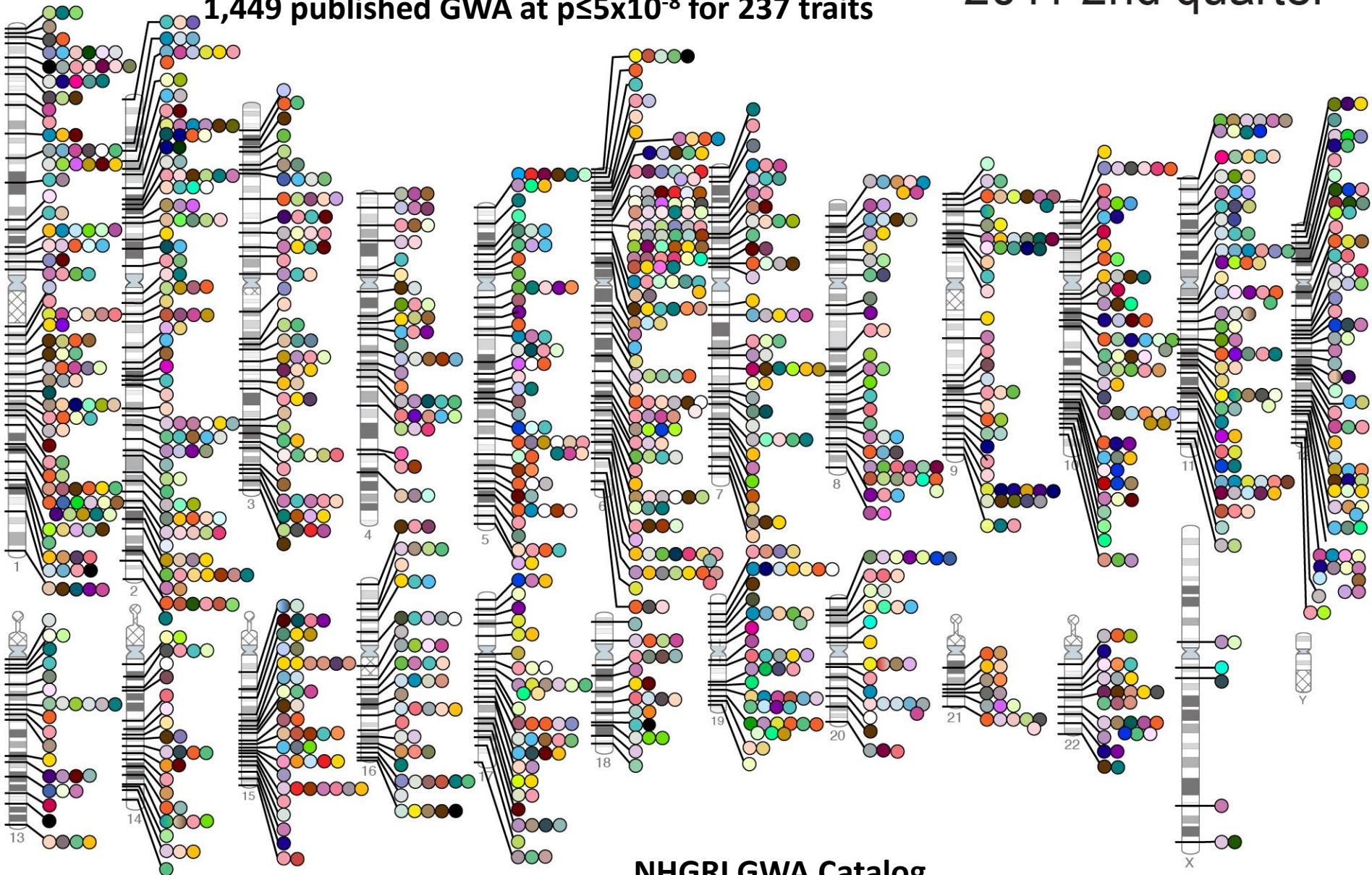
Final
Genetic Mates
Future Genetics
Course evaluation
Class discussion/feedback

Published Genome-Wide Associations through 06/2011,
1,449 published GWA at $p \leq 5 \times 10^{-8}$ for 237 traits

