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Personalized Medicine

Richard H. Scheller

Chief Scientific Officer and Head of Therapeutics

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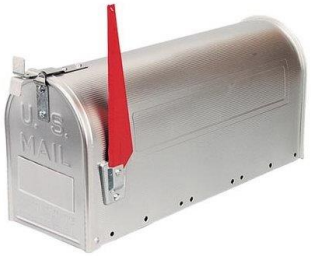
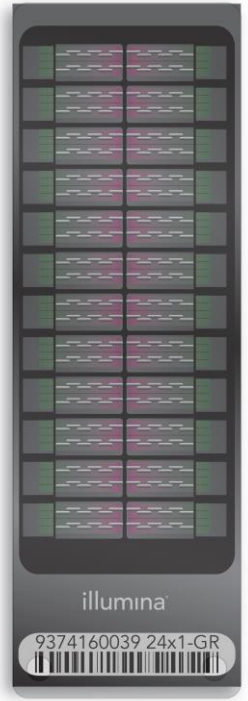


Genotype Data

- **Customized Illumina HumanOmniExpress+ Beadchip**
  - 600K+ SNPs
  - Selected to provide good genome-wide coverage for imputation
  - Coverage of variants of known or suspected medical relevance

- Phase with Beagle, impute with Minimac
  - Currently imputing 15M SNPs using 1000G
    - IBD calculated by HAPLOSCORE
    - Ancestry estimated using our Ancestry Composition algorithm



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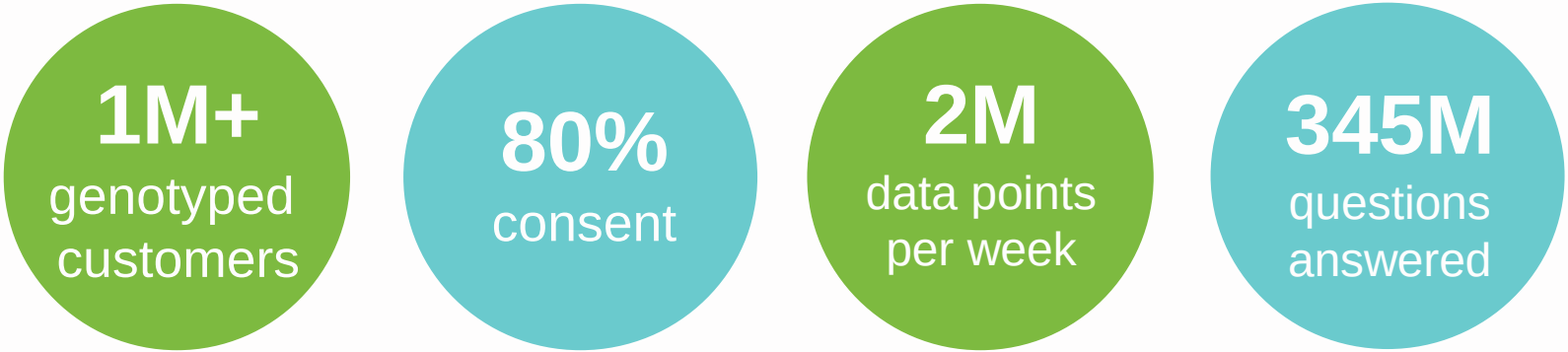
Engaged Consumers Enable a New Model for Research



- Genotype data
- Phenotype data
- Biobanked samples
- Longitudinal data
- Ability to re-contact

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Customer Demographics

77%
European

10%
Latino

5%
African American

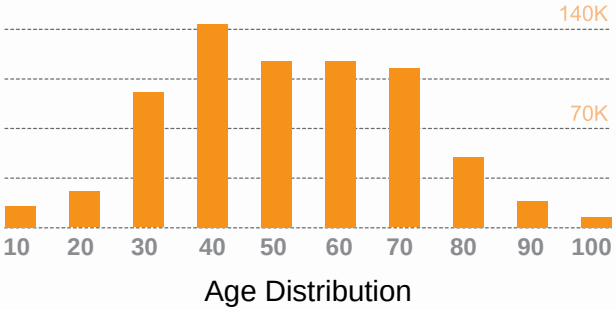
4%
East Asian

2%
South Asian

2%
Other

48%
Female

52%
Male



Age Distribution

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Types of Phenotypic Data Collected

- **Diagnoses**
  - "Have you ever been diagnosed with neuroblastoma?"
- **Medication usage**
  - "Which statin medications have you taken?"
- **Response to medication**
  - "Does Claritin (loratadine) cause you to have a fast or irregular heartbeat?"
- **Family history of disease**
  - "Have any of your grandparents, parents, brothers, sisters, aunts, or uncles ever been diagnosed with mild cognitive impairment?"
- **Health behaviors**
  - "Do you currently smoke cigarettes?"
- **Geographic location**
  - City, State, Country
- **Personality traits**
  - "I am someone who is sometimes shy, inhibited." [Scale of 1-5]
- **Environmental exposures**
  - "Have you ever had a job in which you worked in petroleum products, such as benzene, toluene, or gasoline?"

