaker 1: Lukusa-Tshilobo (RD Congo): Human and clinical genetics in the DR
a rapidly evolving story

11:20   Guest speaker 2: Leon Mutesa (Rwanda): Medical genetic services in Rwanda: achievements, challenges and perspectives

11:40   Guest speaker 3: Arame Ndiaye (Senegal): Medical genetic services in Senegal

12:00 – 12:50   **Free communications**

12: 00 – 12:10   **C06** – Genetic counseling competencies of nurses in Three Nigerian teaching hospitals (**Adejumo Prisca Olabisi, Nigeria**)

12: 10 – 12:20   **C07** – Caractérisation des anomalies de développement sexuel (ADS) à travers la cytogénétique: à propos de 40 cas rencontrés au Sénégal (**Fatimatou Dia, Senegal**)

12: 20 – 12:30   **C08** – Diversité et évolution génétique des tumeurs malignes du sein chez les femmes Sénégalaises (**Fatimata Mbaye, Senegal**)

12 : 30 – 12:40	**C09** – Genetics of congenital heart disease (CHD) in Morocco: Experience of Medical Genetics and Cardio-Pediatrics departments of Fez Hassan II University Hospital **(Ihssane El Bouchikhi, Morocco)**
13:00	**LUNCH BREAK AND POSTER SESSION 2**

Session 8	**Genetics of Infectious Diseases**
	Chair: Melanie Newport (UK) / Cheikh Saad Bouh Boye (Senegal)
14: 00	Guest speaker 1: Daouda Ndiaye (Senegal): Malaria genomics
14: 25	Guest Speaker 2: Christian Happi (Nigeria): Genomic Surveillance Facilitates Ebola Virus Containment and Elucidates Origin, Transmission and Evolution during the 2014 Outbreak
14: 50	Guest Speaker 3: Collet Dandara (South Africa): Pharmacogenomics of antiretroviral
15: 15	Guest speaker 4: Dissou Affolabi (Benin): TB genomic susceptibility in Benin

15:40 – 16:10	**Free communications**
15:40 – 15:50	**C10** – The Predictive Value of IL-28B Gene Polymorphism in Egyptian HCV Patients' Response to Combination Therapy of Pegylated Interferon and Ribavirin **(Samar Kamal Kassim, Egypt)**
15:50 – 16:00	**C11** – Temporal dynamics of genome-wide transcription in malarial children in Burkina Faso **(Aïssatou Diawara, Emirates)**
16:00 – 16:10	**C12** – Real-time expression profile of Mycobacterium tuberculosis Thymidylate Kinase messenger ribo-nucleic acids during in-vitro growth of a Ugandan strain **(Ivan Mwebaza, Uganda)**

16:10	**Coffee break**

Session 9	**Human Genetic Diversity and Health**
	Chairs: Mbacke Sembene (Senegal) / Alice Matimba (Zimbabwe)
16:30	Guest speaker 1: Adebowale Adeyemo (USA): Human diversity and Precision Medicine
16:55	Guest Speaker 2: Muntaser Ibrahim (Sudan): The pivotality of the north East African scenery to early human evolution
17:20	Guest speaker 3: Patrick Curmi (France):
17:35	Guest speaker 4: Amadou Gaye (NIH/Senegal) Study of severe hypertension in African American

18:00 – 18:30	**Free communications (3)**
18:00 – 18:10	**C13** – Whole Exome Sequence Analysis Identifies Two Novel Loci for High Density Lipoprotein Cholesterol in African Ancestry Individuals **(Amy Bentley, USA)**
18:10 – 18:20	**C14** – Southern African Human Genome Programme: Deep whole genome sequencing provides insights into the genetic architecture of South Africans **(Ananyo Choudhury, South Africa)**

18:20 – 18:30   **C15** – Genomic Diversity of African populations and pharmacogenomics in the safe and efficacious use medicines in Africa **(Collen Masimirembwa, Zimbabwe)**

20:30   **GALA DINNER**

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Day 3 (Tuesday, 17th May 2016)

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Session 10	**Genomic Medicine**
	Chairs: Rokhaya Ndiaye (Senegal) / Michèle Ramsay (South Africa)
08: 30	Guest Speaker 1: Benoit Arveiler (France): New Generation Sequencing for molecular diagnosis in clinical laboratories: study of a large series of patients with albinism
08: 55 Neurogenetic	Guest Speaker 2: Kenneth Fischbeck (USA)/ Guida Landouré (USA & Mali); diseases study: the case of Mali
09: 30	Guest Speaker 4: Henriette Poaty (Congo Brazzaville): Les gènes MisMatch Repair et le Syndrome de Lynch
09: 50	Guest Speaker 5: Anatole Laleye (Benin)

10:10	**Coffee break**

10: 30 – 11:20	**Free communications**
10: 30 – 10:40	**C16** – Targeted resequencing of genes involved in neurological conditions in South African patients with Parkinson's disease **(Soraya Bardien, South Africa)**
10: 40 – 10:50	**C17** – Knowledge and experiences of parents with children affected by Sickle Cell Disease in Cape Town **(Katryn van Niekerk, South Africa)**
10: 50 – 11:00	**C18** – Hereditary spastic paraplegias: Identification of a novel SPG57 variant affecting TFG oligomerization and description of HSP subtypes in Sudan **(Yahia Ashraf, Sudan)**
11: 00 – 11:10	**C19** – Genome-wide analysis identifies an African specific variant in SEMA4D that is associated with BMI **(GuanJie Chen, USA)**
11: 10 – 11:20	**C20** – Genome-wide Association Identifies African-Specific Susceptibility Loci in African Americans with Inflammatory Bowel Disease **(David Tea Okou, USA)**

Session 11	**Ethics and genomics**
	Chairs: Alioune Dieye (Senegal) / Jantina de Vries (South Africa)
11:20	Guest speaker 1: Aissatou Toure (Senegal
11:45	Guest speaker 2: Elonna Obiefuna (Nigeria): Indigenous linguistic and cultural concepts of heritability and comprehension of genomic research in Nigeria

12:10– 12:40	**Free communications**
12:10 – 12:20 a Ethiopia).	**C21** – Rapid Ethical Appraisal (REA) tool to design a contextualized consent process for genetic study of podoconiosis in Ethiopia **(Tewodros Tariku Gebresilase, Ethiopia).**
12:20 – 12:30	**C22** – Types of albinism in southern Africa and genetic investigation of pigment-related genes **(Robyn Kerr, South Africa)**
12:30 – 12:40	**C23** – Alleviating the Burden of Beta-Thalassemia in Egypt **(Ghada Yousef El-Kamah, Egypt)**

13H00	**LUNCH BREAK AND POSTER SESSION 3**
Session 12 14H00	**Disorders of Sex Development / Symposium** Chairs: Oumar Faye (Senegal) / Ibrahima Fall (Senegal) Invited Speaker 1: Alassane Diouf, Gynaecologist Invited Speaker 2: Haby Signate Sy, Paediatrician Invited Speaker 3: Oumar Faye, Geneticist Invited Speaker 4: Ambroise Wonkam, Geneticist Invited Speaker 5: Ibrahima Fall, Surgeon Invited Speaker 6: Aida Sylla, Psychologist
15:30	**CLOSING CEREMONY and PRIZE GIVING** **Pr Ibrahima THIOUB**, Vice Chancellor, University Cheikh Anta Diop (Senegal) **Michèle Ramsay**, President of the AfSHG and Chair of the H3Africa Consortium Steering Committee
16H30 – 18H30	**SOCIAL EVENT –VISIT TO GOREE ISLAND**

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GUEST SPEAKERS' BIOSKETCH AND ABSTRACTS

SCOTT WILLIAMS,

CASE WESTERN UNIVERSITY, USA

Scott Williams, PhD, is professor in the Department of Epidemiology and Biostatistics and in the Institute for Computational biology at Case Western Reserve University, School of Medicine. He received his PhD from Washington University, St. Louis, training in the population genetics and molecular evolution of Drosophila. About 20 years ago he switched to the study of human genetics and has been applying tools of population genetics to the genetic basis and the differential distribution of complex disease among populations. He has explored how ancestry and genetic differentiation among populations affects health disparities. A major focus has been on addressing patterns of genetic variation among populations with different disease prevalence. He has also worked on the genetic susceptibility to infectious disease and the co-evolution of pathogens and host genomes as it affects disease risk and severity. Dr. Williams has published more than 200 papers addressing issues of disease risk, disparity, genetic differentiation and methods to address these from both theoretical and practical perspectives.

Abstract

Immunosuppression resulting from HIV infection increases the risk of progression to active tuberculosis disease (TB), both in patients newly exposed to Mycobacterium tuberculosis (MTB) and in those with latent infections. We hypothesized that HIV-positive patients who do not develop TB despite living in areas where it is hyperendemic provide a model of natural resistance. We performed a genome-wide association study of TB resistance, using 581 HIV-positive Ugandans and Tanzanians enrolled in prospective cohort studies of TB, 267 of whom developed active TB, and 314 did not. A common variant, rs4921437, at 5q33.3, was significantly associated with TB (odds ratio = 0.37, p = 2.11 x 10-8). This variant lies within a region of the genome that includes IL12B and is embedded in an active regulatory region, an H3K27Ac histone mark. The locus also displays consistent patterns of linkage disequilibrium across African populations and has signals of strong selection in populations from equatorial Africa. Along with prior studies demonstrating that therapy with IL12, the cytokine encoded in part by IL12B, associated with longer survival following MTB infection in CD4-T-cell deficient mice, our results suggest that this pathway may be an excellent target for development of new TB treatment modalities, especially for HIV-positive patients. Our results also indicate that studying extreme disease resistance in the face of extensive exposure can increase the power to detect associations in complex infectious disease.

AMBROISE WONKAM, CAMEROUN, SOUTH AFRICA

Prof Ambroise Wonkam is professor of medical geneticist, in the Division of Human Genetics, Faculty of Health Sciences, and University of Cape Town, South Africa.

After a MD training from the Faculty of Medicine and Biomedical Sciences, University of Yaoundé I (Cameroon), Dr Wonkam completed a thesis in Cell Biology in the department of Morphology, University of Geneva (Switzerland) and a PhD in Human Genetics (University of Cape Town, South Africa).He was awarded the 2003 Denber-Pinard Prize for the best thesis from the Faculty of Medicine, University of Geneva.

Other salient aspects of Dr Wonkam's background include his education as a medical geneticist at a highly reputable genetics department in Geneva (Switzerland). He subsequently practiced medical genetics in both European and African contexts. Dr Wonkam interests are reflected in more than 80 peer-reviewed publications, which are in laboratory, clinical educational and ethical aspects of medical genetics. His research focuses on disease of Africans: 1) Psychosocial Burden and Genomics modifiers of Sickle Cell Disease; 2) Genetics of hearing loss among Africans and 3) Monogenic conditions that affect the people of African descent.

Prof Wonkam recently won the very competitive Clinical Genetics Society International Award for 2014, from the British Society of Genetic Medicine. Prof Wonkam is secretary of the African Society of Human Genetics, Board member of the International Federation of Human Genetics Societies and council member of Human Genome Organization. His is also member of the steering committee of H3Africa consortium, leading specifically the SCD project.

ROKHAYA NDIAYE DIALLO, SENEGAL

Pr Rokhaya Ndiaye Diallo is an associate professor of Human Genetics, in the Department of Pharmacy of the Faculty of Medicine, Pharmacy and Odontology of University Cheikh Anta Diop of Dakar, Senegal.

After a PharmD training at University Cheikh Anta Diop of Dakar, Pr Ndiaye completed a PhD thesis in 2014 at University Paris 7, France. She was awarded in 2010 a Fullbright senior scholar fellowship in the Department of Pathology of University of Washington, Seattle, USA.

Her research interests focused on the role of genetic variation in cancer susceptibility and genetic basis of single gene disorders in African populations. Her current research projects focused on breast and ovarian cancers, head and neck cancer and rare genetic diseases.

Pr Ndiaye recently won a competitive Award for 2013 and 2015, from the Senegalese Ministry of Higher Education and Scientific Research. She is also member of the African Society of Human Genetics

BARRY BLOOM, USA

Harvard University Distinguished Service Professor and Joan L. and Julius H. Jacobson Professor of Public Health

A leading scientist in the areas of infectious diseases, vaccines, and global health and former consultant to the White House, Dr. Barry Bloom continues to pursue an active interest in bench science as the principal investigator of a laboratory researching the immune response to tuberculosis, a disease that claims more than two million lives each year.

He has been extensively involved with the World Health Organization (WHO) for more than 40 years. He is currently Chair of the Technical and Research Advisory Committee to the Global Programme on Malaria at WHO and has been a member of the WHO Advisory Committee on Health Research and chaired the WHO Committees on Leprosy Research and Tuberculosis Research, and the Scientific and Technical Advisory Committee of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases. Dr. Bloom serves on the editorial board of the Bulletin of the World Health Organization.

Dr. Bloom currently serves on the Ellison Medical Foundation Scientific Advisory Board and the Wellcome Trust Pathogens, Immunology and Population Health Strategy Committee. He is on the Scientific Advisory Board of the Earth Institute at Columbia University and the Advisory Council of the Paul G. Rogers Society for Global Health Research.

His past service includes membership on the National Advisory Council of the National Institute for Allergy and Infectious Diseases, the Scientific Advisory Board of the National Center for Infectious Diseases of the Centers for Disease Control and Prevention, and the National Advisory Board of the Fogarty International Center at the National Institutes of Health, as well as the Governing Board of the Institute of Medicine.

Dr. Bloom was the founding chair of the board of trustees for the International Vaccine Institute in South Korea, which is devoted to promoting vaccine development for children in the developing world. He has chaired the Vaccine Advisory Committee of UNAIDS, where he played a critical role in the debate surrounding the ethics of AIDS vaccine trials. He was also a member of the US AIDS Research Committee.

Dr. Bloom came to HSPH to serve as Dean of the Faculty in 1998. He stepped down December 31, 2008 and is currently a Harvard University Distinguished Service Professor at HSPH. In his capacity as Dean, he served as Secretary Treasurer for the Association of Schools of Public Health (ASPH). Prior to that he served as chairman of the Department of Microbiology and Immunology at the Albert Einstein College of Medicine from 1978 to 1990, the year in which he became an Investigator of the Howard Hughes Medical Institute, where he also served on the National Advisory Board. In 1978, he was a consultant to the White House on international health policy.

Dr. Bloom holds a bachelor's degree in biology and an honorary D.Sc. from Amherst College and a Ph.D. in immunology from Rockefeller University.

He is a past president of the American Association of Immunologists and the Federation of American Societies for Experimental Biology. He received the first Bristol-Myers Squibb Award for Distinguished Research in Infectious Diseases, shared the Novartis Award in Immunology in 1998, and was the recipient of the Robert Koch Gold Medal for lifetime research in infectious diseases in 1999.

Dr. Bloom is a member of the National Academy of Sciences, Institutes of Medicine, the American Association for the Advancement of Science, and the American Philosophical Society.

DISSOU AFFOLABI, BENIN

Contribution of genetic variation to pharmacokinetic variability and toxicity in patients undergoing multi-drug tuberculosis treatment in Sub-Saharan Africa (RAFAgene)

Principal Investigator

Scientific Description: In 2010 there were an estimated 8.8 million incident cases of tuberculosis (TB) globally, with 2.3 million of these reported in Africa, 1.1 million deaths among HIV-negative cases of TB and an additional 0.35 million deaths among people who were HIV-positive. The complex relationship between TB pathogen, host, and drug exposure in the pathogenesis of TB is poorly understood. The treatment regimen that is currently recommended by WHO for new cases of drug-susceptible TB is highly efficacious, with cure rates of around 90% in HIV-negative patients. However, even if all new TB cases were treated and patients were adherent to the treatment, there would still be 10% of patients (i.e. 880,000 patients worldwide, 230,000 patients in Africa) who fail to respond to treatment. Even if adherent to treatment, a proportion of patients, with rifampicin sensitive TB, are slow to respond to medication or are non-responders. The problem is even more complex and serious in HIV infected patients where the efficacy of the current treatments appears to be lower. Still other patients can be treated successfully, but will experience toxicity and thus treatment interruptions. While several potential determinants of the variable response to drug treatment are recognised (e.g. sex, age, ethnicity), much of the variability in response to anti-tuberculosis drugs remains unexplained. In recent years there has been a rapid development in the understanding of the genetics underlying interindividual differences in drug metabolism and treatment efficacy. The field of pharmacogenetics encompasses the study of the heterogeneity in genes related to drug transporters, drug metabolising enzymes and drug targets, in the context of efficacy of treatment and adverse drug reactions. Few studies have been conducted to explore this field for TB disease. Through this study we aim to explore and determine host genetic factors contributing to pharmacokinetic (i.e. drug concentration) and dynamic (i.e. treatment outcome) variability in TB patients. The "RAFAgene" study is a 5 year project which will be nested within two multi-country randomised phase III tuberculosis treatment trials, the OFLOTUB and RAFA trials (reg numbers NCT00216385 and PACTR 201105000291300) conducted in Sub-Saharan Africa. Patients enrolled in the pharmacokinetic studies within these 2 trials will be sampled for genetic analysis (genome-wide and targeted SNPs screening with in vitro confirmation of the biological plausibility of the association between pharmacokinetic and genetic characteristics). The proposed project is led by Dr Dissou Affolabi at the National Hospital for TB and Pulmonary (NHTPD) with partners from the National TB program in Senegal, the University Ignace Deen in Guinea, the University of Cape Town (SA), the Medical Research Council in Durban (South Africa), the University of Liverpool UK and the London School of Hygiene and Tropical Medicine UK.

RUTH CHADWICK, UK

Distinguished Research Professor

She has co-ordinated a number of projects funded by the European Commission, including the EUROSCREEN projects (1994-6; 1996-9) and co-edits the journal Bioethics and the online journal Genomics, Society and Policy. She is Chair of the Human Genome Organisation Ethics Committee, a member of the Advisory Committee of the UK National Stem Cell Network; and has served as a member of several policy-making and advisory bodies, including the Panel of Eminent Ethical Experts of the Food and Agriculture Organisation of the United Nations (FAO), and the UK Advisory Committee on Novel Foods and Processes (ACNFP). She was editor-in-chief of the award winning Encyclopedia of Applied Ethics (1998), of which a second edition has now been published. She is an Academician of the Academy of Social Sciences and a Fellow of the Hastings Center, New York; of the Royal Society of Arts; and of the Royal Society of Medicine. In 2005 she was the winner of the World Technology Network Award for Ethics for her work on the relationship between scientific developments and ethical frameworks.

GUIDA LANDOURE, MALI

Professor Clinical and Genetic Studies of Hereditary Neurological Disorders in Mali

Principal Investigator

Lay Description: Hereditary neurological disorders are very disabling diseases that are under-studied in Africa. Our first aim is to clinically characterize these disorders in the Malian population in order to establish a comprehensive clinical description of the diseases in this region. Our second aim is to identify gene mutations related to neurological diseases, and to explore their effects in cell culture models to further our understanding of their function and interactions and our knowledge of common disease mechanisms. Our third aim is to provide training and post-training incentives for Malian physicians and students in order to maintain them locally and insure that research is current.

MILES AXTON, USA

Myles Axton is the editor of *Nature Genetics*. He was a university lecturer in molecular and cellular biology at the University of Oxford and a Fellow of Balliol College from 1995 to 2003. He obtained his degree in genetics at Cambridge in 1985, and his doctorate at Imperial College in 1990, and between 1990 and 1995 did postdoctoral research at Dundee and at MIT's Whitehead Institute. Myles's research made use of the advanced genetics of *Drosophila* to study genome stability by examining the roles of cell cycle regulators in life cycle transitions. His interests broadened into human genetics, genomics and systems biology through lecturing and from tutoring biochemists, zoologists and medical students from primary research papers. Helping to establish Oxford's innovative research MSc. in Integrative Biosciences led Myles to realize the importance of the integrative overview of biomedical research. As a full time professional editor he is now in a position to use this perspective to help coordinate research in genetics.

Abstract

Useful high impact publications

Attention to accurate representation of claims within a research article together with the evidence and method supporting each claim can expedite peer review. Accurate citation of the claims of others is essential to avoid prematurely closing possibly productive research strategies.

Our recommendation in planning a research paper is to lay out the claims together with the supporting evidence and methods in a three-column table. The rows follow one another logically as one experiment or analysis follows necessarily from its predecessor. This simplified structure permits rapid peer review and can be used to assess student comprehension of the contents and structure of a scientific argument. Where evidence provides increased likelihood or other increased support for the authors' ideas, the claims should be presented in terms of likelihood, conjecture or hypothesis. This simplified and graded schema for claims makes it easier for referees, of whatever linguistic background, to agree or disagree with the authors' claims one by one, expediting peer review. Depending on the level of evidence, the referees and editors can then recommend strengthening the evidence or downgrading the claims accordingly.

Much of the impact of a publication is derived from careful stewardship in release of methods, materials, code and analytical strategy, and making data available, whether publicly or under agreements that protect research subjects and encourage capacity building in the data producing region. The FAIR data principles are simple guidelines for ensuring that machines can find and use data, supporting data reuse by individuals. More (and better) research can be generated by designing data and algorithms to be findable, accessible, interoperable and reusable. FAIR data should be stored together with the tools and workflows that led to these data. Data reuse can improve existing research publications and can result in useful Analysis articles based entirely on existing data.

NICOLA MULDER, USA

Head of Computational Biology Division, Department of Integrative Biomedical Sciences, IDM, University of Cape Town

Professor Mulder heads the Computational Biology Division (CBIO) in the Department of Integrative Biomedical Sciences at the University of Cape Town (UCT) (http://www.cbio.uct.ac.za). She has a PhD in Medical Microbiology, and spent over 8 years at the European Bioinformatics Institute (EBI) in Cambridge, moving into the area of bioinformatics. At the EBI she was a Team Leader, responsible for development of InterPro and the Gene Ontology Annotation Project. At UCT, Prof Mulder works in the area of bioinformatics of infectious diseases, including pathogen and host genomics and biological networks, African population genetics, human variation and disease association studies, and microbiomes. Her group also provides bioinformatics support and training for postgraduate students and local researchers. She plays a leading role in bioinformatics education in South Africa and the rest of Africa, and heads the GOBLET Learning, Education and Training Committee. Prof Mulder is PI of H3ABioNet, a Pan-African Bioinformatics network for H3Africa, which aims to build bioinformatics capacity for genomics research on the continent and develop the infrastructure for managing large-scale genomics data from H3Africa projects.

ABSTRACT

Design of a new African genotyping array

The emergence of genomics data for human populations from genotyping arrays or sequencing is skewed towards populations outside of Africa. Genotyping arrays (chips) have also traditionally been designed for non-African populations, leaving a gap for researchers studying African cohorts. We have done an analysis of how African populations perform on existing chips, which demonstrates the need for a new chip designed using African population data, which is more appropriate for these populations. Up to 5,000 full genome sequences, 3,500 of which are from diverse African ethnic groups have been processed for the new chip design. This presentation will describe the work done to date on the design of the new array and the opportunities it provides.

ZANE LOMBARD, SOUTH AFRICA

BIOSKETCH

Division of Human Genetics, National Health Laboratory Service and University of the Witwatersrand

Dr Lombard obtained her PhD in Human Genetics in 2008, with her PhD research focusing on a bioinformatics-driven approach to disease-gene discovery. She is currently a principal medical scientist and the team lead of the Research & Development group in the Division of Human Genetics, where the focus is on the implementation of next-generation technology for genetic diagnostics. Before this she worked as a Senior Lecturer in Bioinformatics in the School of Molecular & Cell Biology, University of the Witwatersrand. Dr Lombard's research interests include understanding the role that the human genome plays in conveying risk to common, chronic diseases. Therefore, her research group focuses on using molecular genetics and computational techniques to better understand African genetic variation, and how it influences disease risk. She is the co-chair of the H3Africa genome analysis working group, and has taken a lead in the endeavour to establish an African-focused custom genotyping array.

ABSTRACT

An efficient genome-wide genotyping array for African populations – the H3Africa custom chip consortium

H3Africa (Human Heredity and Health in Africa) is a partnership among the National Institutes of Health (U.S.A.), the Wellcome Trust (U.K.) and the African Society of Human Genetics. The main objective of H3Africa is to facilitate a contemporary research approach to the study of the genomic and environmental determinants of disease in Africa, and to improve the health of African populations. It is recognized that currently available genotyping arrays are not ideally suited to studying African populations. Therefore the main aim of the H3Africa custom chip consortium is the design of a cost-effective genome-wide association (GWAS) array, with content appropriate for use in genomic studies of individuals from the African continent. To enable this, a large sequence reference panel (based on whole-genome sequence (WGS) data) of African populations will be designed, and used to select an appropriate GWAS scaffold for the array.

FASIL AYEKE TEKOL, NIH, USA

Bio-sketch:

Fasil Tekola-Ayele, M.P.H., Ph.D., is a research fellow at the Center for Research on Genomics and Global Health, National Human Genome Research Institute (NHGRI), National Institutes of Health (NIH). His research focuses on genetics and epidemiology of type 2 diabetes/metabolic syndrome, podoconiosis, and population genetics. His lead-authored research published in the New England Journal of Medicine in 2012 led to the discovery of genetic variants that confer susceptibility to podoconiosis. His published genome-wide studies on the metabolic syndrome and interleukins in African ancestry populations have found multi-ancestry shared as well as African-specific loci associated with cardio-metabolic diseases. He was co-first author in an international collaborative research namely the African Genome Variation Project that provided new insights into the genetic variation landscape of several African populations published in Nature in 2014. His overall research interest is on genetic and environmental basis of chronic diseases and its public health translation, with a long term goal of contributing to the betterment of global health. Dr. Tekola-Ayele is a recipient of the 2014 Intramural Research Award from the NHGRI/NIH.

Abstract:

Next generation sequence data analysis in complex traits: principles and examples

Next generation sequencing has enabled a deeper interrogation of the genome to investigate the genetic bases of common and rare diseases. This workshop will introduce basic principles of sequence-based genetic studies, sequencing data formats, variant quality control processes, variant analysis and prioritization pipelines, and functional annotations. To demonstrate application of these procedures in genetic studies of complex diseases, practical examples involving whole exome/genome sequencing studies will be discussed. By the end of the workshop, it is hoped that participants will have basic grasp of DNA sequence-based genomic studies and analysis pipelines.

PROSPER LUKUSA-TSHILOBO, DR CONGO

HUMAN AND CLINICAL GENETICS IN THE DR CONGO: A RAPIDLY EVOLVING STORY.

Prof. Dr. P Lukusa-Tshilobo on behalf of the Congolese Society for Human Genetics

Abstract:
The Democratic Republic of Congo (DR Congo), the second largest country in Africa with more than 70 million citizens, is in enormous need of genetic services. People face various hereditary diseases, some of which are highly prevalent in this region. E.g. sickle cell anaemia and albinism rage heavily in DRC where affected individuals are generally helpless, with often lack of correct information about the origin and mode of transmission, and also lack of access to treatment or guidance.

Despite the need of genetic services, until the end of the 20th century, Medical Genetics was not part of the training curriculum of medical schools in DR Congo, and clinical genetic services were lacking.

The first Human Genetics Unit ("Unité de Génétique Humaine") was created in 2007 at the faculty of medicine, University of Kinshasa, with the mission of providing high quality genetic teaching, developing clinical genetic services and initiating human genetic research in the DR Congo.

Since then, several initiatives were taken.

* From 2008 on, postgraduate genetics courses and workshops were organized for medical researchers and doctors working in Kinshasa (the capital city, located at the western part of the DR Congo) and in Lubumbashi (the second main city of the country, in the south-eastern region).

*A few years later, medical genetics courses for undergraduate students were introduced in the training program of medicine faculties in DR Congo: since 2011 at the University of Kinshasa (UNIKIN) and, a year later, at the University of Lubumbashi (UNILU).

*Outpatient genetic clinics were organized in Kinshasa (UNIKIN) and in Lubumbashi (UNILU), both as teaching sessions and as means to get more insight in the needs of the population.

*Two genetics laboratory were created in Kinshasa, one in the Institut National de Recherche Biomédicale (INRB), focusing on molecular and conventional cytogenetics, another at the Faculty of Medicine of UNIKIN, focusing on DNA analysis.   DNA extraction facilities are available at both sites, an essential step for both clinical services and genetics research.

* A solid and sustainable network between Congolese Universities (teaching, clinical and research activities in UNIKIN and UNILU) and INRB (laboratory and bio-repository) has been build and is currently called "Centre Interdisciplinaire de Génétique au Congo (CIGC)".

*The growing interest in the field of human and medical genetics has led to the creation of the Congolese Society for Human Genetics (CoSHG), which was launched during a very successful scientific meeting in Kinshasa in May 2013. A second CoSHG meeting was organized two years later in Lubumbashi, with attendance of African geneticists from Congo-Brazzaville, Rwanda, Bénin and Sénégal. A network linking French speaking geneticists was then created.

*Several research programs were initiated over the last years, already leading to two successful PhD's in the fields of intellectual disability and sickle cell anemia. Six additional PhD students initiated projects on sickle cell anemia, dysmorphology and albinism and cleft lip/palate. A major focus currently is on diagnosis and treatment of sickle cell anemia, with support from the VLIR-UOS (Flanders-Belgium), and participation in the African Consortium named SPARCO.

The enthusiasm of our young genetics team is great, and this together with a growing international network is a solid basis for further steps forward in the fascinating domain of medical and clinical genetics in our country.

LEON MUTESA, RWANDA

Dr Leon Mutesa studied medicine at the University of Rwanda, obtaining an MBChB (Doctorate in General Medicine) in 2003. In 2003 he was awarded a PhD scholarship grant from French speaking Universities CIUF/CUD/Belgium Cooperation and joined the Center for Human Genetics at the University of Liege-Belgium. He began researching on cystic fibrosis (CF) causing mutations in African population where the disease has been under-diagnosed for longtime. In 2009 he graduated with a PhD in Medical Sciences (Human Genetics) and joined the College of Medicine and Health Sciences/School of Medicine at the University of Rwanda as Senior Lecturer then Associate Professor of human genetics and serves as Head of Center for Medical Genetics, where he is currently developing clinical practice, molecular and cytogenetic analyses. From 2009 to 2011 he served as the Head of Department of Clinical Laboratory at Kigali University Teaching Hospital (CHUK) where he was supervising laboratory analysis set up and lab accreditation process. In 2010 Dr Mutesa was awarded a two year-postdoctoral fellowship grant from CIUF/CUD-NUR03 Belgian Cooperation project and jointly conducted his research in Rwanda and at the University of Liege/Belgium in the Department of Human Genetics with collaboration of the Institut fur Zellulare und Molekulare Physiologie at the Universitat of Erlangen-Numberg in Germany. Currently, he is Principal Investigator and manages more than six major international research grants including an NIH U54 grant on molecular screening of HPV.

ABSTRACT

Medical genetic services in Rwanda: achievements, challenges and perspectives

The creation of Center for Human Genetics in Rwanda in 2006 was related to the increasing requests of genetic counseling and other services to the population including diagnostic and prevention.

The objectives of this Center are to perform cytogenetic and molecular testings for diagnostic of genetic disorders; to conduct and promote research in all aspects of human genetics and genomics; and to serve as a center for higher education and specialized training in human genetics and allied disciplines. Under this broad mandate, the center pays attention to application of scientific and technical advances to the development and provision of diagnostic tests for genetic disorders commonly occuring in Rwanda, and train students and laboratory personnel. In addition, the center strives to bring together clinicians, geneticists and other specialists for translational research, provide a forum for discussion of the ethical and legal issues emanating from genetic research and routine work.

Since the center started its activities, several various cases continue to be addressed and these mainly include patients with dysmorphic patterns and multiple congenital anomalies (MCA), global development delay (GDD), intellectual disability (ID), congenital heart defects (CHD), chromosome aberrations in spontaneous abortions and stillbirths, genetics of infertility and miscarriages, disorders of sex development (DSD), unsolved cases of metabolic diseases and other genetic defects like hemoglobinopathies.

Cytogenetic studies have been performed in the majority of these cases and the most common identified chromosomal abnormalities were Down syndrome, Edward's syndrome and Patau syndrome. A large spectrum of other chromosomal rearrangements including Turner syndrome, Klinefelter syndrome, Cat eye syndrome, DiGeorge syndrome, Williams syndrome, Angelman syndrome, Prader willi syndrome, 47,XX,+del(9)(q11), 46,XY,del(13)(q34) and 46,XX,der(22)t(10;22)(p10;p10)mat have been also identified. Most of complementary molecular tests including MLPA, a-CGH, and next generation sequencing (NGS) have been carried out in collaboration with the Center for Human Genetics of the University of Liege, which continues to support our Center for capacity building and knowledge transfer.

ARAME NDIAYE, SENEGAL

Arame Ndiaye, PhD, est Biologiste dans le Laboratoire de cytologie clinique-cytogénétique-Biologie de la reproduction de l'hôpital Aristide le Dantec (HALD) où elle est responsable de l'unité de cytogénétique. Ayant obtenue son PhD à l'Université Cheikh Anta Diop de Dakar, dans la spécialité de Génétique des populations, elle s'est surtout intéressée à la Biologie évolutive des Gerbilles en étudiant leur phylogénie, phylogéographie et cytogénétique au sein de l'UMR 022 du Centre de Biologie et de Gestion des Populations de l'Institut de Recherche pour le Développement. Par ailleurs, elle utilise divers outils de la génétique des populations et de l'écologie afin de mettre en évidence chez différents modèles biologiques (*Gerbillus nigeriae*, *Rattus rattus* et *Tuta absoluta* essentiellement) les routes d'invasions possibles pour ainsi évaluer les risques sanitaires et les dégâts causés aux cultures et proposer ainsi des méthodes de lutte appropriées. Depuis trois ans maintenant, elle a permis de mettre en place au sein d'une équipe dynamique l'unité de cytogénétique qui est de nos jours la seule institution publique au Sénégal à proposer le caryotype pour essentiellement permettre le diagnostic des anomalies de développement sexuel et des aneuploïdies.

Résumé : Dans le cadre de la promotion de la mise en place de service de génétique dans nos structures en Afrique, pour positionner notre continent à l'ère des « omics », nous rapportons ici le processus de mise en place d'un laboratoire de génétique médicale au Sénégal, les étapes, les résultats et les perspectives de ce processus. Partant d'un service hospitalier de **Cytologie** qui a fonctionné pendant des décennies sans aucune activité de génétique faute de ressources suffisantes aussi bien financières, matérielles qu'humaines, au moment où les maladies génétiques quant à elles ne cessent d'augmenter, nous avons dû dérouler plusieurs étapes pour pouvoir accéder progressivement à l'étape de la génomique depuis la cytogénétique conventionnelle. De la détermination du sexe chromatinien en **2008**, avec **1** professeur agrégé, **1** microscope photonique ordinaire, **0** technicien, nous avons pu, en 2009, nous équiper sur le plan des ressources humaines, d'une doctorante en Génétique des populations, puis en 2010, sur le plan des ressources en matériel, d'un Cytovision, acquisition qui nous ont permis, à partir de 2010, d'introduire à côté de la chromatine sexuelle, le caryotype sanguin conventionnel. Dès 2012, nous avons senti la nécessité de former beaucoup de jeunes dans ce domaine où nous étions trop seuls avec, au sein de l'école doctorale, l'ouverture d'un Master en Cytogénétique et **en** 2013, l'acquisition d'un microscope à contraste de phase et d'un microscope à têtes multiples (10 têtes). En 2014 le service s'est enrichi d'une pharmacienne agrégée en Génétique sur le plan ressources humaines et sur le plan ressources matériels d'un thermocycleur, d'un nanodrop, acquisitions nous permettant de nous engager enfin dans la Génétique moléculaire. Par la suite le service compte un PhD en Histologie-Embryologie-Cytogénétique en 2015. Toutes ces acquisitions aussi bien matérielles qu'humaines nous ont permis d'évoluer progressivement vers le caryotype GTG en conventionnel, la recherche de gène SRY par Fish, la fragmentation de l'ADN spermatique, le génotypage HPV, la génomique des leucémies et des cancers du sein. En perspective, les ressources humaines étant aujourd'hui à un niveau acceptable, nous cherchons maintenant à **renforcer nos capacités** surtout matérielles (**thème du congrès**) pour nous positionner à l'échelle internationale, et faire de ce laboratoire un centre de référence en matière de génétique, avec une triple mission d'Aide au Diagnostic, de Recherche et de Formation.

SERIGNE MAGUEYE GUEYE, SENEGAL

Dr. Serigne-Magueye GUEYE is Professor of Urology at University Cheikh Anta DIOP, Dakar, Senegal, Chair of Urology and Andrology, Grand Yoff General Hospital and Director of IFRU-SF (www.ifru.org). He is a former Fulbright Senior Scholar at University of Pennsylvania School of Medicine, Philadelphia, PA, USA.

Active clinician with expertise and focus on urologic oncology, he developed international collaborations in cancer research. He leads studies on prostate cancer in Senegal and male from African descent that include epidemiological data, clinical and outcome as well as biosample collection for genetic studies.

He serves on numerous advisory boards. President of ALIAM (www.aliam.org) and member of the Board of **Directors of Union for International Cancer Control (UICC) (**www.uicc.org**)**, he is past-president of the African Organization of Research and Training in Cancer (AORTIC) and the Pan African Urological Surgeons Association (PAUSA). Recipient of many national and international awards. Dr Gueye and collaborators received the American Association of Cancer Research (AACR) 2011 Landon Award for excellence in international collaboration on cancer research.

CHRISTIAN HAPPY, NIGERIA

Christian Happi, is a Professor of Molecular Biologist and Genomics in the Department of Biological Sciences, Redeemer's University. His research focus is on infectious diseases, especially, Lassa fever, Ebola, malaria, HIV and Human genomics. He is the Pioneer and current Dean of the College of Postgraduate Studies, Redeemer's University and the Director of the World Bank funded African Center of Excellence for Genomics of infectious Disease (ACEGID) in Redeemer's University. Professor Christian Happi, holds a B.Sc (Hons) in Biochemistry from the University of Yaounde, Cameroon (1993), and PhD from the University of Ibadan, Nigeria (2000). After his PhD, he went to Harvard University where he worked as a Postdoctoral fellow (2000-2003). He subsequently worked at Harvard University as a Research Scientist for 4 years (2004-2007). He became an adjunct Professor at Harvard University School of Public Health between 2007-2011.Professor Happi is currently a visiting professor in the Department of Immunology and Infectious Diseases (IID), Harvard School of Public Health (HSPH), and the Department of Organismic and Evolutionary Biology, Harvard University Cambridge. He has also served as visiting Professor in major leading institutions in Europe. He served as a WHO consultant molecular biologist between 2000 and 2009.

ABSTRACT

Genomic Surveillance Facilitates Ebola Virus Containment and Elucidates Origin, Transmission and Evolution during the 2014 Outbreak.

The current epidemic of Ebola in Sierra-Leone, Guinea and Liberia, has demonstrated on one hand how lack of preparedness and coordinated response within countries and from international aid agencies and donors, can lead to an unprecedented human and economic loss in the afflicted countries. On the other hand, the rapid detection of the Ebola virus, and containment of the Ebola outbreak by Nigeria is a clear demonstration of the power of genomics diagnostics tools to detect infectious diseases outbreak as soon as they appear and facilitated their containment.

Early in the epidemic, we used genome sequencing to provide insights into virus evolution and transmission and offered important information for outbreak response, including our developing a 15minutes rapid diagnostic test (RDT) for Ebola Virus Disease (EVD).

We observed a rapid accumulation of interhost and intrahost genetic variation, allowing us to characterize patterns of viral transmission over the initial weeks of the epidemic. This West African variant likely diverged from central African lineages around 2004, crossed from Guinea to Sierra Leone, from Sierra-Leone to Liberia and from Liberia to Nigeria between May and July 2014. The virus exhibited a sustained human-to-human transmission, with no evidence of additional zoonotic sources. Because many of the mutations alter protein sequences and other biologically meaningful targets, they were monitored for impact on diagnostics, vaccines, and therapies critical to outbreak response.

As the epidemic winds down and the afflicted West African countries are celebrating because the World Health Organization (WHO) has declared them Ebola free, the questions that keep wandering in my mind are: Is Nigeria and other West African countries prepared for the next outbreak? How best can we prepare for the next outbreak?

We provide insights on how are using new genomics knowledge and technologies to build capacity and leadership toward preparedness and containment of future infectious diseases outbreaks, promote state-of-the-art genome sequencing and field-deployable genetic tools for microbial infections detection in West Africa, and enable a surveillance network for some of the world's greatest global health threats.

COLLET DANDARA, SOUTH AFRICA
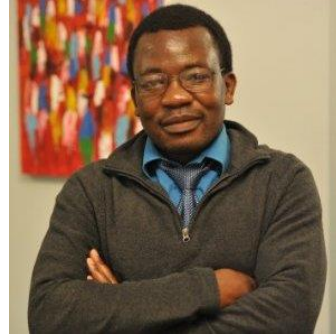
Collet Dandara is a Professor of Genetics in the Division of Human Genetics, Department of Pathology, in the Faculty of Health Sciences at the University of Cape Town. He holds holds a BSc (Hons) and PhD from the University of Zimbabwe. Completed his PhD in 2003, after a sandwiched program with University of Karolinska, Stockholm, Sweden, after which he joined the University of Cape Town as a postdoctoral research fellow until 2007 when he moved to the University of Witwatersrand as a lecturer. In 2009, he moved back to the University of Cape Town as a Senior lecturer, setting up the "Pharmacogenetics and Drug Metabolism Research group. In 2012 he was promoted to Associate professor and in 2015, to full professor. Professor Dandara was awarded TWAS Young affiliate status in 2012. He is a member of the pharmacogenetics subcommittee of the International Union of Pharmacology (IUPHAR) and has published more than 80 articles in international and peer-reviewed journals. He has consistently trained postgraduate students at the levels of Honours, Masters and PhD. Professor Dandara convenes the Human Genetics and Forensic Genetics Honours programs; chairs the faculty of health sciences transformation and equity committee at the university of Cape Town. Through his work, he was one of the finalists in the National Science & Technology Forum (NSTF) in 2015.

His work concentrates on the characterisation of African populations with respect to genes that have pharmacogenetics/genomics relevance. His recent work involves focussing of the pharmacogenomics of antiretroviral drugs. His group has extensively characterised the genetic determinants associated with responses to efavirenz, stavudine and lopinavir. His group is also investigating the pharmacogenetics of risperidone among psychiatric patients.

ADEBOWALE ADEYEMO, USA

Dr Adeyemo is the Deputy Director of the Center for Research on Genomics and Global Health (CRGGH) at the National Human Genome Research Institute. His research interests are the genetic epidemiology of complex diseases and genomics of populations of African ancestry. His current projects include: the genetic epidemiology of cardiometabolic disease, genetics of podoconiosis and genetics of complex disease in childhood (including renal/urogenital disorders, orofacial clefts and cardiac malformations). His research involves the application of high throughput methods (including dense SNP genotype arrays for genome wide association studies, exome arrays, gene expression microarrays and whole exome capture/sequencing) to answer biological and clinically relevant questions in human disease. Dr. Adeyemo qualified in medicine at the University of Ibadan in Nigeria. After completing a residency in Pediatrics and Genetics, he became a faculty member of the College of Medicine, University of Ibadan, Nigeria and a Consultant Pediatrician/Geneticist at the University College Hospital, Ibadan, Nigeria. He subsequently held training fellowships in genetic epidemiology and medical education. He moved to the National Human Genome Center at Howard University, Washington DC in 2003 from where he moved to the NIH in 2008. Dr. Adeyemo has published widely in genetics and genetic epidemiology. He has served on multiple national and international grant review panels. He is currently co-chair of the H3Africa Genome Analysis Working Group and serves on the H3ABioNet Scientific Advisory Board. He is a co-creator of the NHGRI electronic atlas of birth defects for diverse populations (PMIDs 26838780, 26963283). Further information about Dr. Adeyemo can be found at his ORCID profile: http://orcid.org/0000-0002-3105-3231

Abstract:

Human Diversity and Precision Medicine

The promise of precision medicine is the potential to tailor disease treatment and prevention approaches to each patient using all the information available on the individual's genetic variation, environment and lifestyle. While it can be argued that the ideas underlying precision medicine have always been at the foundation of clinical care, the reality had always suffered from major limitations in knowledge and technology. This situation is rapidly changing due to the recent explosion in new knowledge of disease risk and prevention; new technologies that better characterize the genome, transcriptome and metabolome; large-scale databases; new methods for categorizing patients, as well as computational tools/pipelines for analyzing large datasets. Achieving the goal of precision medicine in the context of human diversity is fraught with many challenges. This presentation will review the principles underlying precision medicine and examples of recent successes in the field. The challenges and opportunities represented by human diversity will be discussed as well as examples of new precision medicine initiatives.

BENOIT ARVEILER, FRANCE

ABSTRACT

New Generation Sequencing for molecular diagnosis in clinical laboratories: study of a large series of patients with albinism.

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The molecular diagnosis of genetic diseases has largely benefitted from the development of Next Generation Sequencing (NGS) technologies. This is especially the case for genetically heterogeneous diseases where multiple genes are involved. NGS allows the sequencing of all genes simultaneously, resulting in thus far unreached completeness and substantially reduced turnaround time when compared with the successive analysis of the different genes by Sanger sequencing. Medium throughput and high throughput equipment make possible the analysis of tens or hundreds of genes respectively. Very high throughput enables to sequence the whole exome or even the whole genome of patients in the case of pathologies where a very high number of genes need analyzing, or where defining a panel is illusory (new genes constantly discovered, e.g. intellectual deficiency, or too many unknown genes, e.g. developmental anomalies).

Our laboratory, amongst other diseases, is particularly committed into the molecular diagnosis of patients with albinism. Albinism is a clinically and genetically heterogeneous disorder characterized by nystagmus, hypoplasia of the fovea, and decreased visual acuity, associated with a variable degree of skin, hair and eye hypopigmentation, leading to an increased risk of cutaneous cancer. 19 genes are involved in the various forms of the disease, including oculocutaneous (OCA), ocular (OA, FHONDA) and syndromic (Hermansky-Pudlak, Chediak-Higashi) albinism. Our molecular diagnostic strategy includes investigations by next generation sequencing (NGS; ion Torrent technology) with an AmpliSeq panel (Life Technologies – Thermo Scientific) covering the exons of 18 genes (the recently identified HPS10/*AP3D1* gene is not analyzed as yet, but will be soon). Gross genomic rearrangements, which account for 5-6% of alleles, are analyzed by high resolution array-CGH.

We have analyzed 640 patients. A molecular diagnosis was obtained for 480 (75.7%): 31.8% OCA1; 22.5% OCA2; 2% OCA3; 8.6% OCA4; 2% OCA6; 0.3% OCA7; 5.5% OA1; 0.15% FHONDA; 1.5% HPS1; 0.15% HPS4; 0.75% HPS5; 0.3% HPS6; 0.15% HPS8). 10% of patients carried heterozygous mutations and 14.30% had no mutation in any of the known genes. 25% of patients therefore do not have a molecular diagnosis yet. This may be because mutations reside in regions of the genes that are not routinely analyzed (i.e. regulatory regions or deep intronic regions), or because new albinism gene remain to be identified.

HENRIETTE POATY, CONGO

Abstract

Les gènes MisMatch Repair et le Syndrome de Lynch

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Les gènes du système MisMatch Repair (MMR) codent pour des protéines qui interviennent dans la reconnaissance et dans la réparation des erreurs de l'ADN après réplication du simple brin 3'5' lors de la division cellulaire. Ils sont également impliqués dans recombinaison méiotique, l'apoptose et ils interagissent entre eux. Ces gènes se repartissent en deux familles : MutS (MSH2, MSH6) et MutL (MLH1, PMS2) auxquelles se rajoute le gène EpCam. Une mutation constitutionnelle de l'un de ces gènes est à l'origine du syndrome de Lynch (SL) aussi appelé syndrome HNPCC (cancer colo-rectal héréditaire sans polypose) qui se manifeste dans 60 à 80% des cas par un cancer colorectal (CCR) d'apparition précoce ou parfois par un cancer extra-colique (dont les sites les plus fréquents sont l'endomètre, l'ovaire, l'estomac, le foie). Le SL est le CCR héréditaire le plus fréquent avec une transmission sur le mode autosomique dominant.
S'il est vrai que cette pathologie est facilement détectable dans les pays du nord, le diagnostic dans les pays du sud (notamment au Congo) rencontre des difficultés à cause de l'inaccessibilité de certaines techniques d'analyse en génétique. Nous avons analysé par la technique d'immunohistochimie, les gènes MMR dans 34 CCR familiales (identifiées à partir des critères de Bethesda et des arbres généalogiques typiques). Cette méthode de diagnostic simple, fiable et accessible, nous a permis d'obtenir la prévalence du SL au Congo Brazzaville (soit 5,6% de l'ensemble CCR).

Mots-clés: gène MisMatch Repair, syndrome de Lynch, cancer colorectal héréditaire, syndrome HNPCC.

