Population Genomics at NHGRI: Definition

"application of genomic technologies to population studies"

Frontiers in Population Genomics Research: Workshop Objectives

- Review mission, goals, development, and current activities in population genomics, particularly as relevant to NHGRI
- Identify resources, including genomic technologies, ripe for application in population studies, those on horizon, and those needing development that would greatly facilitate population genomic research
- Recommend research, infrastructure development, and training efforts that NHGRI's OPG should pursue, either in lead or in collaboration with other NIH ICs or other groups, over the next 3-5 years (or longer, but focus on short- to medium-term goals)

Building on Genome Wide Association Studies

Frontiers in Population Genomics Research
Dec 18-18, 2007

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GWA points

Finds common variants only

(Sickle cell vs beta thalassemia)

Locus finding not etiology finding

Odds ratios are small

BUT may identify critical paths to useful treatment (insulin/diabetes)

Focus to date on limited diseases and disparity groups

Ongoing debates on IRB and sharing

Outline

* Additional GWA studies needed
* Preparing for next population-based technologies
* Mining GWA data, pooling and establishing collaborations

Next phase of GWA

Fine mapping to causal variants

Subphenotyping

New disorders

Much larger Ns (>10,000)

Standardized sets of shared controls

Quantitative traits

New technologies (Sequencing)

Gene x Gene

Gene x Environment

Need for non-GWA in populations studies

GWA is limited to finding common variant associations

Failure with allelic heterogeneity

Short term family based studies to find genes

Long term high throughput comprehensive sequencing (finds both high frequency common variants and rare etiologic variants that may be of higher impact)

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Genetics and beyond

Incorporation of novel mechanisms (CNVs, microRNAs, distant enhancers)

Role of expression and environment

Impact of inexpensive sequencing

$100K ~ 100 people

$10K ~ 1000 people

Targeted sequencing (exons, conserved regions)

Outline

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Collaborative Projects

dbGaP/GAIN/GENEVA

Use of existing cohorts

Phenotypes attached to huge collections

Military

Forensic

Blood and Tissue Banks

Newborn Screening

Overseas Collections and Collaborations

What can OPG do? - 1

Generate/collate empiric data on when GWA works and when alternate approaches (linkage) do and GWA doesn't

RFAs might consider joint study designs (in addition to current focus on Epi)

Support collaborative very large N studies (~50,000 with the disease of interest)

Measure true population impact of gene/locus by combining the common variant (low OR) effects with the rare variant (high impact) variants

What can OPG do? - 2

New disorders (?host interactions)

Quantitative/Longitudinal Trait Measures
(?hemoglobin, renal function, cognitive change)

New populations (AA, women etc)

Tie to microbiome analysis

Plan for impact of full/extended sequence analysis

Your favorite here

More Solutions