

## CURATING GENETIC ASSOCIATION LITERATURE FOR COMMON DISEASES

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### INTRODUCTION

Papers describing genetic associations with common diseases are currently being published at a rapid rate. These new papers add to an already large body of literature which includes candidate gene studies, genome wide association studies, review papers, and meta-analyses. Related papers describe the basic epidemiology of these common diseases, gene-environment interactions, gene-gene interactions, and pharmacogenomics (gene-drug interactions), all of which may affect disease predisposition and management.

#### GOALS

- Track gene-disease associations over time to see if they are replicated
  - Ideally different populations by different authors
  - Lack of replication is one historical limitation of genetic association studies and can be a major barrier to the adoption of personalized genomics
- Systematically collect data
  - Magnitude of the gene-disease effect (ie odds ratio)
  - Variant identifier
  - Allele frequency
  - Risk and non-risk alleles
  - Other key information

#### Challenges

- Data presentation by authors
- Which is the risk allele?
- DNA strand issues
- Different coordinate systems, incomplete specification of variant location

#### NAVIGENICS CURATION PROCESS

Top 7 journals as published

Scouting

- RSS feed
- Directed searches
  - PubMed
  - HugeNet
  - NHGRI GWAS catalog
- Curation criteria
  - Replication
  - Study, statistical, and laboratory methods

Evaluation

- Sample size and significance level
- Product fit
  - Actionability
  - Utility and relevance

#### Curation

- Genetic information
- Condition specific information
- Team of epidemiologists and human geneticists
- QC measures include
- ≥2 independent curations

#### Testmaking

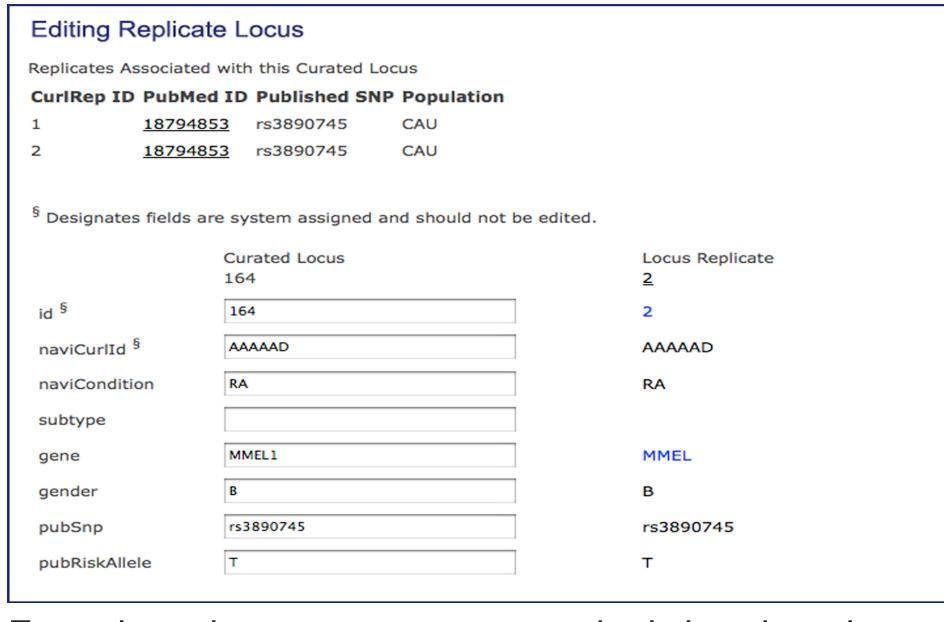
- Affymetrix 6.0 array
- TaqMan (Applied Biosystems)

#### RESULTS

We have built a literature curation database with a web interface that addresses these key needs, using Ruby on Rails with MySQL. Lack of consistent standards for reporting gene-disease associations, either by journal editors or other consortia or agencies, make automated curation infeasible at this time.

#### Features

- Compare multiple independent curations
- Allow remote data entry
- Track changes
- PubMed linkage
  - Journal, author, etc. fill from PubMed id
- HapMap and dbSNP linkage
  - Check alleles and their frequency in ancestral group, strandedness



Two independent reviews are compared side by side and discrepancies are highlighted in blue

# Pubs: New Browse | Curated Locus: Browse | Locus Replicates: Browse | Possible New Cond: New Browse | CSI: Browse | TMG | Pub Snps: New Browse | Test Snps: New Browse | Table Export | Admin | Logout (5) Show publication Curated Locus Associated with this Publication Curild NaviCurild PubMed ID Published SNP Population 178 AAAAAR 18650507 rs4149056 CAU curiDate 2009-02-19 pubPmid 18650507 pubDoi 10.1056/NEJMoa0801936 pubTitle SLCO1B1 variants and statin-induced myopathy--a genomewide study. pubAuthors SEARCH: Link E, Parish S, Armitage J, Bowman L, Heath S, Matsuda F, Gut I, Lathrop M, Collins R pubJournal N Engl J Med pubDate 2008 Aug 21

Curation browser. Publication title, author, journal, and date fill automatically from PubMed id. Publication is linked to curated locus.

SLCO1B1

PGx\_statin\_myopathy

pubGenes

	Editing Curated Locus					
	Curated Pu	Curated Publication (Pubs) Result				
	PubMed ID Authors					
	18794853	Raychaudhuri S, Remmers EF, Lee AT, Hackett R,				
	Replicates Associated with this Curated Locus					
CurlRep ID PubMed ID Published SNP Population Notes						
	1	18794853	rs3890745	CAU		
	2	18794853	rs3890745	CAU		
	Basic pubSnp Test Results					
	Failure	pubMajorAllele (T) mismatch to HapMap2 allele 2 (G)				
	Failure	pubMinorAllele (C) mismatch to HapMap2 allele 1 (A)				
	Success	cess Matched population 'CAU' in HapMap2 as CEU.				
	Warning					
	Warning	dbSnp entry count not checked.				

A variety of QC checks minimize data entry errors

#### CONCLUSIONS

- A custom built curation database with web interface can facilitate curating genetic association literature for common diseases
- QC checks are very helpful, and more could be incorporated, both interally and against external sources