

Principal Investigator

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Funding

NIH

Summary of research:

selection, PCA, polygenic_selection, genetic_component

Application Lay Summary:

1a: Genetic differences between human populations are generally small, but unusually large differences can serve as signals of natural selection, e.g. at the LCT (lactase) gene. We will use an approach called principal components analysis to define subpopulations and detect unusual differentiation. We will also look for signals of polygenic selection spanning many genes associated to a given trait, as in recent work on height. We will primarily focus on quantitative traits measured at baseline in regards to health conditions (i.e. height, bone mineral density, etc.). We will also study type 2 diabetes and depression, through linkage to medical records.

1b: Detection of genomic regions under natural selection will improve power of association studies.

1c: First, we will infer top principal components and compute resulting statistics to assess selection, as described in our recent work (Galinsky et al. in press AJHG). Second, we will develop a new method for inferring polygenic selection by quantifying genetic components of phenotypes that differ between closely related populations. The new method is based on statistics that assess the association between genes and phenotypes while correcting for confounding effects of environmentally induced correlations between geographic ancestry and phenotypes. We will also integrate the new method into a new approach for predicting phenotypes from genetic data that accounts for polygenic selection.

1d: We will analyze the full cohort.

Project Extension Details:

"We plan to use cancer registry data to create cancer phenotypes, and investigate the genetic architecture of these phenotypes."