



Collaborative African Genomics Network

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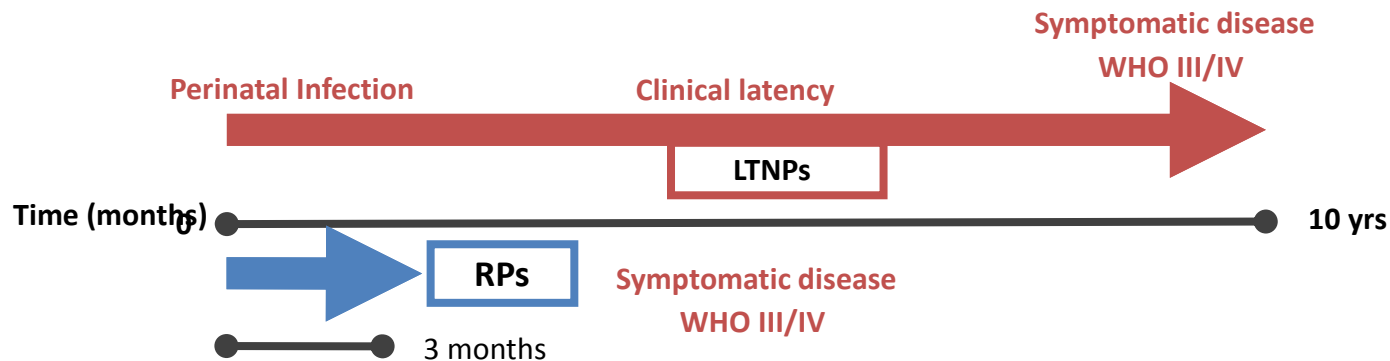
Broad Objectives *CAfGEN*

- A retrospective study on the genomics of paediatric HIV disease progression among long-term non-progressors using children with rapidly progressive disease as controls
- A prospective genomics study on HIV/TB disease progression in children
- Establishment of genomics capacity and provision of enabling technology in Botswana and Uganda
- Community engagement and education in both countries to support current and future genomics research

Sample Collection from two Paediatric Cohorts

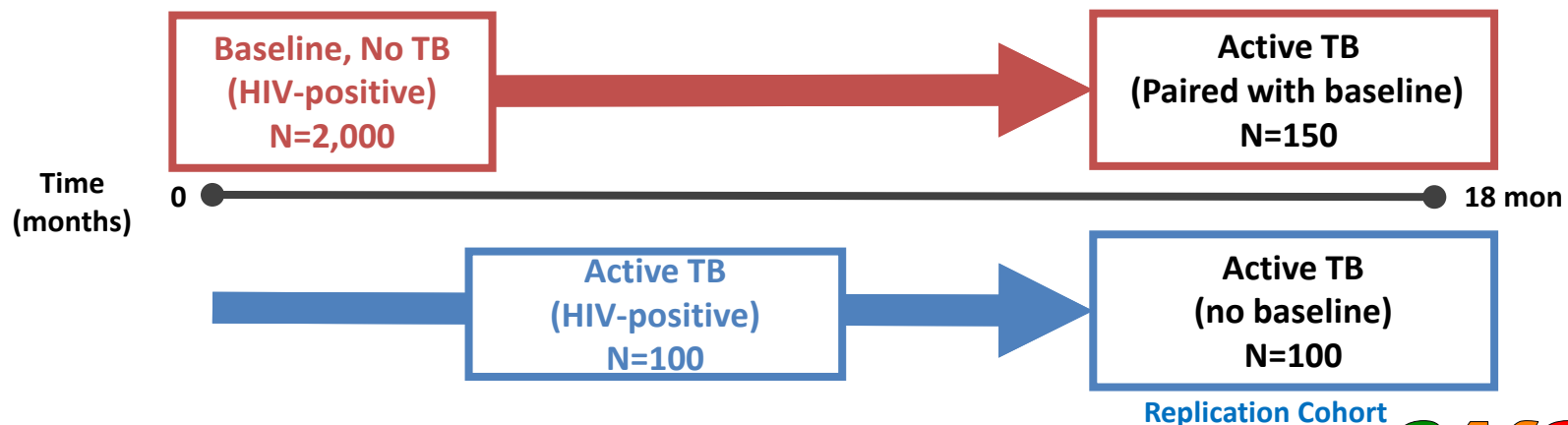
1. Retrospective HIV/AIDS cohort (CP1):

