Genetics 210: Personalized Medicine and Genomics

It's far more important to know what person the disease has than what disease the person has.

-Hippocrates

For: MDs, PhDs and curious students

Spring term. Tue 2:15 – 4:05 Workshop

Thur. 2:15-4:05 Presentation

LKSC 101

Genotyping : $49 copay

Gene210.stanford.edu: info and FAQs

Course Staff

- Course Organizer: Stuart Kim stuartkm@stanford.edu
- Participating Faculty: Euan Ashley, Russ Altman, Atul Butte, Mike Snyder, Aaron Gitler, Carlos Bustamente, Emmanuel Mignot
- TAs:
  - Damek Spacek dspacek@stanford.edu
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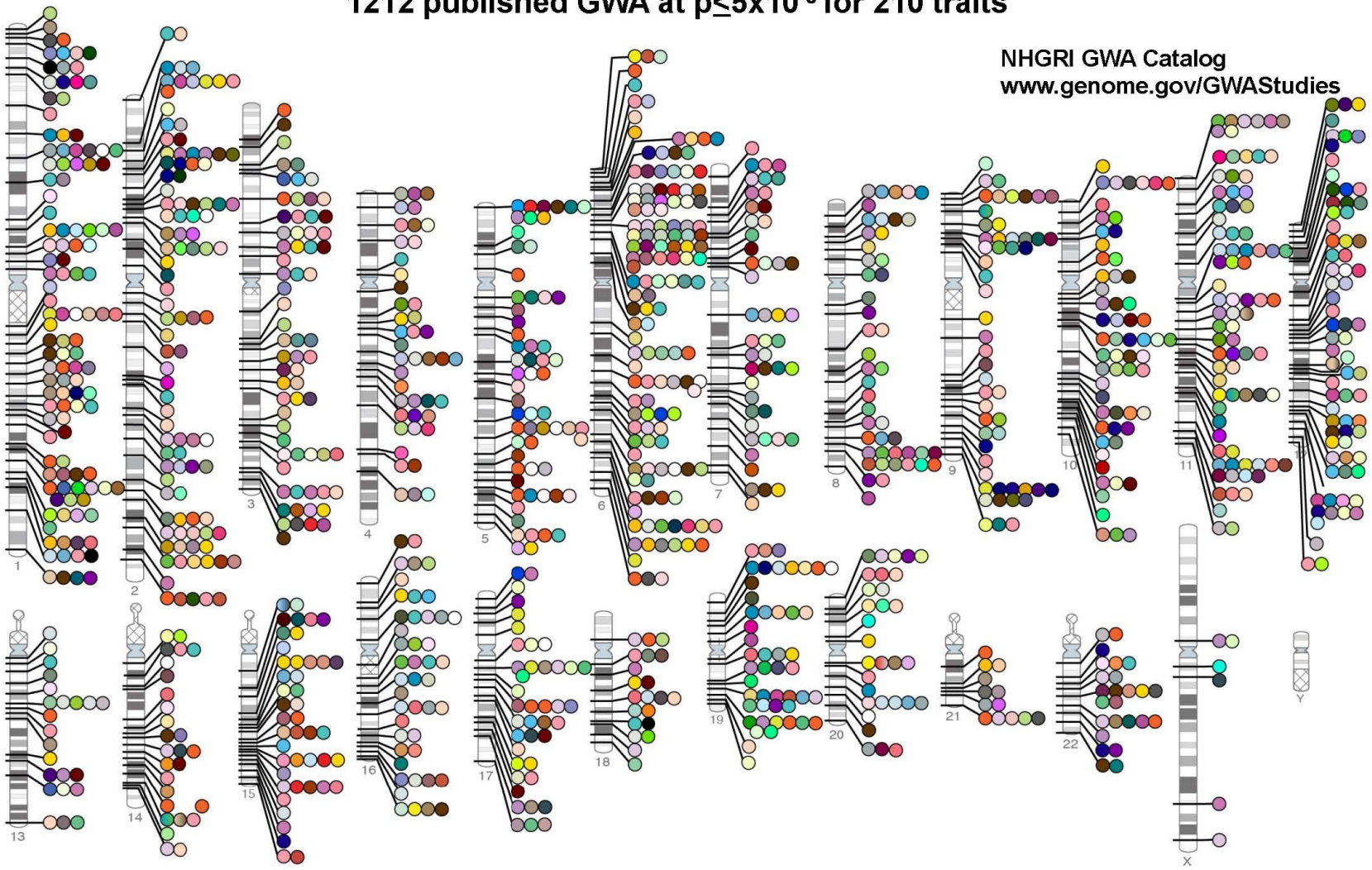
Genetics 210: Personalized Medicine and Genomics

