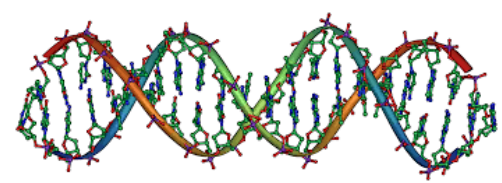


A GWAS for all in the WHI

Themistocles (Tim) Assimes, MD PhD
Stanford University

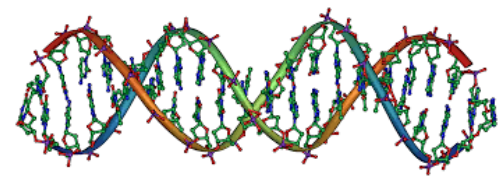
Charles Kooperberg, PhD, Alex Reiner, MD, Riki Peters, PhD,
Fred Hutchinson Cancer Research Center

Rebecca Jackson, MD
The Ohio State University



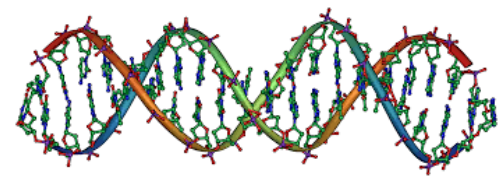
The Rationale

- All human traits have a genetic component
- Large numbers needed for genetic discovery
 - Even larger for gene-environment and gene-gene interactions
 - Modest effects (for both common and rare variants)
- Era of large scale molecular epidemiology studies is here!
 - UK Biobank (500K), MVP (>550K), China Kadoorie Biobank (510k)
- Opportunity for more collaborations and to lead studies
- Maximally leverage investment in WHI biobank
- ↓ ↓ Cost: genotyping ~800k carefully selected polymorphisms: \$45-50 / sample.
- Now easy to add ~15M variants (>0.1%) via imputation



The Rationale (con't)

- Large number and breadth of adjudicated outcomes
 - Cancer, CVD, Linkage to CMS
- Repeated measures of important health related traits:
 - Diet, alcohol, coffee, sleep, psychosocial, osteoporosis, fractures exercise, etc.
- Many other unique phenotypes
 - Bone density, body fat, biomarkers, reproductive, cognition, MRI, mammography, weight loss response to diet....
- About 50,000 participants already have GWAS or Whole Genome Sequencing. Another 96,000 more have genetic (dbGaP) consent.
- Ample blood for multi-omic studies – genetics always the anchor



The Challenge

- ~96k need genotyping, ~45k need DNA extraction
- Total Cost: ~\$8M (< 4 R01s)
 - \$4.7M genotyping + \$2.25M DNA extraction + \$1M salaries/computing
 - DNA extraction could drop to \$0.8M if done outside academic labs
- Ideally, genotyping all in “Year 1 and 2” to maximize scientific utility, and reduce batch effects
- How to fund?
 - Not possible with a regular R01
 - NIH sponsored Center of Inherited Disease Research?
 - Super R01 (a. >\$0.5-1.5M /year, or b. >1.5M)?
 - Industry (e.g. Regeneron-UK Biobank ESP)?