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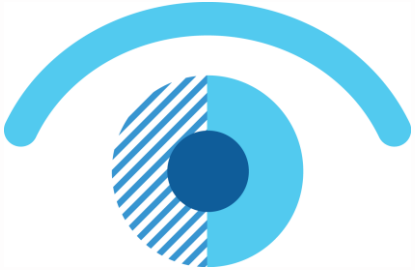
Reports

35+
Carrier Status*

3
Ancestry

4
Wellness



19+
Traits

*Our tests can be used to determine carrier status in adults, but cannot determine if you have two copies of the genetic variant. Each test is most relevant for people of certain ethnicities. The tests are not intended to diagnose a disease, or tell you anything about your risk for developing a disease in the future. On their own, carrier status tests are not intended to tell you anything about the health of your fetus, or your newborn child's risk of developing a particular disease later in life.

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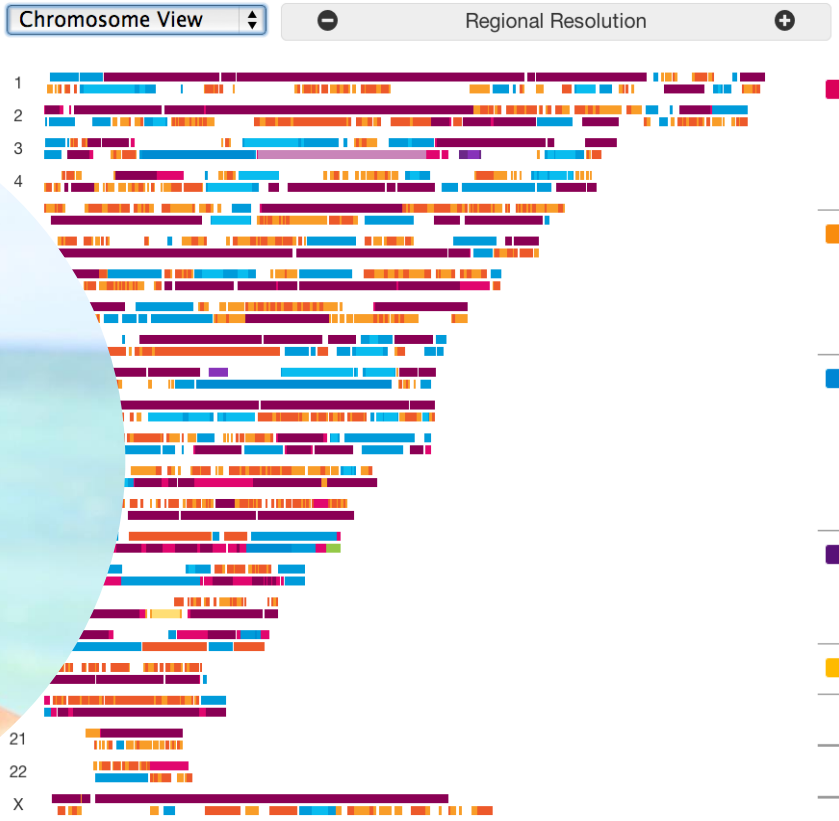
Monica



37.1%	Sub-Saharan African	
33.2%	West African	
1.0%	Central & South African	
2.9%	Nonspecific Sub-Saharan African	
24.7%	East Asian & Native American	
14.1%	Native American	
0.2%	Southeast Asian	
10.3%	Nonspecific East Asian & Native Am	
19.4%	European	
4.0%	Southern European	
2.2%	Northern European	
0.1%	Ashkenazi	
13.0%	Nonspecific European	
0.2%	Middle Eastern & North African	
0.2%	North African	
0.1%	Nonspecific Middle Eastern & North	
0.1%	South Asian	
18.6%	Unassigned	
100%	**Monica De Armond**	

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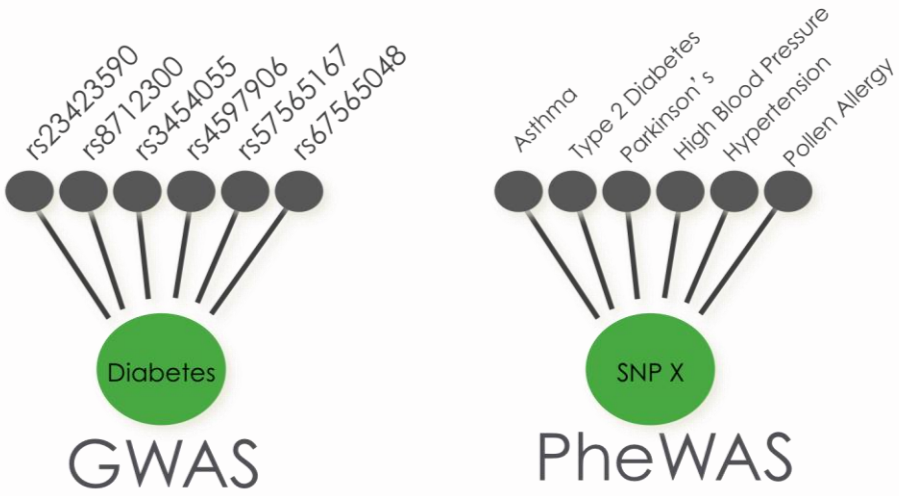
Therapeutics Analytic Strategy



GWAS

- Focus on diseases of interest
- Provides important validation of our platform and underlying data

PheWAS

- Focus on SNP/gene of interest
- Allow us to focus on druggable targets with little or no competition

