Stony Brook University
The Graduate School

Doctoral Defense Announcement

Abstract

Elucidating the Genetic Architecture and Evolution of Quantitative Traits in Southern African Populations with Genomic Data

By

Meng Lin

The genetic architecture of complex traits likely differs across human populations. Yet the characterization of the underlying genetic variants in populations outside of Europe is far from adequate. This dissertation focuses on skin pigmentation as a highly heritable model phenotype, aiming to infer its complexity and adaptation in light skinned, endogamous, and genetically diverse KhoeSan groups from South Africa. Chapter 1 demonstrates the unexpectedly high polygenicity of pigmentation by assaying genome-wide array, exome, and high coverage resequencing data with paired quantitative pigmentation measurements. Both canonical and non-canonical pigmentation loci are associated with variation in the KhoeSan. Previously discovered pigmentation loci only explain a small fraction of the total phenotypic variance, but the largest effect variant (rs1426654) in *SLC24A5* has a relatively high heritability of ~15%. Chapter 2 details the evolutionary insight between the frequency of this *SLC24A5* allele and the light skinned phenotype in KhoeSan. With simulations from a 4-population demographic model with selection, I show that the common haplotype is shared identically by descent with Europeans. Recent migration introduced the haplotype into southern Africa via 'back to Africa' gene flow about 2000 years ago. The frequency of the causal allele is consistent with strong subsequent positive selection, on the order of a ~0.05 selection coefficient. This example is among the strongest selective sweeps discovered in the human genome. In Chapter 3, I propose a novel approach to calculate statistical power when ancestry affects complex diseases. The simulation-based pipeline is developed as an easy and fast application for estimating statistical power in complex disease studies for admixed populations, assuming ancestry proportions and incidence rates. Together, the chapters provide a framework of human complex trait study set in a more complicated, admixed background.

Date: December 8th, 2017
Time: 10:00 a.m.
Place: N-503 Social and Behavioral Sciences

Program: Graduate Program in Genetics
Dissertation Advisor: Brenna Henn