

# HUBERT KAIRUKI MEMORIAL UNIVERSITY



## 1. STAFF RESEARCH ACTIVITIES FROM 2000 TO 2014

### 1.1 Genetic Research

#### 1.1.1 Linkage disequilibrium and human genetic studies

Prof. Sylvester L.B. Kajuna (PI)

This is a systematic evaluation of linkage disequilibrium (LD) in a variety of human populations representing diversity of the species for loci located on diverse chromosomal regions of the human genome to locate gene clusters related to certain diseases.

#### 1.1.2 A study of genetic variation in the ADH and ALDH gene clusters in multiple populations and in alcoholics

Prof. Sylvester L.B. Kajuna (PI)

This project looks at the genetic variation in the primary ethanol metabolizing genes, the relationship of these functional gene variants to susceptibility to alcoholism, and whether the ADH1B\*369Cys allele is associated with a protective effect against alcoholism in Tanzanian and other alcoholics around the world.

#### 1.1.3) Possible Association between Pesticide Exposure, Parkinson's Disease, and Polymorphisms in the Glutathione Transferase (GST) Genes in Tanzanian patients

Prof. Sylvester L.B. Kajuna (PI)

#### 1.1.4 Genetic Links between East Africa, Maldives and Madagascar.

Prof. Sylvester L.B. Kajuna; as Co-Principal Investigator, in collaboration with Prof. H. Soodyal (PI) and Prof. Trefor Jenkins of the National Health Laboratory Service (NHLS) at the University of Witwatersrand, South Africa; and Prof. Gwyn Campbell at the McGill University, Canada.

This study looks at the genetic links between East Africa, Maldives and Madagascar using mitochondrial DNA (mtDNA) and Y-chromosome DNA.

### 1.2 HIV

**1.2.1 A Comparison of the Efficacy and Safety of NK2 against Standard Combination Therapy in Patients with Symptomatic Primary Human Immunodeficiency Virus Type I (HIV-1) Infection: a Randomised Controlled Trial.**

Prof. Sylvester L.B. Kajuna (PI)

**1.2.2 Factors Contributing to Antiretroviral Therapy Non-adherence Among People Living with HIV/AIDS Attending Care and Treatment Clinics (CTC) in Private Hospitals in Dar es Salaam Region**

Miriam Napandilwa (PI)

**1.2.3 Duration of Symptoms and Clinical Outcomes Among Patients With AIDS-Related Kaposi's Sarcoma at Ocean Road Cancer Institute**

Dr. Shaaban I. Mohammed (PI)

**1.2.4 Prevalence of Adverse Pregnancy Outcome and Associated Risk Factors Among HIV Infected Women Delivered at Mwananyamala Hospital From May to October, 2008**

Dr. Grace D. Sangawe (PI)

**1.2.5 The Selection and Dynamics of Nevirapine Resistant HIV-1 Mutants During Single Dose Nevirapine Regimen: the Risk of Drug Resistance Transmission Through Breastfeeding**

Prof. Sylvester L.B. Kajuna (PI)

**1.2.6 Nutritional Status of Pregnant Tanzanian Women: An Assessment of Fatty Acids Critical to Infant Growth and Neurological Development and Impact of HIV/AIDS**

Prof. Sylvester L.B. Kajuna (PI)

**1.2.7 Effects of Plasmodium falciparum Antigen-stimulated Cytokine Production on Human Immunodeficiency Virus Type 1 (HIV-1) Replication.**

Prof. Sylvester L.B. Kajuna (PI)

## 1.3 Malaria

**1.3.1 Hyperphenylalaninemia in Cerebral Malaria**

Prof. Esther Mwaikambo (PI)

This study looks at Phenylalanine and nitrogen dioxide levels in children with complicated cerebral malaria

**1.3.2 Urine Pterin Level Among Children with Uncomplicated Malaria in Dar es Salaam**

Dr. Jackson Mukemba (PI)

**1.3.3 Anaemia and Co-infection of Plasmodium falciparum and Hookworm Among Primary School Children in Kinondoni Municipality, Dar es Salaam Region, Tanzania**

Dr. T.K. Kabalimu (PI)

### **1.3.4 Immune Cytokine Expression and Host Susceptibility to Combination Antimalarial Treatment Resistance in *P.falciparum* Endemic Tanzania**

Dr. Boniphace Sylvester (PI)

## **1.4 Clinical Research**

### **1.4.1 Eclampsia: Magnitude, related Factors, and Outcome of Pregnancy at Amana hospital in Ilala Municipality**

Dr. Monica Chiduo (PI)