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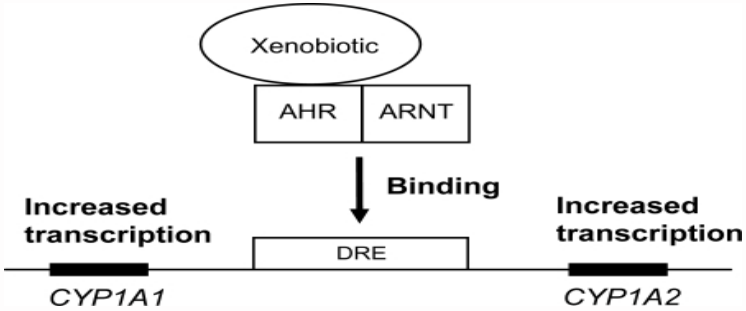
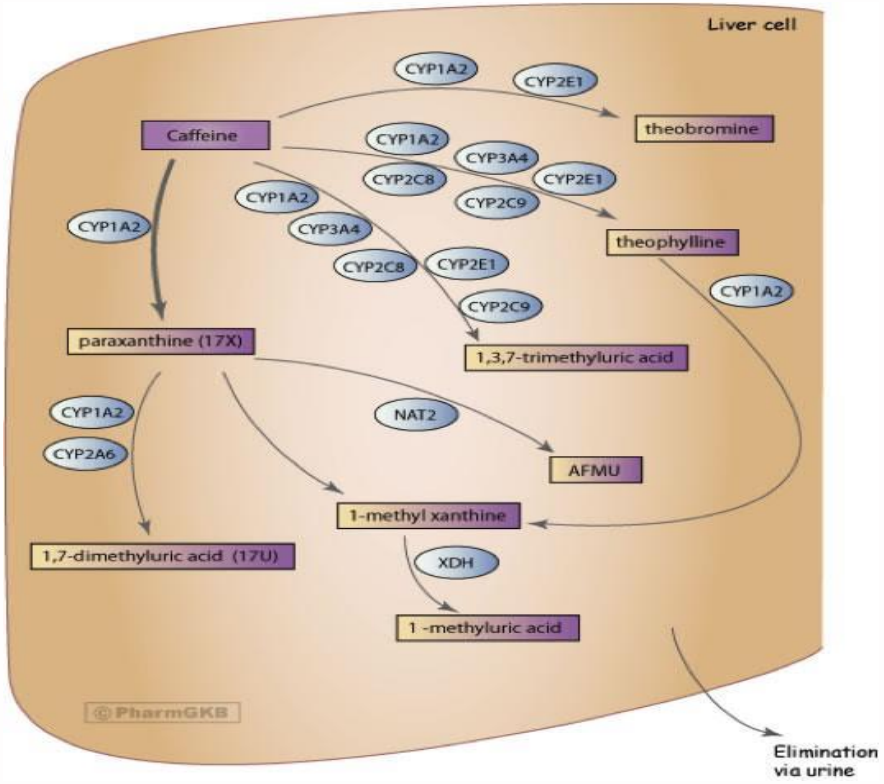
Variants in Caffeine Metabolism





