Collaborative African Genomics Network
Overview of the Objectives CAfGEN in the context of H3Africa

H3Africa Consortium
Johannesburg, South Africa

Gabriel Anabwani
CAfGEN
Goals

• Background to CAfGEN: Mission/Vision
• Illustrate foundation basis of CAfGEN
• Highlight CAfGEN clinical and educational capacity
• Review scientific goals and approach
• Outline unique training and career development plan
• Describe contribution to H3Africa consortium
• Demonstrate capacity and sustainability
Background

H3Africa Objectives:

To develop within Africa the study of genomic/genetic/environmental contributors of human health and disease using cutting-edge genomic research tools

To increase capacity for biomedical research in Africa, in terms of building infrastructure, including data and research resources

To increase the genomic proficiency of researchers and trainees in Africa.
Background: HIV

HIV/AIDS and associated co-morbidities remain a global plague with the greatest burden in SSA
THE HIV BURDEN

Uganda

Botswana

Graph showing the HIV burden in Uganda and Botswana from 1990 to 2010, with categories for adults and children.
Background: TB

- SSA in general and both Botswana and Uganda in particular, have some of the highest annual TB notification rates in the world:
  - Sub-Saharan Africa: 262/100,000
  - Uganda: 193/100,000
  - Botswana: 455/100,000
Background:
Genetic Studies

- Genetic studies have the potential to transform our understanding of both HIV and TB.

- Paradoxically, most such studies have been conducted in non-African, adult populations.
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• HIV-infected children differ from their adult counterparts and have more to ultimately contribute and gain from therapeutic advances, yet genetics studies of this population have been conspicuously absent.
Background: Genetic Studies

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- Why have these studies not been conducted, especially in Africa?
  - Too little genomics expertise
  - Insufficient and inadequate infrastructure
  - Difficulties in obtaining large cohorts with appropriate clinical phenotyping.
What is CAfGEN?

- Collaborative network of clinicians and scientists
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• Collaborative network of clinicians and scientists

• That combines expertise in genetics with expertise in paediatric HIV/AIDS and TB

• Aims to integrate genetic and genomics technologies to probe host factors that are important to the progression of HIV and HIV-TB infection in sub-Saharan African children

• The Goal and Aims of CAfGEN are aligned to those of the H3Africa Initiative
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To create a collaborative, multi-disciplinary, multi-institutional, inter- and intra-country network of African scientists, clinicians, and researchers to use genomics approaches to study gene/pathogen interactions for HIV/AIDS, its co-morbidities, and other diseases among diverse paediatric African populations.
Collaborative African Genomics Network

Baylor College of Medicine

University of Botswana

Botswana-Baylor Children’s Clinical COE

Makerere University

Baylor Uganda Children’s Foundation
Collaborative African Genomics Network (CAfGEN)

Research Projects

1. Phenotyping & Bioarchiving
   - Phenotype Identification
   - Patient Recruitment
   - Core Genomic Infrastructure
   - DNA Collection & Processing
   - Storage / Bioarchive
   - Biorepository Oversight

2. HIV Progression
   - Infrastructure & Equipment
   - Resequencing & Allelotyping
   - Genomics Transfer & Training
   - Whole Exome Sequencing
   - Bioinformatic/Statistical Analysis
   - Validation of Results

3. HIV-TB Progression
   - RNA-Seq
   - SNP Genotype
   - eQTL Analysis

Training and Career Development

Trainee Selection

Short- and Long-Term Training Opportunities

Training Program Development

Faculty / Student Enrichment

Grants Administration

Trainee Administration

Administrative Oversight

IEARD Training

Milestones /Timeline
CAfGEN Specific Aims

**Aim 1:** Recruit well-phenotyped paediatric HIV and HIV-TB infected patients and create a DNA and RNA biorepository from blood and sputum samples that will be linked to a central clinical database.
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Aim 3: Use integrated studies of clinical outcomes, DNA and paired RNA analysis in HIV/TB co-infected children to identify genes that contribute to the progression to active TB.
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**Aim 5:** Establish genetic and genomic technologies and supporting laboratory and physical infrastructure for large-scale genetic/genomic analyses of common diseases in Africa.
CAfGEN Partnerships