Dr Aissatou Toure is a pharmacist biologist specialized in Immunology and a researcher at the Pasteur Institute in Dakar where she heads the Unit of Immunology and conducts research in the area of immunology of malaria. She is member of the scientific advisory group of the European Vaccine Initiative (EVI) and was member till 2012 of the expert group of WHO on malaria vaccines (MALVAC).

In parallel to her scientific activities as researcher in malaria, Dr Toure has different activities in the field of ethics, which represents for her a major area of interest.

Dr Toure is member of the Senegalese National Ethic Committee for Health Research since 2003, tasked with evaluating scientific and ethical aspects of projects in health research, advising health authorities in the area of ethics, training health research in ethics.

Since 2012 Dr Toure is member of the Working Group on the Revision of CIOMS 2002 International Ethical Guidelines for Biomedical Research Involving Human Subjects.

From 2006 to 2013 Dr Toure was a member of the UNESCO International Committee on Bioethics (IBC) and as such participated to the reports elaborated by IBC on various bioethics topics.

From 2003 to 2007, she has been a member of the African Committee (Developing Countries Coordinating Committee or DCCC) of the European program EDCTP (European and Developing Countries Clinical Trials Partnership) serving as focal point for the activities in the field of ethics that included building capacity, strengthening of national ethics committees, etc.

She has been also a member of the Project Advisory Group (since 2004) that advises WHO on the Meningitis Vaccine Project (MVP) on different aspects of the projects including ethical aspects.

Aissatou Toure has also participated to different activities of capacity building in ethics at the national level as well at the international level: participation to the writing of WHO manual on basic concepts for capacity building of health research committee, facilitator in training workshops, organization of international conferences (Bioethics Days for Central and West Africa).

More recently, in 2015 and 2016 Aissatou Toure has support the National Ethic Committee on Health Research of Guinea in strengthening the capacity of the members through several workshops on respectively "Research ethics during epidemics", "Improving Ethics Committees functioning", "Ethics of Biobanking."

She was also member of the Working Group established by WHO during the Ebola outbreak to advice and make recommendations on specific ethical issues raised by the Ebola crisis.

ELONNA OBIEFUNA,NIGERIA

Elonna Marylyn Obiefuna is a graduate of Biochemistry with a master's degree in Environmental health from the University of Strathclyde Glasgow. She is currently working as research scientist, co-ordinating indigenous linguistic and cultural concept s of Heritability and comprehension of genomic research in Nigeria, INDEGENE project with the institute of Human Virology Nigeria. She served the National Health Service Aberdeen, United Kingdom and Carter center covering South East region in Nigeria. She is a member of the H3Africa ethics ad community engagement working groups, member royal environmental institute Scotland, member of the Chattered institute of Environmental Health, and member of the consortium of universities for Global Health. My primary interests are in bioethics, genomic studies and environmental health.

ABSTRACT

Indigenous linguistic and cultural concepts of heritability and comprehension of genomic research in Nigeria

INTRODUCTION/ Large scale genomics research started in Nigeria in 2004 with the International HapMap project and this was accompanied by studies of the ethical aspects of the research. Since that study, there has been other genomics studies and concerns have been expressed about whether participants in such research projects understand the research and their consent to participate in it. This is particularly relevant because of the high prevalence of poverty and low levels of literacy in LMIC like Nigeria. We therefore decided to explore local knowledge about heritability in general and of diseases specifically in order to use these to improve comprehension of consent forms. **METHODS/** We enrolled 50 females and 50 males from diverse ethnic groups and religions living in villages around Abuja, Central Nigeria into 10 focus group discussions and conducted 50 key informant interviews to identify existing linguistic and cultural concepts of heritability that are used to understand common heritable traits and diseases in indigenous communities in Nigeria. The discussions and interviews were transcribed and analysed using Atlas.ti®. **FINDINGS/** Participants in our studies were very keen to discuss their cultural heritage and heritable traits. They were conversant with local terms used to describe many diseases that they considered heritable. Most participants attribute the reason for heritability and inheritable diseases to "blood" – in the sense of a corporeal essence, while others attributed such events to acts of God. Participants acknowledged the occurrence of "dominant" and "recessive" traits. The dominant traits were attributed to strength of the male partner while recessive traits were attributed to several factors including multiple sexual partners. Others thought that heritable traits were due to association with specific individuals, natural causes, types of sexual activities, mental state of the woman peri-conception, the environment, etc. Participants identified various diseases as heritable.

CONCLUSION

Our study showed that Nigerians were aware that some diseases and traits are heritable and some of these were "dominant" while others were "recessive". However participants had limited knowledge of the basis for heritable diseases and its different forms. This suggests that genomic researches in these communities must be accompanied by careful education of the research participants.

ABSTRACTS SELECTED FOR ORAL PRESENTATION

Session 6   Cancer Genetics/Genomics

C01   **Utility of a microarray diagnostic for AML in the South African setting**

Auteurs /Authors :

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1-Department of Immunology and Institute for Cellular and Molecular Medicine, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa;
2-Department of Haematology, Faculty of Health Sciences, University of Pretoria and National Health Laboratory Services, Pretoria, South Africa.

Introduction: Acute Myeloid Leukemia (AML) is characterised by proliferation of the myeloid lineage and accumulation of immature haematopoietic cells in the bone marrow. The disease is typified by diverse genetic abnormalities and marked heterogeneity both in response to treatment and survival. The AMLprofiler is a qualitative in vitro diagnostic microarray, which incorporates seven molecular biomarkers used to diagnose and predict post-therapy survival rates.

Goals: The goal of this study is to contrast the AMLprofiler to routine diagnostic methodologies employed for AML in South Africa, particularly with respect to consistency in results, cost and time to result.

Methods: Bone marrow and peripheral blood samples were collected from patients diagnosed with de novo AML. RNA was isolated and samples processed using Affymetrix Gene Profiling Reagent kits. The scanned AMLprofiler data was sent automatically to the secured server of Skyline Dx, and diagnostic reports generated in under 15 minutes. The findings were subsequently compared to reports generated via the traditional cytogenetic and fluorescent in situ hybridisation (FISH) approaches.

Results: Results generated thus far indicate 100% correlation with findings obtained using standard methodologies. Notably, many samples were determined to be positive for biomarkers not routinely investigated in South Africa, namely CEBPA double mutants, NPM1 variants and altered expression levels of BAALC and EVI1. While 26% of samples presented with no positive marker, the AMLprofiler enabled a further 33% of AML patients to be classified into either favourable or poor prognostic categories.

Conclusion: Preliminary findings of the study indicate benefit for use of the AMLprofiler in South Africa, particularly with respect to the comprehensive nature of the microarray and the decreased time required to generate a final result. The ability of the AMLprofiler to refine risk stratification of AML is a notable benefit that has already been demonstrated in the cohort investigated to date.

Mots clés /keywords :
Acute myeloid leukaemia, microarray analysis, South Africa

C02   **Aspects moléculaires des patients opérés de cancer colorectal à TOURS**

Auteurs /Authors :
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Introduction :
Le cancer colorectal est une affection multifactorielle qui associe des anomalies épigénétiques et des altérations moléculaires à une déstabilisation du génome. En dehors de deux processus bien établis, l'immunité pourrait contribuer aussi au processus de la carcinogenèse

Objectifs / goals :
déterminer la relation entre l'infiltrat lymphocytaire intratumoral et les différentes caractéristiques moléculaires des tumeurs chez 135 patients porteurs de cancer colorectal.

Méthodologie / Method:
L'infiltrat lymphocytaire intratumoral est recherché par marquage immunohistochimique avec les marqueurs CD3, CD8 et CD45Ro. La PCR multiplex fluorescente a permis de rechercher la stabilité des microsatellites. La technique HRM est utilisée pour rechercher le degré de méthylation du gène MLH1 ainsi que la présence de mutation. La PCR classique et la PCR à temps réel suivies du séquençage ont servi à déterminer la nature des mutations géniques.

Résultats / Results :
Nous avons observé une association entre l'infiltrat lymphocytaire et le stade II de la tumeur (p=0,0035) pour CD3, (p=0,0142) pour CD8 et (p=0,0011) pour CD45Ro. Les marqueurs CD3, CD8 étaient associés à la localisation droite de la tumeur (p=0,0296) pour CD3 et (p=0,0110) pour CD8. Les tumeurs infiltrées, étaient associées au statut MSI-H, à une méthylation du gène MLH1 et inversement corrélées à la mutation de K-ras. L'association entre la mutation B-raf et l'infiltrat lymphocytaire CD45RO n'a pas été retrouvée.

Conclusion :
Notre étude met en évidence l'importance de l'infiltrat lymphocytaire observé dans les tumeurs colorectales, ce qui laisse présager de nouvelles stratégies thérapeutiques dans la prise en charge des cancers.

Mots clés /keywords :
cancer colorectal, infiltrat lymphocytaire, marqueurs moléculaires, Tours

C03   **Genetics and Pharmacogenetics Aspects of Chronic Myeloid Leukemia in Morocco**

Auteurs /Authors :
Kassogue Y(1,3), Dehbi H(1), Quachouh M(2), Quessar A(2), Benchekroun S(2), Nadifi S(1)

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2-Department of Onco-Hematology, Ibn Rochd University Hospital, Casablanca, Morocco.
3-Faculty of Medicine and Odonstomatology, University of Sciences, Techniques and Technologies of Bamako

Introduction :
The use of imatinib in the treatment of chronic myeloid leukemia (CML) certainly gave a renewed interest for patients. However, some patients take more time to achieve the desired results or do not respond at all.

Goals :
In order to better understand this variability of therapeutic response which also is a major concern for clinicians and to assess the genetic risk of the disease, we have undertaken a study on the genetic variability of response to imatinib therapy and genetic susceptibility to CML from 2011 to 2015 at the genetics laboratory and molecular diseases.

Methods:
Thus, we selected genes involved in drug and xenobiotics metabolism including cytochrome P450 (CYP2B6), the glutathione S-transferase (GSTM1, GSTT1) and multiple drug resistance gene (MDR1). We used PCR-RFLP or multiplex-PCR to identify these genes in 92 patients and in 100 controls. SPSS Version 16 software or SNPAnalyzer 2.0 software and SNPStats software were used for statistical analysis.

Results :
Our study shows that patients with 15631GG/GT CYP2B6 and GSTM1 null/GSTT1 null genotypes were significantly associated with complete cytogenetic response after 18 months of treatment. However, the primary cytogenetic resistance as well as the loss of hematologic response was more frequent in patients harboring the combined genotype GSTT1 present/GSTM1 present. Side effects were more common in patients carrying the 15631GG genotype (CYP2B6) and GSTT1 null. No significant influence of MDR1 gene on the response to imatinib was observed. In addition, we noted that the GSTT1 null and the 1236T allele of MDR1 are risk factors of CML.

Conclusion :
In the light of our observations, identification of CYP2B6 G15631T, GSTM1 and GSTT1 could facilitate the prediction of therapeutic response in our patients treated with imatinib and to understand the risk that the minor alleles play in the susceptibility of CML.

Mots clés /keywords :
CYP2B6, GSTT1, GSTM1, MDR1, LMC, Therapeutic response, Susceptibility

C04   L'allèle arginine du codon 72 du gène p53 serait un facteur de risque de cancer du sein au Sénégal

Auteurs /Authors :
DIA Y. (1), NDIAYE DIALLO R. (1, 2, 3), DIOP JPD. (1, 3), BA SA. (1,3), DEM A. (4) DIENG MM. (4), KA S. (4),
MBAYE F. (6), MBENGUE B. (3, 5), SYLLA NIANG M. (5), THIAM A. (3), DIOP G. (6), DIOUF D. (4), FALL M. (6),
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Introduction :
Le gène suppresseur de tumeur p53, code une phosphoprotéine de 393 acides aminés structurée en domaines. La
région comprenant les résidus 63-97 est riche en proline et constitue un domaine fonctionnel nécessaire à
l'induction de l'apoptose. Ce domaine présente un polymorphisme au niveau du codon 72 qui se traduit par la
substitution d'une Proline par une Arginine. L'allèle Arginine a été suggéré comme facteur de risque de cancer.
Cependant son implication dans l'oncogenèse mammaire est controversée.

Objectifs / goals :
Etudier l'association entre l'allèle Arginine du codon 72 du gène p53 et le cancer du sein au Sénégal

Méthodologie / Method:
Dans une étude analytique de type cas témoin 80 patientes atteintes de cancer du sein confirmé par l'examen
anatomopathologique et 85 femmes saines indemnes de tout cancer ont été recrutées après consentement
éclairé. Parallèlement 3 familles avec une histoire familiale de cancer du sein ont été recrutées. Un prélèvement
sanguin a été réalisé et l'ADN génomique extrait avec le kit Qiagen. Le génotypage du codon 72 du gène p53 a été
effectué par PCR-RFLP et les données obtenues analysées avec le logiciel SPSS. Les valeurs de p inférieurs à 5%
ont été retenues comme significatives.

Résultats / Results :
La fréquence de l'allèle Arginine chez les patientes et les témoins était de 56,15% et 43,84% respectivement.
L'étude d'association a montré que l'allèle Arginine serait un facteur prédisposant au cancer du sein(p=0,03 ;
OR=1,622 ; IC=1,039-2,532). De même nous avons observé une ségrégation de l'allèle Arginine avec le cancer du
sein chez les 3 familles recrutées.

Conclusion :
L'allèle Arginine du codon 72 du gène p53 serait un facteur de risque de cancer du sein au Sénégal. Nous
envisageons de répliquer cette étude sur une cohorte plus importante afin de confirmer ce résultat.

Mots clés /keywords :
gène p53, codon 72, cancer du sein

C05   Place de la cytogénétique et de la biologie moléculaire dans le diagnostic et le suivi des patients atteints de leucémie myéloïde chronique

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Introduction :
 La LMC est une hémopathie maligne clonale caractérisée par la translocation t(9;22) à l'origine d'une protéine BCR-ABL oncogène. Diagnostiquée tard, des anomalies cytogénétiques additionnelles (ACyA) apparaissent entrainant une résistance aux traitements. Le coût élevé des examens de confirmations, réalisés en Europe, participe à ce retard et est responsable des difficultés de surveillance de la maladie résiduelle.
Objectifs / goals : Evaluer les difficultés diagnostiques et de suivi des patients puis leur impact dans l'évolution de la maladie

Méthodologie / Method:
Il s'agissait d'une étude longitudinale portant sur 60 cas de LMC suivis entre février 2008 et juin 2015. Etaient inclus tous patients dont la LMC était confirmée par la présence d'une t (9 ; 22) au caryotype et/ou du transcrit BCR-ABL par PCR ; puis traités par imatinib mesylate. Nous avons évalué le délai de confirmation diagnostique, l'évolution hématologique à 3 mois, cytogénétique à 12 mois, moléculaire à 18 ou 24 mois selon les critères ELN 2013. Une analyse bivariée nous a permis de ressortir l'impact pronostique du délai diagnostic et celui des ACyA.

Résultats / Results :
Le délai moyen de confirmation diagnostique était de 11,37 mois. Le caryotype conventionnel seul ou associé à d'autres tests était réalisé dans 63,3% des cas et la PCR dans 20%. Etaient observés 11,7% d'échecs de culture cellulaire et 18,4% d'anomalies cytogénétiques additionnelles (8% duplication Phi). L'évolution de la maladie était évaluée chez 43,3% par la cytogénétique et chez 8,3% par la PCR. Elle était marquée par 69,2% de RCyM ; une RMM chez 3 patients ; 16,7% progression et 23,3% de résistances. Le pronostic était lié à la phase avancée au diagnostic et à l'absence de réponse thérapeutique (p < 0,05).

Conclusion : L'absence de plateau technique relevé et le coût élevé des tests constituent un retard au diagnostic mais également une barrière au suivi des patients atteints de LMC dans les pays émergents, selon les recommandations internationales.

Mots clés /keywords :
LMC, cytogénétique, biologie moléculaire

Session 7   Medical Genetic Services

Co6   **Genetic counseling competencies of nurses in Three Nigerian teaching hospitals**

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Introduction :
In this new era of genetics and genomics and personalized care in Africa and world wide, medical genetics is still not firmly established and genetics nursing remains scarce. Nonetheless, high prevalence of cancer and other complex diseases continue unabated.

Goals :
This study determined genetic counseling competencies (Knowledge, Attitude and Reported skill) of nurses in 3 Nigerian teaching hospitals

Methods:
A cross-sectional design was used to study 492 participants using structured questionnaire to elicit nurses' competencies about basic genetics and genetic counselling. The study took place in the Lagos University Teaching Hospital, Obafemi Awolowo University Teaching Hospital Complex and University College Hospital following due ethical approval.

Results :
We studied nurses in all cadres with the highest proportion being Nursing Officer II. Less than a tenth of nurses (7.1%) had a nursing degree. Over a quarter (25.7%) of them had been in service for over 20 years. Over three quarters (80.2%) stated they were taught genetics in nursing school, while less than two-thirds (58.9%) ever heard of genetic nursing. Mean age was 40.2 years ±8.6 and less than a tenth(7.3%) were males. Regarding self-assessment of genetics knowledge, a high proportion of respondents reported they had not been taught several of the topics investigated. In most cases, less than a quarter of all respondents indicated they had excellent knowledge of the different items. For example, only 5.7%, 4.1% and 6.9% respectively reported they knew inheritance patterns, molecular genetics and mendelian inheritance very well. Mean scores for the outcomes were knowledge(15.5±5.5), attitude (94.5±11.4), reported skills (76.3±19.7), and overall competency (186.3±27.7).

Conclusion:
Nurses' competencies about cancer genetics and counseling are less than optimal. This calls for urgent interventions and funding for appropriate education of nurses to be genetically minded in the bid to ensuring patients' positive outcome and personalized care.

Mots clés /keywords :
Knowledge, Attitude, Skills, Genetic counseling, Teaching hospitals

C07 **Caractérisation des anomalies de développement sexuel (ADS) à travers la cytogénétique:**
à propos de 40 cas rencontrés au Sénégal

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Introduction :Les anomalies génétiques constituent un véritable problème pour le monde entier, sa fréquence est estimée selon l'OMS en 2014 à un nouveau-né sur 33 entraînant chaque année 3,2 millions d'incapacités à travers le monde plus particulièrement en Afrique faute de structures sanitaires spécialisées dans la prise en charge des personnes atteintes. En conséquence, le diagnostic précoce serait d'un grand apport pour la prise en charge des patients.

Objectifs / goals :L'objectif est la publication des résultats obtenus sur des activités cytogénétiques nouvellement menées dans le laboratoire de cytogénétique de l'hôpital Aristide Le DANTEC. Nous allons mettre en évidence à partir de 40 cas, les différentes catégories d'anomalies de développements sexuels (ADS) fréquemment rencontrées et permettre de répondre à la question qui nous est souvent posée: mon enfant est-ce un garçon ou fille ?
Méthodologie / Method:Le Caryotype CR avec le marquage en bandes G est une technique qui consiste en une dénaturation enzymatique par la trypsine après obtention des préparations chromosomiques suite à une culture cellulaire. La technique utilisée pour la CB est la coloration de GUARD sur des cellules épithéliales de la muqueuse jugale.

Résultats / Results :55% des cas d'ADS rencontrés concernent des individus présentant un sexe déclaré congruent avec les analyses génétiques effectuées. Aussi bien pour le CR que la CB trois catégories correspondant au sexe masculin (CR : 42,5% ; CB : 65%) féminin (CR : 30% ; CB : 22,5%) et intermédiaire (CR : 5% ; CB : 12,5%). Ces valeurs mettent ainsi en évidence des différences (45%) entre le sexe déclaré à la naissance et les divers tests génétiques réalisés.

Conclusion :Ces résultats montrent aussi bien l'importance du diagnostic génétique dans le cas des ADS que la complémentarité des méthodes génétiques utilisées. Le caryotype a permis de mettre en évidence deux cas d'hermaphrodisme vrai rencontrés dans d'autres pays Africains via des techniques similaires

Mots clés /keywords :
Anomalie de différentiation sexuelle, caryotype, chromatine, cytogénétique, marquage chromosomique,

Co8   **DIVERSITE ET EVOLUTION GENETIQUE DES TUMEURS MALIGNES DU SEIN**
CHEZ LES FEMMES SENEGALAISES

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Introduction :
au Sénégal, comme dans la plupart des pays d'Afrique subsahariens, le cancer du sein constitue le second cancer le plus répandu après celui du col utérin.

Objectifs / goals :
déterminer la diversité et l'évolution génétique des tumeurs malignes du sein chez les femmes sénégalaises.

Méthodologie / Method:
cent vingt (120) patientes sénégalaises atteintes d'un cancer du sein et prises en charge à l'Institut Joliot Curie de l'Hôpital Aristide Le Dantec ont fait l'objet de cette étude. Pour chaque patiente un prélèvement de tissus sains et de tissus cancéreux ont été obtenus. Trois gènes (Cytochrome b, D-Loop et le Bèta-fibrinogène) ont été amplifiès et séquencés. Les séquences ont été corrigées et alignées avec le logiciel BioEdit version 7.1.9. La diversité et l'évolution génétique des tumeurs ont été étudiés avec les logiciels MEGA 6, DnaSP version 5.10.01 et ARLEQUIN version 3.5.1.2.

Résultats / Results :
au total 40 variations dont 22 décrites comme nouvelles et présentant des différences significatives (P<0.05) entre tissus cancéreux et tissus normaux ont été notées au niveau du cytochrome b. Deux des variations de la D-Loop (T146C et T152d) présentent des différences significatives entre tissus cancéreux et tissus sains. Nos résultats ont également révélé qu'au cours de la carcinogenèse, le Cytochrome b est beaucoup plus affecté que la D-Loop. Aucune mutation n'a été retrouvée au niveau du Bèta-fibrinogène.

Conclusion :
puisque la mitochondrie est le site d'initiation de l'apoptose, par conséquent, les mutations du cytochrome b présentent dans la population étudiée et qui sont sous sélection positive peuvent jouer un rôle causal dans le cancer du sein. Le gène nucléaire (Béta-fibrinogéne) semble ne pas être impliqué dans la carcinogenèse mammaire.

Mots clés /keywords :
cancer, sein, diversité, évolution, Cytochrome b, D-Loop

C09   **Genetics of congenital heart disease (CHD) in Morocco: Experience of Medical Genetics and Cardio-Pediatrics departments of Fez Hassan II University Hospital**

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Introduction : Congenital heart disease (CHD) is the most common type of birth defect with a prevalence of 1% of live births and 10% of spontaneously aborted foetuses. Non-syndromic Atrial Septal Defect (ASD) and Tetralogy of Fallot (TOF) account for approximately 10% and 7% of CHDs respectively. While in case of syndromic CHDs, the most prominent syndromes are Down syndrome and Noonan syndrome. Non-syndromic CHDs are said to be associated with mutations in transcription factors expressed in developing heart, such as NKX2.5 and GATA4. In the other hand, Noonan syndrome is rather associated to regulation factors of RAS-MAPK pathway, a molecular signalling cascade expressed in several tissues including heart and brain.

Goals :The aim of this project is to identify the spectrum of mutation and environmental risk factors that may cause syndromic and non-syndromic CHDs in a Moroccan population.

Methods:One hundred patients were recruited in cardio-pediatrics and medical genetics departments of Hassan-II university Hospital of Fez, DNAs were extracted from Blood samples. Then, all samples have undergone amplification by PCR and direct sequencing of NKX2.5 and GATA4 coding regions in non-syndromic ASD and TOF; and seven PTPN11 hot spot exons in cases with Noonan syndrome. The obtained sequences were analysed by Bioinformatic alignment tools. Risk factors were analysed using chi-square and Fisher's exact tests.

Results :we identified five Noonan syndrome patients carrying PTPN11 mutations, six non-syndromic CHD patients with NKX2-5 mutations, and three patients carrying GATA4 mutations. The prevalence of mutations in our cohort is 14.3%, 9.2% and 4.6% respectively in PTPN11, NKX2-5 and GATA4.

Conclusion :Beside the genetic aetiology, consanguinity among other risk factors was proved to be involved. Finally, other interesting genes could also be studied like SOS1, RAF1 and RIT1 in Noonan syndrome patients, and MYH6, TBX20 as well as NKX2-5 and GATA4 promotors in non-syndromic CHDs.

Mots clés /keywords :
Congenital Heart Disease (CHD), Noonan Syndrome, Atrial septal defect (ASD), Tetralogy of Fallot(TOF), PTPN11, NKX2-5, GATA4

Session 8   Genetics of Infectious Diseases

C10   The Predictive Value of IL-28B GenePolymorphism in Egyptian HCV Patients' Response to Combination   Therapy of Pegylated Interferon and Ribavirin

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Introduction :
Hepatitis C virus (HCV) is the major etiological agent of liver disease worldwide. IL-28 is a cytokine that plays a role in immune defense against viruses including HCV. It has been demonstrated that polymorphisms in and near the region of the IL-28B gene locus of chromosome 19 are correlated with spontaneous and treatment induced clearance of hepatitis C virus infection.

Goals :
To evaluate the impact of IL28-B polymorphisms on response to combination therapy (pegylated interferon and ribavirin) in Egyptian HCV-infected patients.

Methods:
Fifty HCV-infected patients were included in a cross-sectional study.They were 44 males (88%), mean age 45.6 ± 9.8 years, and 6 females (12%), mean age 49.3 ± 7.2 years. They received combination therapy (pegylated interferon and ribavirin) based on the degree of fibrosis. HCV viral load and Genotyping of IL28-B gene polymorphism was done by real time PCR. Patients were divided according to the presence or absence of C and T alleles into CC, CT, and TT.

Results:
The frequency of IL-28B genotypes was 58 % for CT, 28% for CC and 14% for TT. A significant difference was found among the three genotypes (CC, CT & TT) regarding response to therapy at 24 weeks (P=0.025) as indicated by declining levels of viral load and liver function tests. The best response has been elicited in CT genotype patients (54% responders versus 4% non-responders) followed by CCgenotype patients (26% responders versus 2% non-responders).

Conclusion :
The presence of the C allele was a determinant factor for response to combination therapy in hepatitis C virus patients. Pre-treatment assessment of IL-18B genotype may help personalizing treatment for HCV patients.

Mots clés /keywords :
HCV, IL-18B, Genotyping, response to anti HCV treatment

C11　　　　　　　**Temporal dynamics of genome-wide transcription in malarial children in Burkina Faso**

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Introduction :
Malaria is a life-threatening disease caused by the parasites of the genus Plasmodium and transmitted by mosquitoes. Plasmodium falciparum is the most lethal of the human malaria parasites. The vast majority of malaria occurs in sub-Saharan Africa affecting mostly children under five. Malaria is a complex disease in which host response to infection is modulated by several factors such as host genetic background and state of immunity, parasite load and virulence, level of exposure and environment.

Goals :
To explore the temporal dynamics of transcription of the human peripheral immune system using RNA Sequencing on samples collected from a Burkinabe pediatric cohort.
Methods:
A longitudinal study was conducted between April and November 2015 in two malaria-endemic villages of Banfora health district in Burkina Faso. Peripheral blood was collected from children, after obtaining informed consent from parents, at baseline (before malaria infection) and during the first malaria episode. Total RNA was extracted then cleared from globin mRNA and RNASeq libraries were prepared. Short reads sequencing was then performed on an Illumina HiSeq 2500 at NYU Abu Dhabi.

Results :
Supervised statistical analysis of host genome-wide gene expression profiles revealed the magnitude and significance of differential expression taking place during malaria infection. Gene set and pathway enrichment analysis identified key signature pathways, molecular and biological processes of host immune system in response to infection.

Conclusion :
Global changes in host gene expression profiles take place in the blood of infected children. The study provides a high-resolution picture of transcriptional changes at the individual level in a highly malaria-endemic region.

Mots clés /keywords :
Malaria, RNA Sequencing, Genome-wide transcription, host gene expression profile

C12   Real-time expression profile of Mycobacterium tuberculosis Thymidylate Kinase messenger ribo-nucleic acids during in-vitro   growth of a Ugandan strain

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Introduction :
Mycobacterium tuberculosis (M.tb) is the causative agent of tuberculosis. Laboratory confirmation of active M.tb infection   is based on culture. Conventional M.tb cultures, however, take 2-3 weeks to observe/rule out growth. M.tb thymidylate kinase (TMKmt) has been identified as a predictive biomarker for M.tb growth and proliferation. Assays premised on TMKmt have been proposed to reduce time-lines for detection of positive M.tb cultures.

Goals :This study aimed at establishing the expression profiles of TMKmt messenger ribo-nucleic acids (mRNA) levels during in-vitro growth of a Ugandan M.tb isolate and thus the possibility of predicting growth of M.tb in solid and liquid media early before any detectable phenotypic growth.

Methods:Archived samples for one of the most prevalent strain in Uganda, Uganda genotype I, and H37Rv (control Strain) were cultured in Liquid broth media. Samplings were taken from the cultures at time 2.5, 3.0, 5.0, 8.0. 9.0, 11.0, 15.0, 21.0, 33.0, 100.0, 124.0, 172.0, and 196.0 hours and used to determine the levels of TMKmt specific mRNA by quantitative reverse transcriptase (RT) PCR using extracted total RNA. Phosphate buffered saline (PBS) and M.tb DNA polymerase gene were used as background negative and positive controls.

Results :The results showed that TMKmt mRNA is expressed all throughout the time of aliquoting though it shoots up at around 3 hours of incubation where it sharply tappers down between 5th and 9th hours only to reach its maximal expression at the 11th hour. Generally Uganda Genotype had a higher expression profile for TMKmt mRNA than H37Rv at any given time between 3th and 100th time of incubation

Conclusion :The expression of TMKmt mRNA in M.tb culture is a promising target for the development of a predictive diagnostic test to reduce time-lines for designation of positive M.tb cultures as well as drug sensitivity testing.

Mots clés /keywords :
Mycobacterium tuberculosis, Diagnosis, mRNA, Expression profile, Uganda Genotype I

Session 9   Human Genetic Diversity and Health

C13   Whole Exome Sequence Analysis Identifies Two Novel Loci for High Density Lipoprotein Cholesterol in African Ancestry Individuals

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Introduction : Much of the genetic epidemiology of high-density lipoprotein cholesterol (HDLC) in African ancestry individuals has focused on replicating findings identified in those of European ancestry, which may miss associations relevant for people of African descent. Also, HDLC is influenced by genetic and non-genetic factors, motivating study of individuals with similar ancestry in different environments, such as West Africans (WA) and African Americans (AA).

Goals : To identify HDLC loci by conducting whole exome sequencing (WES) on WA and AA with extreme HDLC values, followed with analysis of identified loci in larger samples of WA and AA.

Methods: We performed WES on 198 WA and 117 AA individuals with extreme HDLC values. We conducted both a SNP-based analysis of common variants using regression models and a gene-based analysis using SKAT. Common variants in loci identified in these analyses (MAF ≥ 0.05; n=270) were considered in linear mixed models of up to 2,204 AA and 4,919 WA.

Results : Based on WES analyses, we selected 8 variants and 4 genes (SLC36A4, CEL, SLC4A8, KRTAP11) for follow-up in a larger sample of WA and AA. In follow-up analysis, 2 variants were significantly associated with HDLC. The A allele of rs7305599, a variant in the 3' UTR of SLC4A8, was positively associated with HDLC (β 0.88, p=0.008). The C allele of a missense variant in ELF1, rs7799, was inversely associated with HDLC (β -1.02, p=0.01).

Conclusion : This WES-based approach identified two novel HDLC loci (SLC4A8 and ELF1) in African ancestry individuals. There are predicted eQTL hits and enhancer histone marks for the associated variants and evidence for sequence constraint at rs7799, providing support for their potential biological activity. Further work is ongoing to understand the underlying biological mechanism for these associations and to investigate the role of rare variants in identified regions.

Mots clés /keywords :
Whole exome sequencing; high-density lipoprotein cholesterol

C14   **Southern African Human Genome Programme: Deep whole genome sequencing**
provides insights into the genetic architecture of South Africans

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Introduction: The pilot study of the Southern African Human Genome Program (SAHGP) includes 24 high coverage whole genome sequences from three Southern African ethno-linguistic groups (Sotho-speakers : SOT, Xhosa-speakers : XHS and Coloured/admixed individuals : COL).

Goals: This study was aimed at assessing the diversity of ancestral contributions and genetic architecture in Southern African populations using high coverage whole genome sequence data.

Methods: Whole genome sequencing (>30X) was performed on the Illumina platform. A suite of programs including GATK, Vcftools, Plink, ADMIXTURE, GENESIS and several custom scripts were used for data processing, analysis and visualization.

Results: The discovery of ~0.8 Million novel SNPs in this small group of 24 individuals confirms the anticipated potential for novel SNP discovery in Southern African populations. Despite the relatively recent divergence of the Southeastern Bantu-speakers (SEB), the two groups (SOT and XHS) were found to be distinguishable in the Principal Component Analysis. Moreover, analyses based on ADMIXTURE showed these populations to also differ significantly in ancestral component contributions. Characterization of Khoesan (KS) ancestry in the Southern African groups show that, in addition to clear variations in the extent of Khoesan (KS) ancestry, the possible source of KS ancestry also differs between the SEB and COL populations. The Southern African groups were found to show extreme variation in frequency and length of runs of homozygosity (ROH) segments, with the longest and most numerous ROH blocks in Southern African KS groups and the Niger-Congo speaker groups, including the SOT and XHS. In accordance with their history of recent and complex admixture, the shortest and smallest number of ROH blocks was observed in the COL.

Conclusion: We highlight the need to study different African populations to understand their unique patterns of genetic diversity, to discover novel genetic variation and to promote biomedical research on the sub-continent.

Mots clés /keywords :
Whole genome sequence, novel SNPs, Admixture, Population structure, runs of homozygosity

C15   **Genomic Diversity of African populations and pharmacogenomics in the safe and**

efficacious use medicines in Africa

Auteurs /Authors :
Masimirembwa C

Introduction :
Genomic studies in Caucasian and Asian populations have uncovered genetic variability of importance in disease diagnosis and treatment. There is however little data on the genomic diversity of African populations and its implications for medicine

Goals :
To explore the genetic diversity of African populations and to investigate the pharmcogenetics of efavirenz in the treatment of HIV/AIDS patients

Methods:
Two thousand (2000) DNA samples from unrelated healthy individuals belonging to 10 major African ethnic groups, the Yoruba, Ibo and Hausa from Nigeria, the Kikuyu, Luo and Masaai from Kenya, the Shona, Ndebele and San from Zimbabwe, and the Venda from South Africa. The samples were genotyped using the Illumina 600K SNP microarray chip. The samples were also genotyped using traditional PCR methods for 20 SNPs in 6 important pharmacogenes (NAT-2, FMO, CYP2B6, CYP2D6, CYP2C19, GSTM). The data were analyzed using principal component analysis. The pharmacogenetics of efavirenz, were studied in a cohort of 500 HIV/AIDS patients on anti-retroviral treatment. The role of CYP2B6 genetic variants as possible biomarkers for CNS adverse effects associated with the use of efavirenz was explored. A pharmacogenetics guided dosing algorithm was derived using pharmacometric modeling. Cost-effective analysis (CEA) was done to assess the potential value of the algorithm in efavirenz dose adjustments.

Results:
Genomic diversity of African populations compared to Caucasian and Asian populations was observed. The diversity and structure was also reproduced when analyzing genetic variants in genes known to be important in drug safety and efficacy. The results of the efavirenz pharmacogenetics study showed that the low activity CYP2B6*6 variant is more prevalent in African populations, which correlated with more patients having high drug concentrations and higher incidences of CNS side effects. The pharmacogenetics guided dosing algorithm showed that patients homozygous for the CYP2B6*6 required 200 mg/day of efavirenz compared to the standard dose of 600 mg/day.

Mots clés /keywords :
Biobank,Pharmacogenomics, efavirenz, dosing algorithm

Session 10   Genomic Medicine

C16   **Targeted resequencing of genes involved in neurological conditions in South African patients with Parkinson's disease**

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Introduction :
Parkinson's disease (PD) is a debilitating neurodegenerative movement disorder that affects 1-2% of individuals over the age of 60 years. Cardinal features include features such as resting tremor, bradykinesia, rigidity, depression, sleep disturbances, psychosis, and cognitive decline. In Black Sub-Saharan African (SSA) populations, PD is often misdiagnosed possibly due to a lack of access to specialized health care and services. These limitations have greatly hampered studies on PD in these populations and the genetic etiology in these patients is largely undefined. High-throughput mutation screening methods using next generation sequencing technology is needed to comprehensively assess SSA patients with PD, in order to identify the underlying genetic causes.
Goals :
The aim of this study was to investigate the genetic causes of PD in a group of Black South African patients.

Methods:
A customized target-capture panel encompassing 116 genes implicated in Parkinsonism and related conditions as well as a further 53 genes involved in biologically relevant pathways was used in this study. We screened for pathogenic mutations in 21 Black South African patients with PD.

Results :
A total of 98 missense variants were found, 11 of these were novel or of low frequency (≤ 0.003) and were specific to patients and absent in 144 ethnic-matched control individuals. These include DCTN1 p.P209R, DNAJC13 p.E1740D, GBA p.G517R, LRRK2 p.I610T, p.H1758P, p.N2133S and p.T2423S, PARK2 p.G430D and p.Q311K, PSEN1 p.V191A, and PSEN2 p.V139M.

Conclusion :
The large number of missense mutations identified in this small group of patients is indicative of the extensive genetic diversity present in this population. Further functional studies are warranted to determine the potential functional effects of these variants. The inclusion of Black patients in genetic screening studies is necessary to determine the full extent of the genetic etiology of PD.

Mots clés /keywords :
Parkinson's disease; Black African; targeted resequencing; genetic diversity

C17   **Knowledge and experiences of parents with children affected by Sickle Cell Disease in Cape Town**

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Introduction :
Sickle Cell Disease (SCD) is an autosomal recessively inherited blood disorder that causes a debilitating systemic illness. Although the disease was initially found predominantly in tropical and subtropical regions, SCD has now become a global health problem, due to migration of people from countries with a high burden thereof. Consequently, the incidence of SCD in South Africa has increased dramatically over the last decade.
Goals :
This study aimed to explore the knowledge and understanding of SCD among parents of affected children in Cape Town, as well as identify burdens associated with caring for a child with SCD. Furthermore, the study assessed opportunities to improve genetic counselling services available to parents and explored their attitude to preventive policies.

Methods:
A phenomenological approach was used to conduct this research. Seventeen semi-structured interviews were conducted with the parent of a child attending the Red Cross War Memorial Children's Hospital Haematology Clinic. Participants were selected using both purposive and convenience sampling methods. Data collected during these interviews were analysed using thematic content analysis.

Results :
Themes and sub-themes were identified and grouped into three categories: knowledge and understanding; experiences and burdens; and attitude toward preventative policies. While the majority of participants had some knowledge of SCD, several misconceptions were discovered, often relating to participants' prior knowledge of the disease. A number of burdens experienced by participants were revealed, with both practical and psychosocial implications. Finally, it was found that the majority of participants supported all methods of screening for SCD, regardless of whether they would make use of the screening services themselves.

Conclusion :
Findings of this study provide valuable insights on the subject of experiences of parents of children affected with SCD as well as the potential role of genetic counselling services.

Mots clés /keywords :
Sickle cell disease, genetic counselling, qualitative research

C18   Hereditary spastic paraplegias: Identification of a novel SPG57 variant affecting TFG oligomerization and description of HSP subtypes in Sudan

Auteurs /Authors :
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Introduction :
Hereditary spastic paraplegias (HSP) are the second most common type of motor neuron disease recognized worldwide. HSP can be pure or complex according to the absence or presence of additional neurological and non-neurological manifestations. There are more than 67 known HSP genes with different patterns of inheritance. Autosomal dominant HSP forms are the most frequent in western populations while recessive HSP predominates in highly consanguineous communities.
Goals :To estimate the relative frequencies of known HSP genes in Sudanese families with the disease and perform genotype-phenotype correlation to extend the clinical spectrum associated with HSP genes.
Methods:
We used next generation sequencing to screen 74 HSP-related genes in 23 consanguineous families from Sudan and candidate gene sequencing in two other families (total of 25 families).
Results :We established a genetic diagnosis in six families with autosomal recessive HSP (SPG11 in three families and TFG/SPG57, SACS, and ALS2 in one family each). An autosomal dominant HSP (ATL1/SPG3A) was also identified in one additional family. Six out of seven identified variants were novel. The TFG/SPG57 variant (p.Arg22Trp in the PB1 domain) is the second SPG57 HSP variant to be identified worldwide, and we demonstrated its impact on TFG oligomerization in vitro. Patients did not present with visual impairment as observed in a previously reported SPG57 family (p.Arg106Cys in coiled coil domain), suggesting unique contributions of the PB1 and coiled coil domains in TFG complex formation/function and a possible phenotype correlation to variant location. Some families manifested marked phenotypic variations implying the possibility of modifier factors complicated by high inbreeding.
Conclusion :We identified the first Sudanese families carrying novel variants in 6 HSP genes. The difficulty to reach a genetic diagnosis in the majority of studied families suggests the possibility of new genes, unusual models of inheritance or noncoding variations underlying spinocerebellar degeneration.
Mots clés /keywords :
Hereditary Spastic Paraplegia, SPG57/TFG, SPG11, SACS, ATL1, ALS2.

C19   Genome-wide analysis identifies an African specific variant in SEMA4D that is associated with BMI

Auteurs /Authors :
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Introduction :
Obesity, commonly measured by body mass index (BMI), is a major risk factor for several cardio-metabolic disorders. Thus, understanding the etiology of excess weight gain is a scientific and public health imperative. Although over 20 genome-wide association studies (GWAS) have been published for obesity and related traits, none has been conducted in continental Africans.

Goals :
Identify common genetic variants with BMI.

Methods:
A GWAS was conducted in 1,576 West African with a total of 15.4 million SNPs, and replication study was performed in 6,050 African ancestry samples.
Results :

A novel African specific genome-wide significant locus at 9q22.2 (SEMA4D, rs80068415; $p = 2.1 \times 10^{-8}$) was identified. Following de novo genotyping and correction for multiple testing, the rs80068415 finding was replicated in African ancestry samples ($p=1.5 \times 10^{-3}$, adjusted $p= 2.6 \times 10^{-2}$). The frequency of this variant is 1% in Africans and absent in other non-African ancestry populations in the 1000 Genomes dataset. We measured serum soluble Sema4D in 1,485 West Africans and showed that individuals with obesity had significantly higher sSema4D levels than those without obesity ($p < 0.0001$).

Conclusion :
We report the identification of a novel ancestry specific SEMA4D variant for BMI in this GWAS of continental Africans highlighting the importance of conducting genomic studies in diverse populations.

Mots clés /keywords :
BMI, Obesity, African ancestry, SEMA4D

C20   **Genome-wide Association Identifies African-Specific Susceptibility Loci in African Americans with Inflammatory Bowel Disease**

Auteurs /Authors :
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The inflammatory bowel diseases (IBD), comprising ulcerative colitis (UC) and Crohn's disease (CD), are chronic inflammatory gastrointestinal conditions associated with significant morbidity and a rising prevalence in all populations. More than 200 susceptibility loci have been identified in European ancestry populations and a handful has been identified as Asian-specific. African Americans (AAs) suffer the same disease burden as Europeans. They have a higher risk for developing disease complications and worse disease outcome but no African-specific loci have been established. We hypothesized that high-density GWAS of IBD in AAs could identify population specific variants and expose novel disease mechanisms.

We combined two, previously unpublished, AA genome-wide associations scans (GWAS) comprising 2345 IBD cases and 5002 controls.

We identified a novel Sub-Saharan African-specific UC locus (19q31) at the ZNF649 gene. ZNF649 influences the NFκB pathway and TNF activation. We provide the first association from GWAS of BTNL2 (HLA region) to IBD in AAs (BTNL2 was associated with IBD in Caucasians and CD in Koreans by deep sequencing only). We observed multiple African-specific SNPs with suggestive evidence ($5 \times 10^{-8} < p < 6.5 \times 10^{-6}$) of association at the TNC gene for UC (top SNP: OR=2.06 and P=3.68×10^{-6}) and IBD (top SNP: OR=1.65 and P=9.6×10^{-8}); and within the CXCR6 for CD (OR=0.6, P=6.94×10^{-7}). Additionally, we show that many loci originally found in Europeans are shared across ancestries.

In this first AA GWAS for IBD, we provide evidence for the first genome-wide significant African-specific UC locus at the ZNF649 gene, the function of which seems biologically relevant to UC pathophysiology. We show varying contribution of the HLA region to UC in AAs and evidence of genetic heterogeneity underlying UC between AAs and European populations. A high proportion of IBD loci found in Europeans are shared across ancestries, in support of shared pathogenic mechanisms across different ethnicities

Mots clés /keywords :
IBD, GWAS, African-specific, African Americans

Session 11   Ethics and genomics

C21   **Rapid Ethical Appraisal (REA) tool to design a contextualized consent process for a genetic study of podoconiosis in Ethiopia.**

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Conducting biomedical studies in developing countries can be difficult partly due to poor knowledge about research process and research ethics. The situation is complicated when the disease of interest is thought to be familial and a reason for stigmatisation. We used a Rapid Ethical Appraisal tool to assess local factors that were barriers to getting genuine informed consent prior to conducting genetic studies of podoconiosis (non-filarial elephantiasis) in two zones in Ethiopia. The tool includes In-depth Interviews and Focus Group Discussions with patients, healthy community members, field workers, researchers, Institutional Review Board (IRB) members, community elders, religious leaders, and podoconiosis administrators who work closely with patients. Most patients and healthy community members did not differentiate research from routine clinical diagnosis. Participants felt comfortable when approached in the presence of trusted community members. There was a difference in opinion in terms of the need for verbal or written consent between participants, researcher/IRB members, and podoconiosis administrators. Participants better understood genetic susceptibility concepts when analogies drawn from their day-to-day experience were used. The type of biological sample sought and gender were the two most important factors affecting recruitment process. Most researcher/IRB members indicated that returning incidental findings to participants is not a priority in an Ethiopian context. Understanding the concerns of local people in areas where research is to be conducted will help to design contextualized consent processes appropriate for all parties and will ultimately result in getting genuine consent.

C22   **Types of albinism in southern Africa and genetic investigation of pigment-related genes**

Auteurs /Authors :
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Introduction :
Oculocutaneous albinism (OCA) is one of the most common recessively inherited, single-gene disorders in southern Africa and several types have been described. Molecular techniques can now be used to confirm the clinical diagnosis.

Goals :
The first aim of this study was to describe and classify the different types of albinism found in the local South African black population. Secondly, a mutation screen was undertaken to identify disease-causing mutations in a group of black OCA subjects. All subjects were initially screened for the common black OCA2 mutation: the 2.7 kb deletion mutation. Subjects where one or two mutations remained to be identified were included in an OCA2 mutation screen (N=63). Certain individuals with "unclassified" OCA were investigated further.

Methods:
Classification of types involved a descriptive survey in which 96 affected individuals underwent a clinical and/or dermatological examination.
The OCA2 genetic screen involved Sanger sequencing of all 25 exons of the gene. Certain individuals were also investigated at the Tyrosinase (TYR) or Tyrosinase-Related Protein 1 (TYRP1) locus.

Results :
Most subjects had classic OCA2 (79/96; 82%), and a further 11/96 (12%) had the brown oculocutaneous albinism (BOCA) subtype. The remainder of the subjects (6/96; 6%) had rufous oculocutaneous albinism (OCA3 or ROCA), caused by mutations in the TYRP1 gene.
In the black OCA2 patients, four mutations which are likely to be pathogenic were found. Five mutations in three individuals with "unclassified OCA" were identified. No further mutations (besides the 2.7kb deletion) were identified in the BOCA sample.

Conclusion:
The most common types of OCA found locally are OCA2 and OCA3. No patients with OCA1 were described.
Besides the 2.7kb deletion, no other common OCA2 mutation has been found. Approx 20% of mutations remain unidentified. Genotyping of particular unusual cases suggests that genetic variation at more than one pigment locus is responsible for the resulting phenotype.