### **1.4.2 Management of Cholelithiasis in Developing Countries: Five year experience in TMJ Hospital, Dar es Salaam (200-2006), KCMC, Moshi and Bugando MC, Mwanza**

Dr. J.P.Mkiramweni (PI)

### **1.4.3 Cumulative Burden Placed on the Families of Psychiatric Patients Living in the Community**

Dr. Alphage Liwa (PI)

## **2. PUBLICATIONS IN PEER-REVIEWED JOURNALS FROM 2000 -2014**

- 1) Kikwilu E. Mugonzibwa E.A, Rugarabamu PGN, Ntabaye MK. Tanzania High School Students' Attitude Towards Five University Profession Courses. East African Medical Journal, 2000, 77(3): 18 – 22.
- 2) Mugonzibwa EA., Kikwilu E., Rugarabamu PGN, Ntabaye M. Factors influencing career choice among high school students in Tanzania. Journal for Dental Education, 2000, 64(6): 423 – 429.
- 3) Morahan G, Boutlis CS, Huang D, Pain A, Saunders JR, Hobbs M, Granger DL, Weinberg JB, Peshu N, Mwaikambo ED, Marsh K, Roberts, DJ, Anstey NM. A promoter polymorphism in the gene encoding interleukin-12p40 (IL12B) is associated with mortality from cerebral malaria with reduced nitric oxide production. Genes and Immunity 3: 414, 2001.
- 4) Hobbs MR, Undhayakumar V, Levesque MC, Booth J, Tkachuk AN, Pole A, Roberts JM, Kairuki S, Nahlen BL, Mwaikambo ED, Lal AI, Granger DL, Anstey NM, Weinberg JB. A novel NOS2 promoter polymorphism associated with protection from severe malaria in Tanzania and Kenya children. Lancet 360: 1468 – 1475, 2002.

- 5) Weinberg JB, Hobbs MH, Levesque MC, Udhayakumar V, Roberts JM, Kairuki S, Nahlen BL, Mwaikambo ED, All AL, Anstey NM, Granger DL. NOS2 promoter polymorphism as determinants of NO promoter polymorphisms and susceptibility to severe malaria in humans Nitric Oxide 6: 488, 2002 (abstract).
- 6) Rugarabamu PGN, Poulsen S, Masalu JRP: A longitudinal study of occlusal caries among schoolchildren in Dar es Salaam, Tanzania. Community Dent Oral Epidemiology 2002; 30: 47 – 51.
- 7) P.P. Mella: Major Factors that Impact on Women's Health in Tanzania: The way forward. Journal of the International Council on Women's Health Issues Vol. 24(8), p712, 2002. Tylor & Francis Health Sciences Inc. Philadelphia.
- 8) Giuseppe Raviola, M'imunya Machoki, Esther Mwaikambo and Mary jo Delvecchio Good. HIV, Disease Plague, Demoralization and "Burnout;" Resident Experience of the Medical Profession in Nairobi, Kenya, Culture, Medicine and Psychiatry 26: 55 – 86, 2002.
- 9) Weinberg JB, Hobbs MH, Levesque MC, Udhayakumar V, Roberts JM, Kairuki S, Nahlen BL, Mwaikambo ED, All AL, Anstey NM, Granger DL. NOS2 promoter polymorphisms as determinants of NO promoter polymorphisms and susceptibility to severe malaria in humans. Nitric Oxide 6:488, 2002 (abstract).
- 10) M. Gwamaka<sup>1</sup>, J.A. Matovelo<sup>1</sup>, M.M.A. Mtambo<sup>2</sup>, G. K. Mbassa<sup>3</sup>, R. M. Maselle<sup>1</sup>, and Boniphace, S. The Effect of Dexamethasone and Promethazine in Combination with Buparvaquone in the Management of East Coast Fever. Submitted to Onderstepoort Journal of Veterinary Research (South Africa), 2004.
- 11) Morahan g, Boutlis CS, Huang D, Pain A, Saunders JR, Hobbs M, Granger DL, Weinberg JB, Peshu N, Mwaikambo ED, Marsh K, Roberts, DJ, Anstey NM. A promoter polymorphism in the gene encoding interleukin-12p40 (IL12B) is associated with mortality from cerebral malaria with reduced nitric oxide production. Genes and Immunity November, 2002/3: (7)414 – 8.
- 12) Lopansri BK, Anstey NM, Weinberg JM, Hobbs MR, Levesque MC, Ganger DL, Mwaikambo ED. Low plasma arginine in children with cerebral malaria and decreased Nitric Oxide Production. Lancet 361: 676 – 678, 2003.
- 13) Hobbs MR, Udhayakumar V, Levesque MC, Booth J, Roberts JM, Tkachuk AN, Pole A, Coon H, Kairuki S, Nahlen BL, Mwaikambo ED, Lal AL, Granger DL, Anstey NM, Weinberg JB. A new NOS2 promoter polymorphism associated with increased nitric oxide production and protection from severe malaria in Tanzania and Kenyan Children. Comment in Lancet of 2003 Feb 15; 361 (9357) 609 – 10; author's reply 610 – 1.

