AWI-Gen

Wits – INDEPTH Partnership

Genomic and environmental risk factors for cardiometabolic disease in Africans

Collaborative Centre
World Bank – Change in burden of disease (1990 to 2010)

- **HIV/AIDS**
  - North Africa and Middle East: 178%
  - East Africa: 240%
  - Southern Africa: 1065%

- **Neonatal sepsis**
  - North Africa and Middle East: 26%
  - East Africa: 29%
  - Southern Africa: 10%

- **Neonatal encephalopathy**
  - North Africa and Middle East: 56%
  - East Africa: 53%
  - Southern Africa: 56%

- **Malaria**
  - North Africa and Middle East: 61%
  - East Africa: 57%
  - Southern Africa: 57%

- **TB**
  - North Africa and Middle East: 57%
  - East Africa: 57%
  - Southern Africa: 57%

- **Cirrhosis**
  - North Africa and Middle East: 74%
  - East Africa: 74%
  - Southern Africa: 74%

- **Sickle cell**
  - North Africa and Middle East: 66%
  - East Africa: 66%
  - Southern Africa: 66%

- **Diabetes**
  - North Africa and Middle East: 94%
  - East Africa: 99%
  - Southern Africa: 99%

- **Interpersonal Violence**
  - North Africa and Middle East: 79%
  - East Africa: 79%
  - Southern Africa: 79%

- **Major depressive disorder**
  - North Africa and Middle East: 63%
  - East Africa: 63%
  - Southern Africa: 63%

- **Road injury**
  - North Africa and Middle East: 36%
  - East Africa: 36%
  - Southern Africa: 36%

- **Ischaemic heart disease**
  - North Africa and Middle East: 37%
  - East Africa: 37%
  - Southern Africa: 37%

- **Low back pain**
  - North Africa and Middle East: 74%
  - East Africa: 74%
  - Southern Africa: 74%

- **COPD**
  - North Africa and Middle East: 38%
  - East Africa: 38%
  - Southern Africa: 38%

- **Stroke**
  - North Africa and Middle East: 33%
  - East Africa: 33%
  - Southern Africa: 33%

- **Meningitis**
  - North Africa and Middle East: 53%
  - East Africa: 53%
  - Southern Africa: 53%
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, 6.0)

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

- High BMI
- Smoking
- High blood pressure
- Dietary risks
- Alcohol use

High BMI as a risk factor
- Ghana 7th
- Kenya 14th
- Burkina Faso not in top 15
AWI-Gen - Outline

- Projects
- Management
- Ethics
- Phenotyping

- Data Management
- Training
- Challenges
- Progress

H3Africa – AWI-Gen - Accra - May 2013
1. Pilot Project – Soweto (~2000 individuals)
2. Population structure and genome architecture
3. Genetic 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
- Platform
  - Candidate gene/region assessment
  - Metabochip
- Analysis
  - Correlations with quantitative traits

**Progress**
- ~1000 females
- 40 to 60 years
- phenotyped
- DNA normalized
- Sent to service provider for genotyping

**Next steps**
- Prospective phenotyping of ~1000 males
- Sample collection
- DNA extraction & normalisation
- Genotyping & data QC
- Data analysis & interpretation
Aim 2: Population structure and genomic architecture

- **Study design**
  - 30 unrelated trios
  - 40 unrelated individuals

- **Genotyping Platform**
  - Uncertain

- **Outcome**
  - HapMap equivalent for each population
  - Common variant allele frequencies

- **Challenge**
  - Which populations to test
Aim 3: Genetic and environmental contributions to body composition

- Standardised phenotype questionnaire
- Instructions & SOPs
- Equipment purchase
  - Stadiometers
  - Scales
  - Ultrasound machines
- Training
- Field roll out
  - Staggered to ensure QA
  - Years 2, 3 & 4
  - Phenotyping
  - Blood sampling
- Data (demography & phenotype)
  - Collection
  - Central Data Management
Management

- Steering Committee
- SAG
- Education & Training
  - Ethics Governance Group
  - Phenotyping Group
  - Genome Research Group
  - Data Management Group

Financial Management – WHC/INDEPTH - Project Manager and Administrator
Ethics approval for the study

- Wits Ethics Approval (Soweto and Agincourt)
  - Project
  - Two informed consent forms
  - MTA
- Dikgale (South Africa)
- Navrongo (Ghana)
- Nanoro (Burkina Faso)
- Nairobi (Kenya)
Ethics Workshop – December 2012
Ethics Review Board members

Objective: To discuss ethical issues related to genomic science in African communities
Phenotype & Sample collection

Funded

- Demographic information
  - Home language & self-reported ethnicity
  - Medical & health histories
  - Living conditions (SES)
- Body composition
  - Height & Weight
  - Blood pressure
  - Waist & hip circumference
  - Ultrasound subcutaneous & visceral fat

Not funded

- Glucose
- Lipids

Blood samples:
- 10ml EDTA (DNA)
- 15ml Clotted (serum - lipids)
- 5ml NaF (plasma - glucose)
## Body composition and HIV infection

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

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<thead>
<tr>
<th>Location</th>
<th>Expected number HIV infected individuals</th>
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<tbody>
<tr>
<td>Agincourt</td>
<td>462</td>
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<tr>
<td>Dikgale</td>
<td>274</td>
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<tr>
<td>Nairobi</td>
<td>248</td>
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<tr>
<td>Nanoro</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>
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Based on regional averages

Based on country average
Objective: Capacity development

• Assessing needs
• Bringing international partners on board
• Timing of training workshops
• AWI-Gen specific training
  – Data management workshop
  – Phenotyping workshop
• External training opportunities
  – Wellcome Trust courses
  – BioNet courses
Challenges

• Effective communication given poor internet connectivity across African countries (keeping everyone onboard)
• Standardisation across Centres
• Coordinating training activities
• Structure of African populations in study
• Funding & Financial management of the project
• Employing experienced senior scientists
• Management structure
• Ethics approval
• Phenotyping questionnaire
• Data Management Framework
• Pilot project
# Timeline

<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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<td>African genome structure</td>
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<td>Phenotyping and sampling for Cohorts</td>
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<td>Obesity and body composition pilot study – urban South Africa</td>
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<tr>
<td>Genome association study – west, east and south Africa</td>
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