Mots clés /keywords :
oculocutaneous albinism; southern Africa; OCA2 gene

C23   **Alleviating the Burden of Beta-Thalassemia in Egypt**

Auteurs /Authors :

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Introduction :Beta- thalassemia is the most common hereditary chronic hemolytic anemia; the Mediterranean regions, central parts of Africa and Asia have the highest prevalence. In Egypt, the carrier rate was estimated as 5.3 - 9 %. More than 1000 patients are born yearly. The disease creates a social and financial burden for the patients, families and society in general. Even in carefully managed patients, survival rates have increased with no parallel improvement in quality of life. Bone marrow transplantation, as the only curative therapy, is limited by availability of compatible donors & increased risk of morbidity & mortality & prevention could be the answer

Goals :reviewing cases frequenting Hereditary Blood Disorders (HBD) clinic and assessing the progress achieved towards a national preventive program

Methods:670 patients & families subjected to; Clinical evaluation, quality of life assessment, defining haplotype map for beta-thalassemia, Mutations characterization and bioinformatics analysis for newly detected mutations, genotype/phenotype correlation, carriers' detection, prenatal diagnosis for pregnant mothers and ultimately genetic counseling

Results :This is a prospective cross-sectional study performed from 2005 till 2015 in the HBD, NRC. Egyptian beta-thalassemia patients were clinically classified according to our scoring system into mild moderate & severe and accordingly assessed for quality of life that mostly correlated to maternal educational level & frequency of blood transfusion. Beta thalassemia haplotype map was established and 30 beta thalassemia mutations could be characterized compared to much less individually reported in different Egyptian studies. Comparing our spectrum to previous reports, 2 novel mutations were detected, 5 (80%)prevalent mutations are in accordance with other reports; 23 varied from rare to once reported. No intra-familial heterogeneity was detected among sibs helping prenatal decision making. In conclusion, Prevention of thalassemia on a national basis in Egypt is urgently needed. HBD team, established a first step

Mots clés /keywords : beta thalassemia mutations, preventive program,genotype/phenotype correlation

ABSTRACTS SELECTED FOR POSTER PRESENTATION

P01   **FCγRIIIA/B genes in SLE**

Auteurs /Authors :
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Introduction :
Systemic Lupus Erythematosus (SLE) is a multi-systemic autoimmune disease with varied symptoms and clinical presentations caused by genetic and environmental factors. The main targeted tissues and blood vessels are that of the heart, kidneys and skin. The genes, Fc gamma receptors IIIA and IIIB, code for the Fc gamma receptors which are cell surface glycoproteins that are involved in the interaction and removal of antigen-antibody complexes from the body into cells. These genes have been shown to be associated with SLE susceptibility and disease in previous studies.

Goals :
Determine if single nucleotide polymorphisms (SNPs), allotypes and copy number variation present within the Fc gamma receptor genes IIIA and IIIB contribute to the susceptibility of systemic lupus erythematosus (SLE) within the black South African population.

Methods:
DNA from 145 black South African patients who have been diagnosed with SLE will be investigated using TaqMan Genotyping assays to determine SNP differences and an ARMS-PCR will be used to determine the allotype differences. Copy number variation will be investigated through the use of real-time PCR.

Results :
The FCGRIIIA 66L/R/H (rs10127939) and 176V (rs396991) SNPs have shown to have strong associations with SLE pathogenesis when present together, in African Americans and therefore it would be expected to be strongly associated within the South African black population. Two allotypes exist on FCGRIIIB, FCGRIIIB-NA1 and FCGRIIIB-NA2. The NA2 allotype is most strongly associated with SLE among Chinese patients and therefore one would not expect this allotype to be present within the South African black population. Low copy number variation with the FCGRIIIB gene have shown to be associated with SLE. Therefore one would expect to see low copy number of FCGRIIIB within our population.

Conclusion :
The genes FCGRIIIA and FCGRIIIB show a strong association with SLE and therefore confer susceptibility to the disease.

Mots clés /keywords :
Systemic Lupus Erythematosus, FCGRIIIA, FCGRIIIB, polymorphisms, allotypes,CNV, South Africa

Auteur présentateur / presenting author:
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P02   Lopinavir disposition

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Introduction :
Drug metabolising enzymes, CYP3A4 and CYP3A5, and transporters, SLCO1B1 and MRP2, are involved in the disposition of lopinavir (LPV). Interindividual variability in LPV plasma concentration could be due to genetic polymorphisms in these genes.

Goals :
The study was set to determine the extent of genetic variation in CYP3A4, 3A5, SLCO1B1 and ABCC2 and evaluate its significance on LPV plasma concentration in Bantu African HIV-positive patients.

Methods:
Eighty-six (n=86) HIV-positive participants on ritonavir-boosted LPV (LPV/r) treatment were genotyped for CYP3A4*1B, CYP3A4*22 CYP3A5*3, CYP3A5*6 and ABCC2 c.1249G>A using PCR/RFLP and TaqMan assays. Variation in SLCO1B1, including the common variants c.388A>G and c.521T>C, was determined by sequencing. LPV plasma concentration was determined from blood samples obtained 12-h post-dose.

Results :
CYP3A4*22 and SLCO1B1 c.521T>C, which have been shown to influence disposition of LPV in other populations, did not play any significant role in this Bantu African cohort. Both CYP3A4*22 and SLCO1B1 rs4149056G (c.521C) variants were not observed in this sample. LPV plasma concentration ranged from 0.0206 to 38.6 µg/ml. No significant association was also observed between LPV plasma concentration and CYP3A4*1B (P=0.0479). However, the variability in the LPV plasma concentrations observed among patients show that Bantu African populations possibly harbour distinct variants that affect variability to LPV plasma concentration.

Conclusion :
These findings highlight the need to include more African populations or ethnic groups in genomics studies in order to identify variants of pharmacogenomics significance as well as a requirement for huge sample sizes to detect potential associations of these variants with drug concentration or response.

Mots clés /keywords :
Pharmacogenetics, Lopinavir (LPV), Africa, Antiretroviral therapy (ART), CYP3A4/5, SLCO1B1 ABCC2

Auteur présentateur / presenting author:
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P03   **Investigating the prevalence of selected MYO7A mutations amongst a group of sub-Saharan African patients with non-syndromic hearing loss**

Auteurs /Authors :
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Introduction :
Congenital hearing loss occurs in approximately 5.5/1000 birth in South Africa. Mutations in GJB2 and GJB6, that explain most of autosomal recessive non-syndromic hearing loss (ARNSHL) in people of European and Asian descent, have been shown to be insignificant in African populations. In order to resolve ARNSHL amongst African patients, next generation sequencing (NGS) was employed thorough the use of OtoSCOPE®, a diagnostic platform for hearing loss, that investigated 66 genes of hearing loss. Compound heterozygous causative mutations (c.5806_5808delCTC and c.5880_5882delCTT) were identified in the MYO7A gene in one family. These mutations may have relevance in some cases of non-syndromic hearing loss among Africans.

Goals :
The aim of this project was to investigate two specific MYO7A deleterious mutations, in an African cohort with ARNSHL

Methods:
100 patients who were negative for GJB2, GJB6 and GJA1 mutations were selected for the present study. The patients were screened for two MYO7A mutations using newly designed primers. This was followed by analysis of the secondary variants using publically available bioinformatics tools to assess their association with MYO7A.

Results :
Only two of the patients carried the c.5806_5808delCTC mutation (2/100) and only one patient carried the c.5880_5882delCTT MYO7A mutation (1/100). The bioinformatics analysis showed no direct interaction between MYO7A and the secondary variants.

Conclusion :
The targeted MYO7A mutations are not prevalent in the Cameroonian and South African populations

Mots clés /keywords :
NSHL, ARNSHL, Hearing Loss, MYO7A, African NSHL
Auteur présentateur / presenting author:
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P04   **Helicobacter Pylori DNA in Liver Tissues From Chronic Hepatitis C Egyptian Patients**

Auteurs /Authors :
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Introduction : Hepatitis C virus (HCV) is considered the most common etiology of chronic liver disease in Egypt, which may progress to cirrhosis and hepatocellular carcinoma (HCC). Previous studies have documented an association between Helicobacter pylori
(H. pylori) infection and liver cirrhosis with or without HCC.

Goals :This study aimed to investigate the presence of H. pylori DNA in the liver tissue of Egyptian patients with chronic hepatitis C (CHC).

Methods:Fifty-two CHC Egyptian patients were enrolled in this study.Plasma anti-H.pylori IgG was assessed with ELISA. Liver biopsies were tested for presence of Helicobacter DNA using genus specific nested polymerase chain reaction (PCR) and species was identified by sequencing.

Results :Anti-H. pylori IgG was detected in 31/52 (59.6%) CHC patients while Helicobacter DNA was detected in 6 (11.5%) patients, all were H. Pylori by sequencing. Helicobacter DNA was more frequent in patients with high stage liver fibrosis (33.3%) than in those with low stage fibrosis (2.7%) (P = 0.006). There was no association between the presence of H. pylori DNA in the liver and age, gender of patients, liver function tests, AFP levels or viral load

Conclusion :These data confirm the presence of H.pylori DNA in liver of some CHC Egyptian patients and suggest an association of this bacterium with progression of liver fibrosis.

Mots clés /keywords :
HCV; Chronic hepatitis C; H. pylori; Liver fibrosis

Auteur présentateur / presenting author:
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P05   **SNP based literature and data retrieval**

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Background:
Biomedical literature retrieval is a time consuming process. Despite academic search engines being more specific than general search engines, they are still too broad in highly specialized fields of study. Ontological integration of search engines has not yet advanced to the state where they provide optimum results when a user is interested in retrieving academic literature relevant to a reference SNP identifier (refSNP). For this reason, the results retrieved when using refSNPs as keywords, are not specific enough. A new search engine is needed. To bypass the lack of ontological integration, the goal of this project is to design a proof-of-concept SNP search engine that returns results to the user with an indication of the amount of times a refSNP has been mentioned in an article. The purpose is to give the user an empirical estimate of the relevance of an article. The vision is to illustrate the use of low-cost untraditional materials and tools in scientific software development to alleviate commercial exploitation.

Methods:
Extract relevant data from biomedical literature made available by the Pubmed Central open access initiative. Store the new data artefact in a database that provides access to human users and applications. Provide additional features to improve user experience (an easy to use website, a VCF file parser and a medical terminology search feature). Display the email address of the correspondence author of a suggested article prominently in the search results to promote communication between scientists.

Results:
A search engine, called SNiPhunter, was designed. It has an index of 69,463 unique refSNPs and 8,743 author defined keywords in 20,650 biomedical articles. The underlying NoSQL database allows RESTful access, and serves results via a web application and an application programming interface.

Conclusion:
The creation of a viable academic search engine was demonstrated using open access literature in combination with free and open source software.

Mots clés /keywords :
Bioinformatics, Data mining, SNP

Auteur présentateur / presenting author:
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P06   **Cystic Fibrosis: A Molecular Investigation**

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Introduction: Cystic fibrosis (CF) is an autosomal recessive disease resulting from the dysfunction of the cystic fibrosis transmembrane conductance regulator (CFTR) gene, with ~1,900 CF-related variants having been identified globally. Early diagnosis is crucial to the quality of life and life expectancy of the CF patient. In South Africa (SA), diagnosis is generally made at ~13months versus ~6weeks in developed nations. This can be partially attributed to a possible diagnostic panel bias as the current panel is Caucasian-based, as well as a knowledge deficit of the diverse CF-causing variants spectrum on the African continent.

Goals: To evaluate the molecular presentations of CF in SA patients with the overarching aim of developing a better representative Afro-centric diagnostic panel.

Methods: DNA was extracted from whole blood of consented patients – confirmed CF patients, and those with suspicious sweat test results with no clear molecular resolution, across 4 ethnicities from 3 major public hospitals. Next generation sequencing was done for CFTR on the extracted DNA with subsequent bioinformatics analyses and Sanger sequencing used for validation of the identified variants.

Results: The patient cohort comprised 50 individuals. 1,375 variants were identified, with 21 of these being potentially pathogenic. 9 variants have been empirically shown to be CF-causing, 5 are on the current diagnostic panel and 4 are novel. 8 variants that have previously appeared in literature with no associated functional studies were also identified. In summary, about 37% of unresolved variations in the study cohort were identified.

Conclusion: The research strategy appears to work well as seen in the significant decrease of the number of unknown CFTR mutations in the cohort, as well as in the identification of novel variations. This should contribute to the knowledgebase for the development of a better adapted CF diagnostic panel that could eventually lead to earlier accurate diagnosis and consequently, better life quality and expectancy.

Mots clés /keywords :
cystic fibrosis, CFTR, next-generation sequencing, bioinformatics, South Africa, diagnosis.

Auteur présentateur / presenting author:
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P07   **Variance in common cancer genes from African populations**

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Introduction :
The effort to determine the role played by specific genes in the clustering of cancer susceptibility within family groups has been bolstered by rapid advances in various sequencing technologies, as well as variant detection and analysis software. This has resulted in the production of a number of cancer panels, each consisting of multiple genes known or suspected to play a role in disease formation. These panels have been built using predominantly European population genomic data however. Considering the high degree of genetic diversity within and between African populations, there is a potentially large degree of unknown variation contributing to disease formation in these groups.

Goals :

This project attempts to make a comparison of several African and European populations from the 1,000 genomes project against genes from a combination of cancer panels, using the GRCh37 reference genome in order to determine any differences in the roles that certain variants may play in increasing disease risk in African populations.

Methods:
1000 Genomes vcf data relating to 5 African and 5 European populations was collected and modified using the fastaalternatereferencemaker tool (GATK) in relation to the hs37d5 custom reference genome, along with a bed file comprised of the exonic sequences for a comprehensive number of cancer panel genes to specify gene regions of interest. The aligned fasta files will then be analysed using BEAST phylogenetic software to perform Bayesian analysis and construct sequence trees to test the evolutionary relationships between possible causal genes across multiple populations and consequently their respective roles in disease formation and potential as therapeutic targets.

Results :

Conclusion :
We hypothesize that the number and identity of disease associated alleles that act to increase susceptibility in African populations will show deviations from the more derived and less heterogeneous European populations.

Mots clés /keywords :
Breast Cancer; 1000 Genomes; BEAST

Auteur présentateur / presenting author:
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P08   **Novel mlh1 germline mutation in a Moroccan lynch syndrome family**

Auteurs /Authors :
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Introduction :

Hereditary non-polyposis colorectal cancer (HNPCC or Lynch syndrome), is a genetically heterogeneous disorder that is associated with germ-line mutations in the DNA mismatch repair (MMR) genes namely MLH1, MSH2, MSH6, and PMS2. The disease follows autosomal dominant inheritance pattern with high penetrance (85%) and younger age of onset.

Goals :
 we report in this paper the case of a suspected Moroccan HNPCC family referred to our medical genetics unit for counseling.

Methods:
Mutation analysis in MLH1 followed by pre-symptomatic diagnosis was performed on genomic DNA isolated from the family members.

Results :

A novel duplication of G nucleotide at position 911 of MLH1 resulting in a premature stop 3 codons downstream in MLH1 was found. The mutation was associated with HNPCC and two asymptomatic carriers were found in the family.

Conclusion :
There are a variety of the reported novel mutations in hMLH1 gene studies. This is the first mutation ever reported in a Moroccan family associated with colon cancer susceptibility. Identification of these mutations is necessary and can help the management of colorectal cancer in these populations by screening, prevention strategies, and following up the suspected HNPCC families.

Mots clés /keywords :
Lynch syndrome, MLH1, colorectal cancer, presymptomatic diagnosis.

Auteur présentateur / presenting author:
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Auteurs /Authors :
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Introduction: Genetic data provide insight into the migratory history and geographic structuring of modern human populations. The recent origin of modern humans reflects migration from sub-Saharan Africa. The serial founder model of modern human origins predicts that the phylogeny of ancestries exhibits bifurcating, tree-like behavior.

Goals: We tested this prediction using three methods designed to investigate gene flow in autosome-wide genotype data from 3,528 unrelated individuals from 163 global samples. Specifically, whether Cushitic ancestry has an East African or a Middle Eastern origin has been disputed in the literature; we sought to resolve this particular issue.

Methods: We analyzed the distance matrix based on Fst between ancestries using split decomposition analysis. We also analyzed ancestry-specific allele frequencies using f3 and f4 statistics as well as a graph-based model of gene flow.

Results: We found evidence for non-tree-like behavior in the form of four migration events. Our results indicate that Cushitic ancestry is a near-equal mixture of ancestries closely related to Arabian ancestry and Nilo-Saharan or Omotic ancestry. We found evidence for additional migration events in the histories of: 1) Indian and Arabian ancestries, 2) Kalash ancestry, and 3) Native American and Northern European ancestries.

Conclusion: Cushitic ancestry has both East African and Middle Eastern origins. In conjunction with three other global-scale migration events, our results indicate that the serial founder model is not strictly correct and that ancestries can form by both splitting events, as predicted by divergence under isolation, and by mixing events. These findings, based on analysis of ancestry of present-day humans, reveal migration in the distant past and provide new insights into human history.

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P10   ASPECTS EPIDEMIOLOGIQUES ET PRISE EN CHARGE DE LA NEUROFIBROMATOSE DE TYPE 1 (NF1) AU SERVICE DE DERMATOLOGIE DE L'HOPITAL INSTITUT HYGIENE SOCIALE (IHS) DE DAKAR

Auteurs /Authors :
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Introduction :La neurofibromatose de type 1 est maladie génétique neuro-cutanée rare de transmission autosomique dominante. Elle a un retentissement esthétique non négligeable et sa gravité réside dans ses complications. En Afrique subsaharienne, l'absence d'un plateau technique adéquat rend difficile la prise en charge.

Objectifs / goals :L'objectif de notre travail était de décrire la prise en charge de la NF1 dans notre contexte.

Méthodologie / Method:Il s'agit d'une étude rétrospective, de 2010 à 2015, incluant tous les cas de NF1 reçus au Service de Dermatologie de l'Hôpital IHS de Dakar.

Résultats / Results :Nous avions recensé 28 patients avec des données exploitables que chez 21. La fréquence hospitalière était de 5/10000. L'âge moyen était de 35ans et le sexe ratio de 1,3. Une consanguinité existait chez 6 patients et des cas familiaux chez 3. Des céphalées étaient notées chez 6 patients et une HTA chez 2. Tous les patients avaient une gêne esthétique. L'examen retrouvait des neurofibromes nodulaires chez 16 patients, plexi formes chez 9 et mixtes chez 3. Les lésions étaient disséminées avec atteinte du visage chez 13 patients, et des taches « café au lait » étaient notées 12. Une dysmorphie axiale existait chez 5 patients. Des nodules de Lisch étaient objectivés chez 4 sur 5 patients. Deux patients avaient des difficultés d'apprentissage. Une dégénérescence sarcomateuse était suspectée au scanner chez un adolescent. Une prise en charge neurochirurgicale était effectuée chez 2 patients, et des antalgiques étaient prescrits chez les autres. Les 15 patients étaient perdus de vue dès la première consultation et le reste 7 mois après.

Conclusion :La NF1 est rare. Elle met en jeux le pronostic esthétique et parfois vital. Dans notre contexte il se pose un problème thérapeutique du fait de l'absence de moyens adaptés. Cette situation explique la perte de vue précoce des patients.

Mots clés /keywords :
neurofibromatose, difficultés thérapeutiques, perdus de vue

Auteur présentateur / presenting author:
Mr(s) Paulin Sambou

P11   Understanding breast cancer in South African patients by identifying single nucleotide variants, insertions and deletions, copy number variations and gene expression.

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Introduction :
Breast cancer has been identified as the most common cancer present in women worldwide1. Thus far, more than 60 genetic loci have been linked to breast cancer formation2. A number of studies have shown the diversity at which BRCA 1 and 2 mutations are present in different ethnic groups. This study address mechanims in the development of breast cancer by comparing somatic (tumor) to germline (blood) samples in a selection of patients from a local academic hospital in Pretoria, South Africa.

Goals :
To obtain information regarding variants in germline samples which make patients more prone to develop cancer; to analyze the changes that occurred in the somatic samples in relation to single nucleotide variants, insertions and deletions, copy number variations and also gene expressions profiles.

Methods:
Whole exomes of germline and somatic samples have been / are being sequenced using Illumina sequencing technology together with Agilent exome selection to a depth of 30x – 50x. Variant detection has been / is being performed using Bowtie2, the Picard Tools and GATK with Mutect2 being employed for the selection of somatic variants. Variants are filtered and annotated using Snpeff, CANDRA, Oncotator and MutSigCV. Additionally, samples are being analyzed with Affymetrix OncoScan FFPE Express for copy number variant detection and with Nanostring nCounter technology for transcription levels.

Results :
A set of pilot samples have been analyzed for somatic single nucleotide variants as well as insertions and deletions, and a summary of results will be presented.

Conclusion :
A combination of single nucleotide variant analysis, insertion and deletion analysis, CNV analysis and transcription level analysis will aid in the understanding of the development of breast cancer in selected patients from this local academic hospital.

Mots clés /keywords :
Germ line and somatic breast cancer, BRCA, founder mutations, gene expression, copy number variants
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P12   **An Overview of Genodermatoses Cases Presenting at the Genodermatoses Clinic, National Research Centre, Cairo Egypt**

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Introduction :Genetic disorders as genodermatoses, considered rare, are relatively prevalent among the African populations, and are a significant cause of morbidity and mortality in these populations.
Goals :reviewing genodermatoses cases frequenting the Genodermatoses Clinic (GC), classifying them and emphasizing how many rare disorders were disclosed.
Methods:Classifications were based on etiological diagnosis, phenotypic diagnosis in addition to dermatopathological studies when needed.
Cytogenetics & molecular studies of the XPA, AR ichthyosis, XED, EB & hyalinosis among others
Results: Patients were classified clinically to several groups according to our system modified between dermatologists' as Rook's and Emery's clinical classification.
They were classified into groups including; pigmentary skin disorders, chromosomal breakage syndromes, disorders of keratinization, vesiculobullous disorders, connective tissue disorders, Ectodermal dysplasia and others.
During establishing our classification many atypical phenotypes and rare cases were disclosed.
In this overview and classification we emphasize the importance of dermatological clews for identifying some genetic disorders.
We also report the encountered rare disorders and phenotypic variability found during the study.
Cytogenetic and molecular studies helped in prognostic expectations in through correlated percentage of sister chromatid exchanges in XP and micronuclear damages in NF. Molecular studies helped detecting new mutations as in hyalinosis, characterizing some of mutations in Egyptian AR ichthyosis and XP patients & emphasized the importance of collaboration among genetic labs & populations sharing historical and ethnic background.
conclusion: Classifying patients is necessary for proper diagnosis, genetic counseling & management decision.
Reporting rare cases and various throws the light on orphan disorders and helps in their diagnosis and enhances referral to specialized genetic centers which in turn helps better registry and statistical data lacking in developing countries

Mots clés /keywords :
genodermatoses, prevalence and registry.

Auteur présentateur / presenting author:
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P13   **Transcriptional profiling of genes associated with malaria during the course of infection.**

Auteurs /Authors :
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2-Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Ouagadougou, Burkina Faso

Introduction :
Malaria is one of the deadliest infectious diseases in the world. Response to malaria infection, as well as disease progression and severity are influenced by environmental factors, transmission intensity, parasite virulence and host genetic factor. Many genes involved in resistance/susceptibility to malaria have previously been identified but the underlying mechanism of action for most of them is yet to be determined. Variation in gene expression has long been recognized as an important determinant of the cellular mechanisms underlying response to infection. Change in gene expression levels of genes associated with malaria is poorly understood.

Goals :
Here we aim to quantify the transcriptional response to blood-stage infection of 48 human genes involved in various molecular processes and assess the contribution of genotype and infection severity to the response.

Methods:
Total RNA from 48 patients from Burkina Faso was retro-transcribed to cDNA and transcript abundance of the 48 selected genes was quantified using Fluidgm's BioMark HD platform. Data was analyzed using Fluidigm's Real Time PCR software and JMP-Genomics. Unsupervised and supervised statistical analysis was used to analyze the data.

Results :
Statistical analysis of the data revealed the nature and extent of individual transcriptional responses and their relationship to host genotype and parasite load. We identified a subset of genes whose transcriptional response is strongly associated with host genotype and that are likely modulating immune response to infection.

Conclusion :
The results of this study show that transcriptional modulation of genes associated with malaria takes place and that there is significant individual-to-individual variation. These variations are likely modulating severity of the disease.

Mots clés /keywords :
Malaria, Plasmodium, host, genotype, Transcriptional
Auteur présentateur / presenting author:

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P14 Phénotype de l'haptoglobine, statut en fer et susceptibilité à l'infection de Mycobacterium tuberculosis

Auteurs /Authors :
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Introduction :
La propriété anti-oxydante de l'haptoglobine (Hp), variable selon les phénotypes, serait associée à différentes pathologies. Par ailleurs, le phénotype de l'Hp est associé au métabolisme du fer, oligo-élément indispensable à la multiplication de Mycobactérium tuberculosis.

Objectifs / goals :
L'objectif de cette étude était de déterminer les caractères d'une éventuelle association entre le phénotype de l'Hp et la ferritinémie (Ferr) au cours de la tuberculose.

Méthodologie / Method:
Dans un modèle d'étude cas-témoins portant sur 62 sujets tuberculeux et 64 sujets sains, ont été réalisés le phénotypage de l'Hp par électrophorèse en gel de polyacrylamide et la détermination de la Ferr par immunoturbidimétrie.

Résultats / Results :
Les 3 phénotypes majeurs de Hp ont été retrouvé: Hp1-1, Hp2-1, Hp2-2. Le phénotype Hp2-2 était moins fréquent chez les tuberculeux (21.7 % vs 78.3 %, p = 0,014). La ferritinémie moyenne des tuberculeux était plus élevée que celle des sujets sains (87 ± 84 vs 220 ± 206 ng/ml ; p < 0,0001). Cependant, chez les sujets sains, il n'est apparu aucune association entre le phénotype de l'Hp et la Ferr. Chez les tuberculeux, la Ferr des sujets Hp 2-1 était supérieure à celle des sujets Hp 1-1 (285 ± 251 vs 147 ± 128 ng/ml ; p=0,011).

Conclusion :
Les sujets Hp2-2 semblent être moins susceptibles à la tuberculose. Chez le tuberculeux, l'augmentation de la Ferr est fonction du phénotype de Hp. Et en dépit de l'infection à M. tuberculosis, fer-dépendant, c'est le profil inflammatoire qui apparait quel que soit le phénotype de l'Hp et conduit à l'augmentation de la Ferr plutôt que la baisse comme dans une carence martiale.

Mots clés /keywords :
Phénotype – Haptoglobine – Ferritine – Mycobacterium tuberculosis – Tuberculose

Auteur présentateur / presenting author:
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P15   **In-silico analysis of MHC genes in hereditary colorectal cancer shows identical by state SNP sharing affecting HLA-DQB1 binding groove**

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Background :
The role of Human Leukocyte Antigen (HLA) alleles in colorectal cancer susceptibility, development and progression is the focus of ongoing scrutiny. MHC polymorphisms in a Sudanese family with hereditary colorectal cancer were studied using an in silico approach and the results were verified using The Cancer Genome Atlas (TCGA).

Methods:
In this family study, we tested for sharing of nucleotide polymorphisms identified by whole exome capture in major histocompatibility complex region and carried out in-silico prediction of their effects in tumor and control samples. SNPs were analyzed to highlight identical by state sharing, to identify runs of homozygosity, as well as to predict structural and functional effects using homology modeling, damaging effect predictions, and regulatory changes prediction.

Results :
MHC II area showed significantly high degree of homozygosity in tumor samples. Non-synonymous SNPs shared identical by state (IBS) between tumor samples were predicted to affect HLA-DQB1 binding groove. A similar haplotype of these SNPs was identified in a TCGA colonic adenocarcinoma tumor sample. No significant regulatory effects (in the form of transcription factor or miRNA binding site variants) were predicted.

Conclusion :
The results demonstrate IBS SNP sharing of markers affecting HLA-DQB1 binding specificity and probable loss of heterozygosity in MHC II region in colorectal cancer. The significance of this sharing in cancer pathogenesis remains to be established.

Mots clés /keywords :
MHC, Colorectal cancer.

Auteur présentateur / presenting author:
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P16   **Characterisation of the Human genome variation in Tanzania**

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Introduction :
Tanzania has more than 120 ethnic groups. In addition, Tanzania is characterised with diverse environmental factors including land and cultural practise. With such a diverse population, polymorphisms must exist which could determine individual and population differences related to susceptibility/resistance to different diseases. Understanding the diversity of Tanzanian population will greatly contribute to our knowledge and the national/interventional efforts to harness human genome variation and utilise such information for improving health, at local and global level.

Goals :
The overall goal of this study will be to determine common patterns of variation of the human genome in Tanzania.In addition, this study will initial a national biorepository and genetic database.

Methods:
1.   Validation of existing data and samples: A search for existing data and samples will be performed through checking on published studies that have used Tanzanian samples, communication with different research groups within Tanzania. A request will be made to use these samples/data and ethical clearance will be processed.
2.   Sample collection: A total of approximately 1000 human blood samples will be collected from a representative set of major ethnic populations whereby 10-20 populations will be sampled. Blood samples will be collected on filter papers
3.   DNA extraction and sequencing: DNA will be extracted from Whatman filter papers by QIAGEN DNA extraction kits. Whole sequencing/exome sequencing will be performed to capture common and rare variants in the Tanzanian populations
4.   Data management and analysis: Data will be collected in ...... and analysis will be perfomed using R and PLINK platforms

Results :
Findings dissemination: Findings will be disseminated through publications, workshops and TGN meetings

Conclusion :
This will be among the pioneering studies which will establish a platform to investigate the role of genetic variation in diseases and pave a way to personalised medicine in Tanzania

Mots clés /keywords :
genome variation, biorepository, Tanzania

Auteur présentateur / presenting author:
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P17   **Outcomes of Genetic Counselling: Nurses Initial experience at the Oncology Units of a Nigerian Teaching Hospital.**

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Introduction :
Breast cancer is a significant growing disease globally, affecting functional and psychosocial wellbeing.

Goals :
Nurses are expected to broaden the scope of their patient-care by improving their skills and advocate screening via genetic counselling (GC).

Methods:
Breast cancer patients and their first-degree relatives (FDRs) attending Oncology Clinics of the University College Hospital, Ibadan were approached by Nurses trained in GC who explained its concept to them. Patients or FDRs who gave their written consent were counselled using the album/slides for GC in a one-to-one interaction in one of the consulting rooms. Their pedigrees were drawn from the information they provided. They were taken through brief overview of cancer, genetics of cancer, risk factors of breast cancer, sporadic, familial and hereditary breast cancers as well as preventive measures and screening modalities according to level of risk. 34 patients and 5 FDRs received GC from March to June, 2015.

Results :
34 nurses counselled patients/FDRs who were between 28 and 78 years. Patients and FDRs were able to comprehend the concept and implication of genetics in breast cancer which was evidenced by the feedback they gave. All (100%) of the nurses were able to draw the hypothetical three generations family tree correctly, describe its key and able to make inferences from them. Some probands initially declined but after the explanations of the purpose and importance of GC, they gave their consent, acknowledged the session and were very happy. Although there are no facilities for genetic testing in the hospital presently, many counsellees indicated that they would like to test for mutations if or when testing becomes available.

Conclusion:
These results provide initial evidence of the need for genetic counselling for individuals and their first-degree relatives with breast cancer by nurses if they receive training. The need for establishing cancer risk and prevention clinic at this facility is confirmed.

Mots clés /keywords :
Outcomes, Genetic Counselling, Nurses, Oncology

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P18   **Polymorphism of the merozoite surface protein-1 block 2 region in Plasmodium falciparum isolates from symptomatic individual living in rural area of Senegal**

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2- CMP, Copenhagen

Introduction :
Polymorphism and antigenic variation of malaria parasites determine malaria episode and its outcome. The study objectives were to determine Plasmodium falciparum genetic diversity in population with uncomplicated malaria under ACT exposure.

Méthodologie / Method:

P.falciparum isolates collected from 300 individuals with uncomplicated malaria infection living in a rural area of Senegal from 2004 to 2008 were analyzed by a nested PCR amplification of MSP1 and MSP2 genes to compare P.falciparum diversity.

Résultats / Results :
Allelic variation in both msp1 and msp2 were identified in the 88 blood samples. For msp1 67% (59/88) and msp2 44% (39/88) were observed The MSP1_K1 family was widespread (frequency >70%). Regarding MSP2 gene, MSP2_FC27 strains were more frequent, especially in 2006 and 2007. Monoclonal infections were more frequent for MSP1 gene, in 2004 (48.78%) and 2005 (45.05%) and for MSP2 gene than polyclonal ones

Conclusion :
This study demonstrated some differences in the P. falciparum diversity between symptomatic subjects over years living in rural area in Senegal and this should be taken into account when designing MSP1 or MSP2 malaria vaccine

Mots clés /keywords :
Plasmodium falciparum, genetic diversity, MSP1, MSP2, Senegal

Auteur présentateur / presenting author:
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P19   Analysis of global ancestry, ethno-linguistics, and migration illuminates the abundant genetic   diversity contained in Africa and correlates ancestry with linguistic data

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Introduction: Genetic studies have established a sub-Saharan African origin for anatomically modern humans with subsequent migrations out of Africa. Characterizing the genetic variation and relationships among global populations stemming from these events is challenging due to gene flow and admixture. Analysis of ancestry effectively removes the effects of recent instances of these confounding factors, revealing history in the distant past.

Goals: Using the largest multi-locus data set for a study of genetic variation known to date, we investigated the genetic differentiation of early modern humans during global peopling, the extent of human admixture and migration events, and the relationships among ancestries and language groups.

Methods: We assembled publicly available genome-wide genotype data on autosomal single nucleotide polymorphisms. The data set includes 5,966 individuals from 282 global samples genotyped at ~19K SNPs. Thirty of the world's 141 primary language families, accounting for 97.8% of people, are represented in our data set.

Results: The data provide evidence for 21 ancestries, 17 of which are present in Africa. Independent of self-identified ethno-linguistic labels, we found that 97.4% of individuals have mixed ancestry, with evidence of multiple ancestries in 96.7% of samples and 100% of continents. We find evidence for migration events between Eastern and Northern Africa and between Omotic ancestry and the node leading to Northern European, Arabian, Northern African, Southern European, and Western Asian ancestries. The ancestry data support the grouping of Kwadi-Khoe, Kx'a, and Tuu languages and support the exclusion of Omotic languages from the Afroasiatic language family.

Conclusion: Analysis of ancestries provides insights into early modern human history, early migration events, as well as how those events relate to present language families. These data can be used to describe the range of variation observed at multiple levels, from worldwide to continental to population-specific.

Mots clés /keywords :
ancestry, admixture, migration,

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P20   **Exome sequencing in clinical genetics: First Sudanese family with a genetic diagnosis**   **of Leber Congenital Amaurosis type 4**

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Leber Congenital Amaurosis (LCA) is a clinically and genetically heterogeneous inherited retinal dystrophy characterized by early onset visual impairment caused by mutations in not less than 17 genes. AIPL1 mutations cause LCA type 4, comprising approximately 7% of LCA worldwide. The importance of establishing a genetic diagnosis lies in the promise of gene therapy demonstrated in mouse models.

Materials and Methods:
We used whole exome sequencing to screen for disease variants in a Sudanese family with multiple patients diagnosed clinically with LCA, all with different degrees of parental consanguinity. Patients had progressive blindness of an early onset. We sequenced samples from two affected siblings and their unaffected mother. We screened known LCA genes for variants with high predicted impact and prioritized variants that followed an autosomal recessive inheritance.

Results:
We report a Sudanese family with autosomal recessive Leber Congenital Amaurosis resulting from AIPL1 variant rs62637009. This variant is a very rare cause of LCA4 which was, up to our knowledge, described previously only once. This report adds evidence to the pathogenicity of this rare variant. As well, it highlights the importance of considering rare disease variants in clinical genetic studies in African populations.
Conclusion: This is the first genetic diagnosis of LCA4 (AIPL1) in Sudan, highlighting the utility of whole exome sequencing as a diagnostic tool in heterogeneous genetic diseases especially in African populations. Rare disease variants can be identified at a genome-wide scale.

Mots clés /keywords :
Exome sequencing, Leber Congenital Amaurosis, LCA4, AIPL1, Sudan.

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P21   **Exome Array Analysis Identifies TRIM67 and TRMT10A Associations with**
Type 2 Diabetes in Sub Saharan Africans

Auteurs /Authors :
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Introduction :
Most diabetes-associated genetic variants emerging from genome wide association studies are common and non-coding. The extent to which rare and low-frequency protein coding variants contribute to diabetes risk remains an area of intense research.
Goals :
In the present study, we sought to evaluate the potential role of rare and low-frequency coding type 2 diabetes genetic risk variants enrolled from sub-Saharan Africa, a region in which the genomics of type 2 diabetes remains understudied.
Methods:
The study participants consisted of 1775 unrelated Africans (mean age 54 years, 59% female) from the Africa America Diabetes Mellitus (AADM) Study. The subjects included 1,598 (90%) West Africans enrolled from Nigeria and Ghana and 177 (10%) East Africans enrolled from Kenya. Samples were were genotyped using the Affymetrix Axiom Exome 319® Array. All analyses were done under a genetic additive model adjusting for age, sex, BMI and the first three principal components of the genotypes.
Results :
Rare and low-frequency variant gene set analysis revealed three exome-wide significant gene sets (i.e. $p < 4.459 \times 10^{-6}$ after Bonferroni-adjustment for 11,214 tested gene sets): TRIM67 ($p=6.571 \times 10^{-7}$), TRMT10A ($p=1.095 \times 10^{-6}$), and CTTNBP2 ($p=3.064 \times 10^{-6}$). The implicated variants in TRIM67 and TRMT10A are missense or splice site variants. TRMT10A mutations were recently identified as causative of a syndrome that included diabetes or impaired glucose metabolism. A lookup of previously reported coding variants associated with diabetes found two significant loci (SLC30A8, $p=3.848 \times 10^{-3}$ and TBC1D4, $p=0.031$). Single variant analysis did not yield any significant locus after adjusting for multiple comparisons.
Conclusion:
The findings indicate that gene sets of potentially deleterious rare and low-frequency coding variants are associated with type 2 diabetes in continental Africans. The identified loci add to a growing list of candidate genes for type 2 diabetes identified from the exome.

Mots clés /keywords :
Genetic association, exome, Type 2 diabetes, Sub Saharan Africa
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P22　　　　　**Profiling serum miRNAs in Metabolically Healthy Obese African American Women**

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Introduction :
Obesity is a major risk factor for several human diseases. However, some obese individuals do not exhibit obesity associated comorbidities and are therefore classified as metabolically healthy obese (MHO). The mechanisms underlying MHO remain elusive. MiRNAs are differentially expressed in many disorders but have not been investigated in MHO.

Goals :
We sought to investigate the expression of circulating miRNAs in MHO individuals in comparison to metabolically abnormal obese (MAO) individuals and to identify any relationship between miRNA-mRNA and proteins.

Methods:
MiRNA was extracted from the serum of 10 MHO, and 10 MAO enrolled from Washington, DC. The expression levels of 179 miRNAs were determined using RT-PCR. Data analysis was performed with GenEx6 software to identify differentially expressed miRNAs (DEMs) between the two groups. After quality control, 121 miRNAs and 19 individuals were included in the data analysis. Ingenuity Pathway Analysis was used to gain insights into the biological processes associated with DEMs and to generate interaction networks.

Results :
Using an unpaired t- test to compare miRNA expression levels, 6 miRNAs were differentially expressed (p-value < 0.05 and fold change (FC >|2|) in MHO individuals compared to MAO individuals including miR-186-5p, miR-181a-5p and miR-106a-5p. IPA analysis of the 6 DEMs identified a network associated with cancer, endocrine disorders and organismal injury. Four of the 6 DEMs targeted 12 mRNAs (e.g. PPARG, STAT3, and CCXL3), which are key members of canonical pathways especially inflammation. We found indirect relationships between DEMs and previously identified differentially expressed proteins (DEPs) amongst MHO and MAO in this cohort through the intermediate of putative targeted mRNAs.

Conclusion :
The findings suggest that miRNAs are differentially expressed between MHO and MAO.Identified DEMs regulate putative mRNAs that encode key members of MHO-associated canonical pathways. Validation of these results is ongoing in a larger cohort.

Mots clés /keywords :
microRNA, metabolically healthy obesity, African Americans

Auteur présentateur / presenting author:
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P23   **Stability of HIV-1 RNA over long term storage and outcome of viral load quantification and**
HIV   **drug resistance genotyping in Jos, Nigeria**

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Introduction :Maintaining HIV RNA stability in plasma samples stored long term at -80 oC for viral load (VL) quantification and HIV drug resistance genotyping (HIVDRG) can be a major challenge. This is particularly true in Nigeria where erratic power supply is commonplace.   We report VL and HIVDRG results obtained from plasma samples stored from 2006 to 2014.

Methods:Preceding a HIVDRG study in 2014, a pilot VL quantification was carried out on 41 plasma samples purposefully selected from the different chambers of -80 o C storage freezers containing samples collected from HIV patients enrolled for treatment at the PEPFAR-supported HIV Clinic at the Jos University Teaching Hospital from 2006 to 2014. HIV-1 RNA was quantified using Roche Cobas Ampliprep TaqMan 96. The VL values were compared to those previously obtained from paired samples that were tested at the original time of sample collection. HIV-1 Genotyping assay was carried out on 287 separate plasma samples picked from the same freezers. Qiagen QIAmp protocol was used for RNA extraction followed by Viroseq HIV-1 genotyping. An ABI 3130xl Genetic Analyzer was used to generate the DNA sequences which were edited. HIV-1 drug resistance mutations were interpreted using the Stanford database.

Results :In a comparison of the 41 VL values of paired plasma samples (initial vs stored), we did not find evidence of significant degradation of HIV-1 RNA (p: 0.598). Of the 287 plasma samples tested for HIV-1 drug resistance mutations by Viroseq protocol, 169 (58.9%) samples were successfully genotyped.

Conclusion :In resource limited settings, despite challenges of erratic power supply, frequent freezer breakdown due to power fluctuation, and transfer of samples between freezers, with concerted efforts and diligence our data reveal that HIV-1 RNA viability can be maintained for successful VL quantification and HIV-1 drug resistance genotyping over long periods of time.

Mots clés /keywords :
HIV-1, RNA, STABILITY, VIRAL LOAD, DRUG RESISTANCE, GENOTYPING

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P24   **Evaluation de la sensibilité de Plasmodium falciparum a l'Amodiaquine, la lumefantrine, l'Artemether et l'Artesunate au Sénégal.**

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Introduction :
Face a l'émergence de la resistance de Plasmodium falciparum aux dérivés de l'artemisinine,une surveillance rigoureuse de ces molecules devient nécessaire pour détecter et prévenir l'émergence ou la propagation de cette résistance dans le reste du monde. Les études de sensibilité in vitro et le génotypage des marqueurs moléculaires de résistance de Plasmodium falciparum peuvent être utilisées pour une surveillance routinière de la sensibilité des souches aux antipaludiques. Un des gènes démontré associée à la pression médicamenteuse des ACT sur les souches circulantes est le Plasmodium falciparum multi drug résistance protéine 1 (Pfmdr1).

Goals :
Le but de cette étude c'est d'évaluer le niveau de sensibilité de Plasmodium falciparum à l'Amodiaquine, la Lumefantrine, l'Artesunate et l'Artemether dans deux localités du Sénégal (Thiès et Pikine).

Methods:
Le DAPI ex vivo test a été utilisé pour étudier la sensibilité ex vivo de 105 isolats de Plasmodium falciparum. Pour l'étude de polymorphisme du gène mdr1, le hight resolution melting a été utilisée. Les codons N86Y, Y184F et D1246Y de ce gène ont ainsi été étudiés.

Results :
Nos résultats montrent globalement une bonne sensibilité des populations de parasites, des deux localités, aux molécules testées. une absence de pression médicamenteuse de l'artesunate et de l'amodiaquine a été observée.Une forte pression de l'artemether et de la lumefantrine sur les populations de parasite avec la forte présence de l'haplotype NFD a été notée.

Conclusion:
Cette étude permet de mieux s'orienter sur la politique de surveillance de l'efficacité in vivo des ACTs. Ainsi, la surveillance de la combinaison Artemether-lumefantrine est fortement recommandée.

Mots clés /keywords :
sensibilité, Amodiaquine, lumefantrine, Artemether, Artesunate, Plasmodium falciparum et Sénégal

Auteur présentateur / presenting author:
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P25   Evaluation of Serum Fibrosis Markers CTGF and IL-17 Versus Liver Biopsy for
Detection   of Hepatic Fibrosis in Egyptian Patients with Chronic Hepatitis C

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Introduction :
Hepatitis C virus infection in Egypt is the most serious health problem, where 10%-15% of the population is infected (About 9 million), 80% of whom develop cirrhosis and hepatocellular carcinoma. The severity of the disease and diagnostic decision-making is evaluated by liver biopsy; an invasive technique with many drawbacks. Recently, attention has been directed to non-invasive, accurate alternatives using serum biochemical markers.

Goals :
To assess the efficacy of two serum biochemical markers (IL-17 and CTGF) versus the invasive liver biopsy for assessing the hepatic inflammatory and fibrotic status in CHC patients.

Subjects and methods:
Fifty eight chronic HCV-infected patients and 30 normal healthy controls were enrolled in the study. Serum sample were collected for detection of CTGF and IL-17 levels using ELISA. Liver biopsies were obtained from some patients for revaluation of the expression levels of their genes by quantitative Real Time PCR and for histopathological assessment of grades of inflammation and stages of fibrosis.

Results :
CTGF and IL-17 serum levels were significantly higher in HCV patients versus healthy controls. Moreover, there were significant differences in the serum CTGF and IL-17 levels and the relative expression levels of their genes in relation to fibrotic stage and inflammatory grades, respectively ($P< 0.05$). Sensitivity and specificity of IL-17 serum levels in the different grades of inflammation; A0-A1 versus A2-A3, were 83.87% and 55.55% respectively. While the sensitivity and specificity of CTGF serum levels in the different stages of fibrosis; F0-F1 versus F2, were 94.7% and 83.33% respectively and for F2 versus F3-F4, were 35.7%, and 100%

Conclusion :
IL-17 and CTGF are serum promising biomarkers. Their estimation is considered to be non invasive, specific, sensitive and accurate method for assessment of liver fibrosis and inflammation in CHC infection. They can be suggested as an alternative to the invasive liver biopsy.

Mots clés /keywords :
HCV, IL-17, CTGF

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P26   **Etude des mutations génétiques des gènes Kelch 13, Pfcrt et Pfmdr des souches de Plasmodium falciparum isolées à Thiés et Dakar**

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Introduction :
Malgré une diminution des prévalences, le paludisme continue de poser un problème de santé publique au Sénégal. Actuellement le traitement du paludisme simple repose sur les combinaisons thérapeutiques à base d'artémisinine. Mais La résistance de Plasmodium falciparum aux dérivés de l'artémisinine en Asie du Sud menace la lutte antipaludique et les activités d'élimination dans le monde entier. La mutation du gène Kelch 13 a été identifiée comme étant responsable de la résistance à l'artémisinine et ses dérivés. Les mutations des gènes Pfcrt K76T et Pfmdr N86Y Y184F N1042D sont associées à la résistance à la chloroquine, la luméfantrine et l'arteméther. Du fait que les études d'efficacité thérapeutique ainsi que des marqueurs moléculaires de la résistance peuvent servir comme un outil important pour la surveillance mondiale de l'efficacité des antipaludiques.

Objectifs / goals :
Le but de cette étude était d'évaluer la prévalence des mutations des gènes Kelch 13, Pfcrt et Pfmdrdes souches de P. falciparum collectés à Dakar et Thiès durant les saisons de transmission de 2011 à 2014.

Méthodologie / Method:
249 échantillons ont été génotypés. La mutation du gène kelch 13 a été déterminée par séquençage avec la méthode de Sanger. La prévalence des gènes Pfcrt (K76T) et Pfmdr (N86Y, Y184F, N1042D, D1246Y) ont été étudiés par la High Resolution Melting

Résultats / Results :Aucune mutation n'a été détecté sur le géne Kelch propeller domain tous les échantillons ont l'allèle de type sauvage, cependant deux mutations silencieuses A468G et C469T ont été observés. Le codon N86Y du gène Pfmdr a présenté 95.6% (238/249) pour l'allèle sauvage (N86) et 70.6% (176/249) avaient la mutation Y184F. Une légère diminution de la mutation N86Y a été notée (11.50% en 2011 et 9.4% en 2014). Une augmentation de la mutation Y184F a été notée également avec 58% (15/26) en 2011 et 68% (36/53) en 2014. L'allèle sauvage K76 est retrouvé chez 73.09% (182/249) des souches étudiées.

Mots clés /keywords :
résistance, marqueurs moléculaires, artémisinine, K13, Pfcrt, pfmdr

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Introduction
Dans le contexte de diminution de la prévalence de l'endémie palustre, le défi est de pouvoir diagnostiquer les infections asymptomatiques chez les porteurs de très faibles densités parasitaires qui peuvent passer inaperçus à la microscopie. Nous décrivons ici une une technique d'amplification d'ADN en condition isothermale "Loop-mediated isothermal amplification" (LAMP), simple d'utilisation, utilisable sur le terrain et ne nécessitant pas une expertise de biologie moléculaire.

Méthode
Nous avons sélectionné des patients suspects de paludisme dans deux sites de Dakar qui est une région ou le paludisme est hypo endémique. Des prélèvements de sang ont été effectués et à partir desquels nous avons réalisés des lames de goutte épaisse et frottis mince, le test LAMP d'illumigene MALARIA et la PET-PCR. Les résultats de la microscopie et de la PET-PCR ont été comparés à ceux de la LAMP.