2011 2nd quarter



NHGRI GWA Catalog
www.genome.gov/GWAStudies

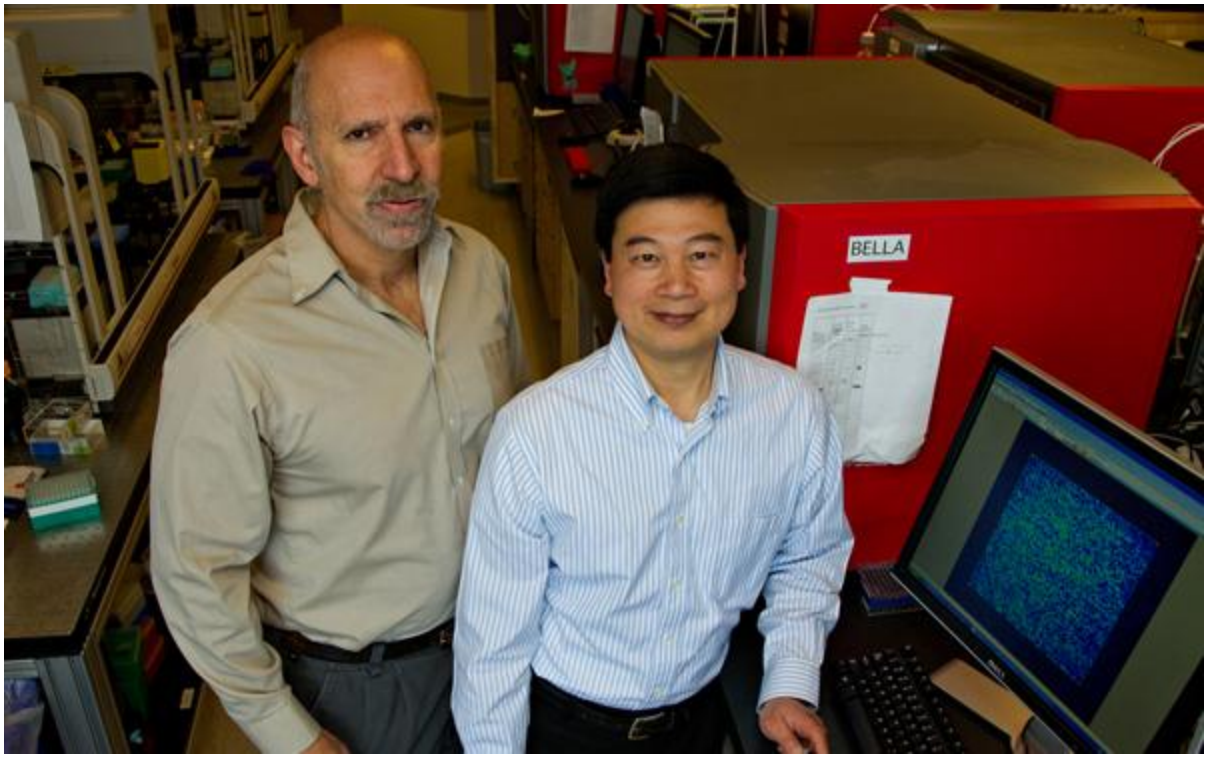
GWAS examples

Date Added to Catalog (since 11/25/08)	First Author/Date/ Journal/Study	Disease/Trait	Initial Sample Size	Replication Sample Size	Region	Reported Gene(s)	Mapped Gene(s)	Strongest SNP-Risk Allele	
05/25/12	Taal HR April 15, 2012 *Nat Genet* Common variants at 12q15 and 12q24 are associated with infant head circumference.	Head circumference (infant)	10,768 European ancestry infants	8,321 European ancestry infants	12q14.3 12q24.31 17q21.31	*HMGA2* *SBNO1* *CRHR1, MAPT*	HMGA2 SBNO1 C17orf69 - CRHR1	rs1042725-T rs7980687-A rs11655470-T	UTI intr int
05/25/12	Bhatnagar R April 12, 2012 *Oral Oncol* Genome-wide disease association study in chewing tobacco associated oral cancers.	Oral cancers (chewing tobacco related)	55 South Asian ancestry cases, 92 South Asian ancestry controls	NR	NS	*NS*	NS	NS	NS
05/25/12	Jylhava J April 12, 2012 *PLoS One* A genome-wide association study identifies UGT1A1 as a regulator of serum cell-free DNA in young adults: The Cardiovascular Risk in Young Finns Study.	Circulating cell-free DNA	1,841 individuals	NR	2q37.1	*UGT1A1*	UGT1A10; UGT1A8; UGT1A7; UGT1A6; UGT1A5; UGT1A9; UGT1A4; UGT1A1; UGT1A3	rs6742078-T	intr
05/25/12	Burri A April 11, 2012 *PLoS One* A genome-wide association study of female sexual dysfunction.	Sexual dysfunction (female)	1,104 European ancestry twins	NR	6q14.3 10p11.22 22q12.3	*Intergenic* *EPC1* *PVALB*	RPL7P27 - HTR1E EPC1 PVALB	rs13202860-A rs2370759-G rs4820255-C	int intr intr