HIV-infected children at the phenotypic extremes of HIV disease progression: 500 long-term non-progressors (LTNPs) and 500 rapid progressors (RPs)



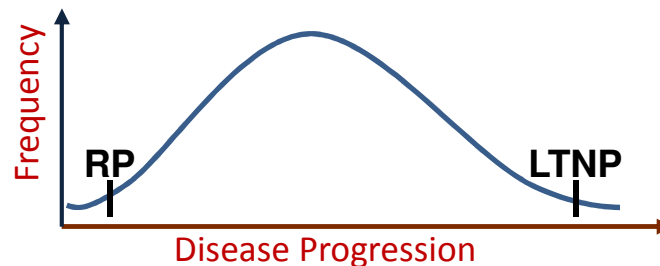
2. Prospective HIV/TB cohort (CP1):

2000 HIV-infected children followed over time for progression to active TB

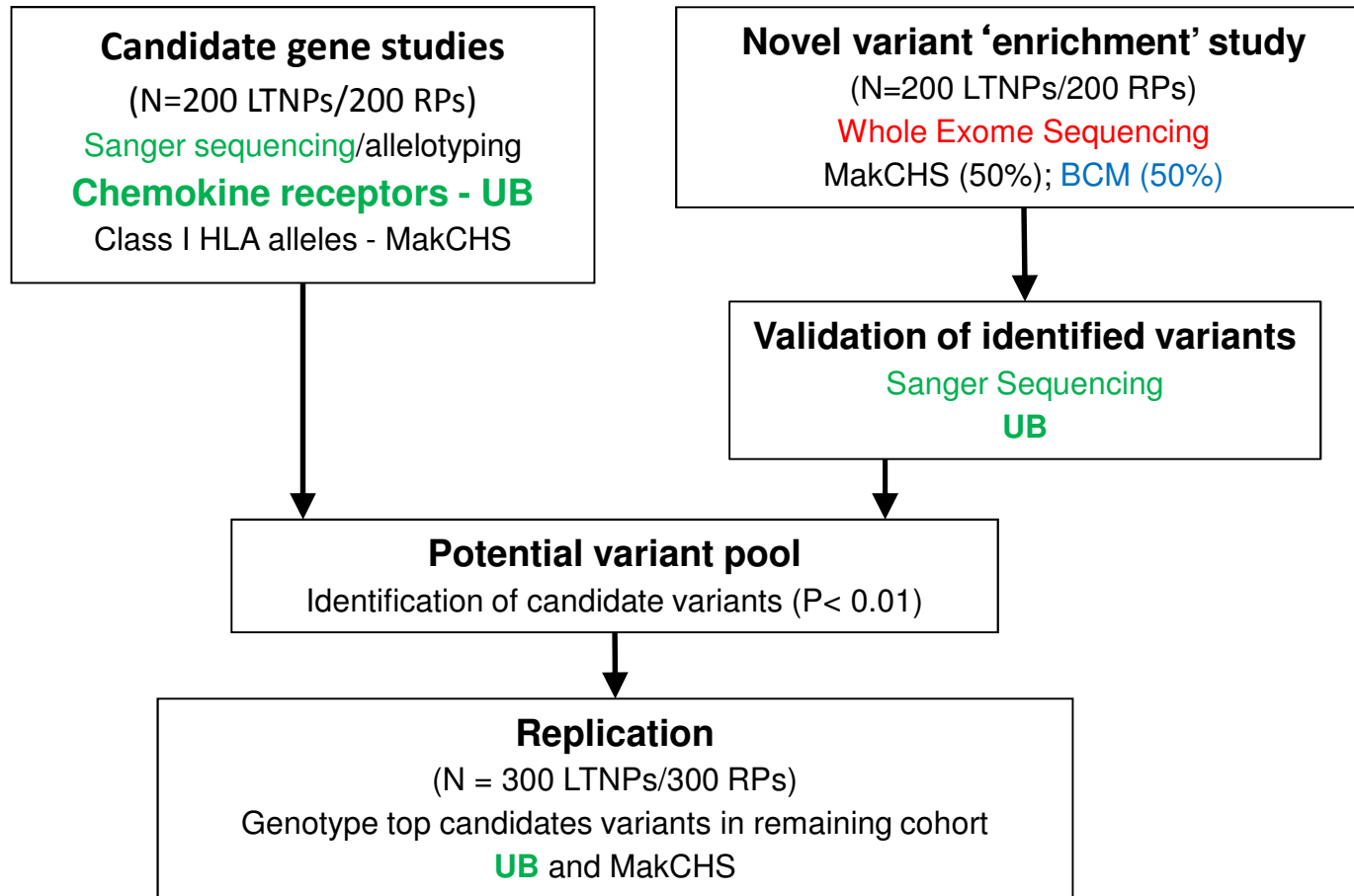


Retrospective HIV/AIDS Cohort (CP2): Approach

- Aim: To identify host genetic variants within the coding regions of candidate genes and throughout the genome that influence disease progression.
- Assess genes that have already been associated with HIV disease progression in other populations: Class I HLA and chemokine receptors, comparing LTNPs to RPs
- Using whole-exome sequencing, identify new host genes affecting paediatric HIV disease among 200 LTNPs and 200 RPs
- Promising variants will be replicated in the remaining 300 LTNPs and 300 RPs



