

NIH COMMON FUND HIGH-RISK HIGH-REWARD RESEARCH SYMPOSIUM

December 15 – 17, 2014

SPEAKER ABSTRACTS – DAY 2 (DEC. 16, 2014)

Integrative Genomic Studies of Evolution and Adaptation in Africa

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Award: Pioneer Award

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Africa is the ancestral homeland of all modern humans, and it is also a region of tremendous cultural, linguistic, climatic, environmental, and genetic diversity. Despite the important role that the African continent has played in human history, groups residing there have remained critically understudied and are underrepresented in the recent explosion of genomic studies. The goal of this project is to characterize genomic and gene expression variation in diverse Africans and to integrate those data with detailed information about normal variable anthropometric traits, as well as traits that play a role in cardiovascular function, nutrition, metabolism, and immune function. This allows us to explore the genetic and environmental factors that play a role in human adaptation, health, and disease. We seek a comprehensive knowledge of variation in African populations that is critical to a deeper understanding of human genetic diversity, the identification of functionally important genetic variation, and the gene-by-environment interactions that underlie traits of biomedical significance.

To achieve the aims of this project, we conducted three field seasons in Eastern and Southern Africa, obtaining DNA, RNA, frozen plasma and detailed ethnographic, nutritional, and health information as well as anthropometric, cardiovascular, and metabolomic phenotype data from ~2,400 individuals from >40 ethnic groups. Here we present integrative analyses of high coverage whole genome sequence and SNP array data, RNA-Seq data, and bi-sulfite sequencing data obtained from blood to characterize patterns of genomic, transcriptomic, and methylation differences across ethnically diverse Africans. Using these data, as well as detailed phenotype measurements of the same individuals, we explore correlations between genetic ancestry and phenotype, and identify regions of the genome that play a role in adaptation to diverse environments. We show that Africans have high levels of variation within and between populations for genomic, transcriptomic, and methylomic data which is distinct from non-African populations. Additionally, we have identified candidate loci that play a role in

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adaptation to infectious disease, diet and high altitude, as well as the short stature trait in African Pygmies. This work provides an unprecedented view of the genomic variation that underlies human health and disease in Africa and also a window into human evolutionary history.