Frontiers in Personalized Medicine

- PW-GW-AS: phenotype wide – genotype wide – association study
- Reverse human genetics

UCSF Kaiser-Permanente
N. Risch and P. Y. Kwok



UCSF Kaiser-Permanente

- 100,000 patients
- Genotype and telomere lengths
- ***many*** health traits

» RPGEH Home

The HUGE Project

About This Program

Participate in this Program

Privacy and Confidentiality

Scientific Collaboration, Current Research Projects

Pregnancy Project

RPGEH in the News

Newsletter Archive

FAQ

Welcome to the website for the Kaiser Permanente Research Program on Genes, Environment, and Health (RPGEH)

The RPGEH, a scientific research program at Kaiser Permanente in California, is one of the largest research projects in the United States to examine the genetic and environmental factors that influence common diseases such as heart disease, cancer, diabetes, high blood pressure, Alzheimer's disease, asthma and many others.

The goal of the research program is to discover which genes and environmental factors—the air we breathe, the water we drink, as well as lifestyles and habits—are linked to specific diseases.

This new knowledge has the potential to improve health and health care delivery by leading to new and improved diagnosis and treatment of disease and even prevention of some disease. One day your doctor may be even able to make a health care plan just for you based on your genetic profile and life experiences. This could include early testing for the diseases you might be likely to get, prescribing medications that will work best for you, and recommending lifestyle changes that will help keep you healthier.

Building a Biobank

Based on the over six million-member Kaiser Permanente Medical Care Plan of Northern California (KPNC) and Southern California (KPSC), the completed resource will link together comprehensive electronic medical records, data on

23andme

research surveys

23andWe begins with you. Learn about yourself while contributing to research.

Related topics: About 23andWe, Research Initiatives, 23andWe FAQ

Featured Research Survey:

Reading the Mind in the Eyes

About this survey | May 2012

This test is a measure of adult "mentalising", the ability to sense other people's emotions based on their facial expressions, and is believed to be an important component of empathy. Find out how you score!

start survey

Click on a survey to get started or to view your results

Your Health Profile

Help us personalize your 23andMe experience by taking 3-5 minutes to answer a few questions about yourself.

Published: June 2011

resume survey

Longevity

About this survey | Published: December 2009

resume survey

Physical Features

About this survey | Published: July 2010

start survey

Headaches

About this survey | Published: October 2009

start survey

Caffeine Usage

About this survey | Published: March 2011

start survey

PLoS Genet. 2010 Jun 24;6(6):e1000993.

Web-based, participant-driven studies yield novel genetic associations for common traits.

Eriksson N, Macpherson JM, Tung JY, Hon LS, Naughton B, Saxonov S, Avey L, Wojcicki A, Pe'er I, Mountain J.

23andMe, Mountain View, California, United States of America. nick@23andme.com

Research Discoveries at 23andme

Getting Attached to Earlobe Genetics

✔ **Thanks!** You took a survey that fueled this discovery.

view discovery

Understanding the Genetics of Freckling

● **Thank you for taking the survey in time for our first publication!** You are a Research Pioneer.

view discovery

Combing Through the Science of Hair Curl

● **Thank you for taking the survey in time for our first publication!** You are a Research Pioneer.

view discovery

Blonde on Blonder

✔ **Thanks!** You took a survey that fueled this discovery.

view discovery

Are We There Yet? Clues to Motion Sickness

✔ **Thanks!** You took a survey that fueled this discovery.

view discovery

Don't It Make Your Brown Eyes Blue

✔ **Thanks!** You took a survey that fueled this discovery.

view discovery

Genes and Geography

✔ **Thanks!** You took a survey that fueled this discovery.

view discovery

The ACHOO Syndrome

● **Thank you for taking the survey in time for our first publication!** You are a Research Pioneer.

view discovery

Eeny, Meeny, Miny, Moe, What's Your Biggest Toe?