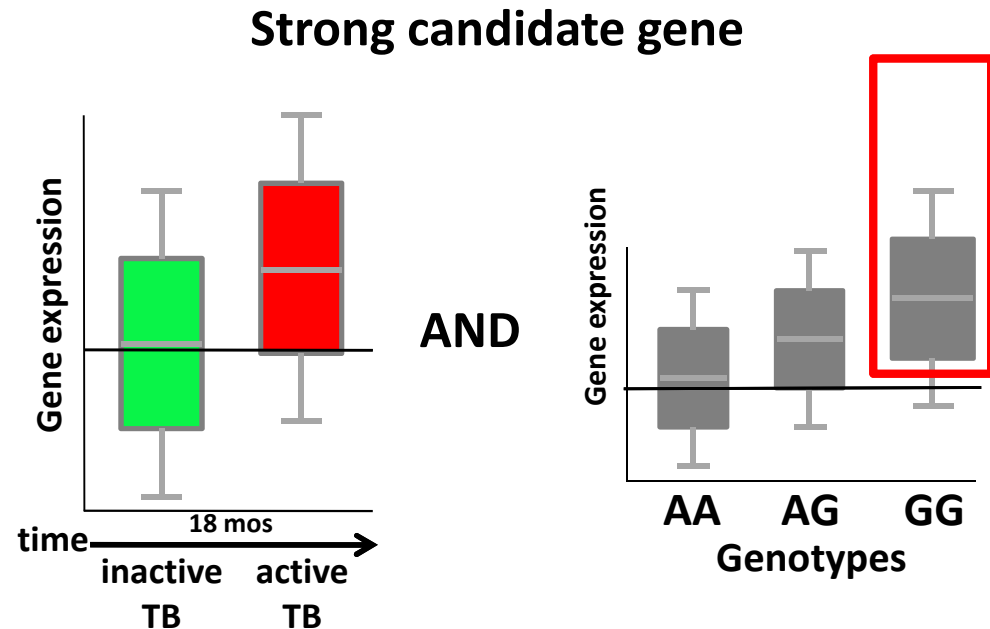
CP2 Approach



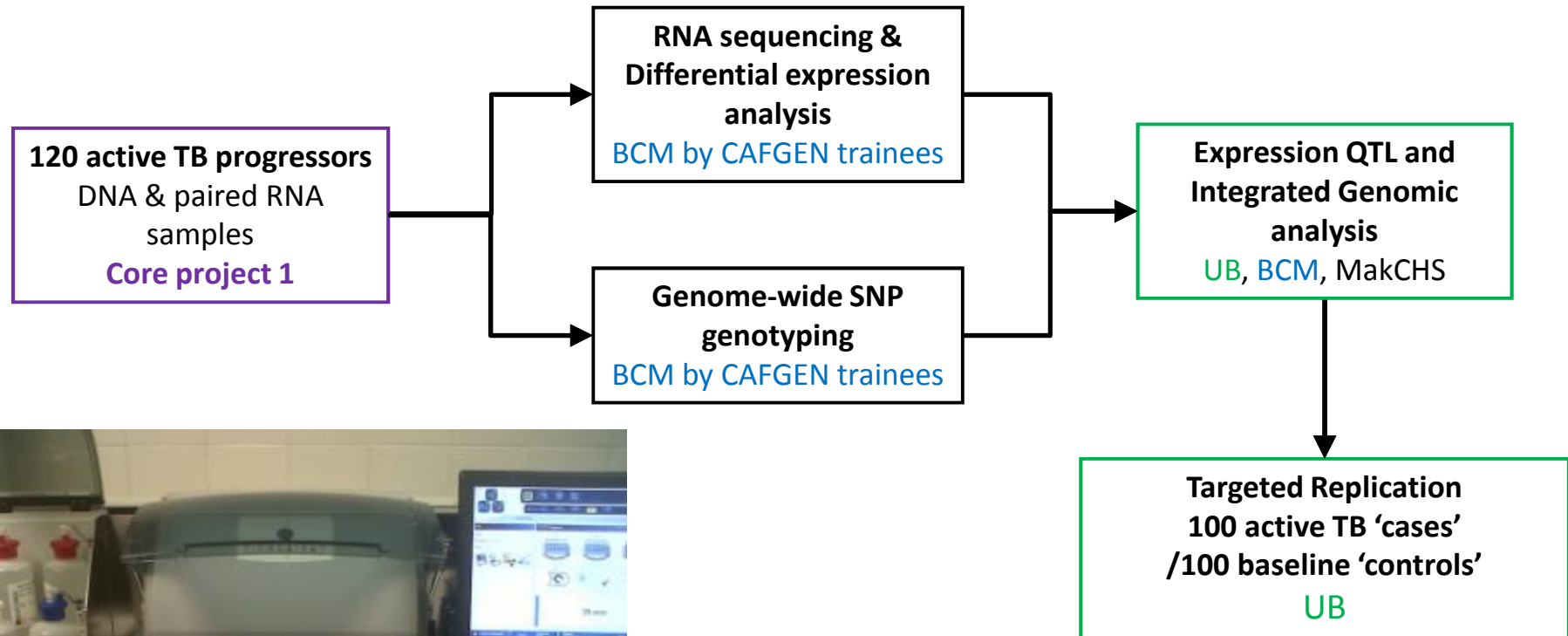
*All analyses will be undertaken by *CAfGEN* trainees assisted by faculty at BCM and Makerere/UB

Prospective HIV/TB cohort (CP3): Aim and Approach

- Aim: To identify genes that show differential expression with the progression to active TB disease in HIV co-infected children.
- Integrate genome-wide genotyping with RNA sequencing to look for SNPs that are causally linked to the progression to active TB in HIV-infected children.
- Strong candidate genes must show both a change in transcript abundance with the transition from inactive to active disease AND...
- The level of expression of the gene must be influenced by the underlying SNP genotype
- Approach adds substantial statistical power to establish the association of SNPs (genotype) with the progression to active TB disease (clinical phenotype) thereby requiring fewer samples than a typical GWAS.



