



# GAIN "2.0": Some Additional Opportunities for WGA Studies in Common Diseases

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GAIN Analysis Workshop II, Bethesda, MD  
October 17-18, 2007



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# GAIN "1.0"

- 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



# GAIN "2.0"

- 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

--OR--

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/remitting 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



# Osteoarthritis

- “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

