Strengthening genomic studies of cardiometabolic diseases in Africa – the AWI-Gen experience
Human Heredity and Health in Africa

Inaugural H3Africa meeting
Addis Ababa - October 2012
Human Heredity and Health in Africa

“To facilitate an Africa-based contemporary research approach to the study of genomics and environmental determinants of common diseases with the goal of improving the health of African populations”

1. Study genomic and environmental determinants of disease
2. Develop capacity for genomic research in Africa (teaching and training)
3. Develop an ethical, legal and social framework for genomic studies

www.h3africa.org
The H3Africa Consortium

8 Collaborative Centers

6 Ethics Grants

The H3Africa Consortium

Guidelines
- Informed consent
- Community engagement

Policies
- Publication
- Data & specimen access and sharing

3 Pilot Biorepositories

Bioinformatics Network

H3Africa GWAS array
Represent common variation across African populations

7 Research Projects

H3ABioNet
- 15 Countries
- 32 Research Groups
- 12 workshops
- 420 participants
H3Africa Footprint 2014

Enabling the genomic revolution in Africa

H3Africa is developing capacity for health-related genomics research in Africa

By The H3Africa Consortium

Science (June 2014) 344 (6190):1347-8
Increase in NCD deaths in Africa

High genetic diversity

GWAS studies
AWI-Gen team & study sites in Africa

- Ghana, Navrongo (Rural)
  - Abraham Oduro

- Burkina Faso, Nanoro (Rural)
  - Halidou Tinto

- Kenya, Nairobi (Urban)
  - Catherine Kyobutungi

- South Africa, Soweto (Urban)
  - Shane Norris

- South Africa, Agincourt (Rural)
  - Stephen Tollman

- South Africa, Dikgale (Rural)
  - Marianne Alberts
BMI in Countries from AWI-Gen Study

Data from - [http://www1.imperial.ac.uk/medicine/globalmetabolics/](http://www1.imperial.ac.uk/medicine/globalmetabolics/)  
Graphs: Carol Liu
AWI-Gen Conceptual Framework

Risk factors:
- Diet
- Exercise
- Infection history
- Genetics

Body Composition
- Obesity

Translation
- Prevention
- Policy
- Novel therapeutics

Outcomes: CMD
- Hypertension
- Diabetes
- Stroke
- Atherosclerosis
AWI-Gen Aims

1. Building capacity for genomic research
2. Population structure and genome architecture
3. Genomic and environmental contributions to body composition and CMD diseases across six Centres in Africa (GWAS with ~12 000 individuals)

Flagship Project: Metabochip study
AWI-Gen workshop October 2015
AWI-Gen Trait Association Study at a glance

**AWI-Gen Study**
- Ethics Review
- Community Engagement

**RESOURCES**
- Biobanked Samples
- Secure Data (EGA)

**Participant**
- Questionnaire
- Anthropometry
- Ultrasound
- Samples
  - Blood
  - Urine

**12000 Participants**
- 40-60yrs
- M:F
- Unrelated

**DATA**
- Demography
- Medical History
- Biomarkers
  - Lipid profile
  - Glucose and insulin
  - Other
- Genetic
  - Population structure
  - Association studies

**Participant enrolment**
- Informed Consent

**Ethics Review**

**Community Engagement**

**Biobanked Samples**

**Secure Data (EGA)**
Participant Recruitment

- **Soweto (South Africa)**: 2000
- **Nairobi (Kenya)**: 1500
- **Navrongo (Ghana)**: 1000
- **Agincourt (South Africa)**: 1500
- **Dikgale (South Africa)**: 1000
- **Nanoro (Burkina Faso)**: 2000

**Total (12000)**

- **Outstanding Enrollment**: 36%
- **Enrolled not yet shipped**: 36%
- **Samples Shipped**: 28%
Baseline data and preliminary analysis

Environment

Biomarkers

Anthropometry

Genetic Variation

BMI
- Waist circumference
- Hip circumference
- Visceral fat
- Subcutaneous fat

SES
- Education
- Substance use (tobacco, alcohol, drugs)
- Exercise

Fasting glucose and insulin
- Lipid profile
### Preliminary Analysis: BMI

#### Male

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Preliminary Analysis: Self-reported CVD

### Hypertension

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### Stroke

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Numbers:

- South 1: 845
- South 2: 837
- South 3: 2018
- East 1: 1580
- West 1: 580
- West 2: 1790
Flagship Project

The Metabochip as a tool to identify genetic markers of obesity risk in the South African black population

Venesa Pillay – PhD Student
Supervisors: Z Lombard, N Crowther, H Soodyall

Female caregivers
n = 1033
Median age 41.8 yrs

Genotyping – UC Davis Genome Center (USA)
QC: SNPs and samples

Association with anthropometric and body composition measures using linear regression
(adjustment for covariates)
PLINK software (vs. 1.9) and GCTA (vs. 1.24.4)
Massai, Kenya

Luwya, Kenya

Yoruba, Nigeria

Bt20, South Africa

South-western Bantu speakers

South-eastern Bantu speakers

Population stratification
Association with total fat mass

rs6425446 $SEC16B$
Universal risk locus for BMI

**Effect ($\beta$) =**
2.32kg fat mass

$CNTNAP5$
GWAS Catalogue not associated with body composition

**Effect ($\beta$) =**
-5.2kg fat mass
**SEC16B**

1. **SEC16B** associated SNPs show association with BMI in European, Asian and African American populations
2. Mouse model: Allele - Sec16b\(^{tm1a(KOMP)Wtsi}\)
   - Association: body weight, cholesterol levels
   - HDL differences show sex specific effect

rs6425446 – downstream of **SEC16B**
## Timeline

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**Year 1a** – Aug 2012 to Jan 2013  
**Year 1b** – Feb 2013 to July 2013  

**Aug 2015 to Feb 2016**  

**July 2017**
H3Africa Timeline for Phase 2

Next call for NIH proposals
May-July 2016

Submission of Proposals
October-Dec 2016

Award of proposals
Aug-Dec 2017

wellcome trust
Acknowledgements

Wits
Scott Hazelhurst
Zane Lombard
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INDEPTH
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Stephen Tollman
Abraham Oduro
Godfred Agongo
Christopher

Halidou Tinto
Hermann Sorgho
Marianne Alberts
Catherine Kyobutungi
Kate Theron

….and all the scientists, clinicians, fieldworkers and participants!