- 14) Lopansri BK, Anstey NM, Weinberg JM, Hobbs MR, Levesque MC, Mwaikambo ED, Granger DL. Low plasma arginine in children with cerebral malaria and decreased Nitric Oxide Production, *Lancet* 361: 676 – 678, 2003.
- 15) Hiroki Oota, Andrew J, Pakstis, Batsheva Bonne-Tamir, David Goldman, Elena Grigorenko, Sylvester L.B. Kajuna, Nganyirwa J. Karoma, Selemeni Kungulilo, Ru-Band Lu, Kunle Odunsi, Friday Okonofua, Olga. V. Zhukova, Judith R. Kidd, and Kenneth K. Kidd. Strong linkage disequilibrium and a small number of haplotypes at the ALDH2 locus around the world. *Annals of Human Genetics*; March, 2004; Vol. 68, 93 – 109; USA.
- 16) Meg A. Palmatier, Andrew J. Pakstis, William Speed, Peristera Paschou, David Goldman, Adekunle Odunsi, Friday Okonofua, Sylvester Kajuna, Nganyirwa Karoma, Selemeni Kungulilo, Elean Grigorenko, O. V. Zhukova, Barsheva Bonner-Tamir, Ru-Band Lu, Joseph Parnas, Judith R. Kidd, Mellissa M.C. DeMille, Kenneth K. Kidd. Population-specific differences in the frequencies of a COMT haplotype associated with Schizophrenia. Published in *Molecular Psychiatry Journal*; USA; April, 2004;
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- 19) Davidson AC, Pakstis AJ, Speed WC, Bartoshuk L, Duffy V, Friedlaender J, Grigorenko EL, Kajuna SLJ, Karoma NJ, Kim JJ, Kungulilo S, Lu RB, Odunsi A, Okonofua F, Parnas J, Schulz LO, Snyder DJ, Zhukova OV, Kidd KK, Kidd JR. "No Evidence for balancing Selection at the TAS2R38 (PTC) Gene". Submitted, 2013; *Annals of Human Genetics*; USA.
- 20) Han Y, Oota H, Osier MV, Pakstis AJ, Speed WC, Odunsi A, Okonofua F, Kajuna SL, Karoma NJ, Kungulilo S, Grigorenko E, Zhukova OV, Bonne-Tamir B, Lu RB, Parnas J, Schulz LO, Kidd JR, Kidd KK. "Considerable Haplotype Diversity within the 23kb Encompassing the ADH7 Gene". *Alcohol Clin Exp Res* 29:2091-2100. (2005).
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- 23) Michael P. Donnelly, Peristera Paschou, Elena Grigorenko, David Gurwitz, Csaba Barta, Ru-Band Lu, Olga V.Zhukova, Jong-Jin Kim, Marcello Siniscalco, Maria New ,Hui Li, Sylvester Kajuna, Vangelis G. Manolopoulos, William C. Speed, Andrew J. Pakstis, Judith R. Kidd, Kenneth K. Kidd "A global view of the OCA2-HERC2 region and pigmentation". Human Genet 131:683-696. (2012)
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- 31) Mshigeni, Keto E. and Ludovick D.B. Kinabo (Eds.). 2012. Lighting a Fire: 31 Inspiring Stories of Eminent Tanzania Scientists, Vol. 1. MKUKI NA NYOTA, Dar es Salaam. 394 pp. + xiv, ISBN 978-9987-08-197-4. Amongst the 31 stories in the book, 5 were from HKMU, viz., The Founder of HKMU, the late Prof. Hubert Kairuki; Prof. Esther Mwaikambo; Prof. Boniface Msamati, Prof. Theonest Mutabingwa, and Prof. Keto Mshigeni, who generated the idea on writing the book intended for inspiring the youth towards studying science subjects, and who steered its publication process.
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- 33) Mshigeni, K. E. 2012. Mushroom industry development in Africa: prospects and challenges. In. Proceedings of the World Forum for Mushroom Industry in Developing Countries, Mudanjiang, China, September 1, 2012: Pages 29- 36.
- 34) S.Kajuna, K.E. Mshigeni; Impact of Climate Change on Health in Africa: Implications for Disease Burden and Control; Discovery and Innovation Journal, December, 2008; Volume 20 Nos.3&4, pages 164 - 168.
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- 37) S.L.B. Kajuna; B. Msambichaka; HIV/AIDS in Africa: Immunology, Genetics and the Challenges for Vaccine Development - accepted and published by the Academic Science Publishers ( Third World Academy of Science s); *Discovery and Innovation Journal*, June, 2007 ; Volume 19 No.2, pages 71 - 78.