- Goals
- Who is this for?
- Course Structure

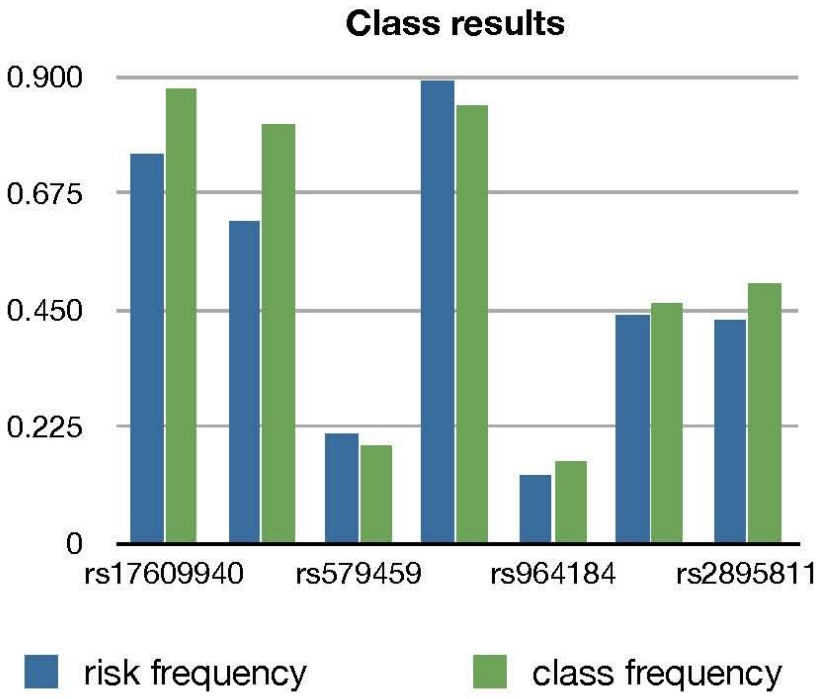
Published Genome-Wide Associations through 12/2010, 1212 published GWA at $p \leq 5 \times 10^{-8}$ for 210 traits



