GAIN “2.0”: Some Additional Opportunities for WGA Studies in Common Diseases

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The first round of GAIN established a significant new infrastructure for managing large-scale creation and distribution of wgas data:

- Public-private partnership governance structure
- Robust study selection process--particularly Technical Analysis Group (TAG)
- Well-established data access, IP, publication policies ➔ informed NIH GWAS Policies
- GAIN Database (DbGaP)
- Appropriate contract mechanisms
Recent discussions with GlaxoSmithKline offer the opportunity to add both additional sample sets for genotyping and completed genotype-phenotype datasets in common diseases:

- Multiple sclerosis (complete genotype-phenotype dataset)
- Rheumatoid arthritis (study samples)
- Osteoarthritis (study samples)
- Potentially others

Intention is to pursue contribution of datasets to the GAIN Database in dbGaP and seek funding from various sources for genotyping of sample sets as appropriate.
GAIN 2.0 Process

1) GSK consults with originating PIs and institutions
2) Initial “TAG” review of study documents and summary data to determine suitability of studies for GAIN:
   - Conducted by NHGRI team with disease expertise from relevant NIH Institutes
   - Examines informed consents, sample ascertainment, power/analysis via document review and interaction with GSK and PI as appropriate
3) GSK/PI obtain local IRB approvals for studies to participate in GAIN
4) PIs/institutions sign GAIN Submitting Applicant Policy Agreement and submit detailed phenotypes submitted for final “TAG”/NCBI review
5) Contracts/MOUs in place; FNIH secures funding for genotyping samples and analytical support for PIs as appropriate
6) Completed genotype-phenotype datasets deposited in GAIN Database

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Samples submitted to genotyping centers; final phenotypes sent to FNIH for transfer to NCBI
Multiple Sclerosis

- “GeneMS” case/control study of ~1000 cases and ~1000 ethnically and gender matched controls
- 3 sites: UCSF, Basel, Amsterdam
- Cases clinically ascertained; most had relapsing/submitting subtype
- Phenotype data very complete (over 100 variables)
- Already genotyped using Illumina 550K platform
- Initial “TAG” review complete; seeking IRB approval to participate in GAIN
Rheumatoid Arthritis

- “Genetics of Rheumatoid Arthritis” (GoRA) case/control study of ~1000 cases and ~1000 unrelated, age and gender matched controls and ~300 parent/sib controls
- All cases clinically ascertained using ACR (1987) criteria and anti-CCP assay
- Cases ethnically matched (Caucasian) from the same geographic area
- Major site: Sheffield, UK
- Samples/data to be submitted for genotyping
- Initial “TAG” review complete; seeking IRB approval to participate in GAIN
“Genetics of Osteoarthritis” (GO) case/control study of ~1000 cases and ~1000 controls matched for age, gender, ethnicity

Cases with primary generalized osteoarthritis clinically ascertained including radiography and bone mineral density

Controls ethnically matched from the same (U.S) geographic area

Samples/data to be submitted for genotyping

Initial “TAG” review scheduled for early November; seeking IRB approval to participate in GAIN