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- 39) **Kajuna SLB**: Kenneth K Kidd; Andrew J Pakstis A Global Survey Haplotype Frequencies for the TAS2R38 (PTC) Gene PTC taste perception. Submitted to the Annals of Human Genetics; USA, 2013.
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## CURRENT RESEARCH ACTIVITIES AT HKMU

### 1. GENETICS

#### 1.1. Linkage disequilibrium and human variation:

In this project we carry out a systematic evaluation of linkage disequilibrium in a variety of human populations representing the diversity of the species for loci located on diverse chromosomal regions of the human genome. Base pair sequences in each type of DNA isolated from human blood samples and cultured lymphoblastoid cells are determined by restriction mapping and verified through comparison of observed fragment patterns to those expected from a known human DNA sequence. Histograms showing the number of restriction site differences between pairs of individuals are constructed and the average number of differences observed between any two humans are determined. From the number of restriction site differences, we estimate the extent of nucleotide sequence divergence for each pair of individuals. Other studies focus on the pattern of variation seen at specific genes that may have some biomedical relevance. In general, studies of these genes are not directly related to the health of specific individuals or populations, but rather to normal and pathologic processes in a broader context with the expectation that better understanding of these genes in human populations is an important part of basic biomedical knowledge for the betterment of human health.

### **1.2. A study of genetic variation at the ADH and ALDH loci in multiple populations and in alcoholics:**

In this project we look at genetic variation in the primary ethanol metabolizing genes; the relationship of these functional gene variants to susceptibility to alcoholism, and whether the ADH1B\*369Cys allele is associated with a protective effect against alcoholism in Tanzanian and other alcoholics.

### **1.3. Genetic Links Between East Africa, Maldives and Madagascar:**

In this project we examine the impact of migrations, gleaned from historical records and trade activities in the Indian Ocean rim, on the gene pool of East African, Maldivian and Madagascar populations. We use isolated DNA from blood and saliva/swab samples to screen for genetic polymorphisms in mitochondrial DNA (mtDNA), Y-chromosome DNA, X-chromosome DNA, and autosomal DNA [single nucleotide polymorphisms (SNPs) and short tandem repeats (STR)] in the same individuals. The collective data would give insights into how females (mtDNA) and males (Y-chromosome DNA) have contributed to shaping the gene pool of Tanzanian populations, and permit a judicious examination of how population specific factors (eg. migration, founder effects, drift, etc.) have contributed in shaping the gene pool of the present-day East African and particularly Tanzanian (including Zanzibar and Pemba) populations.

## **2. HIV/AIDS**

### ***2.1 The Selection and Dynamics of Nevirapine Resistant HIV-1 Mutants During Single Dose Nevirapine Regimen: the Risk of Drug Resistance Transmission Through Breastfeeding.***

In spite of increased use of single-dose Nevirapine to reduce mother-to-child transmission of HIV-1 in resource-limited settings due to its cost effectiveness, little is known about the effects of this regimen on viral loads in breast milk or on the temporal patterns of drug resistance that arise during the early postpartum period. There is also limited data on whether different

subtypes or clades of HIV-1 will develop resistance to Nevirapine at the same rate and as a result of the same mutations. Comparative studies of viruses of different clades are therefore needed in this regard. We therefore, in this

prospective randomized open pilot study, try to assess the dynamics of Nevirapine -resistant mutations occurring after single dose Nevirapine prophylaxis to prevent mother-to-child transmission and the risk of transmission of Nevirapine -resistant HIV-1 variants from mother to child through breastfeeding in a treatment naive Tanzanian population exposed to single dose Nevirapine during delivery.