Résultats
Au total 147 échantillons ont été analysés. La microscopie a permis de détecter 90 échantillons positifs tandis que la PET-PCR et la LAMP ont pu détecter tous les deux 100 échantillons positifs. La sensibilité de la LAMP comparée à la PET-PCR comme méthode de référence a été évaluée à 100% (IC 97,3-100%) et la spécificité à 89,3% (IC 80.3-94%) avec une concordance de 96,3% (IC 92.8-98.1%). La valeur prédictive positive était de 94.6% (IC 89.6-97.2%) et la valeur prédictive négative de 100% (IC 94.6-100%).

Conclusion
Nous avons noté une bonne concordance entre LAMP et PET-PCR avec une meilleure sensibilité par comparaison à la microscopie. La méthode LAMP d'illumigene MALARIA a montré des caractéristiques de performance suffisantes pour être utilisée convenablement dans les zones hypoendémiques du paludisme et dans les régions ou on envisage d'atteindre l'objectif de pre-elimination du paludisme.

Mots clés /keywords :
Plasmodium, diagnostic, LAMP, PCR.

Auteur présentateur / presenting author:
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P28   **Anomalies cytogénétiques additionnelles et résistance au traitement par Imatinib chez les patients suivis pour une leucémie myéloïde chronique au CHU Le Dantec de Dakar.**

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Introduction :
La LMC est un SMP avec présence de chromosome Philadelphie.Il peut exister d'autres anomalies cytogénétiques additionnelles à l'origine de l'apparition de résistance primaires ou secondaires au traitement.

Objectifs / goals :
Rechercher si les anomalies cytogénétiques additionnelles avaient un impact sur la résistance au traitement par ATK.

Méthodologie / Method:
Sur une période de 10 ans, nous avons effectué une étude descriptive colligeant les dossiers de malades présentant une leucémie myéloïde chronique confirmée par la présence du chromosome Philadelphie t(9,22) et /ou son transcrit de fusion Bcl-Abl. Nous avons étudié les paramètres cliniques biologiques, cytogénétiques et thérapeutiques de nos patients. L'analyse des données s'est faite grâce au logiciel SPSS 20.0 et EXCEL 2013.

Résultats / Results :
Nous avons suivi 147 patients présentant une LMC confirmée à l'étude cytogénétique (présence du chi Phi t(9, 22) et ou de son transcrit de fusion, Bcr, Abl). Soixante-dix-sept patients ont eu un suivi régulier clinique, biologique et thérapeutique. Vingt-six patients ont présenté dès l'inclusion des anomalies cytogénétiques additionnelles (ACA) soit 33,76 % à type de trisomie 8, délétion ABL résiduel t (6,8), t (20,9, 22)
 t (2,9), t (3,9, 22) Phi variant etc. Trente-six patients soit 46,7% ont présenté soit une résistance primaire (c'est-à-dire une absence de réponse hématologique après 3 mois de traitement) ou secondaire (c'est-à-dire une perte de la réponse hématologique obtenue à 3 mois ou de la réponse cytogénétique à 6 mois de traitement). Parmi les 30% des patients résistants primaires (n=11), 7 ont eu une anomalie cytogénétique additionnelle à l'inclusion a type de fusion BCR-AB de Trisomie de Duplication, ou de Perte de ABL résiduel.
Conclusion :
Les ACA sont des facteurs pronostiques de risque de survenue d'une évolution péjorative à type de résistance primaire ou secondaire à l'origine d'une accélération de la maladie.

Mots clés /keywords :
MOTS CLES : Anomalies cytogénétiques additionnelles, Résistance ATK, LMC

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P29   Anomalies cytogénétiques au cours de la leucémie lymphoïde chronique

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Introduction :
La leucémie lymphoïde chronique (LLC) est une hémopathie maligne caractérisée par une prolifération monoclonale sanguine et médullaire de lymphocytes B matures. Ses aspects pronostiques basés sur des aspects la clinique et biologiques de la classification de Binet ou de Rai sont actuellement mieux appréhendés avec la cytogénétique.

Objectifs / goals :
Nous nous sommes proposé d'étudier le profil des anomalies génétiques et évolutives des patients suivis dans nos pratiques de prise en charge de la LLC.

Méthodologie / Method:
Une étude rétrospective (2011-2015) descriptive multicentrique est menée chez 20 patients suivis pour une LLC. Ont été inclus ceux qui ont effectué une exploration cytogénétique par FISH à la recherche de del13q14, del 11q22, del17p13 et trisomie 12. Ont été analysés le type d'anomalies cytogénétiques, le score pronostique de Binet et le profil évolutif.

Résultats / Results :
Nous avons inclus 11 patients (3 femmes, 8 hommes) qui ont un âge moyen de 61,1 ans
[50 -80 ans] qui ont tous une hyperlymphocytose sanguine avec une moyenne de 222,9 G/L [12,8-831,1 G/L]. L'analyse cytogénétique a objectivé une anomalie favorable faite de délétion isolée du 13q14 dans 2 cas. Les anomalies de mauvais pronostique sont une double délétion (13q14 + 11q : 1 cas ; 13q14 +17p : 1 cas ; 13q14 + trisomie 12 : 3 cas) et une trisomie 12 isolée (1 cas.) L'anomalie cytogénétique est absente chez une patiente qui est au stade A de Binet. La double délétion est observée chez 4 patients classés stade B/C de Binet. Une délétion du 13q14 associée à une trisomie 13 est notée dans 1 cas de LLC stade A symptomatique. L'évolution est marquée par une rémission primaire chez 5 patients dont 3 qui ont de mauvais facteurs génétiques ont fait une progression (syndrome de Richter : 1 cas ; une anémie hémolytique : 2 cas). Le décès (2 cas) et les pertes de vue secondaires (4 cas) sont notés chez ceux ayant de mauvais facteurs cytogénétiques.

Conclusion :
les facteurs cytogénétiques de mauvais pronostic isolés ou complexes prédominent.

Mots clés /keywords :
leucémie lymphoïde chronique, cytogénétique, pronostic

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P30   Profil des anomalies cytogénétiques rencontrées au cours de la Leucémie myéloïde chronique

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Introduction :
La leucémie myéloïde chronique est un syndrome myéloprolifératif chronique, et par la présence d'un marqueur cytogénétique récurrent : le chromosome « Philadelphie » t (9;22) (q34;q11) ou son équivalent moléculaire (le réarrangement Bcr/Abl).
Le caryotype médullaire au diagnostic permet aussi, de détecter des anomalies cytogénétiques additionnelles non aléatoires, dont certaines sont des facteurs de mauvais pronostic identifiés.

Objectifs / goals :
Cette étude vise à déterminer le profil cytogénétique au diagnostic des patients suivis au CHU A Le Dantec.

Méthodologie / Method:
Sur une période de 10 ans, nous avons effectué une étude descriptive colligeant les dossiers de malades présentant une leucémie myéloïde chronique confirmée par la présence du chromosome Philadelphie t(9,22) et /ou son transcrit de fusion Bcl-Abl. Nous avons étudié les paramètres cliniques biologiques, cytogénétiques et thérapeutiques de nos patients. L'analyse des données s'est faite grâce au logiciel SPSS 20.0 et EXCEL 2013.

Résultats / Results :
Nous avons inclus dans notre étude 77 observations. Il s'agissait de 40 femmes et de 36 hommes (sex ratio = 0,9). L'âge moyen était de 36 ans avec des extrêmes de 9 – 74 ans. Au moment du diagnostic, 42 patients étaient en phase chronique, 16 en phase d'accélération et 6 en phase aigüe. Le caryotypage (conventionnel et FISH) réalisé retrouvait dans 100% des cas le chromosome Philadelphie et/ou le transcrit Bcr/Abl avec dans 13 cas un échec de culture et dans 5 cas le chromosome Philadelphie était masqué au caryotypage conventionnel. Les anomalies chromosomiques additionnelles étaient retrouvées dans 26 cas (39%) à type de délétion de l'ABL résiduel de duplication du chromosome Philadelphie de Trisomie 8 ,de translocations simples, de translocations complexes ou de délétion partielle du bras long du chromosome 6.

Conclusion :
Dans plus de 95 % des cas de LMC, on trouve la translocation t (9; 22). La présence d'anomalies chromosomiques surnuméraires comme la trisomie 8, la duplication du Ph, ou l'isochromosome

Mots clés /keywords :
LMC, profil cytogénétique.

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P31   A South African study for clinical pharmacogenomics.

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Pharmacogenomics explores the underlying genetic composition of genes related in the absorption, distribution and metabolism of drugs. Pharamocogenomics is still in its early stages in several African and European populations, particularly in developing countries.

105 DNA samples from South African populations distributed under Caucasian, Xhosa and Mixed were analysed using the DMET+ platform (Affymetrix, Santa Clara, CA, USA). This resulted in frequencies of 1931 pharmacogenomics biomarkers on 231 genes. The South African dataset was studied, with other European datasets, for clinically actionable pharmacogenomic biomarkers found in CYP2C9, CYP2C19, CYP3A5, VKORC1, SLCO1B1 and TPMT pharmacogenes. Warfarin dosage for the South African population was calculated using the guidelines presented in the International Warfarin Pharmacogentics Consortium. Our results showed how less warfarin dosage (mg/week) is required in South Africans when compared with other European populations.

 Our findings and similar approaches can be used to create medical strategies based on the population's genetic variation, and to integrate clinical pharmacogenomics into African hospitals. If this study is expanded further, with other African populations, it may contribute towards a personalized healthcare service which also reduces healthcare expenditure.

Mots clés /keywords :
Personalized Medicine, Precision Medicine, Pharmacogenomics, African Genomics
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P32 Structuration génétique des tumeurs malignes du sein en fonction de l'atteinte ganglionnaire

Auteurs /Authors :
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Introduction :
De nombreuses altérations génomiques sont connues dans le cancer du sein. Peu d'entre elles peuvent être corrélées à des paramètres clinico-pathologiques et pronostiques. Nos études antérieures ont révélées une forte variabilité génétique entre les tumeurs du sein, mais le taux de cette variabilité diffère selon les caractéristiques tumorales.

Objectifs / goals :
l'objectif de cette étude est de rechercher une corrélation entre la structuration génétique des tumeurs malignes du sein et l'atteinte ganglionnaire qui est un facteur pronostic fondamental.

Méthodologie / Method:
l'étude porte sur cent vingt (120) prélèvements chirurgicaux de tissus cancéreux issus des patientes atteintes d'un cancer du sein. Deux gènes mitochondriaux (le Cytochrome b et la D-Loop) et un gène nucléaire (le Bèta-fibrinogène) ont été amplifiés et séquencés. La structuration génétique des tumeurs qui décrit la distribution de la variabilité génétique a été investiguée grâce à une analyse de variance moléculaire (AMOVA : Analysis of Molecular Variance) en fonction de l'envahissement ganglionnaire à l'aide du logiciel ARLEQUIN version 3.0.

Résultats / Results :
L'analyse de la matrice mitochondriale révèle une structuration génétique entre tumeurs N0-N1 (F_{st} = 0,119 ; P = 0,035) et N0-N2 (F_{st} = 0,148 ; P = 0,002). La valeur de différenciation génétique entre N1-N2 (F_{st} = 0,051 ; P=0,935) traduit l'absence de structuration génétique. Aucune structuration génétique n'a été mise en exergue par la matrice nucléaire (Bèta-fibrinogène) quel que soit le degré d'envahissement ganglionnaire N0-N1 (F_{st} = 0,036 ; P=0,828) ; N0-N2 (F_{st} = 0,056 ; P=0,885) ; N1-N2 (F_{st} = 0,051 ; P=0,843).

Conclusion :
Ces résultats mettent en évidence dans notre population un lien entre l'importance de l'envahissement ganglionnaire et l'hétérogénéité génétique des tumeurs. L'envahissement ganglionnaire reflète une structuration génétique spécifique et qui ne varie pas d'un niveau d'atteinte ganglionnaire à un autre chez la femme sénégalaise.

Mots clés /keywords :
cancer, sein, structure, génétique, ganglions
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P33   **A PROPOS D'UN CAS D'ANOMALIE DU DEVELOPPEMENT SEXUEL**

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Introduction :
Des erreurs apparaissant au cours des étapes de la différenciation sexuelle entrainent des perturbations du développement pouvant aller des ambigüités sexuelles typiques à des états intermédiaires dont les répercutions sont généralement inquiétantes au point de vue sanitaire, social et psychologique. Nous rapportons ici un cas ayant fait craindre une erreur d'attribution d'état civil.

Objectifs / goals :
Dans le contexte actuel des équipements de nos laboratoires notamment de Cytogénétique, en l'absence de Caryotype, la recherche de la chromatine sexuelle peut être d'un apport utile pour nos populations qui, face au « sexe ambigu », sont souvent confrontées à des problèmes socioculturels, le sexe restant encore tabou, mais aussi à un dilemme de déclaration d'état civil.

Méthodologie / Method:

Investigations de Génétique Médicale Clinique :
Prélèvements de cellules épithéliales de la muqueuse jugale, cytoplasmolyse à l'HCL.N. à 56°c et coloration de GUARD pour recherche de la chromatine sexuelle chez un enfant de 7ans référé pour un sexe petit et ambigu.

Résultats / Results :

- Retard du langage et de la marche
- Petite taille : 1m13(pour 7ans)
Faciès élargi et plat ; fentes palpébrales obliques vers le haut et en dehors, Petite bouche, Petits yeux avec un regard en « coucher de soleil »,
Présence d'un micro pénis, Pieds et mains en « coup de vent »
  - La recherche du sexe chromatinien de BARR a donné les résultats suivants :
 Sur deux cents (200) noyaux inter phasiques nus examinés à l'immersion, 10 ont présenté à décrire un corpuscule de BARR, soit un pourcentage de 05% de corpuscules de BARR

Conclusion :
La recherche de la chromatine de Barr, en l'absence de caryotype, reste très utile dans le diagnostic des anomalies du développement sexuel. Aussi, Il y a lieu de mener une bonne politique de communication pour informer et sensibiliser nos populations sur nos possibilités actuelles de résolution de ces problèmes de sexualité.

Mots clés /keywords :
Anomalies - développement - sexuel - corpuscule - Barr - diagnostic
Auteur présentateur / presenting author:
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P34   **Cytogenetic and molecular study of a Moroccan infertile population with**
disorders of sexual development (DSD)

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Introduction :
Infertility affects about 15% of couples on reproductive age. Indeed, microdeletions of the Y chromosome genes were found in 10% of infertile men, in 15% of cases of severe idiopathic oligozoospermia and in 20% of cases of idiopathic non-obstructive azoospermia.

Goals : The purpose of this study is to screen a Moroccan series of 14 infertile patients with disorders of sexual development using molecular techniques.

Methods: We used karyotype for all patients, FISH for the case with 46,XX/45,X/46,XY, SRY gene was analyzed by multiplex PCR and sequencing for patients with 46, XY genotype and female phenotype.

Results : Karyotype results allowed us to identify the etiology of some disorders of sexual development related to chromosomal abnormalities such as Turner and Klinefelter syndromes. In case of congenital adrenal hyperplasia, patients were diagnosed by combining karyotyping with the biological, clinical and radiological examination. The fluorescence in situ hybridization (FISH) technique specified the proportions of mosaic cells and helped us to rectify the karyotype result for the patient's case with 46, XX/ 45, X/ 46, XY. Genetic analysis of five infertile patients with 46, XY genotype and female phenotype showed that the karyotypes of these patients were 46, XY. The mutation screening in sex-determining region Y (SRY) gene was carried out. No mutation has been found in the whole coding sequence of SRY gene.

Conclusion : The genetic analysis of our 14 patients demonstrated that cytogenetic and molecular profiling can be helpful to establish a reliable diagnosis for a considerable part of infertile population. And One could deduce from the SRY gene sequencing that the result of molecular biology can be useful in the absence of clinical, biological and radiological findings well illustrated, and that the search for etiology required exploration of other genes as important as the sex determination gene.

Mots clés /keywords :
disorders of sexual development (DSD), SRY gene, infertile population, multiplex PCR

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P35   Clinical and paraclinical Aspects of Duchenne Muscular Dystrophy in a Group of Cameroonian Patients

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Introduction :
Duchenne Muscular Dystrophy (DMD) is a muscular disease, of genetic origin, inherited in a X-linked recessive mode, and due to a mutation of the dystrophin gene. It is the most common muscular dystrophy in childhood.

Goals :
We intended to investigate the clinical manifestations, echocardiographic and electrocardiograhic abnormalities, and the genetic profile in a group of Cameroonian patients suffering from DMD.

Methods:
We conducted a descriptive cross-sectional study. Clerking and physical examination of participants were performed, as well as cardiac evaluation including an electrocardiogram and an echocardiography. Specific multiplex PCR of the DMD gene were done.

Results :
A total of 17 patients, from 14 families were recruited, all male. The mean age of our study population was 14.03 ± 5.10 years. The mean age at onset of first clinical signs was 4.59 ± 1.50 years, and the mean age at diagnosis was 12.12 ± 5.18 years. Regarding clinical abnormalities, proximal muscle weakness of the lower limbs was found in all participants, and distal muscle weakness of the lower limbs in 70% (7/10) of them. Calf hypertrophy was noted in 76.5% (13/17) of cases. The mean creatine kinase value was 8171.24 ± 7545.29 IU / l (837-31872). An echocardiography has been performed in 8 patients, and an electrocardiogram in 7 patients. Left ventricle systolic dysfunction, dilated cardiomyopathy, and right ventricle systolic dysfunction was observed respectively in 37.5% (3/8), 12.5% (1/8) and 25% (2/8) of our patients. Sinus tachycardia was found in 28.6% (1/7) of our patients, and tall right precordial R waves in 71.4% (5/7) of them. Concerning genetic aspects, specific multiplex PCR was performed in 11 patients. A deletion was found in 45.5% (5/11) of our patients, and a duplication in 27.3% (3/11) of them. The proportion of new mutant has been estimated at 18.2% (2/11).

Conclusion :
At the end of our work, the data indicate that the first clinical signs of DMD in our sample occur in infancy, but the diagnosis is made late in adolescence.

Mots clés /keywords :
Duchenne Muscular Dystrophy (DMD), motor impairment, heart Exploration, muscle enzymes, genetic profile.

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P36   The MRC Keneba Biobank – facilitating integrated research and health care provision in rural Gambia.

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Introduction
The Keneba Biobank is a data and sample repository capturing the rural population of the Kiang West District of The Gambia (described in recent Cohort Profile, Hennig BJ et al IJE 2015).
Goals
Our overall goal is to better understand how health outcomes are affected by both genetic and environmental factors, so as to further the prevention, diagnosis and treatment of illness with a focus on low- and middle-income populations.

Methods
The Keneba Biobank (http://ing.mrc.ac.uk/home/research-areas/the-keneba-biobank/) collects biological samples and routine phenotypic measures from all consenting individuals within the Kiang West Longitudinal Population Study (KWLPS) cohort since May 2012. A custom-designed database and sample tracking system is used for all Biobank-related processes. Participant recruitment is block-randomized to avoid possible seasonal biases. Clinical referrals are made for malaria, hypertension, anemia, diabetes and participants feeling unwell. We are part of the LMIC Biobank and Cohort Network (BCNet, http://bcnet.iarc.fr/).

Results
To date we recruited 10,000 participants (aged 1-92y). Age-group specific data and specimen banked comprise: biological samples (blood/fractions incl. DNA, urine), questionnaire, anthropometry, body composition based on bioelectrical impedance, and blood pressure. Initial analytical tests conducted include fasting glucose, malaria, and full blood count. The repository forms the basis for collaborative studies covering a wide spectrum of health outcomes.

Conclusion
Our three main platforms – the Keneba Biobank, the Kiang West Demographic Surveillance System (KWDSS), and the Keneba Electronic Medical Records System (KEMReS), together serve as an integrated system for research and health care provision to the population living in the vicinity of the MRC Keneba field station. The success of this programme is based on the exceptional long-term relationship between the local population and MRC Gambia staff. This provides the necessary sustainable research capability and capacity to address heal

Mots clés /keywords :
Biobank, Gambia, Demographic Surveillance System (DSS), Electronic Medical Records System (EMRS), MRC Keneba

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P37   **p53 Codon 72 Polymorphism and the Risk of Cervical Cancer in Zimbabwean Women**

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Introduction : In Zimbabwe, cervical cancer is the most common cancer in women and accounts for about 30% of all cancers in females. The development of cervical cancer due to HPV infection is now believed to be associated with host genes such as tumor suppressor gene (p53) of the host. The single nucleotide polymorphism (SNP) of the codon 72 of p53 which results in translation to either arginine or proline has been associated with increased susceptibility to cervical cancer.

Goals : To determine the prevalence of p53 codon 72 polymorphism in Zimbabwean women and risk of cervical cancer

 Methods: : DNA was extracted from blood samples of 73 women undergoing cervical cancer treatment at the Radiotherapy Centre (RTC) of Parirenyatwa Hospital in Harare in Zimbabwe. Sixty two control samples were obtained from undiagnosed healthy group comprising women aged between 30-84 enrolled from the National Blood Transfusion Services of Zimbabwe. Polymerase chain reaction followed by restriction fragment length polymorphism method was used for genotyping for the TP53 codon 72 polymorphism.

Results : The frequencies of the Arg/Arg; Arg/Pro and Pro/Pro genotypes in cervical cancer patients were reported as 15.07%, 43.84% and 41.10% respectively. Odds ratios (ORs) with a corresponding 95% confidence interval were used to calculate the measure of risk and association between the p53 polymorphism and the development of cervical cancer. The p53 Arg/Arg was found to be at increased risk for the development of cervical cancer (OR= 1.78). However its association with the development of cervical cancer was not statistically significant (p-value= 0.29; 95% CI, 0.54-6.12).

Conclusion : The prevalence of the Arg/Arg genotype in our study was lower in cervical cancer women compared to other Black African populations. Further studies are required to ascertain association of genetic markers in tumour suppressor genes with cervical cancer susceptibility

Mots clés /keywords :
p53, codon 72, polymorphism, cervical cancer, Zimbabwe

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P38 Apport de la cytogénétique dans le diagnostic des anomalies du développement sexuel au Sénégal

Auteurs /Authors :
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Introduction :
Les anomalies du développement sexuel (ADS), autrefois appelées ambiguïtés sexuelles, sont les conditions congénitales au cours desquelles les sexes chromosomique, gonadique et anatomique sont atypiques. Dans la nouvelle classification des ADS, le caryotype est incontournable. En l'absence du Caryotype, la recherche de la chromatine sexuelle peut être utile pour nos populations.

Objectifs / goals :
L'objectif de cette étude était de déterminer les sexes chromatinien et chromosomique des patients et de les comparer au sexe déclaré à l'état civil.

Méthodologie / Method:
Il s'agissait d'une étude rétrospective de septembre 2000 à décembre 2012 et prospective d'Août 2013 à Décembre 2013, dans les laboratoires d'histologie, embryologie et cytogénétique de l'université Cheikh Anta Diop de Dakar et de l'hôpital Aristide Le Dantec. Tous les patients ayant été référés pour test chromatinien de BARR et/ou Caryotype en vue du diagnostic d'une anomalie sexuelle ont été inclus. Il a été constitué 71 tests chromatiniens de BARR et 10 caryotypes sélectionnés parmi ceux effectués dans cette période. Nous avons recueilli en même temps certains paramètres épidémiologiques et cliniques.

Résultats / Results :
L'âge moyen des patients était de 10,31ans. Le sexe ratio était de 1,5 en faveur du sexe féminin. Sur 35,21% des bulletins, il était inscrit « ambiguïté sexuelle » comme indication. 41% de nos patients étaient de sexe chromatinien féminin et 39% masculin. Sur 10 cas, 6 avaient une formule chromosomique 46,XY et 4 une formule 46,XX. Dans 25,35% des cas le sexe déclaré à l'état civil ne concordait pas avec le profil génétique.

Conclusion :
Les anomalies du développement sexuel sont des anomalies aux étiologies multiples, pouvant être à l'origine d'erreurs d'attribution du sexe d'état civil. La cytogénétique, plus précisément le caryotype, est indispensable à la nouvelle classification.

Mots clés /keywords :
Ambiguïtés sexuelles- hermaphrodisme- Intersexuation- chromosomes- chromatine de Barr

Auteur présentateur / presenting author:
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P39   **DIAGNOSTIC CHALLENGES AND BEHAVIOR PROBLEMS OF RWANDAN PATIENTS WITH DISORDERS OF SEX DEVELOPMENT**

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Introduction :Disorders of sex development (DSD) comprise a variety of congenital diseases with anomalies of the sex chromosome, the gonads, the reproductive ducts and genitalia. DSDs are always challenging and very difficult to manage. Socio-economic and cultural aspects have a great impact on decision making regarding the management of these conditions. The situation is more complicated in resource-poor settings like in Africa, where access to education and medical care is limited in both quantity and quality of infrastructure, diagnostic tools and medical professionals. In addition, traditional values and beliefs are also very strong in various cultures and sexual issues are taboo subjects.

Methods:The present study is a 5-year prospective descriptive cohort of patients with suspicion of DSDs referred to our genetic clinic between January 2011 and December 2015 for genetic investigations and counseling. All patients underwent abdominal ultrasound or MRI and hormonal analysis before genetic testing including karyotype and molecular tests.

Results :In total, 49 patients aged between 1 and 39 years were clinicaly and geneticaly diagnosed with DSDs associated with behavior problems in most of cases. The majority were diagnosed either with sexual ambiguity and hypospadias, or micropenis, or primary amenorrhea, or poor development of secondary sexual characteristics, or primary infertility. In most of female cases, the ultrasound and MRI revealed absence of uterus and ovaries. The FSH, LH or testosterone hormons revealed major abnormal values in more than 60% of patients. The AIS and Rokitansky syndrome were observed in the majority of these patients. The choice of gender identity after karyotyping raised several psychological and ethical issues in the majority of adults patients. The outcome of surgery was successful for the social integration of some of these patients.

Conclusion: The present study showed that patients with DSDs have major behavior problems in African context.

Mots clés /keywords :
Disorders of sex development DSD - Diagnostic challenges - Behavior problems - Rwanda

Auteur présentateur / presenting author:
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P40 **Prévalence de l'antigène HBs chez une population de femmes enceintes à Dakar, Sénégal**

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L'Hépatite B est un véritable problème de Santé Publique. Le Sénégal est une zone de haute endémicité des hépatites virales et surtout de l'hépatite B. La transmission mère-enfant reste une cause majeure du maintien de l'épidémie dans le monde. Notre étude s'inscrit dans ce contexte.

Objectifs
Etudier la prévalence du portage de l'Ag HBs chez une population de femmes enceintes à Dakar.

Méthodologie
L'Antigène HBs a été recherché chez toutes les femmes volontaires, recrutées pour l'étude, par immunochromatographie.
La recherche des marqueurs d'hépatite B chronique (Ag HBe, anti HBe, quantification virale) a été réalisée chez les femmes enceintes Ag HBs positives par chimiluminescence pour les Ag HBe et anti HBe, et par PCR en temps réel pour l'ADN viral. Les anti HBs ont été titrés chez les femmes Ag HBs négatives par une technique immunologique microparticulaire par chimiluminescence.

Résultats
Cent quinze gestantes ont été incluses dans l'étude de Juillet à Octobre 2014. Leur âge moyen était de 29 6 ans avec des extrêmes allant de 16 à 47 ans. La prévalence de l'Ag HBs était de 12%. La majorité des femmes (90%) affirment ne pas être vaccinées. Parmi les patientes Ag HBs positif (n = 14), aucune n'exprimait dans son sérum l'Ag HBe témoin de la multiplication active du virus et toutes étaient Ac anti HBe positif. Leur charge virale (VHB/ADN) était indétectable. Les transaminases sériques étaient normales.
Les anticorps anti HBs titrés chez les femmes Ag Hbs négatif ont révélé que seules 46 avaient des taux protecteurs vis-à-vis du VHB ; 55 femmes enceintes étaient non protégées.

Conclusion :
Il est recommandé de promouvoir la vaccination avant la grossesse et de faire un dépistage systématique de l'AgHBs chez toutes les femmes enceintes. Pour les femmes AgHBs(+) et AgHBe(-), il est important d'étudier la charge virale afin d'évaluer le risque de transmission périnatale et de le prévenir par une séroprophylaxie dès la naissance, voire même un traitement antiviral en fin de grossesse.

Mots clés /keywords :
Ag HBs – Prévalence – Femmes enceintes - Sénégal

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P41   Cytogenetic, symptomatologic and hematologic characterization of 50 Moroccan patients with Chronic Myelogenous Leukemia

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Introduction :Chronic Myelogenous Leukemia (CML) is a rare myeloproliferative syndrome, it constitutes the first malignant disorder associated specifically to acquired cytogenetic abnormalities, such as the reciprocal t(9; 22) (q34; q11) translocation, known also as the Philadelphia chromosome (Ph), which results in the chimeric BCR/ABL gene. This fusion gene codes for an oncogenic protein of the same name characterized with a high tyrosine kinase activity.

Goals :The aim of this work is to perform clinical, symptomatological and hematological studies before starting the treatment for the patients in whom the Philadelphia chromosome was positive (Ph+). The second goal is to have a full view about the cytogenetic and the hematological pattern in leukemic patients.

Methods:In this study, we have enrolled 50 patients diagnosed to have CML with Ph+. To highlight the Philadelphia chromosome, we carried out karyotyping technique. To detect the 5% of cases overlooked due to karyotype resolution, we used FISH technique for BCR/ABL fusion gene.

Results :We screened 50 patients whose average age is 48 years, we have found that among the performed karyotypes: 41 cases are Ph+, including 38 usual t(9;22)(q34;q11) translocation and 3 complex translocation cases. The 9 remaining cases which were Philadelphia-negative (Ph-), were screened using the FISH technique, and found to carry all the fusion BCR/ABL gene.
Clinical investigation shows that 94% of cases in our series presented a splenomegaly, and more than 73% were in chronic phase. We found also that the white blood cells counts of our patients were remarkably high.

Conclusion :Although we have found interesting results with the two previous techniques, the use of molecular biology, including the technique of RT-PCR, remains essential to rise the resolution at a molecular level, which would allow a better diagnosis, and thus a proper following-up.

Mots clés /keywords :
Chronic Myelogenous Leukemia (CML), cytogenetic, FISH, Philadelphia chromosome (Ph), translocation (9; 22) (t(9; 22)), BCR/ABL fusion gene

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P42   **Formative Evaluation for a Genomics Study of Female Reproductive Cancers.**

Auteurs /Authors :
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1- University of Zimbabwe

Background: Female reproductive malignancies including cervical (CC) and breast (BC) cancers constitute the highest percentage of cancer diagnosed among women in Zimbabwe. However there is little research to understand epidemiological, environmental and genetics risk factors of individual and population variability of susceptibility and treatment response in reproductive cancers in Zimbabwe.

Goals: Understand the distribution of reproductive cancers towards planning for a genomics studies of female reproductive cancers in Zimbabwe.

Methods: Analytic review of epidemiological data from the Zimbabwe Cancer Registry was used to determine the distribution of reproductive cancer incidence rates in Zimbabwe. The World Health Organisation website was accessed for data on Africa.

Results: CC and BC are the leading causes of cancer mortality in Zimbabwe. Incidence rates of CC were 32.5% and 33.9% in 2006 and 2012, while breast cancer statistics were 11.7% and 7% respectively. Overall incidence of CC in Southern Africa is 22.5% while BC is 35%. Mortality rates in 2012 were 12% and 4% for CC and BC respectively, in comparison to African average of 28% and 26%. Furthermore, cervical (33.9%) and breast cancer (9.7%) were the two leading cancers amongst black women.

Conclusions: Zimbabwe has a high burden of female reproductive cancers; particularly CC, the leading female-related cause for cancer mortality. There is an inter-country and possibly interethnic variability in cervical/breast cancer incidences and mortality, which could be linked to geographical and environmental factors, and genetic variability. In future, a restrospective/prospective cohort study will be conducted to determine frequency, distribution, treatment and outcomes from reproductive cancer among adult women (age >18). Surgical, pharmacological and radiological management will be recorded and subsequent outcomes. This work will inform targeted genomics research to determine prevalence of genetic polymorphisms associated with oncogenic mechanisms and pharmacological response

Mots clés /keywords :
Female reproductive cancers; breast cance; cervical cancer; genomics

Auteur présentateur / presenting author:
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University of Zimbabwe

P43   **Penetrance des mutations de la d-loop et du cytochrome b dans l'occurrence des carcinomes ovariens chez les femmes senegalaises**

Auteurs /Authors :
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Introduction :
au Sénégal, les pathologies cancéreuses sont aujourd'hui au sommet des causes de décès. Le cancer de l'ovaire est responsable de 5,8% des décès par cancer et est au 5ème rang des causes de mortalité par tumeur maligne. Les plus forts facteurs de risque actuellement impliqués dans l'éthologie de ce cancer sont ceux d'ordre génétique, avec des mutations spécifiques.

Goals :
le but de cette étude est d'analyser l'incidence des mutations de la boucle de déplacement (D-loop) et du cytochrome b (Cyt b) dans l'occurrence du cancer de l'ovaire au Sénégal.

Methods:
nous avons étudié la variabilité des deux gènes (D-Loop et Cyt b) par   PCR-Séquençage chez trente patientes sénégalaises, atteintes d'un cancer de l'ovaire. Pour chaque patiente nous avons travaillé avec l'ovaire sain et l'ovaire cancéreux. La recherche de mutations, l'évaluation du degré de variabilité des génes mitochondriaux et de la différenciation génétique a été effectuées avec la base de données MITOMAP et les logiciels BioEdit version 7.2.0, MEGA 6 version 6.05, DnaSP version 5.10.01 et Arlequin Version 3.1.

Results :
Il est à noter dans cette étude que, la D-Loop est plus variable que le Cyt b avec 81 nouvelles variations dont 41.28% présentant des différences significatives ($P<0,05$) pour la D-Loop contre 19 nouvelles variations pour le Cyt b dont 19.23% présentent des différences significatives. Nos résultats ont également montré une augmentation significative du tryptophane dans les tissus cancéreux, une légère hausse des taux d'alanine et d'arginine mais aussi que le Cyt b était sous sélection positive.

Conclusion :
Toute augmentation du taux de Tryptophane, d'arginine et d'alanine dans les tissus cancéreux pourrait être corrélée à une augmentation du risque d'apparition du cancer de l'ovaire d'un côté et de l'autre l'arginine et l'alanine pourraient jouer un rôle important dans le traitement du cancer de l'ovaire.

Mots clés /keywords :
cancer, ovaire, mutations, ADNmt, Sénégal

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Auteurs /Authors :
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Introduction :
Recent studies have provided evidence on the efficacy of herbal medicine, most especially anti-diabetes herbal tea (ADHT), in the management of Type 2 Diabetes Mellitus (T2DM) which has resulted to considerable patronage even in developing countries, partly to its affordability. Improved understanding of ADHT and integration of pharmacogenomics will benefit citizens in developed and developing countries. However, there is a dearth of data on genetic variant response and treatment outcomes of such anti-diabetic medications especially in Nigeria.
Goal:
To investigate the in-vitro free radical scavenging activities of ADHT's methanol extract as a first step in assessing individual genetic – drug response to T2DM management.

Method:
This study was carried out at the Department of Biochemistry, Madonna University, Nigeria in 2012 using the 2-2 diphenyl-1-picrylhydrazyl (DPPH) radical, superoxide anion radical (O_2.-), hyrdroxyl radical (.OH) and nitryl oxide radicals (NO.) scavenging assay systems on cold Methanol extracts of a commercially available brand of ADHT. Phytochemical properties of ADHT were also quantified spectrophotometrically.

Results :
Methanol extracts of the tea was rich in flavonoids, flavonols and phenolic compounds. Total phenols were estimated at 1.38 + 0.27 mg gallic acid equivalent (GAE)/mg of dry extracts while flavonoids were 15.00 + 2.011 mg rutin equivalent (RE)/mg. Theses extracts showed a potent DPPH radical scavenging potentials maximally (72.38%) at a concentration of 25ug/ml with IC50 of 31.16 + 17.78 ug/ml. O_2.-anion was also maximally inhibited (90.07% at a concentration of 250ug/ml with IC50 of 11.79 + 26.51 ug/ml). Accumulation of nitrite (NO.) in vitro was also significantly inhibited in a concentration dependent manner.

Conclusion :
Our findings suggest that ADHT may actually improve treatment outcome of T2DM with likelihood of cost-effective personalized treatment, though there is need for further case-control clinical studies to explore the in vivo potentials of ADHT on candidate genes.

Mots clés /keywords :
Pharmacogenomics, Type 2 Diabetes, Adjuvant Self Therapy

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P45   Genetic diversity and drug resistance of HIV-1 strains among antiretroviral therapy(ART) naïve and art treated patients with and witout active tuberculosis in South Omo, Ethiopia

Auteurs /Authors :
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Addis Ababa University

Introduction: The increasing diversity of HIV has profound implications for its   pathogenicity, transmission, diagnosis, treatment, and vaccine development.   In Ethiopia, subtype C accounts for more than 90% of all reported cases so far. In view of ART scale up, and reporting of non C sub type in the country, surveillance of drug resistance and genotyping is important, especially in the current study area where no genotyping study is conducted .

Objective: This study is designed to evaluate HIV-1 genetic diversity and drug resistance-associated mutations among drug-naïve and experienced patients with and without active tuberculosis in South Omo, Ethiopia. In addition, impact of tuberculosis on HIV genetic diversity and viral load will be investigated.

Methods and Materials: Four different study designs and populations will be considered: Recently infected ARV drug-naïve individuals(N=47) , Chronically HIV-1infected   ARV drug-naïve(N=174),   and Chronically HIV-1 infected receiving ART for ≥3 months(N= 328). In addition, to investigate the impact of M. tuberculosis on HIV-1 load and genetic diversity, nested case control study design will be used consisting of HIV/TB group (N=28) and non-TB HIV group(N=56) as control among chronically HIV-1 infected ART naïve patients.

For all types of the study, in addition to socio-demographic and clinical data, 10 ml of blood will be collected from participants using ethylene diamine tetra-acetic acid (EDTA) containing vacutainer. CD4+ lymphocyte count will be done within 2-4 hours of blood collection. Plasma will be separated and stored in multiple aliquot at -40 oC for viral load measurement and molecular characterization using   protease (PR) and reverse transcriptase (RT) gene sequencing.

Pol   gene sequences will be aligned with reference subtypes obtained from HIV sequence database at Los Alamos, and for drug resistance analysis consensus mutations of Stanford University HIVDB will be used .In addition, differentially expressed   plasma proteins, between HIV/TB and HIV /non-TB groups will be analyzed using shotgun proteomics.

Fisher exact test implemented by GraphPad PRISM software (San Diego, CA) will be used for statistical analysis of the difference in subtypes among different risk groups and the genetic variation in PR and RT genes among subtypes.

Expected Result: The research is expected to generate data on: The genetic diversity of HIV-1 in the region, prevalence of transmitted and acquired HIV drug resistance among ARV naïve and experience patients ,and impact of tuberculosis on HIV-1 genetic diversity and viral load.

Hence the data will help in the development of appropriate prevention strategies to limit treatment failure and plan for appropriate treatment6 and vaccine strategi

Mots clés /keywords :
HIV-1,genetic diversity, drug resistance, tuberculosis, South Omo.

Auteur présentateur / presenting author:
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Addis Ababa University: Systems Biology for Molecular Analysis of Tuberculosis

P46　　　　**Anomalie du développement sexuel 46,XX avec hypertrophie clitoridienne et**
pilosité pubienne précoce : à propos d'un cas

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Introduction :
Le terme « ambiguïté sexuelle » a été abandonné au profit d'anomalies du développement sexuel (ADS). Dans la nouvelle classification, les pseudohermaphrodismes masculins correspondent aux ADS 46,XY, les pseudohermaphrodismes féminins aux ADS 46,XX, et les hermaphrodismes vrais aux ADS ovotesticulaires. Ainsi le caryotype est devenu incontournable à la nouvelle classification. Nous rapportons dans ce travail le cas d'une patiente reçue pour hypertrophie clitoridienne.

Objectifs / goals :
l'objectif était de situer le malade dans la classification des anomalies du développement.

Méthodologie / Method:
0,5 ml de sang veineux périphérique a été mis en culture avec une lectine mitogène dans une étuve CO_2 pendant 72h. Ensuite nous avons procédé au blocage par la colchicine, puis au choc hypotonique par le chlorure de potassium. La fixation a été réalisée par le Carnoy 1 avant d'étaler le culot sur les lames pour en finir avec la coloration au Giemsa. Les mitoses ont été observées grâce à la cytovision.

Résultats / Results :
La patiente, de sexe féminin à l'état civil, était âgée de 6ans et demi. Elle est née d'une mère âgée de 23ans avec une notion de prise de médicaments traditionnels au premier trimestre de la grossesse. L'examen clinique notait un développement mammaire classe S1 de Tanner, des grandes lèvres cernant un clitoris hypertrophié type II de Prader et une pilosité pubienne stade P3 de Tanner au niveau des organes génitaux externes .
L'échographie abdominale était normale et l'échographie pelvienne retrouvait des organes génitaux internes de type féminin.
Le résultat du caryotype était 46,XX.

Conclusion :
La patiente a été classée dans les ADS 46,XX. Les anomalies du développement sexuel ont des étiologies multiples. Les ADS 46,XX peuvent résulter d'un trouble du développement des ovaires telle que la dysgénésie gonadique ou d'un excès d'androgènes fœtaux telle que l'hyperplasie congénitale des surrénales ou l'exposition maternelle à des androgènes durant la grossesse.

Mots clés /keywords :
classification de Prader - caryotype - exposition maternelle à des androgènes durant la grossesse

Auteur présentateur / presenting author:
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Université Cheikh Anta DIOP de DAKAR

P47   **Baseline Assessment of Blood Metals Concentration and Fasting Blood Glucose in Understanding Epigenetic Risk Association with Type 2 Diabetes Pathogenesis among Nigerians**

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Introduction :
Recent evidence suggests that the interactions between genes and environment might play a critical role in the pathogenesis of complex diseases, such as Type 2 Diabetes (T2D), however there are limited epigenetic and experimental data from Nigeria on the relationship of environmental heavy metals, essential trace metals with T2D.

Goals :
To determine the level of heavy metal: cadmium (Cd) and trace metals: chromium (Cr) and zinc (Zn) in the serum of patients and their relationship with fasting blood glucose (FBG) of T2D patients.

Methods:
This was a cross-sectional study conducted at the Endocrinology clinics of the Obafemi Awolowo University Teaching Hospital Complex (OAUTHC) at the Ife Hospital Unit (IHU) and Wesley Guild Hospital (WGH), Ilesha. The study population comprised 102 diagnosed diabetic patients attending the Endocrinology clinics. After an overnight fast, blood was drawn from each participant and blood metal concentrations were measured by atomic absorption spectrophotometer after acid digestion while FBG was measured with a glucometer.

Results :
A total of 102 persons were studied, mean (SD) age was 61 (1) years and mean duration of diabetes was 6 years. The mean weight and height were 71 (13.54) kg and 1.61 (0.09) m respectively. Overweight people (BMI>25) accounted for 67% of the study group while 33% had BMI < 25. The mean metal concentrations obtained were 0.0134 ppm for cadmium, 0.0052 ppm for chromium and 0.0088 ppm for zinc while the mean fasting blood glucose was 7.27 (0.21) mmol/L. Serum chromium and zinc concentrations were not significantly correlated with fasting blood glucose while serum cadmium had an insignificant weak positive relationship with fasting blood glucose.
Conclusion :

This is a preliminary investigation on association of environmental heavy metals, DNA hydroxymethylation and microRNA in T2D. Further research is needed to investigate the role of environmental heavy metals on gene expression through epigenetic mechanisms in T2D.

Mots clés /keywords :
Epigenetics, Environmental Heavy Metals, Trace Metals, Type 2 Diabetes

Auteur présentateur / presenting author:
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P48   **Etude cytogénétique des anomalies chromosomiques par le test chromatinien de Barr**
                   et le caryotype au service d'histologie-embryologie et cytogénétique : à propos de 100 cas

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Introduction :
L'analyse des chromosomes est une composante importante du diagnostic et de l'évaluation des désordres génétiques. Approximativement 1000 syndromes chromosomiques influant sur la morbidité et la mortalité de l'espèce humaine ont été répertoriés.

Objectifs / goals :
Les objectifs de cette étude étaient de déterminer les causes les plus fréquentes d'indication d'analyses cytogénétiques, le sexe chromatinien des patients mais aussi les anomalies chromosomiques les plus rencontrées au caryotype

Méthodologie / Method:
Il s'agissait d'une étude rétrospective de septembre 2000 à décembre 2012 et prospective d'août 2013 à octobre 2014, dans les laboratoires d'histologie, embryologie et cytogénétique de l'université Cheikh Anta Diop de Dakar et de l'hôpital Aristide Le Dantec. Tous les patients référés pour test chromatinien de BARR et/ou Caryotype ont été inclus. Nous avons recueilli en même temps certains paramètres épidémiologiques et cliniques

Résultats / Results :
Parmi les patients, 53% étaient déclarés féminin à l'état civil, 40% déclarés masculin, 7% avaient un sexe d'état civil non déterminé. Sur 31% des bulletins l'ambiguïté sexuelle était l'indication. L'âge moyen de consultation était de 8,82 ans. 90% étaient envoyés pour une suspicion d'anomalie gonosomique et 10% pour une suspicion d'anomalie autosomique.. 45% avait un sexe chromatinien masculin, 39% un sexe chromatinien féminin, 15% avait un taux intermédiaire et un patient n'a pas bénéficié du test. 36% des patients ont bénéficié du caryotype et parmi eux, 41,67% avaient une formule 46,XY ; 38,89% une formule 46,XX ; 11,11% présentaient une trisomie 21 ; 2,78% une trisomie 13 ; 5,56% avait une formule en mosaïque.

Conclusion :
Les techniques cytogénétiques sont importantes pour l'identification correcte d'une variété de syndrome. A défaut du caryotype, le test chromatinien de Barr peut être d'un apport utile.

Mots clés /keywords :
chromosomes - ambiguïtés sexuelles - trisomie 21- trisomie 13 - corpuscule de Barr

Auteur présentateur / presenting author:
Dr Mame Vénus GUEYE
Université Cheikh Anta DIOP de Dakar

P49   **Computational Approach to Re-engineering of Predictive Toxicology of Insecticide
and the Reduction of Exposure to Risk of Getting Cancer.**

Auteurs /Authors :
Falade E(1); Marion A(2)

Introduction :
From research, in the quest to eliminate unwanted insects, one need to understand the toxicity of the mechanize structure of chemical in an insecticide for killing or eradication of all targeted insects, the reason is that this toxic chemical can be very harmful when release to the environment
it can be easily absorbed through the skin, eyes or nostril of animals, humans or even plants which can cause some disturbing symptoms like weakness or even death.

Goals :
Reduction of Cancer possibility from insecticides.

Methods:
Computer tools can alternatively use for gathering data on hazard identification, the way they react in humans, group them, and to get their potential effects on human health,

Results :
Possible solutions to the total removal/reduction insecticide effect on the environment especially to man.

Conclusion :
A safe insecticide for use or insecticide with reduce toxicity guarantee cancer free envronment

Auteur présentateur / presenting author:
Mr(s) Falade Emmanuel Eniola

P50 **PNPLA3 I148M Polymorphism and susceptibility to HCV infection in genotype 4 HCV Egyptian patients**

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3-Department of internal medicine Faculty of medicine , Cairo university, Egypt
4 - National Hepatology and Tropical Medicine research Institute, Cairo, Egypt.

Introduction :
Hepatitis C virus (HCV) is a major health problem worldwide. Egypt has the highest HCV epidemic worldwide. Polymorphism in patatin-like phospholipase domain-containing 3 (PNPLA3, adiponutrin) gene has been associated with the risk of developing HCC and was also shown to be associated with fibrosis progression in alcoholic liver diseases, but till now information about this polymorphism and HCV susceptibility is not yet clear. The genotype distribution of this polymorphism differs by race

Goals :
This study is sought to identify the genotype distribution of rs738409 C/G polymorphism in Egyptians and to assess its role in susceptibility to infection by chronic HCV

Methods:
The study included 282 subjects, 135 healthy controls and 147 HCV patients. Genotyping of rs738409 C/G was done by a 5\nuclease Taqman assay.

Results :
Results showed a genotype frequency of 37%, 53.3%, 9.6% for CC, CG, GG in control versus 51%, 38.1% , 10.9% in HCV respectively. A significant (p=0.03) differential distribution of rs738409 C/G was shown between controls and HCV patients. The C allele seems to increase susceptibility to infection by HCV. Nonetheless, this difference in rs738409 C/G genotypes distribution was not significant in HCV patients when stratified according to gender.

Conclusion :
In conclusion individuals carrying the C allele of rs738409 C/G can be considered at higher risk of infection with HCV.