CP3 Approach



Overall Progress Summary

- Program was funded in Jan 2014
- Two-year graduate level training at the Genomics Research Training Program (G RTP) at BCM started in June 2014 in part-fulfillment of PhD for 3 candidates from BW and 3 candidates from UG
- Equipment procured:
 - Illumina MiSeq sequencer for MakCHS
 - ABI 3500 capillary sequencer for UB
 - Freezerworks for both UB/MakCHS
- MTA between BCM and MakCHS
- Community Advisory Boards active at both sites
- 5 IRB approvals for all sites
- Recruitment commenced in Uganda in June 2014 and in Botswana in October 2014

Patients and Samples

- Retrospective study we aimed to recruit 500 HIV RPs and 500 LTNPs; and so far:
 - 457 of the 500 RPs
 - All 500 LNTPs
- Prospective study aimed to recruit 2000 HIV infected children at baseline and follow them for at least 18 months for development of active TB: so far we have screened 773 and recruited 771
 - Botswana – Screened 443 and enrolled 406 With 1 TB incident
 - Uganda – Screened 510 and enrolled 479 With 1 TB incident
- Also aimed to recruit 100 patients with active TB at baseline:
 - So far we have recruited 4 Uganda and 2 Botswana

Sample Processing

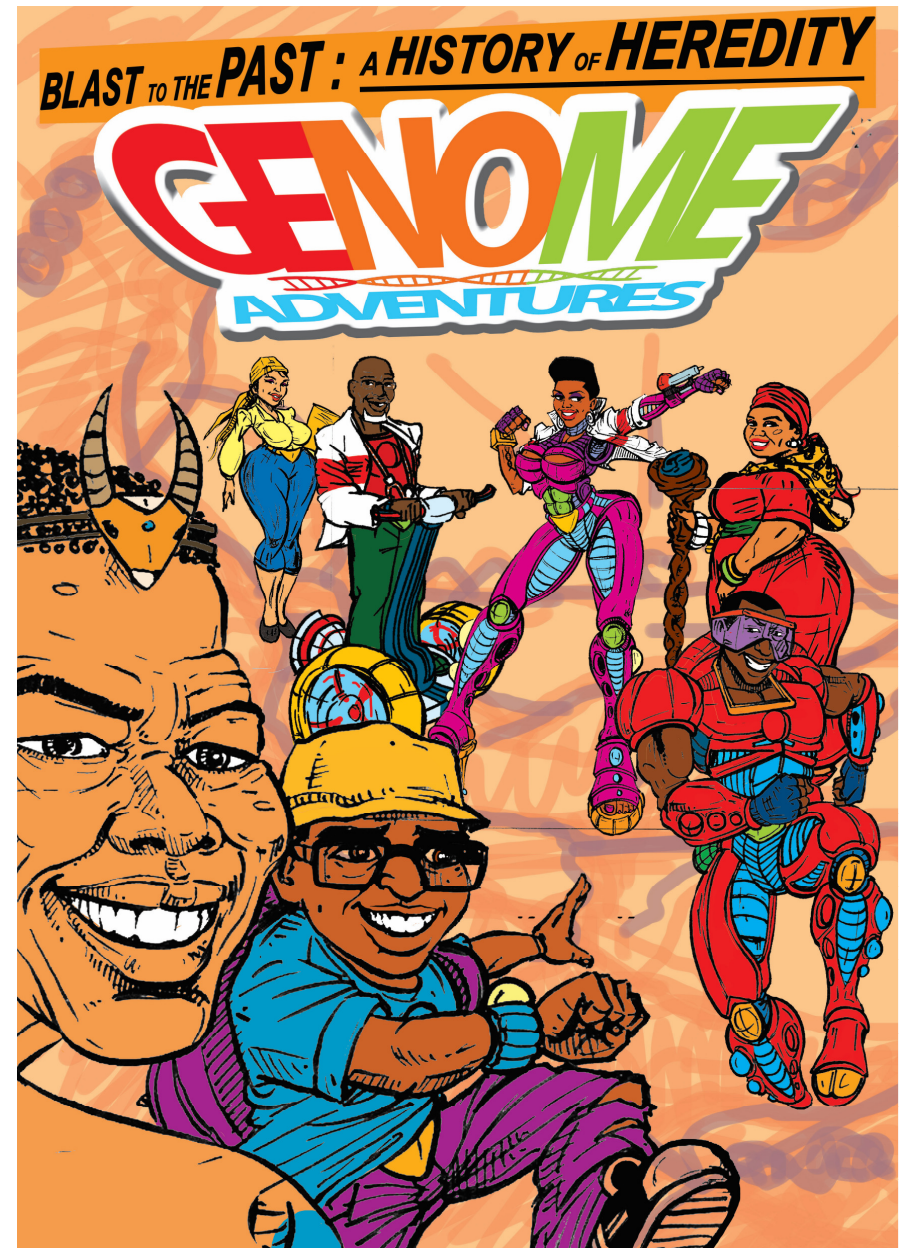
- University of Botswana received 393 retrospective samples of which 268 have had DNA extracted, quantified, quality controlled and archived
 - Received 312 samples for the prospective study
- MakCHS has received 500 retrospective samples of which all 500 have had DNA extracted, quantified, quality controlled and archived
 - Received all 408 samples for the prospective study
- **150 samples** (100 Bw and 50 Ug) were successfully shipped from Uganda to BCM in March for sequencing
- First **50 samples** are currently in **Whole Exome sequencing pipeline** in Human Genome Sequencing Center at BCM
- Additional samples will be shipped by June 2015