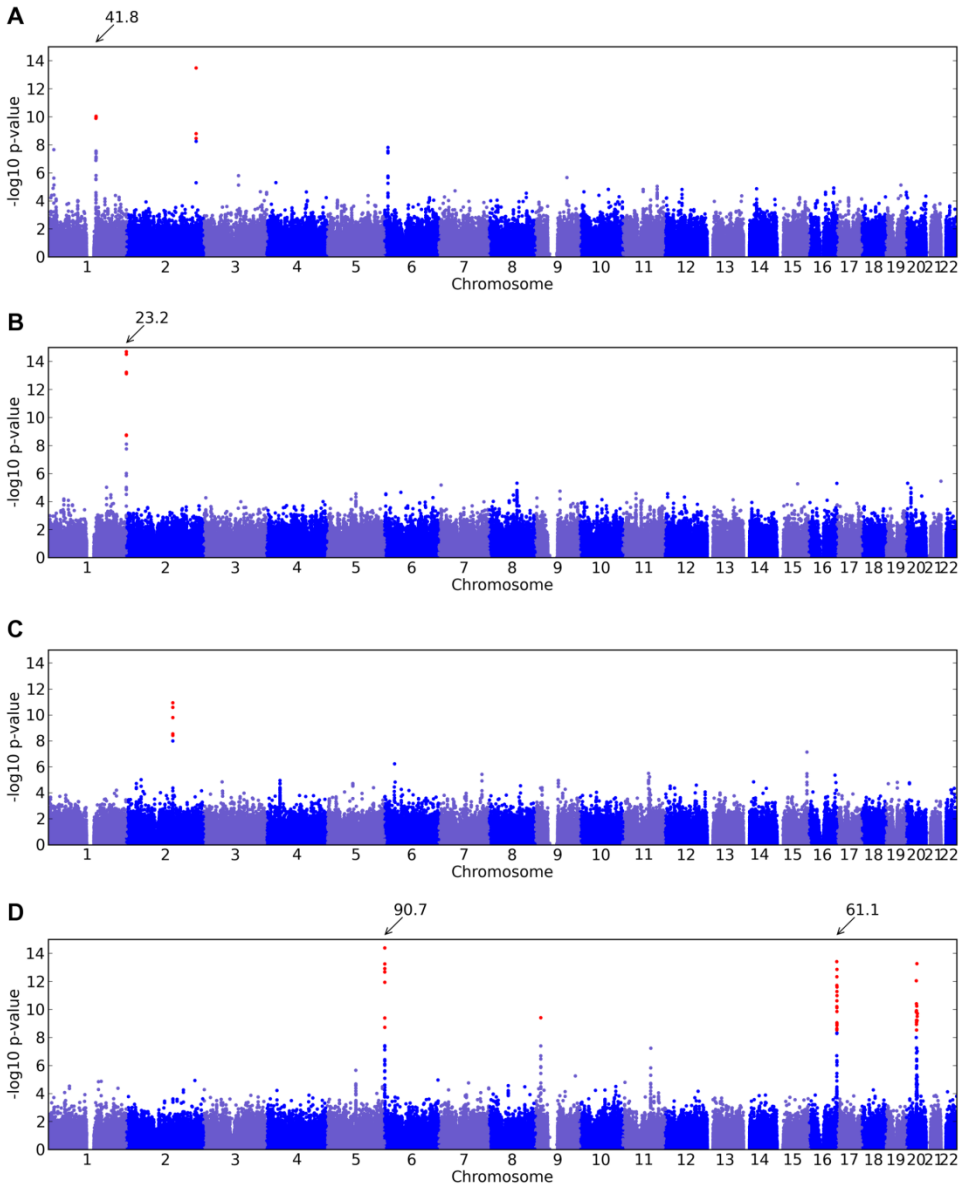
✔ **Thanks!** You took a survey that fueled this discovery.

