AWI-Gen
Wits-INDEPTH Partnership

Genomic and environmental risk factors for cardiometabolic disease in Africans

Collaborative Centre

Project Manager: Ntombizodwa Mthembu
National Institutes of Health - Wellcome Trust H3Africa Research Network

H3Africa Consortium: Policies Harmonisation

NIH Primary Award Institution
WT Primary Award Institution
Collaborating Institution

Other collaborating institutions are in Belgium, Canada, France, the United Kingdom, and the United States of America.
Change in obesity (1980 to 2008)

East Africa (female)
Change = 1.3% per decade (0.6, 2.0)

Southern Africa (female)
Change = 5.2% per decade (1.0, 8.9)

West Africa (female)
Change = 2.4% per decade (1.3, 3.2)

East Africa (male)
Change = 0.4% per decade (−0.2, 1.0)

Southern Africa (male)
Change = 4.3% per decade (2.1, 5.0)

West Africa (male)
Change = 1.0% per decade (0.2, 1.8)

Stevens et al. Population Health Metrics 2012, 10:22
http://www.pophealthmetrics.com/content/10/1/22
Top 5 leading **risk factors** for burden of disease (DALYs) in **South Africa**
AWI-Gen Collaborative Center overview

Wits

Wits Health Consortium

SBIMB
- Wits Bioinformatics
- School of Pathology
- School of Public Health
- DPHRU

INDEPTH Board
- INDEPTH Network
  - Agincourt
  - Dikgale
  - Navrongo
  - Nairobi
  - Nanoro

High Impact Science – Tangible Benefits

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AWI-Gen 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
Top 5 leading risk factors for burden of disease (DALYs) in South Africa

High BMI as a risk factor
- Ghana 7th
- Kenya 14th
- Burkina Faso not in top 15
Project – Aims

1. Pilot Project – Soweto (~2000 individuals)
2. Population structure and genome architecture
3. Genomic and environmental contributions to body composition across six Centres in Africa (~12,000 individuals)
Aim 1: Pilot Project

Urban Soweto study
• Study design
  – Population sample
  – Age 40 to 60 yrs
  – Male & Female
  – Body composition phenotype
• Genomic platform
  – Metabochip
  – Candidate gene/region fine mapping
• Analysis
  – Correlations with quantitative traits related to body composition and cardiometabolic risk

Progress
  – ~1000 females
  – Phenotyped
  – Genotyped

Next steps
  – Preparing DNA from next 1000 individuals for genotyping
  – Bioinformatics training
  – Data analysis
Advantages:
• Cost effective & Rapid results
• Fine mapping (previous associations)
• Replication study
• Data provide a great training opportunity

Disadvantages:
• SNP choice largely Eurocentric
• Previous associations not in African populations
• SNP choices now outdated (designed in 2009)
• Limits novel discovery
Aim 2: Population structure and genomic architecture

- AWI-Gen Study design
  - 30 unrelated trios
  - 40 unrelated individuals
- Genotyping Platform
  - Uncertain (Genome sequencing?)
- Outcome
  - HapMap equivalent for each population
  - Common variant allele frequencies
- Challenge
  - Which populations to test

PCA – ~ 460,000 SNP markers
May et al. (2013) BMC Genomics
### Complexity of population structure

**Africa**

2,146 languages spoken (30.2% of all living languages)

789,138,977 people (12.7% of all people)

<table>
<thead>
<tr>
<th>Country</th>
<th>No. Living languages</th>
<th>Indigenous languages</th>
<th>Immigrant languages</th>
<th>Population size</th>
<th>Diversity Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burkina Faso</td>
<td>70</td>
<td>68</td>
<td>2</td>
<td>10.9 M</td>
<td>0.768</td>
</tr>
<tr>
<td>Ghana</td>
<td>86</td>
<td>81</td>
<td>5</td>
<td>25.1M</td>
<td>0.835</td>
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<tr>
<td>Kenya</td>
<td>72</td>
<td>67</td>
<td>5</td>
<td>37.6M</td>
<td>0.928</td>
</tr>
<tr>
<td>South Africa</td>
<td>44</td>
<td>28</td>
<td>16</td>
<td>44.6M</td>
<td>0.874</td>
</tr>
</tbody>
</table>

Aim 3: Genetic and environmental contributions to body composition

- Ethics approval (Community engagement)
- Standardised phenotype questionnaire
- SOPs
- Central measurement equipment purchase & training
- Training in genomic science
- Staggered field roll out (QA)

**Blood samples (fasting):**
- EDTA (DNA)
- Clotted (serum - lipids)
- NaF (plasma - glucose)

**Added sampling:**
- Spot urine collections
Body composition and HIV infection

In a population sample of 2000 individuals.....

<table>
<thead>
<tr>
<th>Location</th>
<th>Expected number HIV infected individuals</th>
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<tbody>
<tr>
<td>Agincourt</td>
<td>462</td>
</tr>
<tr>
<td>Dikgale</td>
<td>274</td>
</tr>
<tr>
<td>Nairobi</td>
<td>248</td>
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<tr>
<td>Nanoro</td>
<td>22</td>
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<tr>
<td>Navrongo</td>
<td>30</td>
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<tr>
<td>Soweto</td>
<td>304</td>
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</tbody>
</table>

Based on regional averages

Based on country average
Data Collection: RedCAP for AWI-Gen

Demographic Data (89)
- General Information
  - Demographic information
    - Age
    - Country
    - Home language*
    - Ethnicity*
    - Family Ethnicity
  - Family Composition
- Phenotypic Data (231)
  - General Health
  - Infection history
  - Cardiometabolic risk factors
  - Thyroid disease
  - Kidney disease
  - Physical activity
  - Sleep
- Individual measurements (25)
  - Anthropometric measurements
  - Blood pressure
  - Pulse
  - Ultrasound measurements
- Sample Collection (21)
  - Blood collection
  - HIV testing
  - Urine collection
- Checklist (11)
  - Questionnaire
  - Anthropometric measurements
  - BP, pulse and ultrasound measures
  - Blood Samples
  - HIV test
  - Urine sample
  - Travel reimbursement
  - Quality Controller ID

Phenotype Harmonisation with H3Africa Consortium

<table>
<thead>
<tr>
<th>ACTIVITY</th>
<th>YEAR 1</th>
<th>YEAR 2</th>
<th>YEAR 3</th>
<th>YEAR 4</th>
<th>YEAR 5</th>
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<tr>
<td>Training and capacity development</td>
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<tr>
<td><strong>Aim 1: Obesity and body composition pilot study – urban South Africa</strong></td>
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<td><strong>Aim 2: African genome structure</strong></td>
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<td><strong>Aim 3: Phenotyping and sampling for Cohorts</strong></td>
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<td><strong>Aim 3: Genome association study – west, east and south Africa</strong></td>
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Outcomes

- **Capacity development for genomic studies**
  - PhD students, postdocs, scientists
  - Epidemiology, population genetics, genomics, bioinformatics

- **Phenotype and blood profiles**
  - Means and ranges for African populations

- **New knowledge**
  - Pilot study
    - Replication data
    - Logitudinal analysis
    - Training
  - African population diversity
    - African variation enhanced chip (cost effective)
    - African population structure
  - Main research question

Increased understanding of the role of genome variation and environmental factors in cardiometabolic risk across African populations
Acknowledgements

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  Hermann Sorgho
  Marianne Alberts
  Catherine Kyobutungi
  Kate Theron

INDEPTH INTEGRATED COMMUNITY EPIDEMIOLOGY SURVEY

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2013