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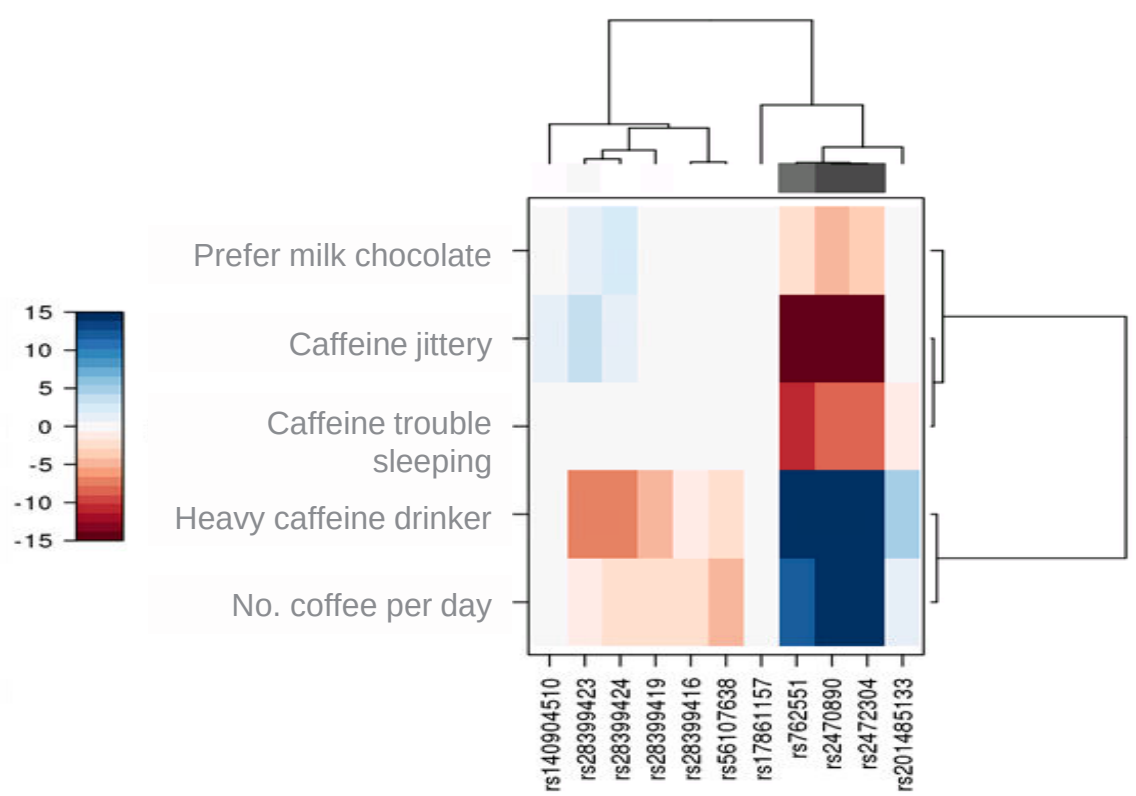
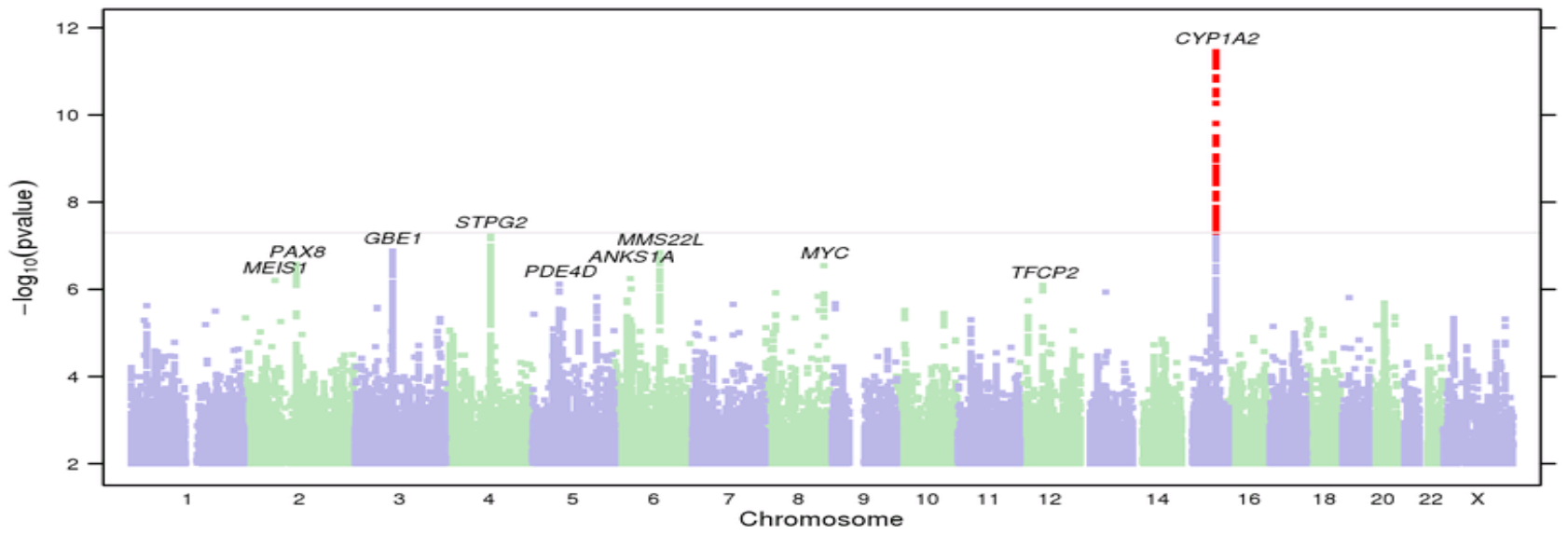
http://www.ncbi.nlm.nih.gov/pubmed/21357676

CYP1A2 PheWAS



Does drinking a caffeinated beverage in the evening usually make it more difficult for you to get to sleep that night?