### Ongoing Research at HKMU between August 2010 to date

#### 1. *Linkage disequilibrium and human genetic studies:*

This project carries out a systematic evaluation of linkage disequilibrium in a variety of human populations representing the diversity of the species for loci located on diverse chromosomal regions of the human genome in collaboration with the Genetics Department; Yale University School of Medicine; New Haven, Connecticut, USA.

**K.Kidd (Principal Investigator); S.L.B. Kajuna (Co- Principal Investigator).**

#### 2. *Assessment of Arginine Flux in Normal Children and Children with Severe Malaria.*

This project looks at uncomplicated malaria in children.

**Prof. Esther Mwaikambo (Principal Investigator); J. Brice Weinberg (Co-Principal Investigator)** Duke University; North Carolina, USA.

#### 3. *Arginine, Nitric Oxide and Severe Malaria*

This project looks at uncomplicated malaria in children

**Prof. Esther Mwaikambo (Principal Investigator); J. Brice Weinberg (Co-Principal Investigator)** Duke University; North Carolina, USA.

#### 4. **GHAWA/AusAID Tanzania Programme:**

*The exploration of caring behaviours in Tanzanian registered nurses and midwives, including nursing and midwifery educators and students.* Rene Michael, Mark Jones, **Pauline Mella**, Phillip Della, Shelley Gower, Pam Roberts.

### Research conducted by Postgraduate Students:

1. *Epidemiology of Road Traffic Injuries Among Patients Presenting to Tumbi District Designated Hospital, Kibaha District, Pwani Region.*

**Dr. Makame Omar Hamad (3<sup>rd</sup> year M.Med Surgery, 2011)**

2. *Prevalence of Metabolic Syndrome in People Living with AIDS Using Highly Active Antiretroviral Therapy at Care and Treatment Centres in Ilala Municipal*  
**Dr. Digna Narciss Riwa (3<sup>rd</sup> year M.Med Internal Medicine, 2013).**
3. *Paediatric Intestinal Obstruction as Seen in Muhimbili National Hospital*  
**Dr. Kiwale (4<sup>th</sup> year Surgery, 2012)**
4. *Prevalence and Factors Contributing to Occurrence of Upper Gastrointestinal Bleeding at Amana Hospital, Dar es Salaam, Dr. Eric Kimaro Muhumba (4<sup>th</sup> year Surgery, 2012)*

#### Recent publications:

1. Mukherjee N, Kidd KK, Pakstis AJ, Speed WC, Li H, Tarnok Z, Barta C, **Kajuna SLB**, Kidd JR "The **Complex Global Pattern of genetic variation and linkage disequilibrium at Catechol-O-methyl transferase (COMT)**". *Molecular Psychiatry* 15:216-225. (2010)
2. Donnelly MP, Paschou P, Grigorenko E, Gurwitz D, Mehdi SQ, **Kajuna SLB**, Barta C, Kungulilo S, Karoma NJ, Lu R-B, Zhukova OB, Kim JJ, Comas D, Siniscalco M, New M, Li P, Li H, Manolopoulos VG, Speed WC, Rajeevan H, Pakstis AJ, Kidd JR, Kidd KK. "**The Distribution and Most Recent Common Ancestor of the 17q21 Inversion in Humans.**". *Am. J of Human Genetics* 86:161-71. (2010)
3. Michael P. Donnelly, Peristera Paschou, Elena Grigorenko, David Gurwitz, Csaba Barta, Ru-Band Lu, Olga V. Zhukova, Jong-Jin Kim, Marcello Siniscalco, Maria New, Hui Li, **Sylvester Kajuna**, Vangelis G. Manolopoulos, William C. Speed, Andrew J. Pakstis, Judith R. Kidd, Kenneth K. Kidd "**A global view of the OCA2-HERC2 region and pigmentation**". *Am. J of Human Genet* (2011)
4. Donnelly, Michael; Paschou, Peristera; Grigorenko, Elena; Barta, Csaba; Lu, Ru-Band; Zhukova, Olga; Kim, Jong-Jin; Siniscalco, Marcello; New, Maria; Li, Hui; **Kajuna Sylvester**; Speed, William; Pakstis, Andrew; Kidd, Judith; Kidd, Kenneth; "**Global distributions and selection at pigmentation alleles in SLC24A5 and SLC45A2**" *Am. J of Human Genetics* (submitted for publication).