view discovery

Phenotype	Size	Top hit	# Loci	Loci
Eye color, blue to brown	4402	>300	6	OCA2, SLC24A4, IRF4, SLC45A2, TYR, (TYRP1)
Freckles	4405	90.68	5	*IRF4*, MC1R, ASIP, **BNC2**, (TYR)
Hair color, blond to brown	3044	87.07	5	OCA2, IRF4, SLC45A2, SLC24A4, MC1R
Red hair	4422	86.28	2	MC1R, ASIP
Eye color, green/blue	2826	51.52	3	OCA2, SLC24A4, TYR
Hair curl	5385	41.80	3	TCHH, **WNT10A**, (**OFCC1**)
Asparagus anosmia	4742	23.18	1	**OR2M7**
Photic sneeze reflex	5390	10.93	2	**2q22.3**, (**NR2F2**)
Footedness	3079	6.75	0	
Attached earlobes	3915	6.59	0	
Morningness	4264	6.50	0	
Braces	4011	6.45	0	
Optimism	3936	6.29	0	
Astigmatism	7701	6.17	0	
Prefer sweet snacks	3100	6.07	0	
Wisdom teeth	3983	5.89	0	
Cavities	5366	5.81	0	
Glasses	5386	5.76	0	
Ocular dominance	3126	5.70	0	
Hand-clasp	5256	5.66	0	
Motion sickness	2987	5.55	0	
Handedness	4268	5.30	0	

Loci are called significant if they contain a SNP with $-\log_{10}$ p-value over 8.4 and suggestively significant if they have one between 7.1 and 8.4. Loci that were not previously associated with the given trait are in bold, those where we report a remapping of a previous hit are in italics, and suggestively significant loci are in parentheses. Size refers to the total number of individuals in the study. The ''top hit'' refers to the largest $-\log_{10}$ p-value for the given trait. The genomic control inflation factor, λ, [59] was between 1.0 and 1.02 for all studies. For more details, including λ, numbers of cases and controls, and covariates used in the analyses, see Supplementary Table 1 of Text S6.

doi:10.1371/journal.pgen.1000993.t001



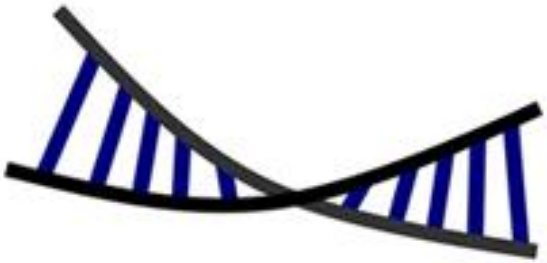
Hair Curl

Asparagus smell

Photic sneeze

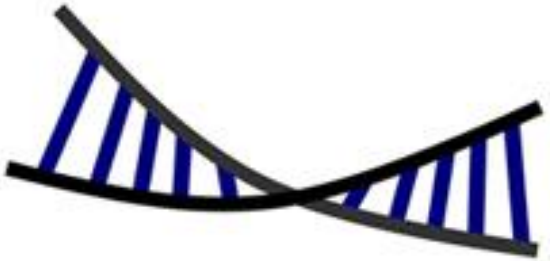
freckling

Forward Genetic Screens

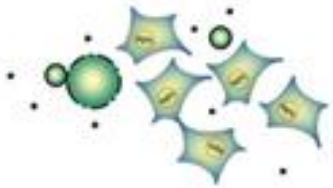


Discover Gene underlying Phenotype

Reverse Genetic Screens



Known Gene



Phenotype Resulting from Alteration

DRD sequencing: Results

- Three genes found with rare compound heterozygous mutations.
  - ***ZNF544* encodes a computationally predicted zinc finger protein with no known function or targets**
  - ***C2orf16.***
  - *SPR* encoding sepiapterin reductase.

Reverse Human Genetics

- Sequence 1,000,000 people
  - Each person is compound heterozygous ~2 gene.
  - DRD patients (2), Snyder (1), Kim (2)
- Entire population has ~2M knockouts
  - For each gene, there are about 100 people lacking that gene (compound heterozygous)
- Find an interesting gene
  - Mutant phenotype is known in model organisms
  - Expression or biochemical activity is interesting
  - Etc.
- Recruit ~100 people that are compound heterozygous for your gene.
  - Guess phenotype based on known function in model organisms
  - Have people come into clinic, take questionaire, etc.
  - This could tell you function of gene in people
- Examples
  - Neurotransmitter receptors/brain function
  - foxP2/speech function
  - Telomerase or insulin signaling receptor/longevity