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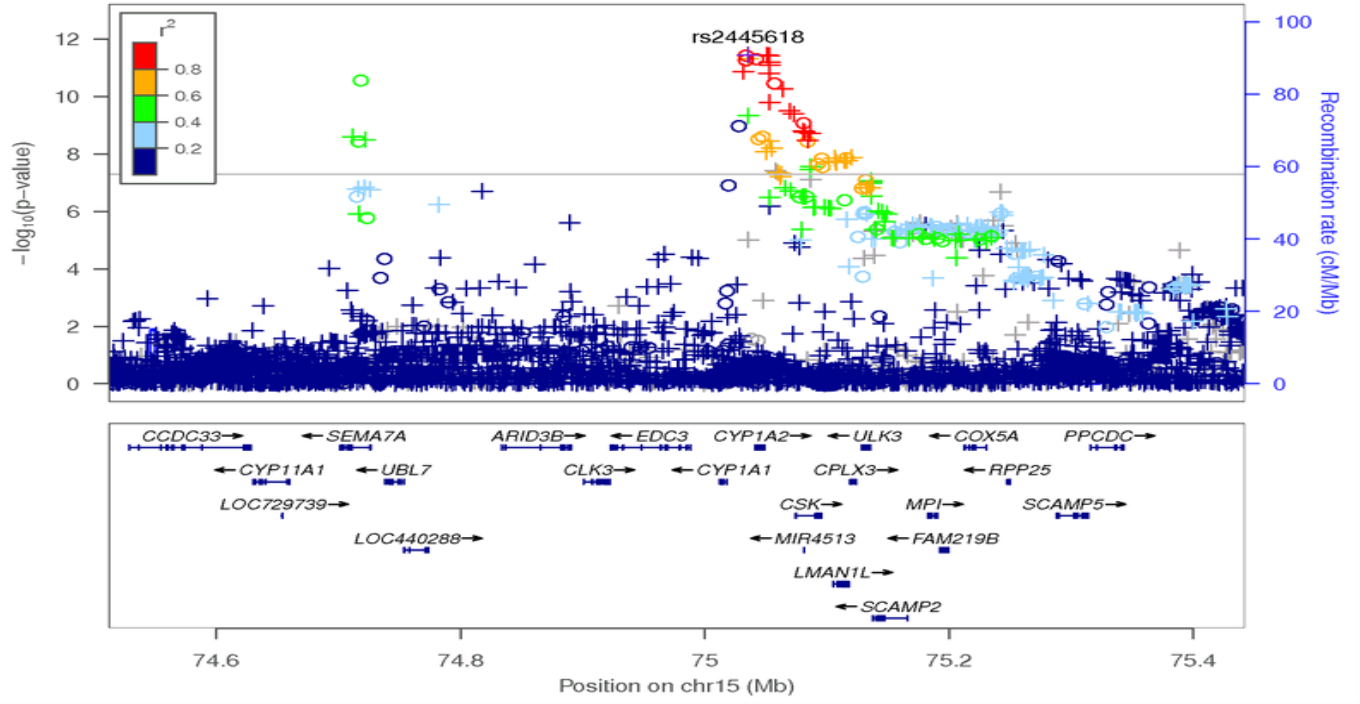
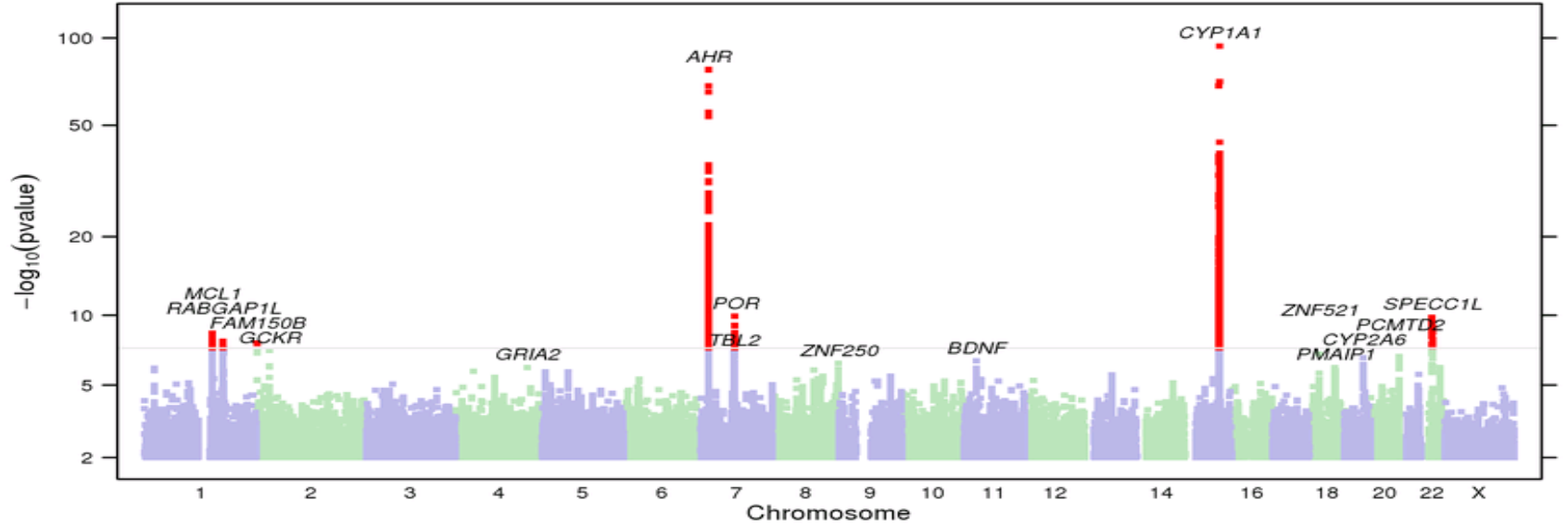


“Heavy caffeine drinkers:” cases report drinking several caffeinated drinks per **day**