Mots clés /keywords :
genetic susceptibility, PNPLA3 gene, polymorphism

Auteur présentateur / presenting author:
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P51   **Investigating the effects of PCSK9 and apoe genetic variation in dyslipidaemia in the south african population**

Auteurs /Authors :
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Introduction :
Dyslipidaemia is a commonly encountered condition that is identified as a major risk factor for cardiovascular diseases. Dyslipidaemia has been shown to have a strong genetic component. Apolipoprotein E (APOE) and proprotein convertase subtilisin/kexin type 9 (PCSK9) are key regulators of plasma lipid levels, thus variation in these gene is of concern. APOE is polymorphic presenting with, APOE2, APOE3 and APOE4. The determination of APOE status is through genotyping for rs429358T>C and rs7412C>T. APOE2, APOE4 and the PCSK9 rs505151G allele have been linked to altered lipid metabolism. We genotyped a cohort of South African dyslipidaemic patients to determine the prevalence of these polymorphisms and evaluate their effect on lipid profiles.

Goals :
We aimed to identify genetic variants that could be used as biomarkers for increased risk of developing dyslipidaemia.

Methods:
Participants (n=245) were recruited from a cohort of 165 dyslipidaemic South Africans and 80 controls attending Baragwaneth hospital from whom blood samples were obtained for DNA extraction. Samples were genotyped for rs429358T>C and rs7412C>T SNPs using PCR-RFLP. PCSK9 rs505151A>G was genotyped for using Sanger sequencing. Genotypes were correlated with lipid profiles while allele frequencies were compared.

Results :
Minor allele frequencies rs429358C, rs7412T and rs505151G in the control and dyslipidaemia group were 0.23, 0.24, 0.23 and 0.27, 0.15 and 0.25, respectively. Frequencies of APOE2, APOE3 and APOE4 were 0.20, 0.60, and 0.19 in the controls, and 0.11, 0.63 and 0.24 in dyslipidaemia cohort, respectively. There were significant differences in the distribution of the APOE isoform variants between controls and patients (p=0.034). However, there were no significant associations between APOE and PCSK9 variants with altered lipid levels.

Conclusion :
These SNPs have been reported to be significantly associated with lipid levels in other populations, thus, African populations may possess a unique profile of genetic variation that need to be identified.

Mots clés /keywords :
Dyslipidaemia

Auteur présentateur / presenting author:
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P52   **Role of plasmodium spp in the pathogenesis of diffuse large cell lymphomas**

Auteurs /Authors :
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Introduction :
Diffuse large cell lymphoma, the commonest non hodgkin lymphoma in Africa, shares clinical, molecular and genetic features with burkitts lymphoma. Besides infection with plasmodium spp, similar factors such as Epstein Barr virus and HIV infections have been implicated in the pathogenesis of the latter entity.

Goals :
To demonstrate the role of plasmodium spp infection in the pathogenesis of diffuse large cell lymphomas.
To demonstrate the overlap of characteristic genetic " lesions" between those seen in burkitt lymphoma and those seen in diffuse large cell lymphoma.

Methods:
Use of Polymerase Chain reaction and Fluorescent In situ Hybridization techniques on serum samples and formalin fixed, and where possible fresh tissue samples of suspected/confirmed cases of Diffuse large cell lymphomas.

Results :
Significant expression of genes coding for proteins derived from plasmodium spp in cases of diffuse large cell lymhphoma. Statistically significant overlap between translocations seen in burkitts and diffuse large cell lymphoma.

Conclusion :
Infection with plasmodium spp plays a significant role in the pathogenesis of diffuse large cell lymphoma, and a much more effective control of malaria could stem its tide.

Mots clés /keywords :
Plasmodium, Burkitts, Lymphoma, Genetics

Auteur présentateur / presenting author:
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P53   **Predicting metabolic biomarkers of Mycobacterium tuberculosis infection in human alveolar macrophage**

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Introduction :
Mycobacterium tuberculosis (M. tb) is a highly persistent pathogen that primarily affects the third world. About one third of the world's population is infected, with 9.27 million new cases and 1.76 million deaths in 2007. This devastating impact of M. tb infection on especially in vulnerable populations is driven partly by the inadequacy of current tools and strategies for diagnosis; which in many cases utilises sputum smear microscopy.

Goals :
We hope to identify metabolic biomarkers of M. tb infection that can be utilised in specific, reliable and rapid diagnostics.

Methods:
A key aspect of M. tb infection is to induce change in the host metabolism. We therefore hope to implement the protocol of Shilomi et al., (2009) to predict biomarkers from iAB-AMØ-1410-Mt-661, an integrated host pathogen genome-scale network reconstruction from RECON 1 (human) and M. tb infection (iNJ661), built by Bordbar et al., (2010) and genotype-phenotype data from Thye et al., (2012). The protocol uses constraint based modelling to predict biomarkers from the metabolic network model.

Results :

Conclusion :
The biomarkers identified can be very useful in developing rapid diagnostic kits for early detection of M. tb infection.

Mots clés /keywords :
Biomarkers, metabolic biomarkers, constraint based modelling, Mycobacterium tuberculosis, network reconstruction

Auteur présentateur / presenting author:
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P54   Evaluation des taux sériques de cd25 libre au cours de la chimiothérapie:
intérêt pronostique dans le cancer du sein

Auteurs /Authors :
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IIntroduction:
Le cancer du sein (CS) est l'une des premières causes de mortalité par cancer chez la femme en Afrique subsaharienne. Les moyens de traitement disponibles ne permettent pas une efficacité thérapeutique parfaite chez les patientes. L'influence néfaste des lymphocytes T régulateurs (Treg) a été évoquée et l'influence de la chimiothérapie sur le comportement de ces cellules reste inexplorée.

Objectif
En vue de mettre en évidence des biomarqueurs immunologiques à valeur pronostique, notre présente étude a porté sur l'évaluation de l'activité des cellules Treg à travers le dosage de l'IL-Rα ou CD25 libre et sur l'analyse de son profil sérologique suivant l'état de rémission des patientes.

Méthodologie:
Trente quatre 34 patientes avec CS, soumises à une chimiothérapie à trois séances par patiente et 42 femmes indemnes de toute tumeur ont été concernées. Un prélèvement de sang périphérique a été fait sur tube EDTA avant les trois cures de chimiothérapie et les taux sériques de CD25 ont été évalués par ELISA.

Résultats: Nos résultats ont montré l'absence de variation discriminante des taux de CD25 sériques entre les témoins et les patientes (221,33 vs 223,87 pg/ml, p = 0,363). Chez les patientes, les taux de CD25 augmente globalement après la première cure. Cette variation concerne essentiellement les patientes à rémission nulle en fin de chimiothérapie. En effet, comparées aux malades à rémission partielle ou totale, les patientes à évolution défavorable ont montré des taux l'IL-Rα croissant au cours du suivi (p = 0,034). Dans le groupe des patientes à rémission totale, aucune variation significative n'a été retrouvée.

Conclusion: Une étude antérieure ayant concerné le même marqueur et rapportant une augmentation de ses taux sériques chez les patientes victimes de récidives à la suite d'une radiothérapie, consolide nos résultats qui orientent vers une exploration plus approfondie des cellules T suppressives de type CD3+CD4+CD25+Foxp3+ ainsi que des cytokines qu'elles produisent dans le CS.

Mots clés /keywords :
Cancer du sein, lymphocytes Treg, CD25 soluble, chimiothérapie

Auteur présentateur / presenting author:
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P55   **Signalling pathways and RBCs invasion by the malaria parasite: A computational analysis**

Auteurs /Authors :
Jelili Oyelade(1); Itunuoluwa Isewon (2); Ezekiel Adebiyi(3)

Introduction :

The invasion of the Red Blood Cells (RBCs) by the Plasmodium spp is conceptually similar. The parasite must engage binding receptors on the RBC, and undergo apical reorientation, junction formation and signaling. The events associated with invasion include, the releasing of essential molecules from the apical organelles and initiation of the actin – myosin moving junction that brings the parasite inside the vacuole that forms in the RBC. An open problem is the identification of the signaling pathways that started the merozoite invasion of a host RBC, on contact with it. It is known that the understanding of these pathways will give insight into parasite virulence and will provide very important information toward the rational design of vaccine against the merozoite invasion.

Goals :
Presently there are nine human malaria vaccines under clinical development, whose target include merozoites. Infact six of the vaccines target solely the merozoites at the blood stage. The successful completion of these vaccines development can obviously be aided by the knowledge of the pathways that signal the merozoites invasion of the RBCs.

Methods:
In this work, we will expand our computational analysis in our previous work (Oyelade, et al) to elucidate for the first time, important signaling pathways as it concerns signaling the malaria parasite, Plasmodium falciparum for apoptosis, cell cycle and metabolism at the blood stages.

Results :
An open problem is the identification of the signaling pathways that started the merozoite invasion of a host RBC, on contact with it.

Conclusion :
The need to urgently get a lasting solution to the malaria causing parasite, Plasmodium falciparum cannot be ruled out. Therefore, understanding of these pathways (the invasion of the Red Blood Cells by the plasmodium spieces) will give insight into parasite virulence which provide very important information toward the rational design of vaccine against the merozoite invasion.

Mots clés /keywords :
Signalling pathways, Red Blood Cell, malaria parasite, invasion, apoptosis, cell cycle, metabolism

Auteur présentateur / presenting author:
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P56   Suivi immunologique des adultes infectés par le VIH sous traitement antirétroviral au Sénégal.

Auteurs /Authors :
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2 : Hôpital Général de Grand-Yoff, Dakar, Sénégal.

Introduction :
Le suivi immunologique joue un rôle essentiel dans la prise en charge de l'infection VIH.

Objectifs
- décrire les caractéristiques sociodémographiques, biologiques, et thérapeutiques des personnes vivant avec le VIH (PVVIH) sous traitement antirétroviral (TARV) suivies en consultation ambulatoire à l'hôpital Général de Grand-Yoff.
- évaluer la réponse immunologique par la mesure du taux d'évolution des CD4 sous TARV

Méthodologie
Il s'est agi d'une étude transversale, à visée descriptive et analytique avec recueil d'antériorités sur deux ans, portant sur le suivi immunologique de l'infection à VIH.

Résultats
L'étude a inclus 82 patients sur une période de quatre mois, de novembre 2015 à Février 2016. L'âge médian au début du traitement était de 42 ans.
La population d'étude est constituée majoritairement de femmes (67%). L'infection à VIH 1 était prédominante (90%). Le taux médian de CD4 à l'initiation du traitement était de 250 cellules/l. Les circonstances de découverte étaient dominées par les infections opportunistes (31%). Près de la moitié des patients (44%) était à un stade OMS 3 et 4 à l'initiation du traitement.
Le taux d'évolution médian des CD4 était respectivement de 32,52% pour les pvvih1 sous Combivir/Efavirenz (n=20), 47,36% pour ceux sous Combivir/Nevirapine (n= 11), 61,51% pour ceux sous Tenolam/Efavirenz (n= 38), et 20,59% pour les patients sous Tenolam/Nevirapine.
Les PVVIH1 en 2ème ligne de traitement, les PVVIH2 et les PVVIH1+2 ont présenté un taux d'évolution médian des CD4 > 80% après 12 mois de traitement. Une mauvaise observance au traitement a été notée dans 13% des cas.

Conclusion :
L'ensemble de ces données permet une optimisation des traitements existants et contribue, grâce à une prise en charge multidisciplinaire, à améliorer la survie des patients.

Mots clés /keywords :
Infection à VIH - Numération des CD4 - Antirétroviraux - Sénégal

Auteur présentateur / presenting author:
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P57   **Consensus Clustering of the transcriptome of malaria patients identifies cluster specific markers associated with severe malaria**

Auteurs /Authors :
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Introduction :
Over the years, clustering has been applied to gene expression data to identify groups of genes that have similar expression patterns to infer sharing of similar function (functional annotation), imply common regulation and predict cis-regulatory promoter sequences. Consensus clustering, also called aggregation of clustering (or partitions), refers to the situation in which a number of different (input) clusterings have been obtained for a particular dataset and it is desired to find a single (consensus) clustering which is a better fit than the existing clusterings.

Goals :
To find groups of malaria patients with similar expression pattern from gene expression data using cluster analysis.
To assess the biological significance of the resulting groups
To find specific cluster markers that are responsible for the observed biological function of each cluster

Methods:
We used three clustering algorithms (K-means Clustering, Self-Organizing Maps and Random Forests with Partition around Medoids PAM) to a RNA-seq data of patients infected with Plasmodium falciparum malaria. To select the optimal no of clusters, we used cluster validity metrics; Silhouette Width index, Connectivity Index and the Dunn Index. The resulting clusters were combined into a cluster ensemble. The consensus clusters were generated by clustering the ensemble. Functional enrichment was done with DAVID. The markers were identified by searching for genes with differential expression.

Results :
We found a number of clusters which we interpret as different sub groups of malaria patients. Genes conferring differential susceptibility to malaria were identified which is in line with reports from previous studies. We also identified cluster markers associated with severe malaria.
Conclusion :
From our results, the consensus clusters generated was insensitive to miss-classification from the individual clustering algorithms. We show that consensus clustering can be used to generate more robust and stable clustering results when compared to a single clustering approach

Mots clés /keywords :
Consensus Clustering, Cluster Markers, Malaria

Auteur présentateur / presenting author:
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P58   Diagnostic des déficits Immunitaires Primitifs au Sénégal

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Introduction :Les Déficits Immunitaires Primitifs (DIP) sont un groupe hétérogène de plus de 250 maladies génétiques. En Afrique, l'incidence est de 107 730 cas par an, cependant, peu de cas sont diagnostiqués en Afrique Sub-saharienne. Au Sénégal, quelques cas de DIP sont diagnostiqués et pris en charge, grâce à la collaboration entre cliniciens et immunologistes.

Goals : L'objectif de ce travail est de rapporter les cas de DIP diagnostiqués au Sénégal.

Methods: Entre Août 2014 et Mars 2016, tous les enfants suspects de DIP, avec une sérologie rétrovirale négative étaient répertoriés.

Results : Nous avons enregistré 18 cas, avec un sex-ratio 0,8 et un âge moyen de 3,41 ans. Les principaux signes d'appels étaient les infections sévères récidivantes, les manifestations dermatologiques, hématologiques et neurologiques. Une thrombopénie était retrouvée chez 5 patients (27,8), une neutropénie chez 2 patients (11,1%), une lymphopénie chez un patient (5,55%). L'immunophénotypage montrait une diminution des T-CD4 chez 5 patients (27,8%) et des B-CD19 chez 8 patients (44,4%). L'électrophorèse des protéines était réalisée chez 14/18 patients, avec un profil inflammatoire dans 85% des cas. Le dosage pondéral des immunoglobulines était en faveur d'une augmentation des IgA chez un seul patient. Trois patients avaient une symptomatologie clinique et biologique très évocatrice: 2 cas d'Ataxie Télangiectasie familiale et 1 cas de Syndrome de Wiskott Aldrich (WAS). Cependant, la confirmation génétique n'était obtenue que pour le patient suspect de WAS.

Conclusion : Les DIP sont des pathologies rares mais non exceptionnelles. Le diagnostic est évoqué sur une forte suspicion clinique, avec orientation biologique mais la confirmation est génétique. D'où la nécessité de développer des stratégies pour faciliter les analyses génétiques, surtout avec la disponibilité des immunoglobulines polyvalentes au Sénégal.

Mots clés /keywords :
Déficits Immunitaires Primitifs, Enfants, Sénégal.

Auteur présentateur / presenting author:
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P59   **Complications infectieuses de la drépanocytose en milieu pédiatrique Dakarois**
Cas des infections ostéo-articulaires

Auteurs /Authors :
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Introduction :La drépanocytose est la maladie génétique la plus répandue dans le monde. Au Sénégal la prévalence de l'HbS estimée à 10 %, avec 0,5% de naissances annuelles d'enfants malades. L'une des particularités de cette maladie est la susceptibilité accrue aux infections sévères chez l'enfant, surtout les Infections Ostéo-Articulaires (IOA).

Goals : L'objectif de ce travail était de déterminer les particularités épidémiologiques, cliniques, bactériologiques et évolutives des IOA chez l'enfant à Dakar.

Methods: Il s'agit d'une étude rétrospective, menée au Centre Hospitalier National d'Enfants Albert Royer (CHNEAR) de Dakar, de 1991 à 2014. Tous les patients suivis pour Syndrome Drépanocytaire Majeur (SMD), âgés de 6 mois à 18 ans et ayant au moins un épisode d'IOA documentée étaient inclus. Les patients âgés de plus de 18 ans, ceux ayant des IOA non documentées ou non suivis, n'étaient pas inclus. Les données socio-démographiques, cliniques, bactériologiques et évolutives étaient recueillies, saisies et analysées avec le logiciel Cs Pro et Excel.

Results : Nous avons colligé 2385 dossiers, dont 182 IOA, soit une prévalence de 7,63%. Seuls 144 dossiers étaient exploitables, avec 136 homozygotes SS (94,44%), 7 hétérozygotes composites SC (4,86%), et une Sβ+ (0,69%). Le Sex-ratio était de 1,03. L'âge moyen était de 83,76 mois (6,98 ans) au moment de l'infection. L'antibioprophylaxie orale était observée dans 41,67%. La couverture vaccinale était de 82,64% pour le PEV sénégalais, 65,97%, pour le vaccin antipneumococcique, 59,72% pour le vaccin antiméningococcique et 68,06% pour le vaccin antityphique. Les principales IOA étaient les ostéomyélites aiguës (52,36%). L'hémoculture, réalisée chez 74 patients (51,39%), était positive chez 33,78%. Salmonella enterica était isolée dans 26,39% des IOA. L'évolution était favorable chez 70,83% des patients.

Conclusion: Les Salmonelles mineures sont fréquentes dans les IOA des SDM et ne sont non prises en compte ni par l'antibioprophylaxie ni par l'actuel vaccin anti typhique.

Mots clés /keywords :
Drépanocytose ; infections ostéo-articulaires ; enfant

Auteur présentateur / presenting author:
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P60   Place de la génétique dans le diagnostic des Déficits Immunitaires Primitifs au Sénégal

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Introduction : Les Déficits Immunitaires Primitifs (DIP) sont des pathologies génétiques peu connues. En Afrique, la prévalence serait de 1 000 000 de cas, cependant,   peu de cas sont rapportés en Afrique Sub-saharienne. Au Sénégal, quelques cas sont enregistrés, dont un avec confirmation génétique.

Goals : Notre objectif est d'évaluer la place de la génétique dans le diagnostic des DIP.

Methods:Depuis 2014, une stratégie de diagnostic des DIP est mise en place au Laboratoire d'Immunologie de l'Hôpital, Aristide le Dantec. Toutes les suspicions de DIP y sont envoyées pour exploration.

Results : Depuis 2014, 18 cas d'enfants suspects de DIP ont été enregistrés. Le sex-ratio était de 0,8, avec un âge moyen de 3,41 ans. Le diagnostic était évoqué sur la base du phénotype clinique, des arguments anamnestiques et des examens biologiques. L'hémogramme, l'électrophorèse des protéines, le phénotypage lymphocytaire et le dosage pondéral des immunoglobulines constituaient les outils d'orientation. Ainsi, un cas familial d'Ataxie Télangiectasie et un cas de Syndrome de Wiskott –Aldrich (WAS) ont été diagnostiqués et pris en charge avec les moyens disponibles. Cependant, la confirmation génétique n'était obtenue que pour le patient suspect de WAS. Cet enfant avait des antécédents d'infection néonatale, de pneumonie et de méningite, associés à un eczéma, une thrombopénie microcytaire à 43000/ mm³ avec VPM à 5,47fl, une lymphopénie TCD4 et TCD8 ainsi qu'une augmentation des IgA et des IgG. La génétique moléculaire à permis de mettre en évidence :
1/ une mutation à l'état hémizygote au niveau de l'exon 1 :Exon 1 : c.37C>T (p.Arg13*)
2/ une duplication d'une cytosine au niveau de l'intron 2 : c.273+11dupC.

Conclusion :Les DIP sont des pathologies génétiques méconnues. Le diagnostic de certitude requiert une analyse génétique, souvent hors de portée des patients. Des efforts sont faits dans la disponibilité des immunoglobulines polyvalentes au Sénégal, mais le défi reste la confirmation sur le plan génétique.

Mots clés /keywords :
Déficits Immunitaires Primitifs ; Wiskott Aldrich ; mutation ; duplication.

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P61   Surveillance of molecular markers in Senegal using RDTs

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Introduction

In Senegal, strategies such as Intermittent Preventive Treatment in pregnancy (IPTp) (SP) and Seasonal Malaria Chemoprevention (SMC) using sulfadoxine-pyrimethamine (SP) and SP plus amodiaquine, respectively have been implemented while artemisinin-based combination therapies are used to treat uncomplicated malaria. These strategies have largely contributed to the decrease of malaria morbidity and mortality in the country. However, the successful control of malaria is highly dependent on continued effectiveness of these drugs which may be compromised by the spread of drug resistance. Therefore surveillance of drug resistance in the malaria parasites is essential.

The objective of this study was to test the feasibility of routinely sampled malaria rapid diagnostic tests (RDTs) at a national scale to assess the temporal changes in the molecular profiles of antimalarial drug resistance markers of P. falciparum parasites.

Methods: A low-cost sampling procedure of RDTs was established at 14 malaria sentinel sites across the country. Overall 4339 RDT positives were collected during 2014 out of which, a subset of 700 RDTs (50 RDTs per site) was randomly selected for initial SNPs analysis of the Pfcrt gene by PCR-SSOP ELISA methodology.

Results: Among the 700 selected and extracted RDTs, 598 (85.4%) was confirmed P. falciparum positive by Pfcrt PCR. The prevalence of the Pfcrt wild type CVMNK haplotype was above 75% in the North-eastern regions including Dakar while a lower prevalence at 65% and 56% was observed in the Central and South regions, respectively.

Conclusion: This study showed that routine sampled positive RDTs can be successfully amplified by PCR and used for routine surveillance of antimalarial drug resistance. Further sampling of RDTs and analysis of other markers of drug resistance (e.g. Pfmdr, Pfdhfr, Pfdhps, K13) are ongoing which will provide temporal trends of these markers and potentially aid drug policy makers in timely decisions regarding choice of antimalarial drugs.

Auteur présentateur / presenting author:
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P62   UTILISATION DE LA PCR DANS LE DIAGNOSTIC DES CANCERS DES VOIES AERO-DIGESTIVES SUPERIEURES : ETUDE PRELIMINAIRE A PROPOS DE 90 CAS

INTRODUCTION
Les carcinomes des voies aérodigestives supérieures (VADS) occupent la sixième place mondiale. L'HPV représente un « nouveau » FDR connu. Cependant, les carcinomes HPV+ ne présentent pas de particularités histologiques d'où l'intérêt d'une analyse biomoléculaire. L'objectif de cette étude était d'évaluer l'utilisation de la PCR pour la recherche de l'HPV dans les carcinomes des VADS.

METHODOLOGIE
Sur une période de 18 mois (1er Janvier 2012- 30 Juin 2014), les blocs parrafinés des cas de carcinomes des VADS confirmés histologiquement au Sénégal étaient envoyés à Paris pour la recherche d'HPV. Le déparrafinage et l'extraction de l'ADN étaient réalisés par le kit NucleoSpin Tissue®. Les techniques de PCR « consensus » avec les amorces « GP5+/GP6+ » et de PCR « spécifique » pour les HPV 6, 11, 16, 18, 33 et 45 étaient utilisées.

RESULTATS
Sur 90 cas inclus, la technique de PCR était concluante dans 54 cas (60%). Le HPV était retrouvé dans sept cas soit une prévalence de 13%. Le génotypage était possible dans six cas (85,7%). Il s'agissait d'un HPV 16 dans cinq cas (71,4%) et d'un cas d'HPV 33 (14,3%). Les cinq cas d'HPV 16 étaient associés au carcinome hypopharyngé, l'HPV 33 de même que l'HPV « indéterminé » étaient retrouvés dans la cavité orale. La localisation hypopharyngée de l'HPV 16 était statistiquement significative (p=0,04). Les patients ayant des carcinomes des VADS HPV+ avaient un âge médian de 42 ans contre 49 ans pour les patients HPV-. Le carcinome épidermoïde était l'unique type histologique retrouvé. Les carcinomes HPV+ ne présentaient aucun aspect histologique spécifique.

CONCLUSION
La technique de PCR donne des résultats satisfaisants même sur les blocs paraffinés. L'HPV constitue un réel FDR des carcinomes des VADS. L'HPV 16 est le plus fréquent et de localisation hypopharyngée.

Mots clés /keywords :
Human Papilloma Virus, PCR, Carcinome, Voies aéro-digestives supérieures, Sénégal

Auteur présentateur / presenting author:
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P63   **A new look at copy number variation in the haptoglobin gene: Associations with haptoglobin level and other iron biomarkers in The Gambia.**

Auteurs /Authors :
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Introduction
The host's iron distribution affects the critical host-pathogen battle for essential iron. Plasma haptoglobin binding free hemoglobin operates as host defense mechanisms to reduce peripheral iron availability to pathogens. A functional haptoglobin gene (HP) copy number variant (CNV), also known as HP1-2, is associated with plasma haptoglobin level, hemoglobin binding capacity and several infectious disease outcomes.

Goals
We aim to examine clinically-significant molecular mechanisms of iron metabolism through our interlinked clinic-laboratory-genotype set-up at MRC Keneba. Here, we assessed the effect of the HP CNV on iron biomarkers and anemia in Gambians living in an environment characterized by the co-existence of iron deficiency and a high infectious disease burden.

Methods
We genotyped 1426 rural Gambians (aged 1-87y) for the HP CNV using a newly developed ddPCR method. Plasma iron biomarkers (iron, ferritin, sTfR, UIBC, TSAT), and c-reactive protein (CPR) were measured by Cobas Integra 400 analysis; hepcidin was measured by ELISA and hemoglobin level was established as part of a full blood count (Medonic). Regression analyses were conducted to assess the effect of the HP CNV on plasma haptoglobin, hemoglobin, and other iron biomarkers as well as anemia, iron deficiency, iron deficiency anemia and anemia of inflammation (as defined in Pasricha S et al 2014).

Results and conclusions
The HP CNV strongly correlates with plasma haptoglobin level ($P<2x10^{-10}$). Associations were also seen with hemoglobin and to a lesser degree other iron biomarkers. However, haptoglobin plasma level does not appear to mediate the association between HP CNV genotype and hemoglobin in Gambians. Further in-depth analyses including the different measures of anemia and the role of the nearby HPR rs2000999 polymorphism, are ongoing.
Understanding the role of genetic variation in iron pathway genes offers major opportunities for us to inform diagnostic, treatment, and prevention approaches in the context of iron-mediated pathologies.

Mots clés /keywords :
HP CNV, haptoglobin genotype and phenotype, iron biomarkers, anemia

Auteur présentateur / presenting author:
Branwen Hennig
MRC, The Gambia

YOUNG RESEARCHER FORUM

ABSTRACTS SELECTED FOR ORAL PRESENTATION

CF01   **Beliefs and attitudes of Egyptian parents influencing participation in a**
pediatric cancer research genetic biorepository

Auteurs /Authors :

Rania M. Labib, Omneya Hassanain, Maram Alaa, Safaa Ahmed, Sherif Abou El-Naga

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Introduction : Biobanks have become a powerful tool that fosters many types of research. The success of biobanks depends upon people's perception and willingness to donate their samples for future research. This is the first pediatric biorepository in the middle-east, hence, little is known about the beliefs and attitudes of parents towards their children participation in a research biorepository.

Goals : To investigate the level of willingness to donate samples for research in an Egyptian Children's cancer hospital and understand factors influencing enrollment.

Methods: A Standardized questionnaire was designed covering multiple items expected to affect the enrollment. This was conducted in-person and data collected included, demographics data, socioeconomic level, educational and religious constraints. Additionally, in the case of refusal, participants were asked about reasons for nonparticipation.

Results : Using extensive communication during the consenting process about our biorepository program research benefits, approximately 3.1% of patients have not been enrolled in the project and 0.3% have withdrawn. Three demographic factors were found having disparate trends in the decision making process to participate or not: father's education (p-value = 0.0001), mother's education (p-value = 0.0001) and father's age (p-value = 0.034).

Conclusion : With parents having a higher level of education and older age, they are more likely to be unwilling to participate in the biorepository. This requires more intensive awareness program to educate them on the importance of research and trusting the process.

Mots clés /keywords :

Socio-demographics; pediatric; biobank; middle-east; genetic; bioethic

Auteur présentateur / presenting author:

Dr Rania M Labib

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CF02 **Replication of GWAS identified loci in the Tunisian population:**

Susceptibility and prognostic implications in Breast Cancer.

Auteurs /Authors :

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2-Genetic Medicine and Immunology Laboratory, Weill Cornell Medical College in Qatar, Qatar Foundation, Education City, P.O. Box 24144, Doha, Qatar.

Introduction : Recent genome-wide association studies (GWAS) have lead to the identification of multiple new genetic variants associated with breast cancer risk. Most of these breast cancer GWAS and replication studies have been conducted in European populations and to a lesser extent in Asians.

Goals : Therefore, we designed a broad study to investigate the susceptibility and prognostic implications of the GWAS breast cancer loci in the Tunisian population.

Methods: In a cohort of 640 unrelated patients with breast cancer and 371 healthy control subjects, we characterized the variation of 9 single nucleotide polymorphisms (SNPs) using the TaqMan® SNP genotyping assays. The chi-square test was used for statistical analysis.

Results : Only 5 (rs1219648, rs2981582, rs8051542, rs889312, rs13281615) out of 9 GWAS breast cancer loci were found to be significantly associated with breast cancer in Tunisians. The strongest associations were found for rs2981582 in the FGFR2 gene and rs8051542 in the TNRC9 gene (OR = 1.55, P = $3 \times 10(-6)$; OR = 1.40, P = $4 \times 10(-4)$, respectively). Homozygous variant genotypes of rs2981582 were strongly related to lymph node negative breast cancer (OR = 3.33, P = $6 \times 10(-7)$) and the minor allele of rs2981582 was associated with increased risk of ER+ tumors (OR = 2.15, P = 0.001) and increased risk of distant metastasis development (OR = 3.57, P = $6 \times 10(-5)$). The association for rs8051542 was stronger for high-grade SBR tumors (OR = 2.54, P = $2 \times 10(-4)$). GG genotype of rs13387042 on 2q35 showed a significant association with the risk of developing distant metastasis (OR = 1.94, P = 0.02).

Conclusion :In conclusion, GWAS breast cancer FGFR2, TNRC9, MAP3K1, and 8q24 loci are associated with an increased risk of breast cancer and genetic variation in FGFR2 gene may predict the aggressiveness of breast cancer in Tunisians.

Mots clés /keywords :

Genome-wide association studies (GWAS),Breast cancer,Susceptibility, Pronostic, Tunisian population.

Auteur présentateur / presenting author:

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CF03   **IMPACT DES MUTATIONS DES GENES MITOCHONDRIAUX DANS LE CANCER DU SEIN CHEZ LES FEMMES SENEGALAISES**

Auteurs /Authors :

Mbaye F (1,2) ; Dem A (3) ; Ka S (3) ; Fall M (1) ; Sembène M (1, 2)

Introduction : Le cancer du sein est une maladie complexe et hétérogène avec une composante génétique souvent modulée par des facteurs environnementaux.

Objectifs / goals : l'objectif de cette étude est de connaitre l'impact des mutations des gènes mitochondriaux dans la carcinogenèse mammaire chez les femmes sénégalaises.

Méthodologie / Method: cent vingt (120) prélèvements chirurgicaux de tissus sains et de tissus cancéreux ont été analysés. Deux gènes mitochondriaux (Cytochrome b et D-Loop) ont été amplifiés et séquencés. Pour tester l'association entre le cancer du sein et les gènes mitochondriaux, les séquences obtenues ont été comparées à la séquence révisée de Cambridge (NC_012920) dans la base de données MITOMAP. Une corrélation entre la durée de survie post-opératoire des patientes et les mutations des gènes mitochondriaux est recherchée avec le test de Kaplan Meir associé au test de log-rank.

Résultats / Results : le Cytochrome b présente des mutations qui altèrent certains acides aminés qui se retrouvent à de fortes fréquences dans la population cancéreuse. Parmi ces acides aminés il y a la méthionine qui est sous sélection positive. La localisation des mutations aux positions 146 et 152 de la D-Loop, très proches de l'origine secondaire de la synthèse du brin lourd de l'ADN mitochondrial, pourrait indiquer leur pertinence fonctionnelle dans la carcinogenèse mammaire. Nos résultats révèlent aussi qu'une région particulièrement instable de la D-Loop (D310) n'est pas fréquemment altérée dans les tumeurs du sein. L'analyse corrélative de l'impact des mutations nucléotidiques, révèle que les mutations au niveau des sites 150 et 152 de la D-Loop agissent négativement sur la survie des patientes (P=0,026 ; P=0,033).

Conclusion : L'ensemble de ces résultats montre que les mutations de l'ADNmt qui affectent le Cytochrome b et la D-Loop peuvent avoir un impact dans la carcinogenèse mammaire chez les femmes sénégalaises.

Mots clés /keywords :

cancer, sein, mutations, ADNmt, Sénégal

Auteur présentateur / presenting author:

Dr Fatimata MBAYE

Université Cheikh Anta Diop de Dakar

CF04   EVALUATION DE L'ACTIVATION ET DE L'APOPTOSE DES LYMPHOCYTES T ET B   SANGUINS DANS LE CANCER DU COL DE L'UTERUS: IMPACT DE LA CHIMIOTHERAPIE ANTICANCEREUSE

Auteurs /Authors :

DIOP M (1), DIOUF D. (3) , MBENGUE B. (1,2), KA S (3) LY A (2) NDIAYE R (2), DIOP G, MBAYE F. (4), THIAM A (2), NDIAYE M, THIAM F (2), FALL M. (4), NDIAYE DIALLO R (2), SYLLA NIANG M. (1), SEMBENE M. (4), DEM A (3) & DIEYE A. (1,2).

GERC Dakar SENEGAL

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Objectif: La prise en charge du cancer du col demeure encore difficile malgré l'existence de plusieurs stratégies thérapeutiques dont la chimiothérapie. Rares sont les études ayant porté sur les effets de la chimiothérapie sur l'immunité. En diminuant les cellules tumorales, les médicaments anticancéreux influeraient-ils indirectement sur la fonctionnalité des lymphocytes ? Pour répondre à cette question, nous avons évalué les proportions de lymphocytes T et B apoptotiques et activées chez des patientes atteintes de cancer du col et des femmes témoins indemnes de tumeur.

Méthodes: L'étude a concerné 35 patientes et 42 femmes saines. Les niveaux d'activation précoce (CD69+) ou tardive (HLA-DR+) et d'apoptose (Apo2.7+) ont été évalués par cryométrie en flux, pour les cellules T et B, avant et au cours de trois séances de chimiothérapie à Cysplatine- 5-Fluorouracile. Les données acquises sur Cell Quest Pro® ont été analysées avec Flow jo® et Statview®.

Résultats: Des 35 patientes atteintes de cancer du col et initialement incluses, 18 sont revenues pour la 2e séance de chimiothérapie et 11 pour la 3e. . Nos résultats ont montré des niveaux d'activation précoce plus élevés chez les patientes avant traitement comparées aux témoins pour les lymphocytes T CD4+ (p <0,001) et CD8+ (p <0,001). Au début du traitement, les taux de cellules CD69+ augmentent significativement (p <0,05). Une hausse des niveaux d'apoptose a été observée pour les cellules T et B. Elle apparait plus accentuée après la 1ère cure et semble évoluer en parallèle avec l'expression de CD69 au cours du traitement. Concernant l'activation tardive des lymphocytes T, diminue au cours de la chimiothérapie.

Conclusion: Nos résultats contribuent à une meilleure maitrise de la relation entre la chimiothérapie et l'immunité. Ils démontrent l'existence d'effets indirects de la chimiothérapie anticancéreuse sur le phénotype lymphocytaire

Mots clés /keywords : Cancer du col, Chimiothérapie, Activation, Apoptose, CD69, HLA-DR, Apo 2.7.

Auteur présentateur / presenting author: Mr(s) Maimouna DIOP

Unité d'Immunogénétique, Institut Pasteur de Dakar , Sénégal

CF05   **BRCA1 AND BRCA2 MUTATIONS IN HEREDITARY BREAST CANCER IN SENEGAL**

Auteurs /Authors :

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Introduction : Breast cancer is the second leading female cancer in developing countries. Majority of breast cancers are sporadic but 5-10% is familial. The mechanism of carcinogenesis in hereditary forms involves several tumor suppressor genes such as BRCA1; BRCA2 and p53. Several mutations conferring genetic predisposition to breast cancer have been described in these genes in Caucasians, Asians and Americans but rarely in African populations.

Objectifs / goals : The objective of this study is to investigate BRCA1 and BRCA2 mutations in susceptibility to hereditary breast cancer in Senegal.

Méthodologie / Method: Probands with familial history of breast cancer followed by the Joliot Curie Cancer Institute at Dakar were recruited after informed consent. Pedigree was drawn for each proband after family survey. DNA was extracted from blood samples for probands and related females. BRCA1 and BRCA2 mutations were screened by whole gene sequencing in collaboration with Paoli-Calmette Institute at Marseille

Résultats / Results : Sequencing of the BRCA1 and BRCA2 genes revealed 2 frameshift mutations: a duplication of 10bp in exon 11 of the BRCA1 gene and a missense mutation T>G in exon 11 of the BRCA2 gene. These mutations have also been identified in related females of each proband, and co-segregate with breast cancer.

Conclusion : Our results show that mutation screening for BRCA1 and BRCA2 in probands with family history of breast cancer is important for cancer prevention in related females by medical follow up. These results will certainly open new perspectives in prevention and medical management of breast cancer in Senegal.

Mots clés /keywords :

Hereditary breast cancer; BRCA1 and BRCA2 genes, genetic predisposition

Auteur présentateur / presenting author:

Dr Jean Pascal Demba Diop, Hôpital Aristide Le Dantec : Laboratoire de cytologie et cytogénétique

CF06   Gut microbiome compositional characterization in colorectal cancer patients from Morocco

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Introduction: Colorectal cancer (CRC) is the third most common cancer in the world and the third leading cause of cancer mortality in Morocco. The colonic mucosa is permanently in contact with the microbiota and its metabolic products, which can potentially induce oncogenic transformation. The molecular mechanisms involved in the etiology of CRC are not yet elucidated due in part to the complexity of the human gut microbiota.

Aim: The aim of this study was to characterize the gut microbiota of CRC Moroccan patients and healthy subjects and to identify bacterial taxa over or under represented in CRC vs. healthy Moroccan individuals. We also aim to test the hypothesis that microbiome of individuals from different geographical locations has significant compositional differences potentially reflecting different genetic backgrounds, diet and lifestyle.

Methods: We analyzed the bacterial composition of stool samples from 11 patients with colorectal cancer and from 12 healthy individuals by 16S ribosomal RNA gene sequencing using MiSeq Illumina platform. The sequences were filtered and analyzed using QIIME metagenomics pipeline.

Results: Our results showed higher Phylogenetic Diversity (PD) and Species Richness (S) in CRC samples. Principal Coordinates Analysis (PCoA) revealed that CRC samples clustered separately from controls (ANOSIM P=0.008, R=0.2039, and PERMANOVA P=0.005, F=1.8976) suggesting an overall different microbiome associated to CRC. Our findings indicate that CRC samples were enriched in Firmicutes (T=50.5%; N=28.4%; P=0.04) and Fusobacteria (T=0.1%; N=0.0%; P=0.02) while Bacteroidetes were enriched in healthy samples (T=35.1%; N=62.8%; P=0.06). Despite the small number of patients included in the study (11 CRC patients, 12 healthy controls), we observed significantly overrepresented genera in the CRC group compared to controls. Porphyromonas (T=0.6%; N=0.0%; P=0.04), Clostridium (T=0.2%; N=0.1%; P=0.02), Ruminococcus (T=0.6%; N=0.5%; P=0.02), and Fusobacterium (T=0.1%; N=0.0%; P=0.03) were over represented in CRC patients while Megamonas (T=0.0%; N=0.4%; P=0.04) were over represented in controls.

Next steps: This is the first study conducted in the Moroccan population that aimed to characterize both healthy and CRC gut microbiome. Data from this small cohort warrant a larger study that will include CRC patients from different Moroccan locations. Additionally, we will use Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt) to infer metabolic differences between healthy and CRC individuals. Understanding the relationship between CRC and the intestinal microbiota will lead to the development of novel strategies for the diagnosis, treatment, and prevention of this disease.

CF07   **Mise en place de techniques moléculaires de détection et de typage du**

Papillomavirus Humain.

Auteurs /Authors :

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1- Hôpital Aristide Le Dantec   2- Hôpital Principal de Dakar

Introduction : Le cancer du col utérin est le deuxième cancer chez les femmes en Afrique, après le cancer du sein. Au Sénégal, deux types de vaccin anti-HPV sont disponibles mais peu d'études moléculaires ont été faites pour guider le choix.

Objectifs / goals : Identifier les types de HPV responsables du cancer du col de l'utérus à Dakar.

Evaluer les facteurs influençant l'analyse moléculaire de HPV.

Méthodologie / Method: Ce travail a porté sur 47 blocs de paraffine de cancer du col utérin diagnostiqués au niveau de l'hôpital Principale De Dakar et de l'Hôpital Aristide le Dantec du 1er janvier 2011 au 31 octobre 2015.

Après extraction de l'ADN par le kit NucleoSpin FFPE DNA de Marcherey-Nagel, les PCR GAPDH (gène de ménage) et GP5+/GP6+ ont été utilisées comme contrôle interne et consensus respectivement dans chaque réaction. Le typage a utilisé la PCR multiplex au SYBR Green des gènes E6/E7 et a ciblé les HPV16, 18 et 33. Les résultats obtenus ont été confirmés par un séquençage nucléotidique du produit de PCR GP5+/GP6+.

Résultats / Results : La PCR consensus était positive pour 21/47 cas de cancer étudiés. Elle était négative pour tous les échantillons datés de 2011, 2012, 2013 et pour 4/5 cas de 2014. Cependant, la PCR consensus était positive pour 20/27 échantillons datés de 2015 et gardé à +4°C. La PCR multiplex était positive pour 17/47 échantillons soit un taux de 36,17 %. Le séquençage a été contributif dans 17 cas et a retrouvé 9 cas de HPV 16, 3 cas de HPV45, les 5 autres HPV retrouvés entaient HPV18, 33, 31, 35 et 39.

Conclusion : Cette étude confirme la fréquence élevée de HPV16 dans le cancer du col et montre que le taux de succès des analyses moléculaires dépend des conditions de conservation.

Mots clés /keywords : Papillomavirus Humain, PCR, détection, Typage

Auteur présentateur / presenting author:

Dr Ahmed FAKHFAKH

CHNU Aristide Le Dantec

CF08　　　　**Predictive utility of a genetic risk score of common variants associated with type 2**

diabetes in a black South African population

Auteurs /Authors :

Chikowore T(1),Van Zyl(1), and Conradie K.R(1)

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Introduction : Type 2 diabetes (T2D) is a complex disease with a polygenic etiology. Limited evidence exists regarding the predictive utility of the common variants genetic risk score (GRS) associated with T2D alone or in combination with other risk factors in the black South African population.

Goals: We set out to evaluate the GRS associated with T2D and its predictive utility alone and in combination with other risk factors.

Methods: Genotyping was done using the GoldenGate assay on the BeadXpress platform among 178 cases and 178 controls. Four types of GRS's were developed which consisted of beta cell related variants (GRSb), variants which had significant associations with T2D in our study (GRSn), variants from the trans-ethnic meta-analysis (GRStrans) and all the 66 selected SNPs (GRSt).The residual probabilities of the logistic regression models of T2D and risk factors of age, sex, urbanisation, fasting glucose, glycated hemoglobin and BMI alone or with GRSn were evaluated using the receiver operating curves (ROC)

Results: Of the GRS's, only GRSn was associated with increased risk of T2D as indicated by an OR (95CI) of 1.21 (1.02-1.43) p-value = 0.015. Stratified analysis of the GRSn was significant in the less than 50years and non-obese categories. The area under the ROC of the T2D risk factors alone was 0.652 (p value < 0.001) and with the addition of GRSn it was 0.665 (p value < 0.001).

Conclusion: The GRS approach has limited clinical utility due to fewer population specific variants associated with T2D in the black South African population. However, its improved predictiveness among non-obese and people less than 50 years, makes it an   attractive approach which might be more effective in the future through the inclusion of rare and population specific common variants in the early identification of high risk individuals for T2D preventative strategies.

Mots clés /keywords :

GRS, type 2 diabetes, black South African

Auteur présentateur / presenting author:

Dr Tinashe Chikowore

North West University

CF09   **Genetic heterogeneity of spastic paraplegia in Mali**

Auteurs /Authors :

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Introduction: Spastic paraplegia (SPG) are neurodegenerative disorders characterized with progressive spasticity and lower limb weakness. All mode of inheritance are seen but recessive SPGs, the most severe, are more prevalent in Africa. However, genetically confirmed cases are rarely reported in sub-Saharan African, and West-Africa in particular.

Goals: We aim to clinically characterize families with spastic paraplegia seen in our neurogenetic clinic, and identify the underlying cause.

Methods: Patients with SPG phenotype were seen in our neurogenetic clinic. Spinal imaging, blood chemistries, vitamin B12 and HTLV-1 and HIV testing were performed to exclude common causes of SPG. DNA was collected for genetic analyses including candidate testing and SPG panel testing.

 Results: We have seen 132 families with a wide range of neurological conditions, and eighteen had symptoms consistent with spinal involvement. HTLV-1 testing was positive in two patients and spinal CT-Scan showed cervical spine injury in three. Thirteen were thought to have a genetic cause. About 63% were autosomal recessive, 21% autosomal dominant, and 16% sporadic. Genetic testing of two candidate genes in our laboratory was negative. SPG next-generation panel testing including 58 SPG genes identified four novel mutations: SLC33A1 (c.623A>G, Glu208Gly), KIF5A (c.1086G>C, p.Lys362Asn), ACOX1 (c.497A>G, p.Asn166Ser), and SPG7 (c.1645G>A, p.Val549Met). The testing was negative four other families; suggesting novel genes. Genetic testing for five families is not complete yet.

Conclusion: We have shown the genetic heterogeneity of SPG in the Malian population. The advances and reducing cost of genetic sequencing give the possibility to diagnose SPGs for a better care in developing countries.

Mots clés /keywords :

SPG, genetic testing, HTLV-1, mutations, Mali

Auteur présentateur / presenting author:

Dr Salimata Diarra

Faculte de Medecine et d'Odontostomatologie

CF10   MOLECULAR DIAGNOSIS OF RWANDAN CHILDREN WITH UNEXPLAINED INTELLECTUAL DISABILITY AND NEURODEVELOPMENTAL DELAY BY a-CGH AND WHOLE EXOME SEQUENCING

Auteurs /Authors :

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Introduction: Intellectual disability (ID) is described by significant limitations in both intellectual functioning and adaptive behavior that begin before the age of 18 years

Goals : The present study aimed at analyzing the potential pathogenic genomic imbalance in Rwandan children with unexplained intellectual disability (ID) and/or developmental delay (DD) and its association with phenotypes, and to investigate the value of array-CGH and whole exome sequencing (WES) in clinical genetic diagnosis.

Methods: Array CGH was performed in 50 rwandan patients with ID/DD associated with multiple congenital anomalies (MCA). Furthermore, whole exome sequencing using Hiseq2000 was performed in three families: two consanguineous and one non-consanguineous. Homozygosity mapping previously performed in consanguineous families, allowed to identify large regions of loss of heterozygoty.

Results : G-band karyotyping of peripheral blood cells showed no abnormalities in the 50 children. The results of the array-CGH revealed that 13 patients (26%) genomic CNVs. Six patients had CNVs associated with known syndromes including William-Beuren syndrome, deletion 22q11.21, duplication 7q23.11, deletion 8p23.1, and deletion 17q21.31; whereas 7 patients presented rare genomic imbalances. The WES allowed identifying mutation in the PEX13 gene responsible of a mild peroxisomal biogenesis disorder in a consanguineous family and a dominant mutation in EFTUD2 gene responsible of the mandibulofacial dysostosis syndrome Guion-Almeida type (MFDGA) in another family.

Conclusion : This research highlights the contribution of genetic factors in the etiology of DD/IDD and MCA, especially the implication of chromosomal abnormalities with an array-CGH detection high rate of 26%. The WES showed a great clinical utility in diagnosis of ultra-rare neurodevelopmental diseases. Applying WES to Rwandan families, a true genetic diagnosis was found in two families. Nevertheless, as we are still facing the challenge that there are no available data about genomic studies in African population

Mots clés /keywords : Intellectual disability, Global development delay, Multiple congenital abnormalities, Array-CGH, Whole exome sequencing, PEX13, EFTUD2, mandibulofacial dysostosis syndrome Guion-Almeida type, Rwandan patients.