Genomics Research Training Program
Genomic technologies
Bioinformatics
Statistical Genetics

Baylor College of Medicine

Genomic technologies
Bioinformatics
Genomics research, education and training (IPGG)

Makerere University

University of Botswana

Botswana-Baylor Children’s Clinical COE

Subject recruitment and sampling
Subject surveillance
Education and training
Community outreach
Botswana and Uganda Centres of Excellence

- State-of-the-art care and treatment for:
  - Over 6,000 HIV infected children at the main COEs
  - Over 14,000 HIV-infected children at their outreach sites
- Provide family education and outreach to the community
- Education and training to health professionals
- Will provide clinical expertise for patient recruitment & sample collection
Potential Expansion of the Clinical Network

- This well-phenotyped paediatric cohort can be expanded to include the larger BIPAI Network

The BIPAI Children’s Clinical Centers of Excellence Network
HIV-Infected Pediatric Cohorts

• Genomic studies need a well-phenotyped cohorts
Two Paediatric Cohorts

1. A retrospective cohort of HIV-infected children at the phenotypic extremes of HIV disease progression:
   • 500 long-term non-progressors (LTNPs)
   • 500 rapid progressors (RPs)

Using WHO clinical criteria
Two Paediatric Cohorts

2. A **prospective cohort** of HIV-infected children with active TB disease:
   - 2,000 HIV-infected children without active TB disease (baseline)
   - 150 participants who subsequently develop active TB disease
   - A replication cohort of 100 patients with active TB disease without baseline samples will also be collected.
CAfGEN Overview

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- Short- and Long-Term Training Opportunities
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- Milestones / Timeline

Administration
- Grants Administration
- Trainee Administration
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CAfGEN Overview

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Collaborative African Genomics Network (CAfGEN)
Genomics Training and Research Program

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<th>Year 1</th>
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<td>Laboratory rotations</td>
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<td>Seminars and Journal Clubs (3 per week)</td>
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<td>Ethics Training</td>
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6 PhD trainees (3 from Makerere and 3 from University of Botswana will be eligible to participate.

Successful trainees will be eligible to receive a Certificate in Genetics and Genomics from Baylor College of Medicine.
CAfGEN Training Network

ELSI

Short Term Trainees

Local Communities

BCM Mentors

Coursework

Symposia

BCM Certification Ph.D. Requirements

Short Courses

NextGen Sequencing
SNP Genotyping

Long Term Trainees

Bioinformatics Statistical Genomics

Core Project 1

Core Project 2

Core Project 3

CAfGEN Training Network

CAfGEN
CAfGEN Training Network

ELSI

Local/BCM Mentors

COEs

Local Communities

Short Term Trainees

NextGen Sequencing
SNP Genotyping

Bioinformatics
Statistical Genomics

Core Project 1
Core Project 2
Core Project 3

Short Courses

CAfGEN
Institutional Commitments

• There is very strong commitment to CAfGEN by all participating institutions
• Strong support from the BIPAI leadership and 5 other COEs across Africa
• Support from respective Ministries of Health
• Protected time for faculty research and training at both UB and Makerere
• Commitment from BCM to allow trainees to take (for credit) graduate courses in genetics and genomics
Co-PIs

- Moses Joloba, Makerere University, Uganda
- Addy Kekitiinwa, Baylor-Uganda CF, Uganda
- Wata Mpoloka, University of Botswana, Botswana
- Oathokwa Nkomasana, University of Botswana
- Graeme Mardon, Baylor College of Medicine, USA
- Gabriel Anabwani, Baylor-Botswana, Botswana
If you want to go fast, go alone
If you want to go far, go together

African Proverb