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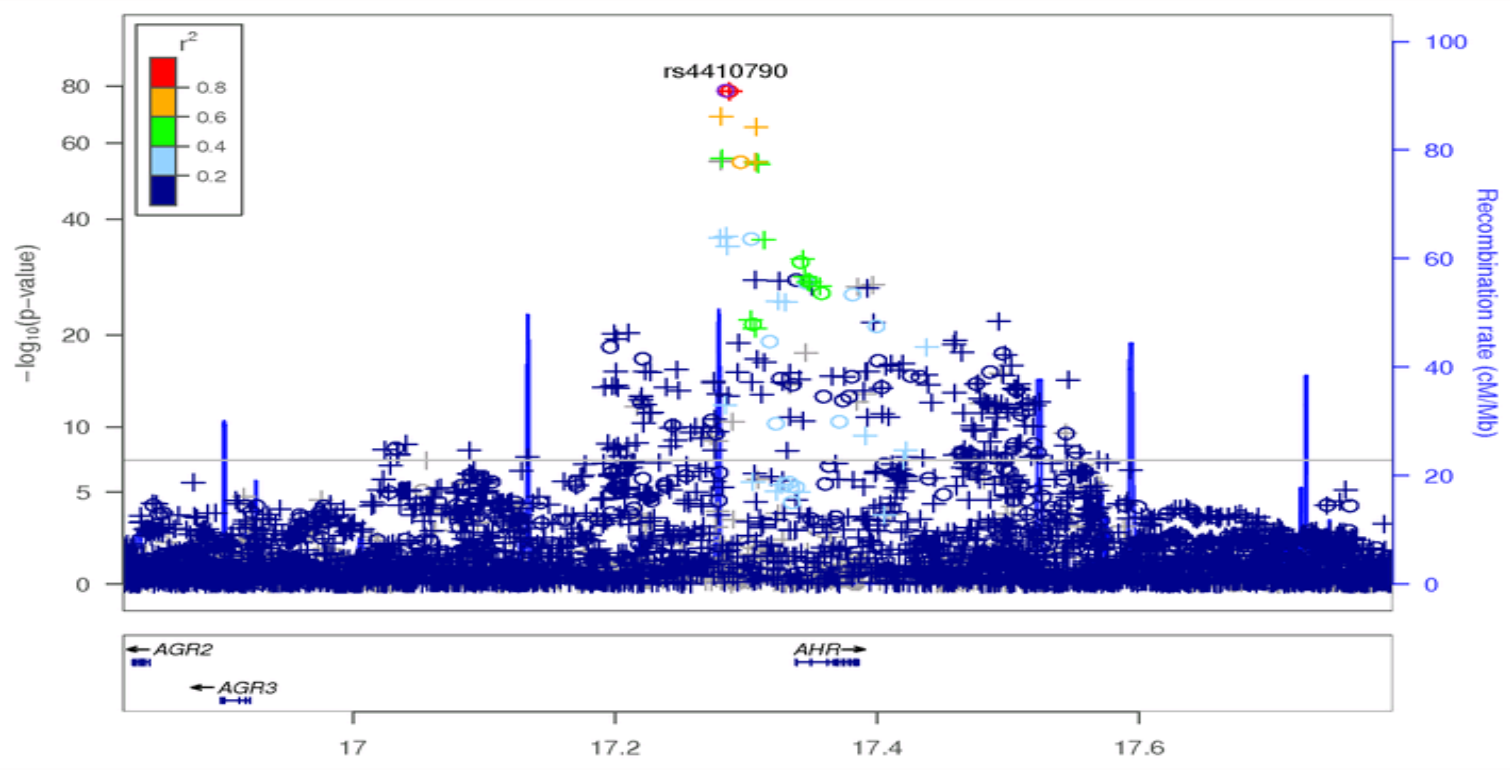

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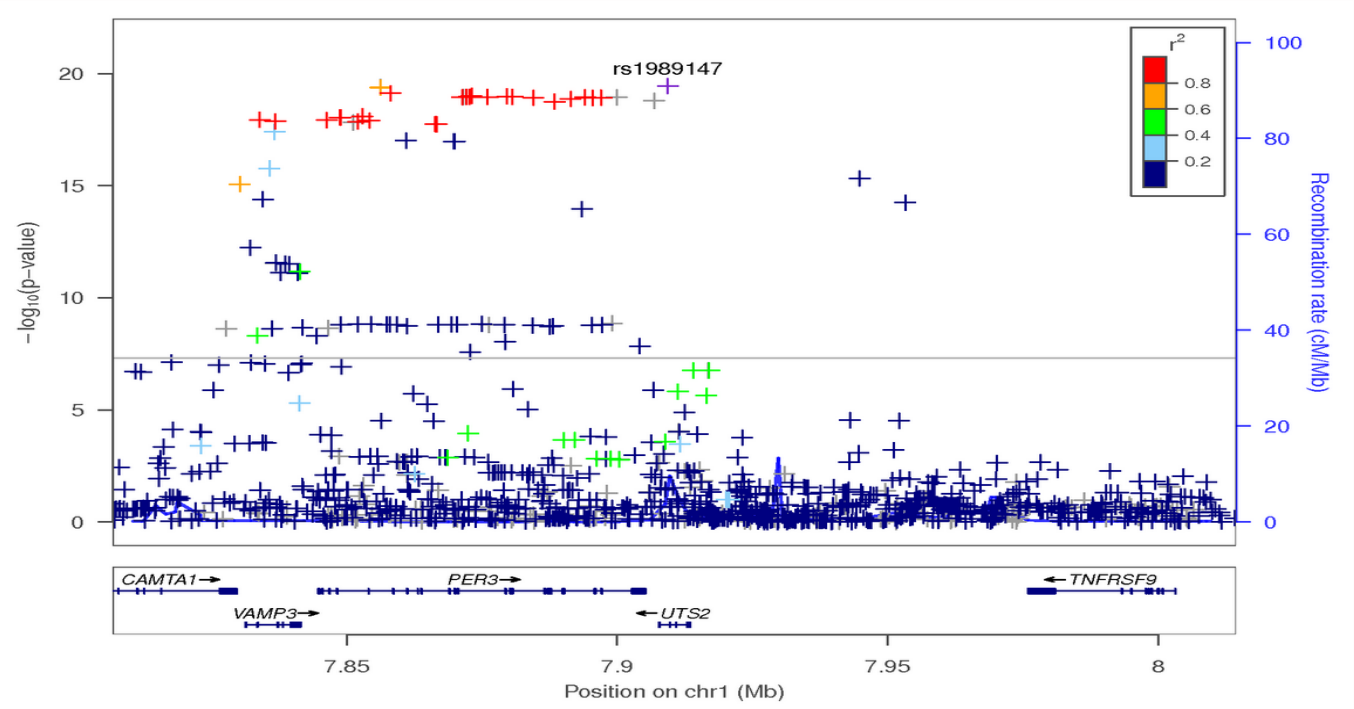
Are you a morning person or a night person?