Auteur présentateur / presenting author: Dr Annette UWINEZA, University of Rwanda/CMHS/School of Medicine and Pharmacy

CF11   Struggling to Breathe: Challenges and solutions to diagnosing cystic fibrosis in Africa

Auteurs /Authors :

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Introduction :The tools of the genomic revolution can be used to address the challenge of diagnosing and treating genetic diseases. Cystic fibrosis (CF) is a monogenic disease that is often difficult to diagnose in Africa. Currently African CF patients live about half as long as their peers in other parts of the world. This is partially due to the fact that insufficient investigations have been conducted to identity causative mutations present in African populations thus leading to delayed or misdiagnosis.

Goals :To assess the diversity of CF-causing mutations in Africa

Methods: A literature search was performed to determine the extent of the molecular investigations that had been done on African CF patients. We also obtained ethical approval for this study and informed consent from 50 patients with confirmed or suspected CF on sweat test and clinical criteria in whom two CFTR mutations were not identified. DNA was extracted from venous blood and the gene responsible (cystic fibrosis transmembrane conductance regulator; CFTR) sequenced using a next generation sequencing (NGS). The data was analysed using an in-house bioinformatics pipeline.

Results : Only 12 African nations had published reports of a search for CF causing mutations. These studies identified 79 mutations, 21 of which were unique to the continent. In our South African patient cohort we were able to identify 21 high quality, potentially pathogenic variants absent from the current genetic test. Our bioinformatics strategy resulted in a decrease in unknown mutations from 63% to 26% among these patients.

Conclusion : The tools of the genomic revolution can assist with the early diagnosis of CF patients which should improve their life expectancy. Afro-centric CF research, as described here, should prove useful in making diagnostic and therapeutic decisions for African and African diaspora CF patients, which should result in improved diagnostic ability and therefore improved outcomes.

Mots clés /keywords :

cystic fibrosis, Africa, South Africa, diagnosis, next generation sequencing, bioinformatics

Auteur présentateur / presenting author:

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University of Pretoria

CF12   Prévalence de l'alpha-thalassémie au sein de la population drépanocytaire sénégalaise

Auteurs /Authors :

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Introduction : La drépanocytose est une affection résultant d'une mutation unique au niveau du gène β-globine, caractérisée par une symptomatologie clinique variable. Différents facteurs génétiques modulateurs ont déjà été validés ou proposés pour leur influence directe ou indirecte sur sa sévérité clinique globale et ses risques de complications spécifiques. Le principal gène modificateur de la drépanocytose validé à ce jour est l'alpha-thalassémie qui oriente la clinique vers les complications vaso-occlusives de la maladie alors qu'elle protégerait contre la survenue des complications hémolytiques.

Objectifs / goals :Au Sénégal, peu de données relatives à la prévalence de l'alpha-thalassémie dans la drépanocytose étant disponibles, notre étude visait dans un premier temps à en déterminer la fréquence allélique globale sur un échantillon représentatif de la population drépanocytaire pédiatrique.

Méthodologie / Method:Trois cent drépanocytaires âgés de 1 à 17 ans (sex-ratio H/F = 1.29) ont été recrutés de façon prospective de janvier 2015 à décembre 2015. Une technique de GAP PCR MULTIPLEX a été utilisée pour rechercher les délétions alpha-thalassémiques les plus communes, à savoir les délétions -3.7, MED, SEA, -20.5 et -4.2. La fréquence allélique de l'alpha-thalassémie a été calculée et sa répartition équilibrée dans la population a été vérifiée au moyen de l'équilibre de Hardy-Weinberg.

Résultats / Results :Seule la délétion -3.7 kb a été retrouvée. Sa prévalence était de 21% avec 19% pour la forme hétérozygote et 2% pour la forme homozygote. L'application de l'équilibre de Hardy-Weinberg et le test de chi2 ont montré que cette délétion était répartie de façon homogène au sein de notre population d'étude (p=0,72>0.05).

Conclusion :Eu égard à la prévalence non négligeable de la délétion -3.7, soit 21%,et de sa répartition homogène au sein de notre population et compte tenu de son implication prouvée dans la symptomatologie de la drépanocytose, il serait important de pouvoir réaliser cette recherche en systématique.

Mots clés /keywords :

Drépanocytose, alpha-thalassémie, gènes modificateurs

Auteur présentateur / presenting author:

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CF13   **The Association Between Drug Resistant Phenotype and Geno types of M. tuberculosis**

Isolated from pulmonary tuberculosis patients in central Ethiopia.

Auteurs /Authors :

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Introduction :Drug-resistant tuberculosis is a major threat to global control of the TB epidemic.Drug-resistant phenotype are not equally distributed among M. tuberculosis Geno types, suggesting that different M. tuberculosis Geno types may have different preference for developing drug-resistant phenotype. It is relevant to understand whether specific Geno type families are over represented among drug-resistant cases and, in particular, if these resistant strains are successfully transmitted within the community.

Goals :The aim of the study was in order to examined the relationships between drug-resistant phenotype and Geno type of M. tuberculosis

Methods:The study included sputum samples collected from 281 pulmonary smear positive TB cases. The Samples were cultured and Identification of M. tuberculosis strain was done using spolygotyping. Susceptibility testing was done for four first line drugs(rifampicin, Isoniazid, Etambutol and streptomycin) using proportion method on Löwenstein Jensen media and molecular method using Genotype MTBDR plus assay.

Results :The relationships between drug-resistant phenotypes and M. tuberculosis lineages or strains were analyzed for 263 isolates .The highest total resistance for any tested drugs were observed in lineage H3, T, T3-ETH, T1, consists 43.2%,34.8%,23.7% and 20% of isolates respectively.Although the numbers are small, significantly higher risk of resistance to the tested drugs   (P=0.025) was observed among patients with a Haarlem strains particularly with sub lineage3 compared to patients with the other strains. All of the four MDR were grouped in major lineage EA and found in a cluster.

Conclusion :Our study showed a significant association between Haarlem strain infection and resistance to first line anti-TB drugs. MDR strains were found in a cluster which indicates the high rate of recent transmission of M. tuberculosis drug-resistant strains.Therefore, important measures have to be taken in order to control the extensive transmission of resistant strains.

Mots clés /keywords : Mycobacterium tuberculosis, Drug resistance strains, Phenotype and geno type of M.tb

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CF14   **Application of MCODE algorithm to Plasmodium falciparum interactome**

Auteurs /Authors :

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Introduction : Proteins are essential parts of organisms and participate in virtually every process within cells by interacting with a similar protein(s) with similar molecular functional at an enzymatic or structural level, thus forming a collection of interactions called an interactome. Understanding protein interactions gives more insight on deducing its function which plays a great role in protein structure prediction, understanding molecular biology, molecular mechanism of cellular processes and drug design. Post-genomic era research on P. falciparum parasite has revealed the prevalence of unknown proteins in the protein interaction network, hence our motivation to address this.

Goals : The aim of the study was to identify unknown proteins in the PPI network of P. falciparum and provide functional annotation for them, motivated by the prevalence of unknown proteins with little knowledge and understanding about their activities in the parasite.

Methods: In this, a graph-based clustering algorithm called Molecular Complex Detection (MCODE) was implemented in C++ to identify protein complexes in the parasite's interactome. Functional annotation for the identified proteins in the complexes was carried out using sequence similarity, protein structure alignment and assessment, phylogenetic analysis, gene functional enrichment and protein family classification for each complex that was identified.

Results : We predicted functions for two proteins (PFL0350c and PFL1395c) with previously unknown functions. PFL1395c was predicted to be a histone acetyltransferase enzyme that regulates gene expression in the parasite, while PFL0350c is predicted to be carrying out DNA binding and bending of linear DNA distorted structures in P.falciparum.

Conclusion : We have been able to use computational approaches to gain understanding and knowledge about the interactions among unknown proteins in the parasite's interactome with respect to the molecular activities and structures which are key parameters for designing malaria vaccines and drug target.

Mots clés /keywords :

protein-protein interaction, MCODE algorithm, Plasmodium falciparum, functional annotation, protein function, unknown proteins

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CF15   THE PATHWAY GENOME DATABASE OF ANOPHLES GAMBIAE AGAMP3

Auteurs /Authors :

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Introduction : A comprehensive genomic sequence annotation for the malaria vector Anophles gambiae AgamP3 has simplified efforts to construct a standardized pathway genome database(PGDB)for such a complex organism.The completion of her genome sequences has given opportunity to develop various methods to facilitate effective malaria control strategies.

Goals : Biochemical networks are the central processing units of life that encompasses biochemical pathways.But is the biochemical research for this organism able to elucidate a better image of her metabolic architecture? Can her biochemical reactions be functionally linked together? If yes, what would their results yield? Thus, this work aimed at constructing a Pathway genome database/ biochemical networks (also called Biochemical pathways) for the malaria vector, Anopheles gambiae (A. gambiae) AgamP3.

Methods: A.gambiae genomic sequence information was extracted from NCBI as residence on AnoBase and further annotations from Kegg, VectorBase and UniProt with Pathologic program was used to build AnoCyc, Two standardized annotation tools.DomainSweep and GoPet from DKFZ HUSARopenservers were deployed.The first was used identify the domain architecture within a protein sequence,assign correct functional assignment for an uncharacterized/ unassigned protein sequences and-second-assigned-molecular-functions to protein-sequence and cDNA.

Results :'AnoCyc ver1.1' http://biocyc.org/organism-summary?object=ANO

In this version,we have we present 14974 genes, of which 14324 code for polypeptides and 650 code for RNA.This produced 2380 known enzymes against the 2297 found in the first edition.Also,Information on transport processes between the different compartments includes 75 transporter metabolites and 12 transport reactions.

Conclusion:AnoCyc ver1.1 involved more rigorous and thorough annotation with quality information,great features and many useful details about the genome gambiae.A useful combination/meaningful computational analysisofour PGDB enhances use of genomics explain-mode-of-resistance/predict-insec

Mots clés /keywords :

PGDB, Anopheles, Biochemical network, pathologic

Auteur présentateur / presenting author: Dr Marion Olubunmi Adebiyi**,** Covenant University

CF16 **Le domaine basique de la protéine Tat(44-61) du VIH-1 : Etude par fluorescence de son interaction avec des oligonucléotides.**

Auteurs /Authors :

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Introduction: La protéine Tat entière de VIH-1, connue comme transactivateur de transcription, et sa séquence basique 44-61 (Tat(44-61)) sont capables d'activer fortement l'hybridation des séquences ADN complémentaires représentant cTAR et dTAR. Par cette propriété, Tat est susceptible de jouer un rôle dans la transcription inverse. A ce jour, les aspects cinétiques de cette réaction, ont été étudiés en détail. En outre, l'étude des effets de mutations de Tat(44-61) sur sa faculté de promouvoir l'hybridation a fourni des informations sur l'importance relative des différents résidus

Objectifs / goals : Étude des interactions de Tat(44-61) avec les oligonucléotides cTAR, dTAR et TAR ARN par fluorescence

Études des modifications conformationnelles de Tat(44-61) durant ces interactions par la cinétique.

Méthodologie / Method: Nous avons utilisé plusieurs techniques de fluorescence pour tenter de mieux comprendre comment Tat(44-61), un peptide essentiellement désorganisé, se structure lors de son interaction avec des séquences nucléotidiques cibles telles que cTAR, dTAR et TAR ARN

Résultats / Results : Les études par spectroscopie de fluorescence suggèrent que dans son complexe avec chaque oligonocléotide, le peptide adopte une conformation plus compacte qu'en solution. Nous avons également utilisé Tat(44-61) muté en position Y47 ou Q60 par un acide aminé artificiel porteur d'une chaine latérale de type chromone. Cette dernière produit une fluorescence à deux bandes N* et T* par transfert intramoléculaire de proton à l'état excité (ESIPT) dont l'intensité relative est très sensible à la polarité du milieu (sonde ratiométrique). Cette approche nous a indiqué que le résidu 47 est dans un environnement polaire lors de l'interaction avec les trois oligonucléotides, ce qui est compatible avec les données antérieures.

Conclusion : Le ciblage de l'interaction de Tat avec ses cibles oligonucléotidiques pourrait être une piste pharmacologiquement valable

Mots clés /keywords :

Tat protéine ; VIH-1 ; cTAR ; dTAR, TAR ARN ; fluorescence.

Auteur présentateur / presenting author:

Dr Mor FALL

CHU Aristide Le Dantec, Pharmacie.

CF17   Genome sequence of tsetse bracoviruses: insights into symbiotic virus evolution

Auteurs /Authors :

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Introduction: The whole genome sequence of the tsetse fly (Glossina morsitans morsitans) revealed presence of putative bracoviral sequences (n=310). The sequences are highly similar to those identified in parasitic braconid wasps. Bracoviruses encode proteins that lower host immunity allowing for the development of parasitoid larvae in the host.

Objectives: Comparative genomics of five tsetse fly species (G. austeni, G. brevipalpis, G. f. fuscipes, G. m. morsitans and G. pallidipes) and the housefly (Musca domestica) genomes was done to determine the presence, prevalence and genetic diversity of bracoviruses.

Methods: Four viral Maverick (mobile elements) genes were identified using computational techniques and used as evolutionary models of bracoviruses. The genes were then validated using molecular techniques.

Results: These genes were observed to be present in multiple copies. G. austeni had the highest number (n = 18) and G. brevipalpis the least (n = 6). This is the first record of homologous bracoviruses in multiple Dipteran genomes. Phylogenetic reconstruction of each gene revealed two major clades, which represent the two types of Mavericks, which are concurrently present. Selection pressure acting on these genes and their flanking regions was evaluated using dN/dS ratio. They were under varying magnitudes of purifying selection except for the poxvirus A32, which was under positive selection.

Conclusion: This indicates that the genes were inserted at conserved regions and co-evolve with the host genome. We discuss the identification of bracoviruses in the tsetse genome and highlight their future potential as a tsetse fly control strategy.

Mots clés /keywords :

bracoviruses; genome sequence; tsetse flies; maverick; symbiosis

CF18 **Genetic variants found in apolipoproteins gene loci and their association with**

HIV progression amongst hiv perinatally infected children in Botswana

Auteurs /Authors :

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Introduction
Understanding the molecular functioning of a disease and its host response mechanisms is critical in exploring ways to prevent or manage the disease and HIV is not an exception to this. Botswana, which is part of the Sub-Saharan Africa, has scarce data on adult HIV-1 host genetics and to our knowledge, no genetic data has been reported on children, yet children pose a good cohort to study because of very little impact fromenvironmental factors e.g. smoking. Host immune factors are important determinants of susceptibility to pathogens in adults and children (Singh & Spector, 2009).Such include Apolipoproteins, which are a family of mRNA-editing enzyme catalytic polypeptide (APOBEC) that have been implicated in many diseases such as HIV, Cancer, murine leukemia virus (MLV) and Rous sarcoma virus (RSV) (Wiegand & Cullen, 2007;).Polymorphisms have been reported in Apolipoproteins and some of these variants are shown to be associated with HIV disease progression.
Objectives
This study is will address Apolipoprotein gene polymorphisms in HIV disease progression amongst perinatally infected children in Botswana. It is a retrospective approach that consist of a cohort of 200 Long term non-progressors (LTNP) who are termed 'cases' and 200 rapid progressor(RP) who are controls.
Methodology
Genomic DNA that has been extracted from patients' whole blood will be sequenced using Sanger sequencer Genotypes and allele counts will be subjected to Hardy Weinberg to ensure that allele and genotype frequencies are constant and not a result of evolutionary events. Statistical significance and regression plots showing clinical data (CD4 counts) and genotypes will be derived to demonstrate genotype and allele association with disease progression. Levels of APOBEC3 mRNA (gene transcripts) in total RNA from the HIV cohort will be quantified by real time PCR. A total of 100 tRNA will be reverse transcribed to cDNA and the cDNA will be used for APOBEC3quantification, calibrated to a reference gene.. Statistical significance will be assessed to determine relative quantification of the gene in cases and controls. Levels of APOBEC3 in serum will be assessed to examine if polymorphisms affect levels of protein production. This will be achieved through analysing proteins by SDS PAGE and quantifying using ELISA. Protein quantification will also be assessed against genotype to determine disease association.
Next Steps
Genomic DNA has been extracted and the next step is targeted sequencing using gene specific primers. We already purchased a sequencer and have had training on sequencing. We envisage that the next objective will be easily carried out. I have also receiveda travel fellowship by the Welcome Trust to attend the Molecular approaches to Clinical Microbiology in Africa, Gambia, and March 2016, where I will learn about approaches to genotyping and statistical data as well as Bioinformatics.

CF19   The African Initiative for Multi-omics Education and Research:

Focus on the Human Microbiome Research in Africa

Auteurs /Authors :

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Introduction: The findings from human microbiome studies are transforming our understanding of the pathogenesis and/or management of several diseases, including asthma, inflammatory bowel diseases, obesity, cancer, Type 1 diabetes and sickle cell disease, as well as the development of the immune response. However, little is known about African populations, and there is no "African Microbiome Initiative".

Goals: This systematic review aimed to summarize the state of research on the human microbiome in Africa, including the therapeutic role of the microbiome for the management of certain local diseases.

Methods: Using predefined keywords, we searched in six electronic databases for human microbiome studies conducted in Africa. In addition, we searched all references cited in eligible studies. The literature search was updated on 22 January 2016.

Results: We included 71 human microbiome studies, including studies targeting Khoi San (n= 1) and Hunter-Gatherers (n= 7). 16S rRNA gene sequencing was the technique most widely used (59%; 42/71) to characterize the microbiota. The main body sites studied were the gut (53%), vagina (20%) and the oral cavity (13%). The diseases targeted were HIV/AIDS (n= 10), malnutrition (n= 7), diarrhoea (n= 4), and periodontitis (n= 4). These microbiome studies were performed in individuals of all ages. Kenya, Uganda, Malawi, South Africa and Tanzania were the sites of the majority of studies.

The principal investigators of 96% (68/71) of the studies were from developed countries. The USA NIH was the main funding source (41%), followed by the Bill and Melinda Gates Foundation (17%) and the European Commission (10%).

Conclusion: There is a need for more human microbiome research in Africa, for African researchers to take the lead in microbiome research on the continent and for studies to focus on diseases of public health concern in Africa.

Mots clés /keywords : Africa, human, metagenomics, microbiome, systematic review

Auteur présentateur / presenting author: Dr Mamadou Kaba**,** Division of Medical Microbiology, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

CF20   **Study of host genetics factors in the resistance / susceptibility to**

Trypanosoma brucei gambiense infection in Guinea.

Auteurs /Authors :

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Introduction: Disease susceptibility can arise as a consequence of adaptation to infectious disease. Long considered as invariably fatal, observations are increasingly indicating that infection by T. b. gambiense can result in a wide range of clinical outcomes in its human host. Recently, self-cure processes have been described in HAT patients in different disease stages. Findings have showed in contrast to patients, trypanotolerant subjects were characterized by a strong inflammatory response with elevated levels of IL8, IL6, and TNF. Other findings have showed that four single DNA polymorphisms located on genes coding for cytokines were correlated with a variable risk for development of the disease.

Objective: Determine genes involve in resistance/susceptibility to slipping sickness to understand the factors underlying this clinical diversity.

Methodology: With the candidate gene approach, we will select a number of chromosomal regions encompassing genes having a relationship with the pathology as reported in the literature: these are going to be genotyped across all samples.

Then we will do an unbiased search on the entire genome to find chromosomal regions that may be involved in the phenotype of control of pathology using the Genome Wide Association study (GWAS) approach.

From there, we are going to do association analysis to identify mutations potentially involved in resistance/susceptibility.

Preliminary Results: After parasitology and laboratory tests, we have got 476 samples of DNA, constituted of 251 cases, 73 seropositives and 152 controls. Five candidate genes are selected for genotyping to all the sample.

Next Steps: DNA samples of 30 patients have been sampled and sent to whole-genome sequencing, and all the data will be pooled to select a panel of SNPs to design a SNP Chip for further genotyping.

CF21   HLA class II allele polymorphisms in patients with pulmonary Tuberculosis at Mulago hospital in Kampala Uganda

Auteurs /Authors :

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Introduction: Mycobacterium tuberculosis (Mtb) is reported to infect about a third of the world's population but only 10 % are thought to develop active tuberculosis (TB) disease. Host immunity regulated by human leukocyte antigens (HLA) is an important determinant of the outcome of the disease. Here we investigate HLA class II gene polymorphisms in susceptibility to TB, and whether particular HLA class II alleles were associated with TB in Uganda.

Methods: Forty two HIV negative newly diagnosed TB cases with positive ZN sputum smear, positive MTB sputum culture, and an equal number of randomly selected unmatched HIV negative controls from the index case's house hold had their samples analyzed using SSP One lambda typing assay. HLA antigens (DRB and -DQB) gene polymorphisms were analyzed to determine phenotypic frequencies. Results were compared by Fisher's exact test as appropriate using the SPSS program.

Results: The HLA-DQB1*03:03 allele was significantly less frequent in patients compared to healthy controls (10 % in controls versus 0 % in patients, p=0.003). After correction for multiple comparisons the difference remained significant (p=0.018).

Next steps:

1.   An additional study is needed in a genetically characterized population to determine if HLA- DQB1*03:03 allele is protective. To rule out the influence of a small sample size and population multiple confounders, the study needs to be re-done within a larger well characterized cohort.

2.   We recommend the use of automation and sequencing platforms for this assay due to test shortfalls we experienced in SSP testing methods.

3.   To confirm that APC cells presenting MTB peptides (ESAT-6 and CFP-10) in context of HLA DQB1*0303 are more superior presenters than with other alleles.

CF22   **Ancestral African Genomes Provide Insight into Human Evolution and**

Relationship with Neanderthal

Auteurs /Authors :

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Humans went through several stages of evolution in the past 400,000 years showing remarkable variations both within and between populations in a number of phenotypic traits, such as pigmentation, height, food tolerance, heat and cold stress responses, and immune responses. This diversity is a culmination of genetic, environmental and cultural adaptations that have occurred under various selective pressures acting over different phases of human evolution. To understand the relationship between modern and ancient humans, a number of adaptive genes were analyzed in Sudanese based on mitochondrial deep ancestry and compared to Neanderthal and global samples collected from 1000 Genomes and UCSC browsers. Our results showed remarkable variations both in SNP numbers and genotypes patterns. Most Sudanese samples showed higher heterozygosity compared to other global samples, possibly attesting to the higher effective population size of East Africans reported earlier. More than 1.5% difference in the number of Neanderthal-like alleles among Africans was recently reported with a suggestion that these differences are likely due to recent non-African admixture in these populations. Here, we observe a considerable number of SNPs were found to be shared between Sudanese genome samples, global modern humans and Neanderthals. For example, the derived allele of an exonic SNP (rs1426654) in SLC24A5 (a gene that affects skin pigmentation) was shared among the majority of samples and the Neanderthal genome. Other similar patterns were seen in olfactory receptor (OR) group of genes. Interestingly, these variations are exonic and thus likely reflect very ancestral sites of selective pressure and adaptation.

Mots clés /keywords :

Evolution, Adaptation,Humans, Neanderthal.

Auteur présentateur / presenting author:

Dr Maha Mohammed Osman Mohammed

Researcher

CF23   **A Comparison of Retinal Gene Expression Levels in Human and Mouse**

Auteurs /Authors :

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Introduction : Leading causes of blindness in human includes various retinopathies and age-related macular degenerations whose etiology requires pre-clinical studies in mice. However, evolutionary differences between mouse and human make it impossible for human physiological attributes of vision to be accurately replicated in the two species. How much of the vision phenotypic differences are reflected at the molecular level is still unknown.

Goals : To analyze mRNA levels in the retina and retinal pigment epithelium (RPE)in human and mouse, to compare the pattern of gene expression levels between the retina and RPE and to identify specific and conserved patterns of genes that remain co-expressed during evolution.

Methods: Publicly data generated by standard Illumina poly(A)+ mRNA-seq protocol was used to study genome-wide gene expression patterns in the retina and RPE of three wild-type mice and three normal humans. In-house differential expression analysis pipeline was developed to compare the expression differences between the retina and RPE in humans and mice.

Results : High number of genes was found to be differentially expressed between the RPE and retina in both species (mouse 5158; human 3857). About 25% of these genes showed a conserved pattern of expression in mouse and human, suggesting a larger group of genes implicated in human- or mouse-specific visual processes. Few of the genes with the strongest expression difference in mice alone included the gene Cartpt, a key marker of direction selective retinal ganglion cells found to be downregulated in the RPE versus retina. Genes with strongest expression difference in human alone included ONECUT1, a transcription factor specific for horizontal cells found to be downregulated in the RPE versus retina.

Conclusion : The majority of gene expression changes in the retina and RPE are specific to human and mouse, suggesting that the causal molecular agents of species-specific vision physiology in the two species may likewise be different.

Mots clés /keywords : retina, retinal pigment epithelium, RNA-seq, mouse, human

Auteur présentateur / presenting author: Mr(s) Edson Ishengoma

Nelson Mandela African Institution of Sciences and Technology

CF24   **Y chromosome haplotype diversity for 17 STR further attests to the linguistic-genetic link and the large east African population size**

Auteurs /Authors :

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1-Institute of Endemic Diseases UoK; 2-Eritrea Institute of Technology; 3-HDDRL, University of the Witwatersrand and the National Health Laboratory Services

Introduction : Y chromosome STRs analysis has become increasingly important for forensic and human population genetics study. Analyzing Y-STRs from populations of East Africa not only enrich the forensic database but may also augment the efforts that have been done to answer some of the important questions regarding the origin and spread of E and J haplogroups and Afro-asiatic languages.

Goals : To investigate the distribution of Y-STR haplotypes in the populations from Eritrea and Sudan, and to put them in global context

Methods: Samples from 94 unrelated males from Eritrea, southern Sudan and Sudan were analyzed for distribution of 17- loci Y-STR, twelve of those were subsequently employed in phylogenetic and population differentiation analyses along 281 individuals from 40 global populations to place the Y-STR variation of east Africans within a global context.

Results : The 12 Y-STR loci analysis allowed 314 haplotypes to be defined out of which 283 are unique. Haplotypes differences between individuals from east Africa conforms the relatively larger male effective size and emphasize the necessity of including Ne measures in population and forensic studies. Haplotypes shared between east African populations and individuals from Algeria and Saudi Arabia, all belong to J haplogroup, indicating a recent genetic history of the region. The 12 Y-STR loci analysis of global samples displayed in various metrics: network, multidimensional scaling, principal component analysis and phylogenetic tree constructed from haplotypes belonging to E and J haplogroups using BEAST attests once more to the role of East African population to the origin and diversification of the haplogroups.

Conclusion : The study revealed a pattern consistent with genetic variation being mirrored by linguistic and geographic patterns a feature possibly indicating the profound force of genetic drift. The overall analysis still conforms to results of cluster and phylogenetic analysis obtained by SNPs in autosomes, Y chromosome and mitochondrial DNA.

Mots clés /keywords :

Y chromosome, Short tandem repeat, Y-STR, Y-SNP, Eritrea, Sudan, East Africa

Auteur présentateur / presenting author:

Dr Eyoab Iyasu Gebremeskel

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CF25   **Anomalie du développement sexuel 46,XY avec gynécomastie et orchi-épididymite :**

à propos d'un cas

Auteurs /Authors :

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2- Laboratoire Histologie-Embryologie, Département de Biologie et d'explorations fonctionnelles, Faculté de Médecine, Pharmacie et d'Odontologie, Université Cheikh Anta Diop, Dakar

3- Département de Biologie animale, Faculté des Sciences et Techniques, Université Cheikh Anta Diop, Dakar

Introduction: La naissance d'un enfant présentant une malformation constitue un choc émotionnel pour les parents. Les anomalies du développement sexuel sont les conditions congénitales au cours desquelles, les sexes chromosomique, gonadique et anatomique sont atypiques. Antérieurement appelés « ambiguïté sexuelle » ou « intersexuation », ces termes sont devenus anachroniques et perçus comme péjoratifs par les familles atteintes. Nous rapportons ici le cas d'un patient élevé en garçon, présentant une anomalie du développement sexuel avec une gynécomastie l'ayant fait abandonner l'école.

Objectifs / goals : L'objectif de cette étude était de déterminer les sexes chromatinien et chromosomique du patient afin de voir s'ils étaient en adéquation avec le sexe d'état civil.

Méthodologie / Method: Un test chromatinien de Barr a été réalisé sur un frottis de la muqueuse buccale par cytoplasmolyse à l'acide chlorhydrique normal (HCL.N) et coloration de GUARD et une technique de caryotype conventionnel a été effectué sur un prélèvement sanguin périphérique.

Résultats / Results : Le patient, de sexe masculin à l'état civil , est âgé de quinze ans. Il a une posture masculine et présente à l'examen une gynécomastie bilatérale classe S5 de Tanner, un micropénis avec une augmentation de volume des bourses. Les deux testicules sont palpés avec une hypertrophie testiculaire gauche. L'échographie testiculaire a conclu à une orchiépididymite gauche chronique avec hydrocèle abondante cholestérolique. Le pourcentage de corpuscule de Barr est de 4% et le caryotype retrouve une formule 46,XY.

Conclusion : Le sexe d'état civil concordait avec les sexes chromatinien et chromosomique. Cependant l'épanouissement social d'une personne dépendant de plusieurs facteurs impliquant une différenciation sexuelle normale, un accompagnement psychologique est nécessaire pour une meilleure prise en charge. En effet, une anomalie du développement sexuel peut avoir de graves répercussions psychosociales comme chez ce patient ayant abandonné l'école à cause de moqueries de ses camarades.

Auteur présentateur / presenting author: Dr Mame Vénus GUEYE, Université Cheikh Anta DIOP de Dakar

CF26   **Relationship between socio-economic status and chronic kidney disease in**
a multi-ethnic cohort – The HELIUS study

Auteurs /Authors :

D.N. Adjei, D. Adu, C. Agyemang.

Background: Chronic kidney disease (CKD) is a worldwide health problem. Ethnic minority groups in high-income countries have been shown to be disproportionately affected by CKD for reasons that are still unclear. Lower socioeconomic status (SES) has been suggested to be associated with CKD. However, evidence seems to suggest differential association of SES with CVD health outcomes in different ethnic groups. Data are lacking on the evidence of SES influence on CKD in ethnic minority groups. We therefore assessed the association of SES with CKD in a multiple population.

Study Design: Cross-sectional analysis of baseline data from the Healthy Life in an Urban Setting (HELIUS) cohort study.

Setting & Participants: A random sample of 21492 adults (4543 Dutch, 3032 South Asian Surinamese, 4112 African Surinamese, 2321 Ghanaians, 3592 Turks, and 3892 Moroccans) aged 18 to 70 years living in Amsterdam, the Netherlands.

Predictors: Socioeconomic status (level of education and Occupational status).

Outcomes & Measurements: CKD status was defined using the 2012 KDIGO (Kidney Disease: Improving Global Outcomes) severity of CKD classification. CKD was defined as albumin-creatinine ratio ≥ 3 mg/mmol (category ≥ A2) or glomerular filtration rate, < 60 mL/min/1.73 m2 (category ≥ G3). Comparisons among groups were made using odds ratios (ORs).

Results: The odds of CKD was higher in all ethnic minority groups, ranging from 1.6 (95% CI, 1.3-2.0) in Moroccans to 2.7 (95% CI, 2.2-3.3) in South Asian Surinamese, compared with Dutch. In an age-and-sex adjusted model, participants with elementary educational level and below had higher odds of CKD in all ethnic groups compared with those with higher educational level. These odds were lower in all ethnic groups ranging from 1.4 (95% CI, 1.0-2.1) in African Surinamese to 1.7 (95% CI, 1.1-2.5) in African Surinamese, compared with the Dutch. Similar findings were recorded among those with elementary occupational levels among all ethnic groups compared with the Dutch.

Limitations: Cross-sectional design.

Conclusions: These findings suggest an influence of SES on CKD for most groups. A reduction of socioeconomic inequalities may reduce CKD and related complications in all ethnic groups.

CF27   IMPLICATION DE L'EXON 2 DU GENE MED12 DANS DES CAS DE FIBROMES UTERINS CHEZ LES FEMMES SENEGALAISES

Auteurs /Authors :

Kénémé B (1); Mbaye F (1,2) ; Ka S (3) ; Dem A (3) ; Sembène M (1,2)

Introduction : Les fibromes utérins sont des tumeurs bénignes, associées à une morbidité significative constituant un problème de santé publique. Les femmes d'origine africaine ont un risque trois fois plus élevé comparées aux femmes caucasiennes.

Objectifs / goals : l'objectif de cette étude est de caractériser par PCR séquençage, l'exon 2 du gène MED12 permettant ainsi de déterminer l'implication de ce gène dans les fibromes utérins.

Méthodologie / Method: les patientes atteintes de fibromes utérins (30) ont été recrutées au niveau de l'hôpital militaire d'Ouakam. Chez chaque patiente, il a été effectué un prélèvement de tissu tumoral et un prélèvement de sang. Il a été effectué, chez des témoins un prélèvement de sang. La position des mutations par rapport au gène MED12 a été déterminée avec le logiciel Surveyor version 5.0.0. Dnasp version 5.10, MEGA version 6.06 et le programme Arlequin version 3.5.1.3 ont été utilisés pour ressortir les paramètres de la variabilité, de la différenciation ainsi que de l'évolution démo-génétique de notre population d'étude.

Résultats / Results : nos résultats ont indiqué des mutations dans les tissus tumoraux (64%). Parmi ces mutations, 37,5 % sont hétérozygotes (c.130G>A, c.130G>C, c.130G>T, c.131G>A, c.133T>G), 31,25 % sont des substitutions simples (c.130G>A, c.130G>C, c.183G>A, c.260A>T, c. 278G>T) et 31,25 % des délétions (c. 130-132delGGT, 74delA). La plupart de ces mutations affectent la glutamine du codon 44. Le nombre de sites polymorphes et le nombre total de mutations sont respectivement 8 et 9. Les diversités haplotypique et nucléotidique sont respectivement 0,4138 et 0,0016. Les distances génétiques sont 0,002 (témoin/tissus cancéreux), 0,000 (tissus cancéreux/sang malades). Les FST obtenus entre les groupes ne sont pas significatifs (p>0,05).

Conclusion : cette présente étude a indiqué pour la première fois, l'implication de l'exon 2 du gène MED12 dans la pathogénicité des fibromes utérins chez des femmes sénégalaises.

Mots clés /keywords :

fibrome, utérin, exon 2, MED12, Sénégal

Auteur présentateur / presenting author:

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Université Cheikh Anta Diop de Dakar

CF28   **Statin pharmacogenetics**

Auteurs /Authors :

Soko Nyarai (1)(2); Collet Dandara (1); Raj Ramesar (1); Gerard Kadzirange (2); Collen Masimirembwa(1)(2)

1-University of Cape Town

2-African Institute of Biomedical Science and Technology

3-University of Zimbabwe

Introduction :Genetic variation in the transporters BCRP and OATP1B1 affects systemic exposure of rosuvastatin and hence contributes to statin induced myopathy.

Goals :This study investigated the role of these transporters in the pharmacokinetics of rosuvastatin among individuals of African ancestry.

Methods:Genetic variants in SLCO1B1 (c.521T>C; rs4149056) and ABCG2 (c.421C>A; rs2231142) were screened for among 815 healthy individuals from nine African ethnic groups (Kikuyu, Luo and Maasai, Igbo, Yoruba and Hausa, Shona and San). A subset of the healthy volunteers, (n=30 Zimbabweans) participated in a further open label, single oral dose trial to evaluate rosuvastatin pharmacokinetics. 20mg of rosuvastatin was administered to each participant and 5ml of blood collected hourly over a period of 12 hours post drug administration. Drug concentrations were quantified using Ultra High Performance Liquid Chromatography coupled to a tandem mass spectrometer detector. Non-compartmental analysis was used to determine pharmacokinetic parameters and profiles of each individual. From these 30 individuals, 8 individuals were selected for whole exome sequencing based on their different drug exposure levels as measured by their highest drug plasma concentration (Cmax). The eight whole exomes were sequenced using the Ion Torrent system by Life Technologies and the variants were annotated using Annovar.

Results :Frequencies of both polymorphisms was low ranging from 0.0% (San) to 7.0% (Kikuyu) for SLCO1B1 rs4149056 and 0.0% (Shona) to 5.0% (Kikuyu) for ABCG2 rs2231142, respectively. In the Zimbabwean subset rosuvastatin maximum plasma concentration varied 11 fold with a mean plasma Cmax of 12.22ngml-1. None of the 30 healthy individuals presented with either the SLCO1B1 c.521C or the ABCG2 c.421A variants, although other rare variants were identified in these exomes.

Mots clés /keywords :

rosuvastatin, SLCO1B1, ABCG2, African, Zimbabwean, pharmacogenetics, pharmacokinetics

Auteur présentateur / presenting author:

Dr Nyarai Desiree

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CF29   **Genome-wide Search for Genetic Loci Influencing Circulating Visfatin Levels**

Auteurs /Authors :

Sally N. Adebamowo(1); Ayo P. Doumatey(1); Fasil Tekola-Ayele(1); Amy R. Bentley(1); Guanjie Chen(1); Hanxia Huang(1); Jie Zhou(1); Daniel Shriner(1); Olufemi Fasanmade(2); Godfrey Okafor(3); Benjamin Eghan Jr.(4); Kofi Agyenim-Boateng(4); Samuel Owusu(5); Albert Amoah(5); Joseph Acheampong(4); Thomas Johnson(2); Johnnie Oli(3); Clement Adebamowo(6); Francis Collins(7); Georgia Dunston(8); Adebowale A. Adeyemo(1); and Charles N. Rotimi(1).

1-Center for Research on Genomics and Global Health, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, USA; 2-University of Lagos, Lagos, Nigeria; 3-University of Nigeria Teaching Hospital, Enugu, Nigeria; 4-University of Science and Technology, Kumasi, Ghana; 5-University of Ghana Medical School, Accra, Ghana; 6-Department of Epidemiology and Public Health, School of Medicine, University of Maryland, Baltimore, MD, USA; 7-National Institutes of Health, Bethesda, MD, USA; 8-National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, USA.

Introduction: Visfatin is an adipokine produced primarily by brown adipose tissue. Animal experiments and epidemiological studies have suggested a role for visfatin in insulin secretion, type 2 diabetes (T2D) and obesity.

Goals: We conduct the first genome-wide association study (GWAS) to identify genetic factors influencing circulating visfatin levels.

Methods: The study participants were 1382 individuals of African ancestry, enrolled in the AADM study. Their mean age(SD) was 54(10) years, 60% were women. Serum visfatin was measured on fasting samples using the BioRad Bio-Plex Pro™ Human Diabetes Immunoassay. Samples were genotyped on Affymetrix Axiom® PANAFR SNP array and Affymetrix Axiom Exome 319® Array. The resulting genotypes were filtered for quality and imputed into the 1000 Genomes Consortium phase 1 v.3 cosmopolitan reference, yielding a total number of ~14M SNPs with imputed allelic dosage frequency >0.01 and r2 >0.3. Association tests were performed under an additive genetic model with adjustment for age, sex, BMI, T2D and the first 3 principal components of the genotypes.

Results:The GWAS yielded a genome-wide significant cluster of 4 SNPs ~30kb upstream of the CNTNAP2 gene on chromosome 7: rs112623225 (p=2.6 x 10-9), rs17480133 (p=2.5 x 10-9), rs4726781 (p=5.1 x 10-9) and rs4726782 (p=4.2 x 10-8). These variants alter several regulatory motifs in key transcriptional factors including E4F1, DEC, NKX2, ARID5A, FOXA and POU1F1, most of which are expressed in adipocytes. ARID5A is overexpressed in adipocytes and whole blood, the two primary sites of visfatin abundance. Also, these variants are in a H3K27ac mark that is found near active regulatory elements. Two of the SNPs are cis-eQTLs for CNTNAP2. The strongest association of the visfatin locus (NAMPT) was for an intronic SNP rs57265962 (p=0.03).

Conclusions: The findings suggest that non-coding genetic variants near CNTNAP2 regulate circulating visfatin levels. More studies are needed to extend the reported associations and to identify mechanisms by which this locus regulates visfatin.

Mots clés /keywords : Visfatin, CNTNAP2, GWAS

Auteur présentateur / presenting author: Dr Sally N. Adebamowo**,** Center for Research on Genomics and Global Health, National Human Genome Research Institute, National Institutes of Health, USA

CF30   Transcriptome analysis of human adipogenesis reveals novel patterns of gene expression

Auteurs /Authors :

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1- Department of Immunology and Institute for Cellular and Molecular Medicine, Faculty of Health Sciences; SAMRC Extramural Unit for Stem Cell Research and Therapy, University of Pretoria, South Africa

Introduction :Adipogenesis is the process of fat cell formation. Accumulation of excess adipose tissue leads to obesity. Obesity is a risk factor for type-2 diabetes, cardiovascular disease and cancer

Goals : To use transcriptomic techniques to systematically study adipogenic differentiation in human adipose derived stromal cells (ASCs) in order to identify genes that are important in driving adipogenesis that could potentially be manipulated to control this process in order to combat obesity

Methods:RNA isolated from both adipogenic induced ASCs and their respective controls on days 1, 7, 14 & 21 was hybridized to Affymetrix HuGene 2.0 ST arrays for gene expression analysis.

Results : It was observed that 61, 124, 138 & 149 genes were significantly up-regulated on days 1, 7, 14 & 21 respectively. KLF15, LMO3, FOXO1 & ZBTB16 transcription factors (TFs) were up-regulated throughout adipogenesis which together are essential for driving this process. CEBPA, PPARG, ZNF117, MLXIPL, MMP3 & RORB TFs were only up-regulated from day 14 – 21, which coincides with adipocyte maturation. These TFs could serve as markers characterizing this stage of adipocyte differentiation. Similarly, we identified genes significantly up-regulated only from day 1 -7 & day 7-21 which could serve as potential markers for early-stage and general adipocyte differentiation, respectively. Up-regulated genes were associated with neural and blood vessel development, tumor growth, invasion and metastasis, while down-regulated genes were associated with osteogenesis and immune response. Furthermore, we observed that genes involved in adipocyte differentiation share common pathways with certain obesity related pathophysiological conditions such as cancer, cardiovascular and metabolic diseases.

Conclusion :This study revealed potential biomarkers for different stages in ASC adipogenic differentiation which could serve as good candidates to modify adipogenesis in order to combat obesity and further links obesity to certain pathophysiological conditions

Mots clés /keywords :

Human adipose-derived mesenchymal stromal cells, adipogenesis, adipocyte

differentiation, microarray, gene expression, obesity

Auteur présentateur / presenting author:

Dr Melvin Anyasi Ambele

University of Pretoria

CF31   Association of variants in APOL1 and MYH9 with micro-albuminuria among

SCD patients from Cameroon

Auteurs /Authors :

Geard A (1); Pule G (1); Wonkam A (1)

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Introduction : Sickle Cell Disease (SCD) is a monogenic hemoglobinopathy that is highly prevalent in Africa. Kidney Disease is a proxy of severity, developing only in a subset of patients. Micro-albuminuria is considered a primary indicator of renal dysfunction that has been associated with specific genetic modifiers.

Goals : We have investigated the association of single nucleotide polymorphisms (SNPs) in APOL1 and MYH9 with micro-albuminuria among Cameroonian SCD patients.

Methods: A total of 413 SCD patients were included. Patients were genotyped for the 3.7kB alpha-globin gene deletion using gap-PCR and seven targeted single nucleotide polymorphisms (SNPs) in APOL1 and MYH9 using PCR, SNaPshot, TaqMan and Sanger Sequencing. Logistic regression analysis was used to study the association between genotypes and socio-demographic variables, crude micro-albuminuria, as well as the albumin-to-creatinine ratio (ACR).

Results : The cohort had a median age of 15 (9-23) with micro-albuminuria significantly associated with age (p=0.0041). 60.9% and 2.5% of patients had crude micro-albuminuria and macro-albuminuria, respectively. Using ACR data, micro-albuminuria had a prevalence of 73.4%. Comparison of the present Cameroonian data to sequence data extracted from the 1000 Genome Project indicates a large MAF difference among various African populations (rs11912763 and rs16996648). 41.4% of patients' had co-inherited the 3.7kb alpha-globin gene deletion. The albumin-to-creatinine ratio (ACR) was significantly decreased in heterozygotes for rs11912763 (p=0.0419) in patients greater than 15 years old (n=69), but not with other targeted SNPs. There was no association between the 3.7kB alpha-globin gene deletion and micro-albuminuria.

Conclusion : Micro-albuminuria is a highly prevalent condition in this cohort. Micro-albuminuria's association with age is indicative of a directly proportional relationship between age and renal dysfunction. This population of virtually micro-albuminuric patients could explain the significant association of only one SNP with ACR.

Mots clés /keywords :

Sickle cell disease, kidney disease, Africa, APOL1, MYH9

Auteur présentateur / presenting author:

Dr Amy Frances Geard

University of Cape Town

CF32   **A translational approach to elucidating disease mechanisms –**

A case study of GPx4 in cardiometabolic disease

Auteurs /Authors :

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Introduction and Goals: Reactive aldehyde derivatives (LPPs) have been linked to obesity-related pathologies, but their causal role remains unclear. Glutathione peroxidase 4 (GPx4) is a selenoenzyme that selectively neutralizes lipid hydroperoxides, and human gpx4 gene variants have been associated with obesity and cardiovascular disease in epidemiological studies. This study tested the hypothesis that LPPs underlie cardio-metabolic derangements in obesity using a high fat, high sucrose (HFHS) diet in gpx4 haploinsufficient mice (GPx4(+/-)) and in samples of human myocardium.

Methods: Wild-type (WT) and GPx4(+/-) mice were fed either a standard chow (CNTL) or HFHS diet for 24 weeks, with metabolic and cardiovascular parameters measured throughout. Biochemical and immuno-histological analysis was performed in heart and liver at termination of study, and mitochondrial function was analyzed in heart. Biochemical analysis was also performed on samples of human atrial myocardium from a cohort of 103 patients undergoing elective heart surgery

Results: After the HFHS diet, WT mice displayed moderate increases in 4-hydroxynonenal (HNE)-adducts and carbonyl stress, and a 1.5-fold increase in GPx4 enzyme in both liver and heart, while gpx4 haploinsufficient (GPx4(+/-)) mice had marked carbonyl stress in these organs accompanied by exacerbated glucose intolerance, dyslipidemia, cardiac fibrosis and liver steatosis. Mitochondrial dysfunction, decreased fat oxidation capacity and increased reactive oxygen species was also present in obese GPx4(+/-) but not WT hearts, along with up-regulation of pro-inflammatory and pro-fibrotic genes. Patients with diabetes and hyperglycemia exhibited significantly less GPx4 enzyme and greater HNE-adducts in their hearts, compared with age-matched non-diabetic patients.

Conclusion: This demonstrates that GPx4 also serves a critical role as an adaptive countermeasure in human patients.

Mots clés /keywords :

Gpx4, mitochondria, obesity, cardiometabolic disease

Auteur présentateur / presenting author:: Dr Lalage Katunga, Saint Louis University

CF33   Pasteur_galaxy: An open and sustainable Galaxy instance for NGS data analysis

Auteurs /Authors :

Oussema Souiai(1) , Mohamed Alibi(1), Ines Tiouiri(1), Kais Ghedira(1), Alia Benkahla(1)

(1) Institut Pasteur de Tunis

Introduction : The exponential growth of Omics and more specifically the NGS data has raised up a great technical challenge to experimentalists who are unused to bioinformatics skills and do not dispose of sufficient computing power.

Goals: The Pasteur_Galaxy project has the following main objectives:

- Provide the academic scientific community with an open and sustainable powerful Galaxy instance with a guaranteed availability. The platform offers access to numerous and up-to-date tools for genetic, meta-genomics and transcriptomic data analysis with help and support.

- Provide the possibility for H3ABioNet nodes and more broadly the H3Africa community to share their data and results.

- Propose innovative developments and new helpful tools packaged for Galaxy (available in the Pasteur_Galaxy toolshed).

- Developing of new tools and services for Galaxy (wrappers and/or toolshed packages).

Methods: Integrative analysis of data from various sources is needed to provide biological insights into biological systems.

Through, the invaluable financial support provided by H3ABioNet, we settled and managed a 72 core, 512 Gb of RAM and 12T of storage server. To facilitate the access to the server we settled the Pasteur Galaxy server (Pasteur_Galaxy), an open and powerful free web-based platform for integrative analysis of NGS data.

Pasteur_Galaxy is based upon Galaxy, one of the most popular bioinformatics workflow management systems, which is considered as a standard for sharing bioinformatics data, tools and results. As a Galaxy instance, Pasteur_Galaxy aims at providing a large range of bioinformatics tools for the analysis of various types of NGS data. Galaxy supports reproducible computational research by providing an environment for performing and recording bioinformatics analyses.

Next steps and perspectives : Enhance server capacity by extending the computational capacity. Upgrade the list of tools with regard to community needs.

Configure Galaxy to work with a suitable scheduler (Torque/Maui) which is already installed on the server.