Continental Training

- In January 2015, UB held a week-long genetic association course with application to analysis of sequence and genotype data for 12 participants from Botswana, South Africa, and Uganda
- Several of short in-house trainings have been held at the Baylor COEs in Uganda COE and Botswana , including:
 - Protocol training for study team members
 - GCP and HSP training for study team members
 - GCLP training for laboratory staff
 - SOPs and clinical quality management plan trainings for study team members

Community Engagement and Education

- Awarded an Engaging Science Grant from the Wellcome Trust to educate media and public on genes and heredity in Botswana using media workshops and comic books
 - Community Stakeholders Workshop: 37 participants
 - Media Workshop (Journalists & Cartoonists): 24 participants
 - Comic books under development - first of 4 books due in May 2015



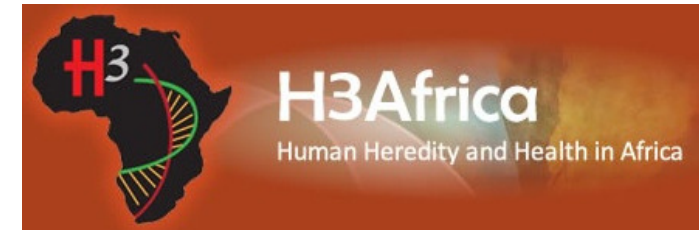
Next Steps

- Establish Genomics Training Programmes at UB/MakCHS
 - MakCHS – Department approval at the final stage
 - Provision for the Department of Genomics in UB
- Monitor trainees
- Shipment of samples across institutions for genomics
- Publish and disseminate Genome Adventures comic books
- Bioinformatics training in Makerere University in July/Aug 2015

Concluding Remarks

- We have made excellent progress so far
- Prospective study will require more time (6-12 months) to complete





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Botswana

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