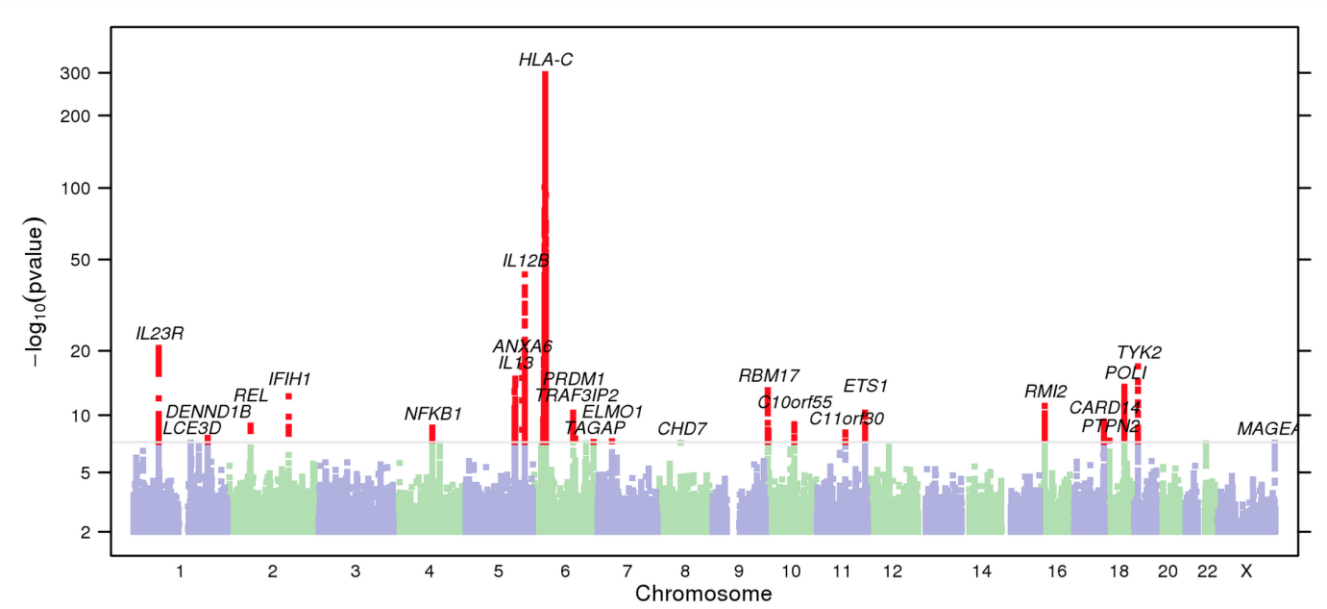


96,434 cases morning person

107,545 cases night person

GWAS Example: Psoriasis

We ask about psoriasis in 7 survey locations, e.g.: *"Have you ever been diagnosed with psoriasis?"*



Robust Sample Size:
25,000 Cases
445,000 Controls

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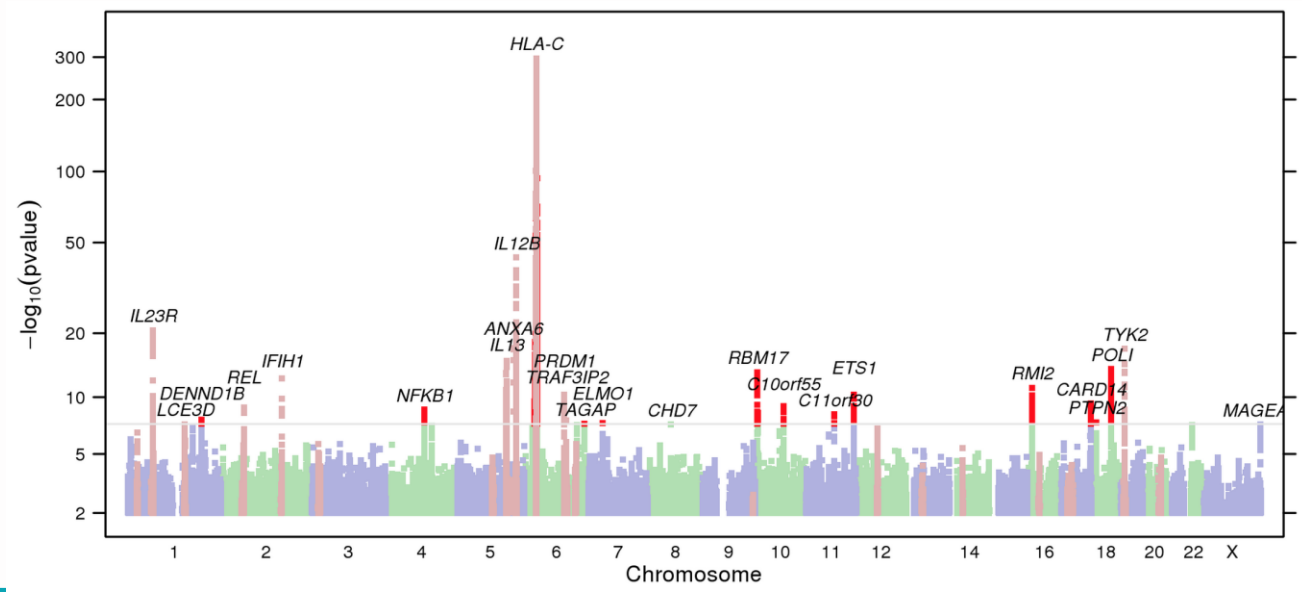
We ask about psoriasis in 7 survey locations, e.g.: *"Have you ever been diagnosed with psoriasis?"*