Mots clés /keywords :

Metagenomics, SNP, DNAseq, RNAseq, Galaxy

Auteur présentateur / presenting author: Dr Souiai**,** Institut Pasteur de Tunis

ABSTRACTS SELECTED FOR POSTER PRESENTATION

PY01   Overdominance effects between Malaria and Visceral Leishmaniasis in the 5q31 region

Auteurs /Authors :

Mutaz Amin

Abdelbadea Elhassan

Kirk Rocket

Muntasir Ibrahim

A group of SNPs in 5q31, genotyped from Hausa tribe of Koka village in eastern Sudan; an area endemic with malaria and visceral leishmaniasis;, were analyzed by The Leishmaniasis research group and found to have significant excess of heterozygozity level and departure from HWE and assumed to be due to natural selection resulting from notorious deadly outbreaks since various ethnic groups from western Sudan settled the area although sequence information in the 5q31 region did not detect functional SNPs that could be associated with such drastic phenotypes. Malaria was thought to inflict inferior selective pressure due to the mild clinical phenotype observed. Taking advantage of follow up phenotype data sets available from the MalariaGen study we re-analyzed these genotypes using different bioinformatics software to determine their effect on the regulation, function and expression of interleukins, miRNA binding and splicing mechanism. The SNPs were found to potentially affect the binding of many transcription factors that regulate the expression of IL-4 and IL-13, and stability of IL-5 mRNA. Association of haplotypes susceptibility revealed that the haplotype of low cytokine TH2 profile is associated with higher risk of malaria infection (P-value= 0.02). Through modulating TH2 cytokine response; the excess heterozygosity in 5q31 is explained with the phenomenon of overdominance between malaria and visceral leishmaniasis, acted by natural selection and driving the locus towards optimum response.

Mots clés /keywords :

Heterozygosity, Natural selection, Single Nucleotide Polymorphisms, Overdominance

Auteur présentateur / presenting author:

Dr Mutaz Amin Abdelgalil Mustafa

PY02   **Towards understanding human leukocyte antigen (HLA) diversity in southern African populations: implications for transplantation and disease association studies**

Auteurs /Authors :

Tshabalala M (1); Mellet J (1); Christoffels A (2); Pepper MS (1)

1-Institute for Cellular and Molecular Medicine, Department of Immunology; SAMRC Extramural Unit for Stem Cell Research and Therapy, University of Pretoria, South Africa; 2-South African National Bioinformatics Institute, University of Western Cape, South Africa

Introduction :Despite the increasingly well-documented evidence of high genetic and ethno-linguistic diversity amongst African populations, little is known about their HLA diversity. HLA is part of the host defense mechanism mediated through antigen presentation to effector cells of the immune system, and also plays a key role in recognition of 'self' (a key feature in transplantation). With the high disease burden in southern Africa, HLA diversity data is becoming increasingly important in the design of population specific vaccines and improvement of transplantation outcomes.

Goals :To highlight the paucity of classical HLA diversity data amongst southern African populations despite the key role in disease association studies, vaccine design and transplantation.

Methods:HLA data was retrieved from Pubmed literature searches, the publicly available Allele frequency database and dbMHC.

Results :HLA data from ten studies (1137 individuals) of southern African origin were identified from the public domain. The order of allele numbers/loci was HLA B > HLA A > HLA DRB1 > HLA C > HLA DPB1. South Africa had the highest amount of publicly available HLA data (no data for Angola, Lesotho, Malawi, Namibia, Swaziland). HLA B and HLA C allele frequencies were generally low (< 0.2) with some class II frequencies ≥ 0.555. Most (>50 %) of the reported sub-Saharan alleles were from southern African populations highlighting diversity in this region. Novel alleles (A*30:01:02, A*30:02:02, A*68:27, B*42:06, B*45:07) were reported amongst black South Africans.

Conclusion :This study revealed the limited amount of HLA diversity data amongst southern Africans. It is currently difficult to find donor-recipient matches for most Black Africans, largely due to the lack of donors in registries and unknown HLA diversity in these populations. In-depth studies on HLA diversity in southern Africans will further guide HLA-disease association studies; improve population specific vaccine development and donor recruitment into registries.

Mots clés /keywords :

HLA, HLA diversity, southern Africa, disease burden, transplantation outcomes

Auteur présentateur / presenting author:

Mr(s) Mqondisi Tshabalala

University of Pretoria

PY03   **Enhancing Ethiopian Youth's literacy about gene * environment contributions about health using the context of podoconiosis**

Auteurs /Authors :

Kibur E. (1); Desta A (2); Collen, M(3), Gail D(4), Getnet, T(4)

Introduction :Improved understanding of gene-environment contributors to health conditions can enhance preventive actions of the public to reduce risky health behaviors.

Goals :The goal of this project is to study the youth's perceptions of podoconiosis(a non-filarial elephantiasis) with the ultimate aim of exploring approaches and settings for improving literacy regarding gene-environment contributors to podoconiosis as a model for other preventable health conditions.

Methods:This study explored youth's mental model using qualitative methods. Data were collected from rural youth in Southern Ethiopia, Woliata Zone, in December 2015. Two focus group discussions and 30 in-depth interviews were conducted with affected and non-affected youth. Data were transcribed and verbatim translated from the local languages into English. The transcribed data were coded and analyzed using qualitative software, from which key nodes were identified and youth mental model constructed.

Results :Findings indicated that the youth harbor various misconceptions about the etiology and prevention of the disease. The study found a number of misconceptions related to the cause of podoconiosis among non-affected youth. The results showed that some youth overemphasize genetics as a sole determinants of podoconiosis and this resulted in a belief that the occurrence of the disease in affected families is inevitable. Moreover, contagion (blood contact) and breast feeding were understood as genetic factors for the transmission of the disease. The study also documented wrong perceptions about the impact of the environment on podoconiosis. We also found better understanding among affected youth on the concept of preventability regardless of the type of cause, which are believed to stem from the interaction with health care providers in the community.

Conclusion :Evaluating these findings with expert's model and quantitative data is paramount to attest knowledge gap and explore suitable settings for improving literacy regarding gene*environment contributors to podoconiosis.

Mots clés /keywords :

Gene, Environment, podoconiosis, causes, prevention, youth

Auteur présentateur / presenting author:

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PY04   DISTRIBUTION OF SICKLE CELL DISEASE-RELATED GENETIC MARKERS IN MALARIA-FREE SUB-SAHARAN AFRICAN COUNTRIES

Auteurs /Authors :

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Introduction :Sickle Cell Disease (SCD) is a monogenic disease. SCD occurs mostly in Sub-Sahara Africa and co-occurs where malaria is endemic. The β-gene has five haplotypes; Bantu, Benin, Senegal, Cameroon and Indian - Arab haplotypes. There is an unusual combination of restriction polymorphisms which is called atypical haplotypes, different to the defined haplotypes by the change of one or more restriction sites.

Goals :To calculate the frequency of SCD-related genetic markers (SCD mutation, haplotype) in the cohorts from malaria-free countries (South Africa, Zimbabwe and Malawi).

Methods:Molecular genotyping of the SCD mutation involved amplification of a 380 bp segment of followed by restriction enzyme analysis using restriction endonuclease Del 1. Restriction fragment length polymorphism (RFLP)-PCR was also used to genotype and describe the haplotype background in the β-globin gene cluster from Xhosa (South Africa), Shona (Zimbabwe) and Chewa (Malawi), respectively.

Results :For SCD diagnosis, all South African samples were homozygous unaffected (HbAA); Zimbabwean cohort 35 (89.74%) were HbAA and 4 (10.26%) heterozygous (HbAS); and Malawian cohort 39 (84.78%) were HbAA and 7 (15.23%) heterozygous HbAS. For the SCD haplotype background, a high frequency of atypical haplotype (SA = 53 (66.25%), ZIM = 42 (65.6%), MAL = 36 (51.5%) was observed in all cohorts. Benin haplotype had the second highest frequency (SA = 15 (18.75%), ZIM = 8 (12.5%), MAL = 19 (27.25%)).

Conclusion : the Frequency of sickle mutation is highest in malaria endemic regions due to positive selection and the partial resistance to the Plasmodium falciparum. Furthermore, the conservation of the haplotype background is associated with regions of high SCD burden and thus malaria as well. Understanding SCD genetic markers in the absence of malaria could inform the global SCD community on the importance of gene/environment interaction, positive selection of traits and hopefully the clinical care for SCD in malaria-endemic and free regions

Mots clés /keywords :

Sickle Cell Disease, Haplotype, Polymormiphism, Monogenic, Plasmodium falciparum and β-globin gene

Auteur présentateur / presenting author:

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PY05   UTILISATION DE LA PCR DANS LE DIAGNOSTIC DES CANCERS DES VOIES AERO-

DIGESTIVES SUPERIEURES : ETUDE PRELIMINAIRE A PROPOS DE 90 CAS

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INTRODUCTION
Les carcinomes des voies aérodigestives supérieures (VADS) occupent la sixième place mondiale. L'HPV représente un « nouveau » FDR connu. Cependant, les carcinomes HPV+ ne présentent pas de particularités histologiques d'où l'intérêt d'une analyse biomoléculaire. L'objectif de cette étude était d'évaluer l'utilisation de la PCR pour la recherche de l'HPV dans les carcinomes des VADS.
METHODOLOGIE
Sur une période de 18 mois (1er Janvier 2012- 30 Juin 2014), les blocs parrafinés des cas de carcinomes des VADS confirmés histologiquement au Sénégal étaient envoyés à Paris pour la recherche d'HPV. Le déparrafinage et l'extraction de l'ADN étaient réalisés par le kit NucleoSpin Tissue®. Les techniques de PCR « consensus » avec les amorces « GP5+/GP6+ » et de PCR « spécifique » pour les HPV 6, 11, 16, 18, 33 et 45 étaient utilisées.
RESULTATS
Sur 90 cas inclus, la technique de PCR était concluante dans 54 cas (60%). Le HPV était retrouvé dans sept cas soit une prévalence de 13%. Le génotypage était possible dans six cas (85,7%). Il s'agissait d'un HPV 16 dans cinq cas (71,4%) et d'un cas d'HPV 33 (14,3%). Les cinq cas d'HPV 16 étaient associés au carcinome hypopharyngé, l'HPV 33 de même que l'HPV « indéterminé » étaient retrouvés dans la cavité orale. La localisation hypopharyngée de l'HPV 16 était statistiquement significative (p=0,04). Les patients ayant des carcinomes des VADS HPV+ avaient un âge médian de 42 ans contre 49 ans pour les patients HPV-. Le carcinome épidermoïde était l'unique type histologique retrouvé. Les carcinomes HPV+ ne présentaient aucun aspect histologique spécifique.
CONCLUSION
La technique de PCR donne des résultats satisfaisants même sur les blocs paraffinés. L'HPV constitue un réel FDR des carcinomes des VADS. L'HPV 16 est le plus fréquent et de localisation hypopharyngée.

Mots clés /keywords :
Human Papilloma Virus, PCR, Carcinome, Voies aéro-digestives supérieures, Sénégal
Type de présentation / presentation mode : poster

Auteur présentateur / presenting author:

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PY06   The Associationof Tumour Necrosis Factor-alpha Single Nucleotide Polymorphisms

(TNFα-SNPs) with Breast Cancer in Ibadan, Nigeria.

Auteurs /Authors :

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Introduction :Breast Cancer remains a global health problem, therefore its early detection using good diagnostic biomarkers are important for a successful treatment and prevention. Tumour necrosis factor alpha Single Nucleotide Polymorphisms (TNFαSNPs) have been implicated in the presentation of some human cancers.

Goals :This pilot study was carried out to determine the role of TNFα SNPs in breast cancer amongst Nigerian women,for its possible use as biomarkers in early detection of breast cancer.

Methods:A total of 75 participants (50 breast cancer patients and 25 controls) were recruited from the University College Hospital, Ibadan for this study. Blood samples (5ml) were collected from participants and DNA was extracted using Qiagen DNA purification kit. Genotyping of TNFα SNPs from the purified DNA in breast cancer and control samples were carried out using Polymerase Chain Reaction - Touch down (PCR-TD) technique with allele specific primers.

Results: The results showed that frequencies of TNFα SNPs varied between control and breast cancer patients. Breast cancer patients showed significant increase in allele frequencies of TNFα-1032C and 859T while allele frequencies of TNFα-488A/238G/308G and 308A were significantly lower amongst breast cancer patients when compared to controls ($p<0.05$), indicating a positive and negative association of specific TNFα SNPs with breast cancer respectively.

Conclusion : Specific genotypic variations in TNFα-SNPs might be a potential risk factor for breast cancer among the Nigerian population, raising the possibility of their use as biomarkers, for early risk indicators, in the diagnosis of breast cancer in Nigeria.

Mots clés /keywords :

Breast cancer, TNFα SNPs , Biomarkers, Women, Nigeria

Auteur présentateur / presenting author:

Dr ALAMUKII NANFIZAT ABIKET

UNIVERSITY OF IBADAN, NIGERIA

PY07   VARIATION IN THE CYP2D6 GENE MAY PREDICT AMITRIPTYLINE EFFICACY IN PATIENTS WITH DIABETIC PERIPHERAL NEUROPATHY

Auteurs /Authors :

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Introduction: Diabetes is a public health problem worldwide with greater prevalence in low and middle-income countries. In South Africa, 2.6 million people are living with diabetes. One of the most common complications of diabetes is peripheral neuropathy. Amitriptyline is the drug of choice for treatment of painful peripheral neuropathy in the South African public health sector. This drug is metabolized by the CYP2D6 and CYP2C19 enzymes. The CYP2D6 gene is highly polymorphic and is primarily responsible for amitriptyline metabolism.

Goals: The present study was conducted on diabetic peripheral neuropathy (DPN) patients to determine if variation in CYP2D6 could explain amitriptyline efficacy and the occurrence of adverse drug reactions (ADRs).

Methods: Thirty-one participants currently on amitriptyline treatment for the management of painful DPN were randomly recruited. The CYP2D6 gene sequences were determined using Sanger sequencing. Predicted phenotypes were assigned from the genotypic data using activity scores, which was compared to observed phenotypes reported by study participants in a seven-day questionnaire.

Results: A decrease in ADRs and drug efficacy appeared to be correlated with an increase in predicted metabolic activity of CYP2D6.

Conclusion: The findings of this study reflect a potentially clinically relevant genotype-phenotype correlation. These encouraging results will be validated in a larger and well-characterized study population. Based on power calculations, a minimum of 120 DPN patients will be assessed for clinical, demographic and behavioral variables. Variation present in pharmacogenes will be investigated using whole exome sequencing and comparisons will be made to establish phenotype-genotype correlation.

Mots clés /keywords :

Amitriptyline; diabetic peripheral neuropathy; pharmacogenomics; whole exome sequencing

Auteur présentateur / presenting author:

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Department of Immunology, and Institute of Cellular and Molecular Medicine

PY08   **Genetic variation in CYP4F2 and VKORC1 -1639: Pharmacogenomics**
                            implications for response to warfarin

Auteurs /Authors :

Zinhle Cindi, Keleabetswe Mpye, Nstekhe Mphiko, Edson Makambwa, Miguel Larceda, Collet Dandara

Introduction :Warfarin is the most commonly used drug in the management of thromboembolic disease. However, there is a huge variability in the time, number of doses or starting doses for patients to achieve the required international normalised ratio (INR) which is compounded by a narrow therapeutic index. Many genetic-association studies have reported on European and Asian populations which have led to the designing of specific algorithms that are now being used to assist in warfarin dosing.However, very few or no studies have looked at the pharmacogenetics of warfarin in African populations.

Goals : This study was therefore carried out to investigate the role of genetic variation in CYP4F2 and VKORC1 on the time it takes to reach INR among South African Mixed Ancestry and Black African patients.

Methods:DNA was extracted from 383 participants and subsequently genotyped using PCR/RFLP for the CYP4F2 c.1347 (V433M) (rs2108622) and the VKORC1 g.-1639 (rs9923231) SNPs. The genetic variation was correlated with the time patients took to reach INR.

Results : The distribution of CYP4F2 c.1347C>T genotypes were as follows; C/C (0.49), C/T (0.36) and T/T (0.15). The VKORC1 g.-1639G>A presented with the following genotypes; G/G (0.57), G/A (0.35) and A/A (0.08). We report minor allele frequency of 30% and 25% for CYP4F2 c.1347T and VKORC1 g.-1639A, respectively. The analysis on the effects of genetic variants on time to reach therapeutic index will be presented at the conference.

Conclusion: CYP4F2 c.1347T was present at a frequency of 25% in the study cohort which is similar to observations among Asians but lower than observations in Europeans. The VKORC1 g.-1639A presented with a frequency of 8% which is lower than observed in Asians and higher to Europeans. Both variants are associated with need for reduced doses of warfarin to inhibit the actions of the vitamin K reductase complex. Thus, the distribution of the genetic variants affecting warfarin metabolism for this population, differ from other populations.

Mots clés /keywords :

Warfarin, pharmacogenomics, INR,

Auteur présentateur / presenting author:

Dr Zinhle Cindi

Auteurs /Authors :

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Introduction :MicroRNAs (miRNAs) are involved in carcinogenesis and tumor progression by regulating post-transcriptional gene expression. However, the miRNA regulatory networks in CRC are far from being fully understood.

Goals :The objective of this study is to identify the colorectal cancer (CRC) specific miRNAs and their target mRNAs using bioinformatic approaches.

Methods:depending on the fact that 80% of the miRNAs are located in the 3UTR region, all 3 UTR regions were analyzed using polymiRTS database 0.2 from whole exome sequence of CRC hereditary family (2 cancers, 3 controls). We used another approach in which dysfunctional genes were analyzed for regulatory miRNA using MiRwak2.0. For potential functional annotation DIANA miRPath v.2.0 was used, in addition to CoMeTA for pathway analysis.

Results :Two miRNA were found to be dysfunctional as compared to normal controls (has-miR- 130a-5p, has-miR23a-3p). has-miR29 was identified as a candidate based on MiRwak 2.0. and association with CRC using DIANA tool (P value =0.0018). Interestingly, the Osteoclast differentiation (OD) signaling pathway showed the highest (p value= 0.0001). Association between the panel and several cancers pathways was also observed, the highest Acute myeloid leukemia (p value= 0.0006).

Conclusion :Considering the complexity of cancer, and the exome analysis of members of this family reported earlier miRNA appear to add yet a different layer of regulation that complements and intersects with other layers and networks towards the ultimate carcinogenesis goals and phenotypes.

Mots clés /keywords :

MicroRNAs, Target mRNAs, Colorectal cancer

Auteur présentateur / presenting author:

Dr Ommniyah Elfatih Yousif

PY10   **Contrasting evolutionary patterns of protein coding genes of Plasmodium vivax,**

depicts a complex and deep history of the parasite

Auteurs /Authors :

Musab.M .Albsheer (1); Basher Salim (2); Mzamil Mahdi Abdel Hamide(2); Muntaser E.Ibrahim (3)

Introduction

Plasmodium vivax is a protozoan parasite with an extensive worldwide America and Asia distribution, being highly prevalent and emerged recently in Sudan and Ethiopia   and in Sudan considered as endemic country and recent studies suggests that these parasites have unique biological and genetic features. The msp1 gene has shown high rate of nucleotide substitutions, deletions, insertions, and its mosaic structure reveals frequent events of recombination, may be between highly divergent parasite isolates.

Goals :

To elucidate the genetic diversity, natural selection and evolutionary relationships of P. vivax in samples collected from central and eastern Sudan targeting PvCSP and icb5-6 fragment of the MSP1 gene

Methods:

A total of 200 P.vivax-infected blood samples collected from patients in Sudan were used CSP-PCR and RFLP to determine the mixed genotype infections (vk210 and vk247) if any. Were select 24 samples for region flanking PvMSP1-icb5-6 all amplified by PCR and sequenced. To carry out detailed nucleotide sequence analysis, the icb5-6 fragment was divided into five subfragments (5c, sV1, M, sV2 and 3C .The polymorphic characteristic, natural selection and minimum spinning haplotypes network were analyzed using the DnaSP v.5.0 ,MEGA5, Arlequine and HapStar programs.

Results and discussion:

From a total 105 haplotypes worldwide (80 in MSP and 25 in CSP)Sudanese parasites had 14 haplotypes 12 in msp1 icb5-6 of which 10 were distinct and two shared, one with Thailand and the other with Bangladesh, while PvCSP had 2 haplotypes were vk210 one distinct and the second shared with Ethiopia and India. PvCSP haplotypes seems to have appeared due to recent expansion while the MSP1 icb5-6 subfragment sV1 and M have more haplotypes diversity suggesting the region to be under balancing selection and compatible with Tajema D and Fu values.

conclusion:

Recombination may play role in resulting genetic diversity. These data will be discussed with implication to the origin, evolution and dispersal of the parasite

Mots clés /keywords :

Plasmodium vivax, Sudan, Circumsporozoite protein, Merozoite surface protein1,Haplotype network ,Genetic polymorphism , evolution ,Balancing selection.

Auteur présentateur / presenting author:

Dr Musab Mohamad Mohamad Ali Albsheer

PY11   **Identifying ancestral European populations for coloured and Afrikaner people of**

Southern Africa using genome-wide SNP data

Auteurs /Authors :

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1-University of Oxford

2-University of the Free State

Introduction :

The 'coloured' people of South Africa are a multi-way admixed population which arose following the arrival of colonial Europe in South Africa, they are admixed between the early European settlers, indigenous KhoeSan people and the slave populations of the Cape.The Afrikaner people have a somewhat similar story of emergence but were socially and economically separated as well as supplemented by immigrants from across Europe. Both groups make up a substantial part of the Southern African population and have a some-what tied history. Work addressing the ancestry of the coloured people has been conducted though samples were largely restricted to the Western parts of the region and only addressed specific local ancestry from South and South-East Asia. No such work has been done on the Afrikaner people. Considering the diversity in the newly arriving people in Southern Africa over the last ~1000 years and the geographic tiering in which people encountered and interacted, we predict that there would be clear geographic structure in ancestry for both Afrikaner and coloured populations across the region.

Goals :

We will map genetic variation in ancestry across both ethnic groups across the region. We will also attempt to identify any regional structure to the European ancestry in both populations.

Methods:

We will samples self-identified Afrikaner and coloured people from Southern Africa (South Africa, Botswana, Lesotho, Zimbabwe and Namibia) based on population age, geographic position and the history of the population. Samples will be genotyped for high density genome-wide SNP data and analysed to identify local ancestry and geographic structure to the local ancestry within each population.

Mots clés /keywords :

Southern Africa; Admixture; Genome-wide SNP; Afrikaner; Dutch East-India Company; Slave-trade; Indigenous people

Auteur présentateur / presenting author:

Dr Ryan Daniels

Zoology Department, University of Oxford

PY12   **Willingness to have genetic testing for breast cancer among female bankers and lecturers in Ibadan, Nigeria**

Auteurs /Authors :

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Introduction :

Mutation in some breast cancer genes (BRCA1/2) is associated with earlier age onset and higher mortality of breast cancer (BC) among African women. A high prevalence of BRCA 1/2 mutation was reported among some BC patients in Ibadan. Genetic testing services for breast cancer is well established in the developed countries compared to African populations that bears a disproportionate burden of BC.

Goals :This study examined the knowledge of lecturers and bankers about BC genetics and their willingness to utilize the genetic testing services when it is made available in Nigeria.

Methods:A cross sectional study was conducted among 165 lecturers and 189 bankers. Data on socio-demographic characteristics, knowledge about breast cancer genetics and willingness to have genetic testing for breast cancer were collected using a pretested self-administered questionnaire. Factors associated with knowledge of BC genetics and willingness to have BC genetic testing were tested using the Chi-Square test and binary logistic regression.

Results :The mean age of the respondents was 34.9 years (SD = 10.9). About 60.2% of the respondents were currently married. Most respondents had limited knowledge of breast cancer risk factors (85.0%) and breast cancer genetics (84.7%). The proportion of women willing to have genetic testing for breast cancer was 87.3%. Health care access (OR = 2.35, 95% CI, 1.07 - 5.13), religion (OR = 3.51, 95% CI, 1.03 – 11.92) and perceived personal risk if a close relative had breast cancer (OR = 2.31, 95% CI, 1.05 – 5.08) independently predicted willingness to get tested.

Conclusion :There was high level of willingness to utilize genetic testing for BC despite limited knowledge about breast cancer genetics. Promotion of BC genetics education as well as efforts to make the BC genetic testing services available in Nigeria at reduced cost remains essential.

Mots clés /keywords :

Genetic testing, BRCA 1/2, Breast Cancer, Nigeria.

Auteur présentateur / presenting author:

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PY13   **Aromatic networks in DNA and proteins suggest biophysical targets for**

degenerative and infectious disease

Auteurs /Authors :

Kurian P(1,2); Mason T(1,3); Craddock TJA(4); Abbas M(1); Dunston G(1)

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4 – Nova Southeastern University

Introduction: Kurian et al. [J.Theor.Bio.(2016)] have shown that quantum coherent energy transport may be implicated in the coordination of DNA double-strand breaks (DSBs). A hallmark of quantum transport is palindromic DNA sequence, which forms due to tandem or inverted genomic repeats. Such palindromic complexes are utilized in viral integration, immunodiversity, and meiotic recombination, and this mirror symmetry can be conserved evolutionarily in a sequence-independent manner. Restriction endonuclease experiments confirm that synchronized DSBs cease when enzyme-DNA symmetry is violated. Biopolymers with similar induced-dipole networks exhibit comparable quantum coherent behavior when excited by ultraviolet photons [J.R.Soc.Interface(2014)]. Goals: We seek to establish the quantum nature of genomics and biology--how collective electronic phenomena can produce physiological-scale effects. This new paradigm can inform understanding of degenerative and infectious diseases, specifically in populations of African descent. Here we present preliminary theoretical and computational data on quantum effects from 1)palindromic symmetries in infectious disease, 2)microtubule stabilization in neurodegeneration, and 3)serotonin receptors in inflammatory responses. Methods: Aromatic compounds--cyclic, planar molecules whose delocalized pi electrons confer unusual stability and non-reactivity--are ubiquitous in DNA, RNA, and protein. We examined aromatic lattices in 1)DNA base-pair sequences, 2)tryptophan networks in microtubules, and 3)tryptophan networks in serotonin receptors for the feasibility of quantum coherence and implications for biological function. Results: Coherent excitations in aromatic lattices of DNA and proteins promote global stabilization, synchronization, and/or synergy of the human systems above. Conclusion: These studies address critical barriers to progress in the fields of degenerative and infectious disease by motivating biophysical targets for interventions that affect genomic regulation, cytoskeletal signaling, and other coherent cellular processes.

Mots clés /keywords :

biophysics;coherence;microtubule;amino;nucleotide;DNA;genome;ultraviolet;UV;biophoton;Alzheimer's;aromatic;tryptophan;cytoskeleton;tubulin;cog*;neuro*

Auteur présentateur / presenting author:

Dr P. Kurian

National Human Genome Center, Howard University College of Medicine

PY14   Caractérisation moléculaire de souches de Salmonella Grumpensis isolées d'infections nosocomiales néonatales à Dakar

Auteurs /Authors :

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Les infections nosocomiales sont fréquentes en néonatalogie et peuvent engager le pronostic vital. L'objectif principal de ce travail était de caractériser au plan moléculaire les souches de S. Grumpensis isolées d'une épidémie d'infection nosocomiale dans l'Unité de Néonatologie du Centre Hospitalier Universitaire de Dakar, Sénégal

L'étude portait sur 17 souches de Salmonella Grumpensis multi-résistantes isolées entre Mars et Mai 2011. L'identification des souches a été réalisée par biotypie et le sérotypage, selon le schéma de KW. L'étude de la sensibilité aux ABT a été réalisée par la technique de diffusion en milieu gélosé selon les recommandations du CA-SFM 2010. Le typage moléculaire des isolats a été réalisé par PFGE.

La détection des intégrons et la recherche des gènes de résistance (bêta-lactamines, quinolones et tétracyclines) a été réalisée par PCR. L'étude de la transférabilité du matériel génétique a été effectuée par la conjugaison bactérienne.

Le sérotypage a permis d'identifier le sérotype Grumpensis. L'ABG a montré un profil homogène de résistance aux ABT; 15 souches sur 17 étaient productrices BLSE. La PFGE a montré que ces isolats appartiennent à un pulsotype unique et confirme le caractère épidémique de la souche. Seuls les intégrons de classe 1 ont été détectés : 14 sur 17 (82,35%), leur caractérisation a permis de retrouver la cassette aadA1. Au total nous avons détectés des gènes de résistance aux aminopénicillines, aux céphalosporines (OXA-1, SHV-1, TEM-1, CTX-M1, CTX-M2, CTX-M9) et carbapénèmes. Les gènes qnrB et qnrS, codant la résistance aux quinolones, ont été respectivement retrouvés chez 13 et 10 souches. Toutes les souches résistaient aux tétracyclines. Seul le gène TetA a été retrouvé chez 11 souches (64,70%). La conjugaison bactérienne a montré que le support de la résistance était plasmidique.

L'émergence de souches de Salmonella multi-résistantes est une réalité au Sénégal, il faudra en priorité rationnaliser l'utilisation des antibiotiques tant en Médecine humaine que vétérinaire.

Mots clés /keywords :

Salmonella, Infections nosocomiales, multi-résistance

Auteur présentateur / presenting author:

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Laboratoire bactériologie-virologie UCAD/Albert Royer

PY15   **Meta-analysis of exome-array studies in Africans identifies novel loci**

associated with lipid traits

Auteurs /Authors :

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Introduction: Genetic loci associated with lipid traits identified using genome-wide association studies, mainly in European ancestry populations, have provided insights into pathogenesis of dyslipidemia and cardiomatabolic complications. Recent replication efforts in African populations succeeded in replicating only about one-third of these loci, indicating the need for multi-ethnic studies. Here we studied the genetic basis of lipid traits in African populations.

Goals: To identify genetic loci associated with lipid traits and to test replication of previously reported lipid loci in African ancestry populations.

Methods: We performed meta-analysis of serum lipids (HDL, LDL, and triglycerides (TG)) from exome-array studies of participants of the Africa America Diabetes Mellitus study (n=4218 west and east Africans) and the Howard University Family Study (n=1789 African Americans), genotyped on the Illumina HumanExome BeadChip v1.0 and the Affymetrix Axiom Exome 319® Array. Single-variant and gene-based analyses were performed in each cohort followed by meta-analyses.

Results: Five missense variants showed Bonferroni-corrected statistically significant association with lipid levels, of which four were novel (HDL: CETP, $P=7.78 \times 10^{-18}$; LDL: APOE, $P=2.41 \times 10^{-27}$ and KLK9 $P=5.92 \times 10^{-7}$; TG: APOA5, $P=1.89 \times 10^{-7}$ and CDC42BPB, $P=3.96 \times 10^{-7}$). Two of these variants are rare or absent in non-African ancestry populations. Two gene-sets showed significant association with HDL and TG (CETP, $P=3.21 \times 10^{-9}$; NUP133, $P=6.18 \times 10^{-7}$). Of a total of 15 exonic variants associated with the three lipid traits in previously published studies, 6 variants showed directionally consistent and statistically significant replication in our sample ($P<0.05$).

Conclusion: Large-scale meta-analyses of exome-array studies in African populations identified novel loci associated with dyslipidemia traits. Both ancestry-specific and multi-ethnic genetic loci are involved in pathogenesis of dyslipidemia with implications for cardiometabolic disorders.

Mots clés /keywords :

exome, dyslipidemia, African ancestry, genetic-epidemiology

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PY16 Apport de la cytogénétique chez un patient présentant un

syndrome myéloprolifératif atypique

Auteurs /Authors :

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Introduction :Les syndromes myéloprolifératif (SMP) sans chromosome Philadelphie constituent un groupe hétérogène qui regroupe les syndromes myélodysplasiques (SMD) et les SMD- SMP. Les anomalies cytogénétiques sont peu fréquentes (25-30%) et sans spécificité. La mutation de SETBP1 située en 18q21.1 est décrite au cours des SMP atypiques. Nous en rapportons une observation.

Observation : Un patient guinéen, âgé de 50 ans a consulté le 03 Avril 2014, pour amaigrissement, une fièvre vespérale et une asthénie physique, évoluant depuis 1 mois. Il n'a pas de splénomégalie.

L'hémogramme a montré une hyperleucocytose à 153,2G/L avec prédominance de neutrophiles (49%), une myélémie polymorphe (métamyélocytes : 10%, myélocytes : 17%, promyélocytes : 14%, érythroblastes 1%), sans anémie (Hémoglobine : 12,6g/dl) ni thrombopénie (208 G/L). Le myélogramme a confirmé l'hyperplasie granuleuse sans hiatus, suspecte de la LMC. Le caryotypage et la FISH n'ont montré ni le chromosome Philadelphie ni le transcrit BCR/Abelson.[(47,XY,+8[15]/46XY [5] : le diagnostic de LMC est éliminé.

Au mois de novembre 2015, le patient consulte à l'institut Bergonié de Bordeaux en France où les analyses cytogénétiques complémentaires n'ont pas permis de retenir les hypothèses de SMP classiques devant : la négativité des mutations V617F de JAK2 (1%), CALR exon 9 (3%) et MPL exon 10 (6%).

La positivité de la mutation de SETBP1 (NM_015559, exon 4), C.2612T> C, p.Ile871Thr a permis de retenir une SMP atyipque. Sous Hydroxyurée, le patient est en rémission hématologique complète avec un recul de 22 mois.

 Conclusion : Ce tableau clinique rend compte de la difficulté diagnostique des SMP atypiques dans nos régions. La mutation de SETBP1 est mutuellement exclusive de JAK2 et de TET2. Elle est décrite plus dans la LMC atypique (31,7%) qu'au cours des SMD-SMP non classables (2,3%) cadre nosologique dans lequel rentre notre cas clinique. L'association avec la trisomie 8 est classique au cours des SMP.

Mots clés /keywords :

Syndrome myeloproliferatif atipique, mutation de SETBP1.

Auteur présentateur / presenting author:

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Introduction: African populations are genetically characterized by unique ethnic heterogeneity and extremely short Linkage Disequilibrium (LD) patterns that make large-scale Genome Wide Association Studies (GWAS) highly prone to confounding by population structure. Despite extensive development during the last decade, mixed model approaches suffer from an expensive computational complexity, $O(MN2)$, and vary in their effectiveness to ascertainment bias in the study sample, besides their implicit assumption of the normality of the phenotype.

These reasons motivated the exploration of Particle Swarm Optimization (PSO) as an effective simple meta-heuristic for addressing these issues taking advantage of its cognitive and social properties, as well as its inherent parallel nature, especially that it doesn't require prior assumptions about the distribution or dimensionality of the data. Successful similar examples of using PSO include micro-array data clustering, and research suggests its feasibility for large-scale datasets. Yet, it has been modestly employed in the context of GWAS analysis, almost solely so for deducing SNP-SNP interactions in breast cancer studies.

Goals:
1.To devise a PSO based algorithm for clustering large scale GWAS data based on ancestry, and benchmark its performance;
2.To extend the developed algorithm such that it captures both genetic differences as well as specific cohort differences in generating the association signal between the single nucleotide polymorphism (SNPs) and phenotypes.

Methods: The hypothesis presented here is that the use of data mining approaches (e.g. PSO) could be helpful in extracting the association signal on one hand, and also in correcting for the hidden correlations due to structure and relatedness in the sample on the other hand. For this reason, research begins by a proof of principle employing PSO for inferring the ancestry and clustering of simulated datasets without explicit model assumptions. Comparisons are made with similar approaches in terms of accuracy, relevance of the extracted feature set, cost

Mots clés /keywords :

GWAS, PSO, clustering, population stratification

Auteur présentateur / presenting author:

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PY18   **ETUDE DU CODON 72 DU GENE p53 COMME FACTEUR DE RISQUE**

DANS LES CANCERS DE LA CAVITE BUCCALE AU SENEGAL

Auteurs /Authors :

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Introduction : Les cancers de la cavité buccale sont classés au sixième rang des cancers dans le monde. Au Sénégal l'incidence n'est pas bien connue. Parmi les facteurs impliqués dans la carcinogénèse, les mutations du gène suppresseur de tumeur p53 ont été très étudiées chez les populations asiatiques, américaines et européennes. Peu d'études ont été réalisées en Afrique.

Objectifs / goals : Le but de ce travail était d'étudier le rôle du polymorphisme du codon 72 du gène p53 (Proline/Arginine) dans la survenue des carcinomes épidermoïdes de la cavité buccale au Sénégal.

Méthodologie / Method: Après un consentement libre et éclairé, 60 patients atteints de cancers de la cavité buccale ont été recrutés au niveau du service de Stomatologie et de Chirurgie Maxillo-faciale de l'hôpital Aristide Le Dantec. Pour chaque patient un prélèvement de sang, une biopsie de la tumeur et un lavage buccale ont été pratiqués.

Le génotypage du polymorphisme du codon 72 du gène p53 a été réalisé par PCR-RFLP chez les patients et des témoins indemnes de tout cancer, recrutés dans la population générale. Une étude d'association par régression logistique a permis de déterminer le risque relatif du codon 72 du gène p53 dans le développement de ces cancers.

Résultats / Results : Les résultats obtenus ont montré que la présence de l'allèle arginine du codon 72 n'augmentait pas le risque de développer un cancer de la cavité buccale dans notre population d'étude. Nous n'avons également retrouvé aucune association entre le codon 72 et les caractéristiques histologiques des tumeurs.

Conclusion : L'allèle arginine du codon 72 ne prédispose pas aux cancers de la cavité buccale dans notre population d'étude. Cependant le screening de la totalité du gène p53 sur une cohorte plus importante devrait permettre de statuer sur l'implication de ce gène dans la carcinogénèse buccale.

Mots clés /keywords :

codon 72 gène p53 ; cancers de la cavité buccale ; allèle arginine

Auteur présentateur / presenting author:

Mr(s) Seydi Abdoul BA, GERC

IMPLICATION DES MUTATIONS DU CYTOCHROME B DANS L'EVOLUTION DES TUMEURS BENIGNES DU SEIN CHEZ LES FEMMES SENEGALAISES

Auteurs /Authors :

Faye J.L (1) ; Mbaye F (1,2) ; Doupa D (1) ; Ka S (3) ; Dem A (3) ; Fall M (1); Ndiaye R (4) ; Sembène M (1,2)

Introduction : la compréhension du processus mutation-sélection qui influence la variabilité du génome humain est un sujet d'intérêt fondamental en génétique médicale. Nous avons focalisé l'essentiel de notre étude à l'influence de la sélection sur la variabilité génétique du Cytochrome b dans l'évolution des tumeurs bénignes du sein. Ceci nous permettra de mieux comprendre la diversité génétique des tissus et à terme de faciliter l'identification des mutations impliquées dans la tumorogenèse.

Objectifs / goals :l'objectif de cette étude est de déterminer l'implication des altérations génétiques du Cytochrome b dans l'évolution des tumeurs bénignes du sein chez les femmes sénégalaises.

Méthodologie / Method: nous avons, par PCR-séquençage, rechercher des mutations du Cytochrome b chez un groupe de tumeurs bénignes et un groupe de tissus sains servant de témoin. Par la suite, nous avons évalué l'importance de la variabilité génétique entre les deux groupes et déterminé l'effet de la sélection naturelle sur la variabilité observée.

Résultats / Results : l'analyse de la variabilité génétique du Cytochrome b a permis d'identifier six mutations (A15824G, C15849T, C15839T, C15849A, T15519C et G15521A) présentes uniquement au niveau des tumeurs bénignes avec des différences significatives. Par ailleurs, l'analyse de signature de sélection a indiqué que ces mutations sont sous sélection positive. Ces observations témoignent de l'implication et de l'importance fonctionnelle des mutations du Cytochrome b dans l'évolution des tumeurs bénignes du sein chez les femmes sénégalaises.

Conclusion : cette étude ayant un rôle prédictif, nos résultats ouvrent la voie à de futures études biochimiques, protéomiques et cliniques afin de déterminer l'effet de ces mutations dans le métabolisme énergétique des cellules tumorales pour une optimisation de la prise en charge des patients et de leurs suivis cliniques.

Mots clés /keywords :

tumeurs, bénignes, sein, Cytochrome b, variabilité, évolution, Sénégal.

Auteur présentateur / presenting author:

Dr Jean Luc FAYE

Université Cheikh Anta Diop de Dakar

PY20 **LES TUMEURS BENIGNES DU SEIN CHEZ LES FEMMES SENEGALAISES :**

DIVERSITE ET EVOLUTION GENETIQUE DE LA D-LOOP

Auteurs /Authors :

Badji M.N. (1) ; Mbaye F (1, 2) ; Doupa D (1) ; Ka S (3) ; Fall M (1) ; Ndiaye R (4) ; Dem A (3) ; Sembène M (1, 2)

Introduction :en Afrique subsaharienne, comme au Sénégal, le cancer du sein est le deuxième après celui du col de l'utérus chez la femme. Toutefois, bien que l'essentiel des études sur la pathologie mammaire concerne le cancer, l'écrasante majorité des lésions mammaires, palpables ou non sont bénignes et certaines d'entre elles peuvent devenir cancéreuses.

Objectifs / goals : ce travail de recherche est ainsi réalisé afin de mieux comprendre l'impact de la diversité et de l'évolution génétique de la D-Loop dans les lésions bénignes du sein chez les femmes sénégalaises.

Méthodologie / Method:

la variabilité de la D-Loop a été étudiée par PCR-Séquençage, chez trente patientes atteintes d'une tumeur bénigne du sein et prises en charge à l'institut Joliot Curie de l'hôpital Aristide le Dantec en comparaison avec un groupe de témoins. La distribution de la fréquence des variants entre Témoins et Tumeurs bénignes a été étudiée selon le test exact de Fisher avec le logiciel MitoTool v. 1.1.2. Les séquences ont été au préalable comparées à la version révisée de la Séquence de Référence de Cambridge (rCRS).

Résultats / Results :

les résultats ont révélé une présence significative de variants spécifiques aux tissus bénins du sein. La mutation G247A serait impliquée à une augmentation du risque. Les patientes d'haplogroupe mitochondrial L seraient significativement plus susceptibles de contracter ces lésions bénignes du sein. Une corrélation significative a été associée aux haplotypes C309CC et 7CT6C de la D310, qui constitueraient respectivement des groupes à risque accru et susceptible à la contraction de lésions bénignes du sein.

Conclusion :

l'ensemble de ces résultats a permis d'avoir une vision globale sur l'influence des mutations pathogéniques sur la diversité et l'évolution génétique de la D-Loop observées chez les patientes sénégalaises atteintes d'une tumeur bénigne du sein.

Mots clés /keywords :

tumeur, bénigne, sein, D-Loop, diversité, évolution, Sénégal.

Auteur présentateur / presenting author:

Dr Marc Noel BADJI

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PY21   **Preliminary investigation of the transmission of tuberculosis between**

farmers and their cattle in smallholder farms in northwest Ethiopia

Auteurs /Authors :

Nuru A(1,4); Mamo G(3); Zewdie A(1); Mulat Y(5); Yitayew G(2); Medhin G(1); Pieper R(6) Ameni G(1)

1-Aklilu Lemma Institute of Pathobiology 2-Bahir Dar Regional Health Research Laboratory Centre 3-College of Veterinary Medicine and Agriculture 4-Faculty of Veterinary Medicine 5-Felegehiwot Comprehensive Specialized Hospital 6-J. Craig Venter Institute

Introduction : The feeding habits and close physical contact that prevails between Ethiopian farmers and their cattle promote the transmission of tuberculosis (TB) between the farmers and their cattle.

Goals :investigate the transmission of TB between farmers and their livestock in smallholder farms in and around Bahir Dar, northwestern Ethiopia

Methods:Sixty eight human TB lymphadenitis (TBLN) cases visiting Felegehiwot Comprehensive Specialized Hospital in Bahir Dar City and 660 (330 owned by households with TB cases and 330 owned by TB free households) cattle were investigated. Culturing of fine needle aspirate, comparative intradermal tuberculin (CIDT) testing, interviewer administer questionnaire and spoligotyping were used to conduct this study. In addition, SITVIT2 database and the online tool "Run TB-Lineage" were explored to determine the shared international spoligotype (SIT) number and lineages/sub-lineages

Results :This study did not show the transmission of TB between farmers and their cattle in the smallholder farms of northwestern Ethiopia. There was no difference (P<0.05) in prevalence of bovine TB in cattle owned by households with TB cases and cattle owned by TB free households as all cattle owned by both groups were none reactors. On the other hand, culture positivity was confirmed in 56%(38/68) of the suspected TBLN cases. Spoligotyping of these 38 human isolates resulted in 29 different patterns (strains), of which 86.2% (25/29) were M. tuberculosis and the remaining 13.8% (4/29) were M. africanum. Although M. bovis was not isolated from human TBLN cases in the study area, 64.7% (44/68) of the respondents did not have awareness on the zoonotic importance of bovine TB and 66.2% (45/68) consumed raw milk.

Conclusion :The transmission of TB between farmers and their cattle was not observed in this study. Nevertheless, the recorded low level of farmers' awareness and higher proportion of row milk consumption habits of the respondents will not exclude the importance of zoonotic TB in the study area.

Mots clés /keywords :

Cattle, Farmer, Transmission, Tuberculosis

Auteur présentateur / presenting author:

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PY22   **Screening of exon 11 of BRCA1 gene using the high resolution melting approach**

for diagnosis in Moroccan breast cancer patients

Auteurs /Authors :

El Khachibi M(1); Diakite B(1); Hamzi K(1); Badou A(1); SenhajiA M(1); Amina B(3); Jouadi H(2); Barakat A(3); Benider A(2); Sellama N(1)

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Introduction :

Identification of specific mutations in cancer patients may lead to the discovery of genes, which can affect susceptibility and/or prognosis. It has previously been reported that mutations in BRCA1 and BRCA2 genes are linked to breast cancer.

Goals :

We evaluated the use of the High Resolution Melting (HRM) approach to screen for mutations in exon 11 of BRCA1 gene in Moroccan patients.

Methods:

HRM analysis was used to screen exon 11 from 71 breast cancer patients in order to detect different variants. Conventional Sanger sequencing was used to confirm the presence of possible mutations. Distribution of different SNPs was determined by SNaPshot analysis software.

Results :

In order to assess the efficacy of the HRM approach to screen for mutations, especially in diagnosis, we first used two samples with previously known mutations, "2924delA and 3398delC". Indeed, these previously known sequence variants were detected by the HRM approach and yielded melting curves with atypical shape relative to wild-type control sequences. We then analyzed, 69 samples from breast cancer patients using the HRM method, and were able to detect two samples with atypical curves. Sequencing of the two samples, using the conventional Sanger approach, confirmed the presence of the same SNP (c.2612C>T) in both samples.

Conclusion :

Our results strongly suggest that the HRM approach represents a reliable and highly sensitive method for mutation scanning, especially in diagnosis.

Mots clés /keywords :

Breast cancer, BRCA1, Exon 11, HRM

Auteur présentateur / presenting author:

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PY23   **The influence of NAT2 gene polymorphism on tuberculosis treatment responses among ethnic groups at South Omo, Ethiopia**

Auteurs /Authors :

This a proposal on the above title and will include an other authors

Adane Worku

Introduction : N-acetyltransferase 2 (NAT2) is an important enzyme in clinical pharmacology. Polymorphisms in NAT2 account for variability in the acetylator phenotype and the pharmacokinetics of metabolized drugs. The frequency in variability of the acetylator phenotype differs depending on ethnicity.

Goals : To determine the influence of NAT2 gene polymorphism on tuberculosis treatment response among ethnic groups at South Omo.

Methods :Institutional based longitudinal cohort study design will be used.   Patients positive for AFB and/or GeneXpert MTB/ RIF will be recruited for the study. The study participants in the cohort will be followed up at four time points (baseline, 2nd weeks, 2nd months and 6th months) during the course of the treatment. Clinical (BMI), bacteriological (AFB, GeneXpert MTB/RIF and Culture by LJ medium), molecular (Spoligotyping) and immunological (Cytokine ELISA) techniques will be used to evaluate TB treatment response. An efficient methods will be used for NAT2 gene analysis (restriction fragment-length polymorphism and sequencing). Appropriate descriptive statistics and bioinformatics software will be used for the analysis The degree of association between independent and dependent variables will be assessed with 95% CI and p-value of <0.05

Next step :Currently 32 patients have been recruited for the follow up from five ethnic groups (Ari= 15, Hamer= 9, Nyangatom= 6 Mursi=1 and Dasenech=1). The sample collection is continued. at the end we need ELISA, RFLP and Sequencing for analysis.

Expected Out Come: Population will be grouped in to slow, intermediate and fast acetylator. The result will be correlated to treatment response and the ethnic diversity. Frequency of acetylator status in inter and intraethnic group will be reported.

Mots clés /keywords :

NAT2, Tb patients, Ethnicity

Auteur présentateur / presenting author:

Dr Adane worku

Addis Ababa University

PY24   **Effect of herbal extracts and CYP450 expression pattern in WHC01 oesophageal cancer cells: Implication for herb-drug interaction in cancer therapy**

Auteurs /Authors :

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Introduction : Medicinal plants are commonly used in resource-constrained countries to support health care systems. The use of herbal medicines for treating diseases including cancer in addition to allopathic medication is a common phenomenon in Africa and other parts of the world with data available showing that patients hardly inform their physicians about the self-combination therapy being used. It is suggested that extrahepatic expression of CYP450s might play an important role in the CYP-mediated metabolism of xenobiotics. In cancerous cells, the expression of individual forms of CYP450 affects the potential for the metabolism of anticancer drugs by cancerous cells directly with localised expression of CYP450 in cancer or tumour cells leading to the activation or deactivation of chemotherapeutic medications. Not much has been done in evaluating the effects of commonly used medicinal plants.

Goals : The purpose of this study was therefore, to investigate the effects of Hyptis suaveolens and Boerhavia diffusa on CYP450 expression and some genes that play an important role in apoptosis and cell cycle regulation in WHC01 cells.

Methods: RT-PCR and western blott was used to evaluate the gene expression levels of CYP450, apoptotic and cell cycle genes using an oesophageal cancer cell line, WHC01. DNA cell cycle analysis was performed using flow cytometry.

Results : Hyptis suaveolens and Boerhavia diffusa exhibited differential expression on CYP1A2, CYP2C9 and CYP2C19. Differential expression was observed for apoptotic and cell cycle associated genes and DNA cell cycle analysis showed an arrest of cell cycle in the G0/G1 phase.

Conclusion : Herbal medicines play a vital role in treatment options available to patients for a population in health transition. The differential expression of CYP450s, apoptotic and cell cycle genes in the presence of herbal medicines calls for more studies to understand drug-herb interaction. It is important to advice patients on co-administering herbs and cancer drugs.

Mots clés /keywords :

Herb-Drug interaction, CYP450, WHC01 cancer cells,Herbal medicine

Auteur présentateur / presenting author:

Mr(s) NICHOLAS EKOW THOMFORD

UNIVERSITY OF CAPE TOWN

PY25   **Etude analytique, descriptive des cancers colorectaux au Sénégal :**

analyse préalable d'une étude génétique

Auteurs /Authors :

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2-Unité de formation et de recherche (UFR), Santé Université Gaston Berger, Saint Louis,

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Introduction : Au Sénégal, les cancers colorectaux représentent 2,5% de l'ensemble des cancers soit 20% des cancers du tube digestif .Cependant, cette prévalence est sous-estimée du fait de l'inaccessibilité des soins de qualité à tous et de l'occidentalisation du mode de vie. En plus de ces facteurs environnementaux, des facteurs génétiques sont également incriminés. Et pour envisager une étude de ces facteurs génétiques, il importe de décrire les caractères épidémiologiques et analytiques.

Objectifs / goals : Décrire les caractères anatomopathologiques et épidemiologiques chez des patients atteints de cancers colorectaux au Senegal

Méthodologie / Method: Nous avons mené une étude prospective, descriptive et analytique de 2012 à 2015 au niveau de l'hôpital général de grand Yoff. A partir des registres du laboratoire d'anatomopathologie, 41 dossiers de patients ont été sélectionnés par tri à postériori à partir d'un nombre beaucoup plus important. Les données ont été analysées grâce au logiciel Excel. Le seuil de significativité est retenu pour des valeurs de p value inférieure ou égale à 0,05.

Résultats / Results : L'âge moyen de nos patients est de 50 ans et la majorité avait plus de 60 ans. Le sexe ratio de 0,76 est en faveur des femmes. Notre population d'étude était dominée par les wolofs, plus de la moitié (51%) suivis des peulhs (21%) et les autres ethnies étaient faiblement représentées. Les adénocarcinomes étaient le type histologique dominant à localisation préférentielle le colon gauche. Le stade de diagnostic suivant la classification TNM était moins avancé (pT3).

Conclusion : Ces résultats confirment les données de la littérature, la deuxième étape qui est l'étude génétique est aujourd'hui incontournable dans la recherche des spécificités liées à des susceptibilités de variations individuelles ou de l'environnement

Mots clés /keywords :

Cancers colorectaux, Sénégal

Auteur présentateur / presenting author:

Dr Arame Ndiaye

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Auteurs /Authors :

Somia A. Mohammed 1,2, Faisal M. Fadlelmola 1

Introduction : The rapid development of micro array technologies in recent years has led to the possibility of acquiring a large spectrum of different molecular data types. Micro array technology has become a powerful tool to analyze the gene expression of tens of thousands of genes simultaneously.gene expression data are usually collected together with additional clinical information and gnomic data from other high throughput technologies such as array-based comparative genomics hybridization (array CGH) or SNP (single nucleotide polymorphism) arrays.

Goals : Main goal of project is to build a web-based tool which provides analyses and interactive capability high-dimensional gene expression data together with associated clinical data. The different data types are organized by a comprehensive data manager.this way useful to help researcher to discover new genes,or use specific gene

Methods: By using incremental model to build framework   for integrated fixable micro array tool use whole data (array CGH) from micro array Determine the expected presence of a gene in a chromosome and integrate with gene expression. We need to create software connectors as basis for our integrative solution . Software connectors represent architectural elements used to model interactions among either computation or data components of a system.

Results : The result that we want to get them Genomic data integration is a key goal to be achieved towards large-scale genomic data analysis. This process is very challenging due to the diverse sources of information resulting from genomics experiments. In this work, we review methods designed to combine genomic data recorded from micro array gene expression.

Conclusion : In conclusion, we need the foregoing integration are good and effective to build a good connectors and take advantage of existing databases and analysis algorithms to achieve our goal by adding new tool to help African scientists as especially all those interested in the world

Mots clés /keywords :

Micro-array, comparative genomics hybridization , single nucleotide polymorphism,software connectors.

Auteur présentateur / presenting author:

Dr Somia Abdelmonem Ahmed Mohammed

PY27   **What are the genes associated with cardiomyopathies in African children?**

Auteurs /Authors :

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1- Jos University Teaching Hospital

Introduction : Cardiomyopathy is the most common acquired heart disease in African children less than five years. Environmental and social factors are associated with the development of paediatric cardiomyopathies. It is well-established that there are several genetic mutations associated with cardiomyopathies in children. While these genes have been described in non-African populations, there is no documentation of these in African children. This study aims to determine the predominant genetic mutations present in children with cardiomyopathies.

Goals : The main aim of this dissertation is to determine if there are genetic mutations in African children with cardiomyopathies. This study also aims to identify the predominant genetic mutations present in these children.

Methods: This cross-sectional study will be nested at the Paediatric Cardiology Unit, Department of Paediatrics, Jos University Teaching Hospital. Children with all phenotypes of cardiomyopathies will be consecutively recruited. Genetic variants associated with the different phenotypes will be identified using genome-wide associated study (GWAS). Single nucleotide polymorphisms (SNPs) associated with these different phenotypes will be identified.

In children with both parents alive, GWAS will also be performed on both parents to identify a possible familiality in the transmission of associated variants. In addition, a general question about any cardiac condition in siblings and other family members will be enquired for.

Results :

Not yet available.

Mots clés /keywords :

Genes, Cardiomyopathy, Africa, Children

Auteur présentateur / presenting author:

Dr Esin Nkereuwem

Jos University Teaching Hospital

PY28   Genetic diversity and drug resistance of HIV-1 strains among antiretroviral therapy(ART) naive and ART treated patients with and witout active tuberculosis in South Omo, Ethiopiawitout active tuberculosis in South Omo, Ethiopia

Auteurs /Authors :

Tachbele E; Ameni G; Leges M? Addis Ababa University

Introduction: The increasing diversity of HIV has profound implications for its   pathogenicity, transmission, diagnosis, treatment, and vaccine development.   In Ethiopia, subtype C accounts for more than 90% of all reported cases so far. In view of ART scale up, and reporting of non C sub type in the country, surveillance of drug resistance and genotyping is important, especially in the current study area where no genotyping study is conducted .

Objective: This study is designed to evaluate HIV-1 genetic diversity and drug resistance-associated mutations among drug-naïve and experienced patients with and without active tuberculosis in South Omo, Ethiopia. In addition, impact of tuberculosis on HIV genetic diversity and viral load will be investigated.

Methods and Materials: Four different study designs and populations will be considered: Recently infected ARV drug-naïve individuals(N=47) , Chronically HIV-1infected   ARV drug-naïve(N=174),   and   Chronically HIV-1 infected receiving ART for ≥3 months(N= 328). In addition, to investigate the impact of M. tuberculosis on HIV-1 load and genetic diversity, nested case control study design will be used consisting of HIV/TB group (N=28) and non-TB HIV group(N=56) as control among chronically HIV-1 infected ART naïve patients. For all types of the study, in addition to socio-demographic and clinical data, 10 ml of blood will be collected from participants using ethylene diamine tetra-acetic acid (EDTA) containing vacutainer. CD4+ lymphocyte count will be done within 2-4 hours of blood collection. Plasma will be separated and stored in multiple aliquot at -40 oC for viral load measurement and molecular characterization   using   protease (PR) and reverse transcriptase (RT) gene sequencing.Pol gene sequences will be aligned with reference subtypes obtained from HIV sequence database at Los Alamos, and for drug resistance analysis consensus mutations of Stanford University HIVDB will be used .In addition, differentially expressed   plasma proteins, between HIV/TB and HIV /non-TB groups   will be analyzed using shotgun proteomics. Fisher exact test implemented by GraphPad PRISM software (San Diego, CA) will be used for statistical analysis of the difference in subtypes among different risk groups and the genetic variation in PR and RT genes among subtypes.

Expected Result: The research is expected to generate data on: The genetic diversity of HIV-1 in the region, prevalence of transmitted and acquired HIV drug resistance among ARV naïve and experience patients ,and impact of tuberculosis on HIV-1 genetic diversity and viral load.

Hence the data will help in the development of appropriate prevention strategies to limit treatment failure and plan for appropriate treatment6 and vaccine strategi

Mots clés /keywords :

HIV-1,genetic diversity, drug resistance, tuberculosis, South Omo.

Auteur présentateur / presenting author:
Mr(s) Erdaw Tachbele
Addis Ababa University: Systems Biology for Molecular Analysis of Tuberculosis

PY29 **Molecular Epidemiology of Mycobacterium tuberculosis complex and Drug sensitivity patterns in Pastoralists of South Omo Zone, Southern Ethiopia**

Auteurs /Authors :

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Introduction : Mycobacterium tuberculosis complex (MTBC) consists of Mycobacterium tuberculosis, M. africanum, M. bovis and M. canetti, which are causative agent for human tuberculosis (TB). One third of the world population has been infected with these bacteria latently. Ethiopia is one of the high TB burden countries. In Ethiopia the prevalence of TB in pastoral communities is almost double compared to other communities. Different strains of M. tuberculosis are associated with different geographic regions. Therefore studying the strains diversity circulating and their response to drugs will have immense contribution for TB control program.

Goals : To investigate molecular epidemiology and drug sensitivity patterns of Mycobacterium tuberculosis complex in pastoralists of South Omo Zone, Southern Ethiopia.

Methods: Sputum and fine needle aspirate samples from TB suspected and confirmed individuals were cultured on LJ media. Culture positive isolates were kept in freezing media and distilled water. Isolates in distilled water were incubated to release DNA materials. RD9 typing, genus multiplex and spoligotyping were done. http://tbinsight.cs.rpi.edu/run_tb_lineage.html, www.mbovis.org/spoligodatabase, and http://www.pasteur-guadeloupe.fr:8081/SITVIT_ONLINE/ were used to interpret results of spoligotype. Drug sensitivity test was done using line probe assay (LPA).

Results : Culture AFB positive isolates (123) were 113 (91.9%) mycobacteria and 10 (8.1%) non mycobacteria. Within genus mycobacteria isolates: 87 (77%) were members of MTBC. Spoligotying analysis indicated that, 59 (67.8%) Euro-American, 17 (19.5%) East-African-Indian, 4 (4.6%) Mycobacterium Africanum, 4 (4.6%) Indo-Oceanic and 1 (1.1%) East-Asian. Only 73% had known SIT numbers in 23 clusters. The most common isolates were SIT 149 (T3-ETH) (9.2%). M. bovis had a contribution of 2.3% for human tuberculosis. Based on LPA drug sensitivity test, there was 1.15% MDR and 2.3% rifampicin mono resistant.

Conclusion :Additional isolates and further analysis will be required for better conclu

Mots clés /keywords :

M. tuberculosis, M. bovis, Drug sensitivity, South Omo

Auteur présentateur / presenting author:

Mr(s) Biniam Wondale Damtew

PY30   **Usefulness of polygenic risk scores associated with type 2 diabetes**

in black South African population

Auteurs /Authors :

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Introduction: Type 2 diabetes (T2D) is postulated to have a polygenic etiology. Recently, polygenic risk scores of variants associated with T2D have been noted to be useful in predicting risk in multiple ethnicities as opposed to single variants that have been reported to be population specific. However, the evidence of this phenomenon is limited among the black South Africans.

Goals: This study was done to determine polygenic scores associated with T2D and their usefulness in the black South African Population.

Methods: Sixty six variants associated with T2D in multiple ethnicities were successfully genotyped using the BeadXpress platform. Four types of polygenic risk scores were computed, which consisted of all the 66 variants which was termed GRSt, significant variants (GRSn), beta related variants (GRSbeta) and trans ethnic shared variants associated with T2D (GRStrans).

Results: GRSn which consisted of 4 variants, was the only polygenic risk score associated with increased T2D risk indicated by OR (95CI) of 1.21 (1.02-1.43) p-value = 0.015. Stratified analysis indicated the GRSn to be significantly associated with T2D among the non-obese and people less than 50years old .Receiver operating curves (ROC) were use to assesses the ability of the convectional risk factors (age, sex, urbanisation, fasting glucose, glycated hemoglobin and BMI) alone or with GRSn to identify a case. The area under the ROC of the T2D risk factors alone was 0.652 (p value < 0.001) and with the addition of GRSn it was 0.665 (p value < 0.001).

Conclusion: The polygenic risk scores of variants associated with T2D, derived from European and Asian ethnicities are less predictive in the black South African population. Inclusion of rare and population specific variants in the GRS might in the future yield a more clinically useful polygenic risk score for early identification of high risk T2D patients.

Mots clés /keywords :

polygenic risk score; GRS; black South Africans

Auteur présentateur / presenting author:

Dr Tinashe Chikwore

North West University

PY31   **Comparative analyses of Podoconiosis susceptibility Genes in Patients**

from Cameroon and Ethiopia

Auteurs /Authors :

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Introduction : Podoconiosis is a Non-infectious elephantiasis ("swelling of limb like an elephant's") caused by long term exposure of bare feet to irritant soil. Globally, it is estimated that there are at least four million people with podoconiosis. Countries where podoconiosis is common are mainly found in tropical Africa, central and south America and northern India. The disease has been shown to be confined in some Families. Family pedigrees collected in Ethiopia shows high heritability (>60%), evidence for an autosomal co-dominant inheritance. More over recent GWAS still in Ethiopia indicates disease susceptibility associations in HLA class II region, chr 6. Although Podoconiosis has been demonstrated in Cameroon, no study has been carried out to investigate the involvement of host genes in the development of the disease.
Goals : In the present study, we intend to determine if the genes responsible for susceptibility in Ethiopian podoconiosis patients can be replicated in podoconiosis patients from the North West region of Cameroon.
Methods:Saliva samples were collected from 400 clinically confirmed podoconiosis patients alongside 400 unrelated healthy individuals. DNA was extracted using the oragene kit and genotyping was performed using the allumina platform at the Sanger institute. Data analyses are ongoing, we intend to concentrate on the top 80 single nucleotide polymorphisms (SNPs) identified by the earlier GWAS in Ethiopia, to perform HLA fine mapping, and compare background HLA haplotypes between Ethiopian & Cameroonian populations.
Results :Data analyses are ongoing and the results shall be available for discussion during the conference.
Conclusion:Through this study, more insight in the genes responsible for susceptibility to podoconiosis and their conservation within and between different populations will be illustrated. This could lead to an improved understanding of the pathogenesis of the disease, improved preventive measures and new therapeutic approaches to manage the disease in the affected areas

Mots clés /keywords :
Podoconiosis, genes, Susceptibility, Cameroon, Ethiopia, SNPs
Auteur présentateur / presenting author:
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PY32 **Knowledge of concepts of heritability of diseases and comprehension in Nigeria**

Auteurs /Authors :

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Introduction :Large scale genomic research in Nigeria was pioneered in 2004 by the International HapMap project. These studies were accompanied by ethical concerns. Recently, there has been other genomic studies, and concerns have been expressed on research understanding and consent before participation. This is particularly relevant because of the high prevalence of poverty and low levels of literacy in LMIC like Nigeria.

Goals :To explore local knowledge about heritability in general and of diseases specifically in order to use these to improve comprehension of consent forms.

Methods: 50 females and 50 males from diverse ethnic groups and religions living in villages around Abuja, Central Nigeria into 10 focus group discussions and conducted 50 key informant interviews to identify existing linguistic and cultural concepts of heritability that are used to understand common heritable traits and diseases in indigenous communities in Nigeria. The discussions and interviews were trnscribed and analysed using Atlas.ti®.

Results : Participants identified various diseases and attributed the reason for heritability and inheritable diseases to "blood" – in the sense of a corporeal essence, while others attributed such events to acts of God.

Participants acknowledged the occurrence of "dominant" and "recessive" traits. The dominant traits were attributed to strength of the male partner while recessive traits were attributed to several factors including multiple sexual partners. Others thought that heritable traits were due to association with specific individuals, natural causes, types of sexual activities, mental state of the woman peri-conception, the environment, etc.

Conclusion: Our study showed that Nigerians were aware that some diseases and traits are heritable and some of these were "dominant" while others were "recessive". However participants had limited knowledge of the basis for heritable diseases and its different forms. This suggests that genomic researches in these communities must be accompanied by careful education of the research participants.

Mots clés /keywords :

Knowledge, concepts, inheritable Diseases, Heritability.

Auteur présentateur / presenting author:

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Institute of Human Virology Nigeria

PY33   IMPACT DE LA CHIMIOTHERAPIE ANTICANCEREUSE SUR L'ACTIVATION PRECOCE DES LYMPHOCYTES T DANS LE CANCER DU SEIN

Auteurs /Authors :

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Introduction: Le cancer du sein malgré les progrès thérapeutiques reste le 2e cancer dans le monde en termes de fréquence. Au Sénégal, il est au 2e rang des cancers gynécologiques et mammaires. Le rôle de la réponse immunitaire n'y est pas entièrement compris mais certaines observations suggèrent qu'il serait influencé par la chimiothérapie. Une nouvelle stratégie thérapeutique combinant chimiothérapie et immunothérapie encore appelée chimiothérapie vectorisée est en cours d'étude. Elle nécessite cependant une meilleure connaissance de l'influence des anti-tumoraux sur la réponse immunitaire.

Objectif : La présente étude a eu pour d'évaluer le profil d'activation lymphocytaire chez des patientes atteintes de cancer du sein et traitées avec l'association 5-Fluorouracile- Doxorubicine- Endoxane.

Méthodologie: L'étude a concerné 34 femmes atteintes de CS avec un âge moyen 47 ans (24 - 78 ans) et 42 femmes témoins indemnes de tumeur, appariées sur l'âge. Un prélèvement de sang périphérique sur tube EDTA a été fait avant les trois cures de chimiothérapie. L'isolement puis le marquage des cellules sanguines mononuclées par les Ac anti-CD3-PE, anti-CD4-APC, anti-CD8-PerCP et anti-CD69-FITC ont permis l'évaluation des pourcentages de LT activés par cytométrie en flux.

Résultats: Nos résultats ont montré que la première cure de chimiothérapie s'accompagnait d'une augmentation significative des proportions de lymphocytes TCD3+ de type CD4+ et surtout TCD8+ exprimant le marqueur CD69+. Cette hausse intéressant aussi les cellules B CD19+CD69+, n'était pas observée avec le marqueur d'activation tardive HLA-DR, qui diminuait légèrement au fur et à mesure des cures de chimiothérapie. L'activation précoce augmentait après la deuxième cure pour les lymphocytes TCD4+ tandis qu'elle diminuait pour les cellules TCD8+.

Conclusion: Nos résultats ont montré une augmentation de l'activation lymphocytaire avec le traitement anticancéreux. Cependant, il convient d'évaluer le niveau d'apoptose et la production cytokinique des lymphocytes pour mieux caractériser cette activation.

Mots clés /keywords :

Cancer du sein, lymphocytes T, lymphocyte B, CD69, HLA-DR, chimiothérapie

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PY34   **I-HAB's DNA Quality Control Improvement Strategies**

Auteurs /Authors :

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Introduction: The principal goal of the Institute of Human Virology H3Africa Biorepository (I-HAB) is to achieve best practices in providing reliable sample processing support, secure storage and shipping of high quality biological samples that promote genomic science on the African continent. I-HAB's strategy for improving the quality of Isolated DNA involves spectrophotometric, spectrofluorometric, and restriction digestion and gel electrophoretic methods. Furthermore, samples tested in I-HAB have been sent to other H3Africa (H3A) biorepositories for re-testing blindly and to IBBL for proficiency testing (PT) program.

Goals: To provide high quality DNA samples suitable for down-stream processes such as next generation sequencing.

Methods: DNA QC was performed in I-HAB using spectrophotometric, spectrofluorometric, restriction digestion and agarose gel electrophoresis methods. Samples tested in I-HAB were shipped to other H3A-biorepositories for re-testing and replica whole blood samples used for DNA extraction in I-HAB were sent to other H3A-biorepositories for DNA extraction and QC.

DNA samples provided by IBBL were measured in I-HAB while IBBL originating Whole Blood sample was used for DNA extraction and extracted was tested in IBBL.

Results: Excellent correlation was observed between sample quality and purity. Spectrophotometric methods provide higher DNA concentrations compared to spectrofluorometric consistent with the ability of the later to discriminate between double and single stranded DNA. Indices of sample integrity were determined by agarose gel electrophoresis. Samples measured in I-HAB compared favourably to those re-tested in other bio-repositories with minimal observed differences. IBBL PT results showed that I-HAB performed very satisfactorily and satisfactorily for DNA extraction and QC, respectively.

Conclusion: Different methods used for DNA QC in I-HAB provide complementary results. Exchange of samples tested in I-HAB with other biorepositories and IBBL have served as useful benchmark for continued improvement of the DNA QC program.

Mots clés /keywords :

DNA Extraction, DNA Quality Control, DNA Quality, DNA Purity, DNA Integrity, IBBL Proficiency testing (PT) program

Auteur présentateur / presenting author:

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Institute of Human Virology H3Africa Biorepository

PY35   **Is Spinal Muscular Atrophy uncommon in Mali?**

Auteurs /Authors :

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Introduction : Spinal Muscular Atrophy (SMA) is an autosomal recessive disorder and the most common severe inherited disorder of childhood. Previous studies have showed higher carrier frequencies in caucasian populations than those of African descent. While a recent study done in Mali showed a much lower SMA carrier frequency, our study has identified SMA in two families.

Goals : Clinically characterize families with SMA phenotype. Identify the genetic defect in those families.

Methods: Patients were seen in our clinic. Blood chemistries including CK levels were done. DNA was extracted for SMN1 copy determination.

Results : Four families totaling six affected individuals in cohort showed symptoms in favor of SMA. Three of them were consanguineous. All patients had normal pregnancy and delivery, and motor and psychic development was normal until age four months when parents noticed difficulties with sitting. Patients never crawled or standed nor did they walk but they could sit.

Clinical examination showed reduced language, generalized atrophy and hypotonia but no facial weakness, more proximal weakness, chest deformity (triangular) with dorsal kyphosis, reduced to absent reflexes, and fasciculations in some patients. There was no cognitive, hearing, and sensory impairment. CK levels were normal.

Genetic testing in two families identified homozygous deletion of the SMN1 gene. Patients were 3 and 4-year-old, but no breathing difficulties were noticed. This suggests that they have type 2 SMA.

Conclusion :Although previous reports have showed very low SMA carrier frequencies, our study shows that this disease is not uncommon in Mali. This may be due to a selection bias as SMA patients are more likely to be seen by pediatricians or gynecologists, and collaborative team work may overcome this difficulty. A larger cohort study would help in the global clinical and genetic understanding of this disease.

Mots clés /keywords :
Spinal amyotrophy, SMN, Mali
Auteur présentateur / presenting author:
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PY36   Huntington's disease in Mali: clinical and genetic spectrum

Auteurs /Authors :

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Introduction : Huntington's disease (HD) is an autosomal dominant neurodegenerative disease characterized by progressive motor, cognitive and psychiatric symptoms. It is due to an expanded trinucleotide CAG repeats within the Huntingtin gene (Htt) on chromosome 4. The disease has been rarely reported in Africa particularly in West Africa due to the lack of specialists and limited access to molecular testing.

Goals : We aim to clinically characterize families with HD features in our Neurogenetics Clinic, and to identify the underlying genetic defect.

Methods: Patients were examined by neurologists and families with suspected HD symptoms were included. DNA was collected for genetic analysis. Brain imaging and blood chemistries were performed to exclude other causes.

Results : We enrolled 132 families with a wide range of neurological conditions. Seven families including eleven patients of which six men presented symptoms consistent with HD. Age of onset was 34 to 60 years. Among motor symptoms, chorea was seen in all but one patients followed by oculomotricity impairment and rigidity. Psychiatric symptoms were noticed in six patients and cognitive impairment in four. In addition, the majority of patients reported weight loss. Genetic analysis showed a heterozygous expansion of the CAG repeats in two families, 42 and 45. Although gel electrophoresis of Htt PCR products indicated repeats expansion in three other cases, sequencing results are not available yet to confirm the diagnosis.

Conclusion : To our knowledge, this is the first large study reporting clinically and genetically confirmed HD in West Africa. Studies of a larger cohort will improve our understanding in the disease variability and management in this region of Africa. Moreover, characterizing African families will set the field for future therapeutic assays.

Mots clés /keywords :

Huntington disease, clinical features, genetic testing, Mali

Auteur présentateur / presenting author:

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PY37   **Elucidating the genetic basis of motor developmental disorders in Malian families**

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Introduction: Motor developmental disorders are common in Africa. However, their genetic basis is rarely reported.

Goals: To clinically characterize these disorders and establish their genetic causes.

Methods: Patients were examined by neurologists and other specialists according to the presence of non neurological symptoms. Brain and skeletal imaging, cardiological and abdominal ultrasounds, and blood chemistries were done to confirm organ systems involvement. DNA was extracted in all available patients and family members for genetic analysis. FISH analysis, and exome sequencing coupled with linkage and homozygosity mapping in negative families will be performed. The effect of putative variants will be assessed by RNA and protein expression studies such as quantitative RT-PCR, Western Blot and immunohistochemistry. We also plan to collect more family members to increase our chance to discover the underlying genetic defect.

Preliminary results: Four families totaling 23 patients were enrolled. The age of onset ranged from birth to one year. Symptoms included psychomotor delay, psychiatric features, microcranus and bone deformation. Blood chemistries have found low calcium in some patients. Two consanguineous families had features consistent with mucopolysaccharidosis. Although no other organ system involvement was found, liver enzymes were slightly increased. Bone X-rays showed rounded vertebra and spinal CT-scan discal herniations. One family with dominant pattern and incomplete penetrance in which sixteen individuals presented an unusual phenotype including bone deformities, psychiatric symptoms, and seizures. Genetic studies are underway.

Conclusion: Our preliminary results show families with unusual clinical features and raise the possibility to find novel genes or variants that can be studied in other populations. As recessive families are more common in our cohort, establishing the genetic basis of these disorders will help identify people at risk and lower the transmission rate of these disorders.

Mots clés /keywords :

motor developmental disorders, genetic testing, MalI

Auteur présentateur / presenting author:

Mr(s) Abdoulaye Yalcouye

Faculte de Medecine et d'Odontostomatologie

PY38   **Aspect moléculaire de la résistance de souches de Escherichia coli uropathogènes sécrétrices de BLSE, isolées au Laboratoire de Bactériologie-Virologie du CHNU Le Dantec**

Auteurs /Authors :

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1- CHU Aristide Le Dantec 2- Bio 24

Introduction : La multirésistance particulièrement liée à la sécrétion de Bêtalactamases à Spectre Etendu (BLSE) compromet le plus souvent les issues thérapeutiques. Elle est d'autant plus inquiétante car ayant comme conséquence la dissémination des gènes plasmidiques codant pour ces enzymes de résistance. Peu d'études ont porté sur ces gènes de résistance dans les Infections du Tractus Urinaire (ITU) au Sénégal

Objectifs / goals : Ce travail avait pour objectif d'étudier au plan moléculaire les gènes de résistance des souches de Escherichia coli sécrétrices BLSE isolées au Laboratoire de Bactériologie-Virologie du CHNU Aristide Le Dantec en 2013.

Méthodologie / Method: L'identification des souches a été faite sur la base de la bactériologie classique. La sécrétion des BLSE a été confirmée au plan phénotypique selon les recommandations du Comité de l'Antibiogramme de la Société Française de Microbiologie 2015 (CA-SFM). Les gènes CTX-M-1, CTX-M-9 ont été recherchés par PCR classique et la révélation des produits a été faite sur gel d'agarose à 1%. Le séquençage nucléotidique a été réalisé et les séquences obtenues ont été soumises au site NCBI-Blast pour le contrôle des résultats de la PCR et le typage des gènes.

Résultats / Results : 40 souches de E. coli, dont 26 (57.5%) communautaires et 14 (42.5%) hospitalières ont été isolées. Les gènes CTX-M-1, CTX-M-9 ont été retrouvés respectivement chez 95% et 25% des souches. Chez les hospitalisés, 100% et 28.6% des souches isolées présentaient respectivement la CTXM-1 et la CTXM-9. Par contre chez les externes, la proportion de souches porteuses des gènes CTX-M-1 et CTX-M-9 était de 92% et de 23%, respectivement.

Conclusion : Ces résultats montrent la large diffusion des gènes de résistance. Ces résistances peuvent être associées à celles des quinolones et/ou des carbapénèmes et entrainer ainsi une impasse thérapeutique, d'où la nécessité de renforcer la lutte et d'élargir les recherche vers d'autres gènes de résistance.

Mots clés /keywords :

Infection du tractus urinaire, Escherichia coli, BLSE, CHNU Aristide Le Dantec, gènes de résistance.

Auteur présentateur / presenting author:

Dr Mba Elhadji Bambo Diakhaby

PY39   **The genetic specificity of spinal cerebellar ataxia in Mali**

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Introduction: Spinal cerebellar ataxia (SCA) are clinical and genetic heterogeneous disorders with a global incidence of about 1-5/100,000, but these diseases are rarely reported in West-Africa.

Goals: To clinically characterize families presenting with ataxia in our neurogenetic clinic, and to identify the underlying genetic defect.

Methods: Patients with ataxia will be seen in our neurogenetic clinic, and DNA will be extracted from peripheral blood for genetic analysis. Brain and spine imaging and blood chemistries were performed to exclude common causes.

Results: We have assessed 132 families with a wide range of neurodegenerative conditions. Twenty seven families presented findings consistent with SCA, and 15 showed autosomal dominant pattern. The age of onset ranged from 5 to 50 years, with some showing anticipation. Genetic analysis has identified an abnormal CAG expansion in the ataxin 2 in seven families, and in ataxin 3 and 7 genes in four families each. Some of these SCAs have shown regional clustering, suggesting a founder effect. Although some presented seizures, their genetic testing of SCA genes causing seizures was negative; suggesting a clinical variant or other genetic or environmental factors. Genetic analysis of the remaining families are underway.

Conclusion: In this study, we identified 26 families with SCA and 15 were genetically confirmed; making this disease the most common hereditary neurological disorder in our cohort. While SCA3 is the most common SCA worldwide, SCA2 was the most frequent in our cohort. Although the genetic analysis is still underway, the clinical features suggest possible new SCA entities or variant. Studying families with high number of patients will allow refine or consolidate the natural history of diseases.

Mots clés /keywords :

SCA, genetic testing, haplotype studies, Mali

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PY40   **Association of Variants in APOL1 and MUH9 with micro-albuminuria among Sickle Cell Disease**

Patients from Cameroon

INTRODUCTION: Sickle Cell Disease (SCD) is a monogenic hemoglobinopathy that is highly prevalent in Africa. Kidney Disease is a clinical proxy of severity, developing only in a subset of patients. Micro-albuminuria is considered a primary indicator of renal dysfunction that has been associated with specific genetic modifiers.

AIM: We have investigated the association of single nucleotide polymorphisms (SNPs) in APOL1 and MYH9 with micro-albuminuria among Cameroonian SCD patients.

METHODS: A total of 413 SCD patients older than 5 years were included. Patients were genotyped for the 3.7kB alpha-globin deletion using gap-PCR and six targeted single nucleotide polymorphisms (SNPs) in APOL1 and MYH9 using SNaPshot and Sanger sequencing. Logistic regression analysis with an additive model was used to study the association between genotypes and sociodemographic variables, crude micro-albuminuria, as well as the albumin-to-creatinine ratio (ACR).

RESULTS: The cohort had a median age of 15 (9-23) with micro-albuminuria significantly associated with age (p=0.0041). 60.9% and 2.5% of patients had crude micro-albuminuria and macro-albuminuria, respectively. Using ACR data, 73.4% of patients had microalbuminuria. Using sequence data extracted from the 1000 genome Project, comparisons with Cameroonian data from the present study indicates a huge MAF difference among different African populations (e.g rs11912763 and rs16996648). 41.4% of patients' had co-inherited alpha-thalassemia. All the studied SNPs were not significantly associated with crude micro-albuminuria. The albumin-to-creatinine ratio was significantly decreased in heterozygotes for rs11912763 (p=0.0419) in the subset of the cohort greater than 15 years old (n=69), but not with the other targeted SNPs. There was no association with 3.7 kb alpha-globin deletion and micro-albuminuria.

CONCLUSION: Micro-albuminuria is a highly prevalent condition in this group of Cameroonian patients. Micro-albuminuria's association with age is indicative of a directly proportional relationship between age and renal dysfunction. This population of virtually micro-albuminuric patients could explain the significant association with only one SNP rs11912763 with ACR. .

NEXT STEPS: Further studies should include association with variants with specifically adult SCD and inclusion of variants in HMOX1 "

PY41   **Investigating the prevalence of selected MYO7A mutations amongst a group
of sub-Saharan African patients with non-syndromic hearing loss**

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Background

Congenital hearing loss occurs in approximately 5.5/1000 birth in South Africa. Mutations in GJB2 and GJB6, that explain most of autosomal recessive non-syndromic hearing loss (ARNHL) in people of European and Asian descent, have been shown to be insignificant in African populations. In order to resolve ARNSHL amongst African patients, next generation sequencing (NGS) was employed thorough the use of OtoSCOPE®, a diagnostic platform for hearing loss, that investigated 66 genes of hearing loss. Compound heterozygous causative mutations (c.5806_5808delCTC and c.5880_5882delCTT) were identified in the MYO7A gene in one family. These mutations may have relevance in some cases of non-syndromic hearing loss among Africans.

Objectives

The objective of this project was to screen, using molecular methods, two specific MYO7A deleterious mutations, in an African cohort with ARNSHL, and to analyse the interaction of secondary variants with MYO7A.

Methods

Patients and controls: A previously well described group of 100 patients affected with ARNSHL together with 200 ethnically-matched normal hearing control samples.

Molecular Methods: Genetic screening was performed using direct Sanger Sequencing.

Bioinformatics analysis: Pathogenicity of the mutation and influence of secondary variants were analysed using SCRIPT bioinformatics tool.

Preliminary Results

The presence of c.5806_5808delCTC was detected, in heterozygosity, in 1 of the 100 patients and in none of the 100 controls population. Similarly c.5880_5882delCTT was not detected in control populations; its detection among isolated case of hearing loss is ongoing.

Conclusions

This study is a proof of concept of the use of NGS in resolving cases of ARNSHL amongst patients of African descent. The absence of the mutations in other cases of non-familial hearing loss could indicate that these are private mutations specific to the families' studied and could not deserve routine investigation in isolated patient with hearing loss. The single patient carrier could carry a second MYO7A undiscovered mutation which affects the second allele that will need further investigations."

PY42   Xhosa translation of the Internalised Stigma of Mental Illness Scale for use in
                 South African Xhosa people with schizophrenia and rheumatic heart disease

O. Matshabane, J. de Vries, P. Appelbaum, P. Marshall, B. Mayosi, D.J Stein, M.M Campbell.

Abstract

Standardised measuring instruments are commonly used in stigma research, however cultural and linguistic factors may be barriers to conducting such research with Xhosa-speaking South Africans. It is therefore important to apply a thorough translation design in preparing stigma measures for use with Xhosa speakers. The aim of this article is to describe the process of translating the Internalised Stigma of Mental Illness Scale (ISMIS) into Xhosa for use in a South African stigma study that compares stigma experiences across Xhosa people with Schizophrenia and those with Rheumatic Heart Disease. The ISMIS was translated into Xhosa using a five stage translation design. First the measure was forward-translated into Xhosa by four Xhosa speaking healthcare professionals. Next the group met as a committee to discuss and debate the resultant translations and select preferred translation choices for each questionnaire item. The resultant ISMIS Xhosa translation was then quantitatively piloted in a sample of 50 Xhosa people with schizophrenia and 50 Xhosa people with rheumatic heart disease living in the Western Cape of South Africa, and qualitatively piloted in a smaller sub-sample of 5 Xhosa people with schizophrenia and 5 Xhosa people with rheumatic heart disease using cognitive interviewing. Furthermore, the tool was back-translated into English by an independent Xhosa speaking translator. The translation team met together to review the piloting data to resolve any discrepancies. Results of the piloting process suggest that this translation design worked well, however some challenges included the difficulty in finding conceptually equivalence Xhosa vocabulary for English concepts relating to stigma and discrimination experiences."

PY43   **Enhancing Ethiopian Youth's Literacy about gene * environment contributions about health using the context of podoconiosis.**

Kibur Engidawork, Desta Ayode, Colleen, McBride, Gail, Davey & Getnet, Tadele.

Introduction: Improved understanding of gene-environment contributors to health conditions can enhance preventive actions of the public to reduce risky health behaviors. The goal of this project is to study the youth's perceptions of podoconiosis (a non-filarial elephantiasis) along with the factors that account for such perceptions. This will be done with the ultimate aim ofexploring approaches and settings for improving literacy regarding gene-environment contributors to podoconiosis as a model for other preventable health conditions.

Method: This study explored youths' mental model using qualitative methods. Data were collected from rural youth in Southern Ethiopia, Wolita Zone, in December 2015. Two focus group discussions and 30 in-depth interviews were conducted with affected and non-affected youth. Data were transcribed and verbatim translated from the local languages into English. The transcribed data were coded and analyzed using qualitative software, from which key nodes were identified and youth mental model constructed.

Results: Preliminary findings indicated that the youth harbor various misconceptions about the etiology and prevention of the disease. In particular, the study found a number of misconceptions related to the cause of podoconiosis among non-affected youth. The results showed that some youth overemphasize genetics as a sole determinant of podoconiosis and this resulted in a belief that the occurrence of the disease in affected families is inevitable. Moreover, contagion (blood contact) and breast feeding were understood as genetic factors for the transmission of the disease. The study also documented inaccurate perceptions about the impact of the environment on podoconiosis. We also found better understanding among affected youth on the concept of preventability regardless of the type of cause, which are believed to stem from interaction with health care providers in the community.

Conclusion: Our lay mental model generated from the qualitative data informed incomplete understanding of the youth about the joint contributions of gene and environment in causing podoconiosis. We suggest that evaluating these findings with experts' model and quantitative data   is paramount to attest clear knowledge gap and explore suitable approaches and settings for improving literacy regarding gene-environment contributors to podoconiosis."

PY44　　　　　**Exploring the effect of stroke on the alimentary and urogenital microbiomes of Nigerians patients**

Melikam ES, Owolabi MO Akinyemi RO Ovbiagele B

Introduction: Whereas the burden of stroke is declining in high income countries, it is rising in low and medium countries (LMICs) where the fatality rates are also higher.

The putative immunosuppressive effect associated with cerebral damage (such as caused by stroke) may contribute to the high rates of reported post-stroke infective complications accounting for the poor clinical outcomes especially in LMICs.

Consequently, prophylactic administration of antibiotics is a very common practice in most Nigerian Tertiary hospitals. However, there is insufficient evidence on the influence of immunosuppression conferred by stroke as well as the prophylactic administration of antibiotics on the microbiome of the alimentary and urogenital tracts which are susceptible gateways through which foreign bodies including microbes could gain entrance into the human body. An understanding of the above could lead to development of appropriate prophylactic and therapeutic interventions to improve outcome.

Objective: To characterize microbial communities from fecal and urine samples of adult Nigerian stroke patients using metagenomic techniques and evaluate the effect of stroke and antibiotic use on outcome.

Methodology: One hundred consenting stroke patients (age > 18) who present at the University College Hospital, Ibadan with the first-ever stroke episodes will be recruited. Consenting stroke-free controls (non-stroke status confirmed by the Questionnaire for Validating Stroke-Free Status already validated in Nigeria; age > 18) will be recruited (Hospital/Community-Based).

Data on socio-demographics, lifestyle habits, previous medical conditions, use of medications by enrolled subjects will be captured. Samples will be obtained from all subjects at baseline. DNA extracts will be purified using the QIAmp DNA Stool Mini kit (Qiagen) for fecal samples and the Norgen's Urine DNA isolation kit for urine samples following the manufacturer's protocol. Followed by bioinformatical analysis.

Next Steps:

Collect prospective data on antibiotic use, type, duration and outcome in stroke patients who received care at UCH in the past 12months.

Commence subject enrolment and sample collection after obtaining consent.

Implement procedures for specimen processing and analyses as stated above at equipped laboratories."

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Background
Infections by certain viruses, bacteria, and parasites have been identified as risk factors for some cancers.
Aim
To evaluate the numbers of cancers in Nigeria from 2012-2014 attributable to infections using data from Population Based Cancer Registries [PBCR] in Nigeria.
Methods
We considered cancers associated with Epstein-Barr virus [EBV], Human Papilloma Virus [HPV], Hepatitis B and C Virus [HBV/HCV], Human Immunodeficiency Virus and Human Herpes Virus 8 [HIV/HHV8], Helicobacter pylori and Schistosoma haematobium that have been classified as oncogenic by IARC. We obtained data on infection associated cancers from the registry databases of 3 PBCR in Nigeria; Abuja, Enugu and Calabar cancer registries. We used Population Attributable Fraction for infectious agents associated cancers in developing countries that were calculated using prevalence data and relative risk estimates in previous studies.
Results
The 3 PBCR reported 4,861 cancer cases from 2012-2014; 1,875 in males and 2,986 in females. There were 412 infection-associated cancers in males accounting for 22% of total cancers in males, and 351 [85%] of these were attributed to infections. In female, there were 727 infection-associated cancers accounting for 24% of all cancers in females and of these, 674 [93%] were attributable to infections. Cancers of the Cervix [n=430] and Liver [n=152] as well as Non-Hodgkin's Lymphoma [n=129] were the commonest infection-associated cancers in both sexes. The commonest infectious agents associated with cancers were HPV[n=453], HIV/HHV8 [n=199], HBV/HCV [n=143] and EBV [n=125].
Conclusion
Our finding suggests that 85% of infection-associated cancers in males and 93% infection-associated cancers in females can be prevented with vaccination, safer risk behaviours or anti-infective treatments."

PY46   **Phenotype and Functional Characterization of T Cell Subset from Lymph Node Lesions and Peripheral Blood of Calves Exposed to Natural Mycobacterium bovis Infection**

Fekadu Desta, Gobena Ameni and Rawleigh Howe

Background: It is generally accepted that protection against bovine tuberculosis (BTB) is made by cell-mediated immunity , and it is takes place mainly at the site of infection. This implies the relevance of studying the response to BTB at the site of the lesion. Nonetheless, there is little or no information on the characteristics of immune response to BTB at the site of lesions.

Methods: Peripheral blood mononuclear cells (PBMC) and lymph node cells (LNC) of the infected lymph nodes were isolated and investigated by flow cytometry. In the phenotypic study fresh cells were stained for CD3, CD4, CD8, WC1 $\gamma\delta$ and CD25 T cell surface markers. For functional analysis, the cells were stimulated with bacillus Calmette-Guérin , phorbol 12-myristate 13-acetate (PMA), ionomycin or medium for the investigation of proliferation of cells and cytokine response including gamma interferon- γ (IFN-γ), tumor necrosis factor alpha- α (TNF-α) and interleukin-4 (IL-4).

Results: The proportion of CD25+ expressing fresh cells was significantly higher (P<0.05) in CD4+ and CD8+ T cells isolated from lymph node than CD4+ and CD8+T cells isolated fromperipheral blood; this was especially apparent in vaccinated calves. However, such difference in expression CD25+ was not observed in WC1 $\gamma\delta$ T cells of lymph node and peripheral blood. To the

contrary from fresh cells, after stimulation, the proportion of CD25+ expressing cells was greater (P<0.05) in T cells of the peripheral blood than T cells of lymph node, and this was more apparent in vaccinated calves. Similarly, proportion of IFN-γ and TNF-α producing cells to PMA + ionomycin stimulation were significantly lower (P< 0.05) in the lymph nodes than in the peripheral blood. There was a significant difference in IFNγ and TNFα responses in the   lymph   node   and peripheral blood of vaccinated and non-vaccinated calves.   IL-4 producing cell were not evident in PBMC and LNC.

Conclusions: This preliminary study revealed that there is a difference in the phenotypic and functional characteristic of T cells of the peripheral blood and T cell isolated from the site of lesion in known BTB positive calves."

PY47   **Experience, Knowledge, Attitudes and Consequences of Stigmatisation Among Stroke Survivors:**

Implications for Genetic Testing

Introduction: Stroke is a leading cause of deaths, disabilities and neurologic admissions worldwide especially in low and middle income countries (LMICs).

Although neurorehabilitation have undoubtedly assisted in enlivening stroke survivors' hope of reintegrating with the society, stigmatisation could impair this hope with consequences. There is dearth of information regarding stigmatisation among stroke survivors although there are for other cardiovascular and chronic illnesses. Obtaining this information from persons stigmatised on account of stroke will provide useful evidence of their perceived and experienced stigma and assist in designing effective interventions for its reduction.

Objectives: To determine stroke survivors' experience of stigma; their knowledge, ability to identify stigmatising attitudes and its consequences (including levels of participation, quality of life, self-esteem and self-efficacy) in uptake of health services among stroke survivors in Nigeria.

Methodology: A mixed methods design will be employed. Purposive sampling technique will be used to recruit four hundred and twenty three (423) stroke survivors' across eight neurologic health facilities in Nigeria. The validated Stigma Scale for Chronic Illness (SSCI-v8) instrument which have demonstrated great potential for measuring stigma among other neurologic disorders will be used to quantify stroke survivors' experience of stigma. To further explore the study objectives, a focus group discussion (FGDs) probing stroke participants' knowledge on stigma, their ability to identify stigmatising attitudes and its consequences including levels of participation, quality of life, self-esteem and self-efficacy in uptake of health services including genetic testing for stroke will be conducted. A total of 72 stroke survivors, with maximum number of 8 participants per group will be recruited for FGDs across the selected health facilities.

Implications: This study will be conducted alongside the SIREN/THRIVES studies. Stigmatisation may have implications for attitudes and practice of genetic testing for stroke among Africans.

Key words: Stroke, Stigmatisation, Knowledge, Quality of life, Genetic testing"

PY48   **Genetic variants that influence HIV disease progression of**

prenatally infected patients in Botswana.

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Introduction: HIV Disease progression from to AIDS is variable among patients and can be influenced by genetic variants. Variants in chemokine receptor and HLA genes have been documented to affect progression in Europeans populations1, which have been widely studied compared to sub-Saharan African populations. At the extreme ends of the disease progression spectrum are Long Term Non-Progressors (LTNPs), who remain healthy and maintain stable CD4+ cell numbers without antiviral intervention for at least 10 years, and Rapid Progressors (RPs), who develop AIDs within 2-3 years of infection.

Objectives: Use whole exome sequencing (WES) data from LTNPs and RPs to identify host genetic variants that influence HIV disease progression in HIV prenatally infected patients in Botswana.

Methodology: Variant Calling Files (VCFs) generated from raw WES data of 62 LTNPs and 102 RPs were imported into Variant Tools2 for QC and annotation. Significant differences in allele frequencies between the two groups were tested using Fisher Exact. Variants (p-value < 1.0×10^{-4}) were selected and possible impact of amino acid substitutions determined in PolyPhen-2, SIFT and Mutation taster. Amino acids coded by genes with these variants were ranked by their relative evolutionary importance using Evolutionary Trace3.

Preliminary Results: We have identified single nucleotide variants exclusive to LTNPs and RPs that potentially predispose HIV infected individuals to rapid or long term non-progression to AIDS. Among these is a missense variant only observed in LTNPs (p-value 4.7×10^{-5}) in a transmembrane protein which has recently been implicated in contributing to lowering HIV-1 infection in the central nervous system.

Next Steps: Validate the variants by Sanger sequencing and replicate these findings in additional patients.