We validate well known associations with psoriasis



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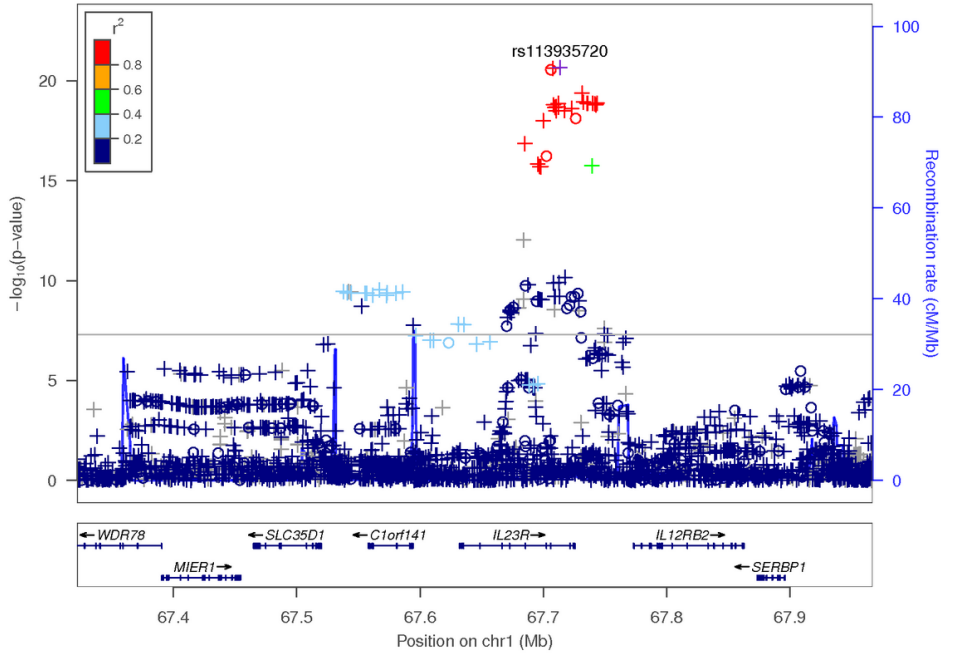

Robust Sample Size:
25,000 Cases
445,000 Controls

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OPEN ACCESS Freely available online

PLoS one

Efficient Replication of over 180 Genetic Associations with Self-Reported Medical Data

Joyce Y. Tung[1]*, Chuong B. Do[1], David A. Hinds[1], Amy K. Kiefer[1], J. Michael Macpherson[1], Arnab B. Chowdry[1], Uta Francke[1,2], Brian T. Naughton[1], Joanna L. Mountain[1], Anne Wojcicki[1], Nicholas Eriksson[1]

1 23andMe, Inc., Mountain View, California, United States of America, **2** Department of Genetics, Stanford University, Stanford, California, United States of America

- Associations compared for 50 phenotypes with published data curated by NHGRI
- In 84.6% of replications for case/control conditions, the 95% CI for the OR contained the published OR

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Multiple Large Cohorts

12,400 with Parkinson's	**243,000 APOE e4 carriers**	**78,000 with cancer**	**159,000 with depression**
710,000 confirmed controls	672,000 non-e4 carriers	657,000 confirmed controls	520,000 confirmed controls
90,000 with asthma	**35,000 with psoriasis**	**191,000 with cardiovascular disease**	**3,100 with colorectal cancer**
444,000 confirmed controls	650,000 confirmed controls	545,000 confirmed controls	711,000 confirmed controls

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In-Depth Study of Asthma

- Approximately **80,000** customers contacted via email → **8,000** chose to participate in 2 weeks

- Participants will be asked to take symptom survey **1x/month for 6 months**

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Genetics is Good for Drug Discovery

- Genetic evidence can help us see that modulation of the target is tolerated
- That modulation of the target is associated with disease
- If we find both LoF and GoF variants in the same gene – we have probably found the causal gene
- We can look for other phenotypes that might indicate safety issues

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Acknowledgements

- 23andMe Research & Therapeutics teams
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- Dave Hinds
- Joyce Tung