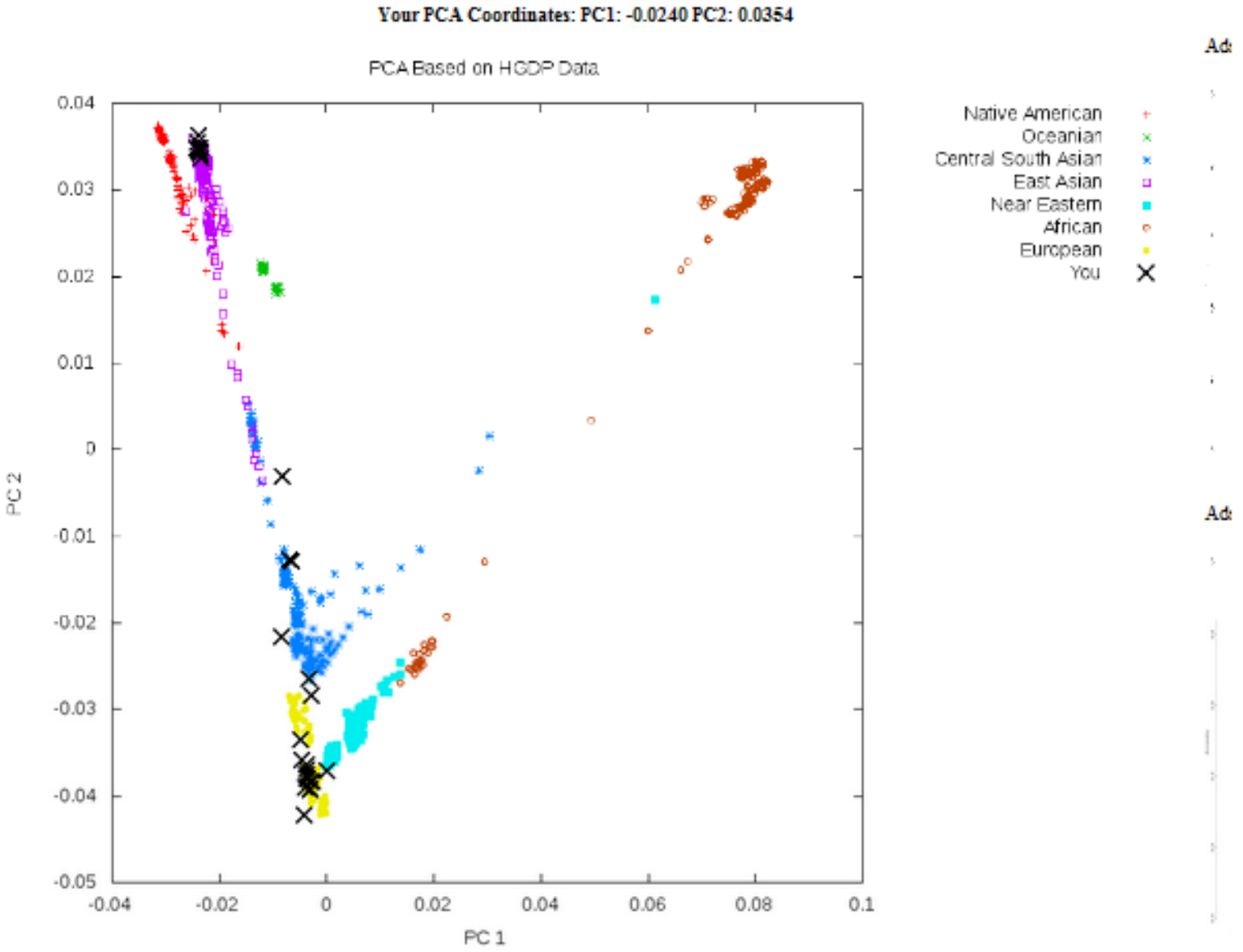
2011 Participatory Presentations

Date	Subject	Presenter
March 30	Human Genetic Variation and GWAS	Stuart Kim
April 6	Interpreting Genomic Data in Clinical Medicine.	Euan Ashley
April 20	Pharmacogenetics	Russ Altman
April 27	Human Ancestry.	Carlos Bustamante
May 4	Networks.	Atul Butte
May 18	Next generation technology.	Mike Snyder
May 25	Narcolepsy	Emmanuel Mignot
June 1	Aging	Stuart Kim

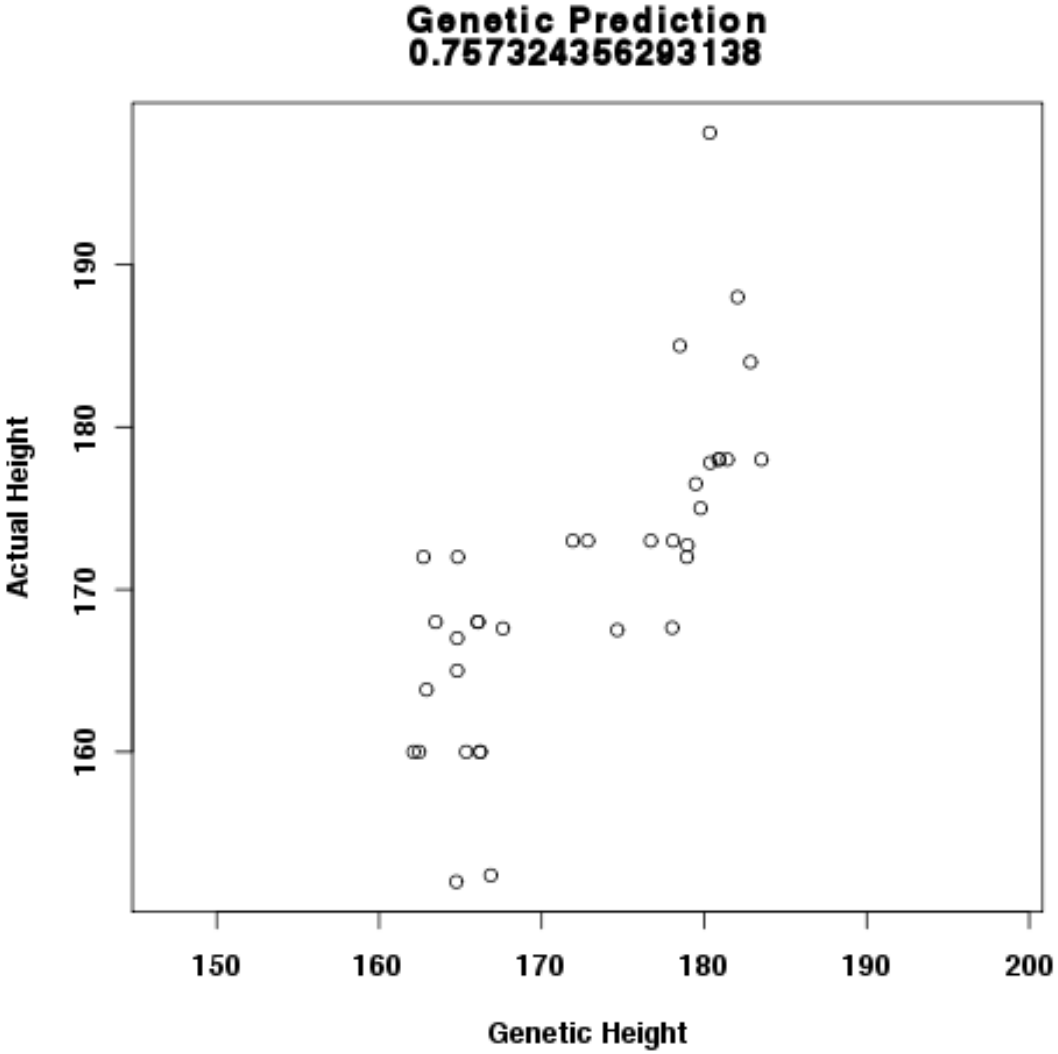
snp	risk	risk.count	nonrisk.count	risk.frequency	class.frequency
rs17609940	G	28	4	0.75	0.875
rs11556924	C	21	5	0.62	0.8076923077
rs579459	C	6	26	0.21	0.1875
rs12413409	G	27	5	0.89	0.84375
rs964184	G	5	27	0.13	0.15625
rs4773144	G	12	14	0.44	0.4615384615
rs2895811	C	16	16	0.43	0.5



Human Ancestry



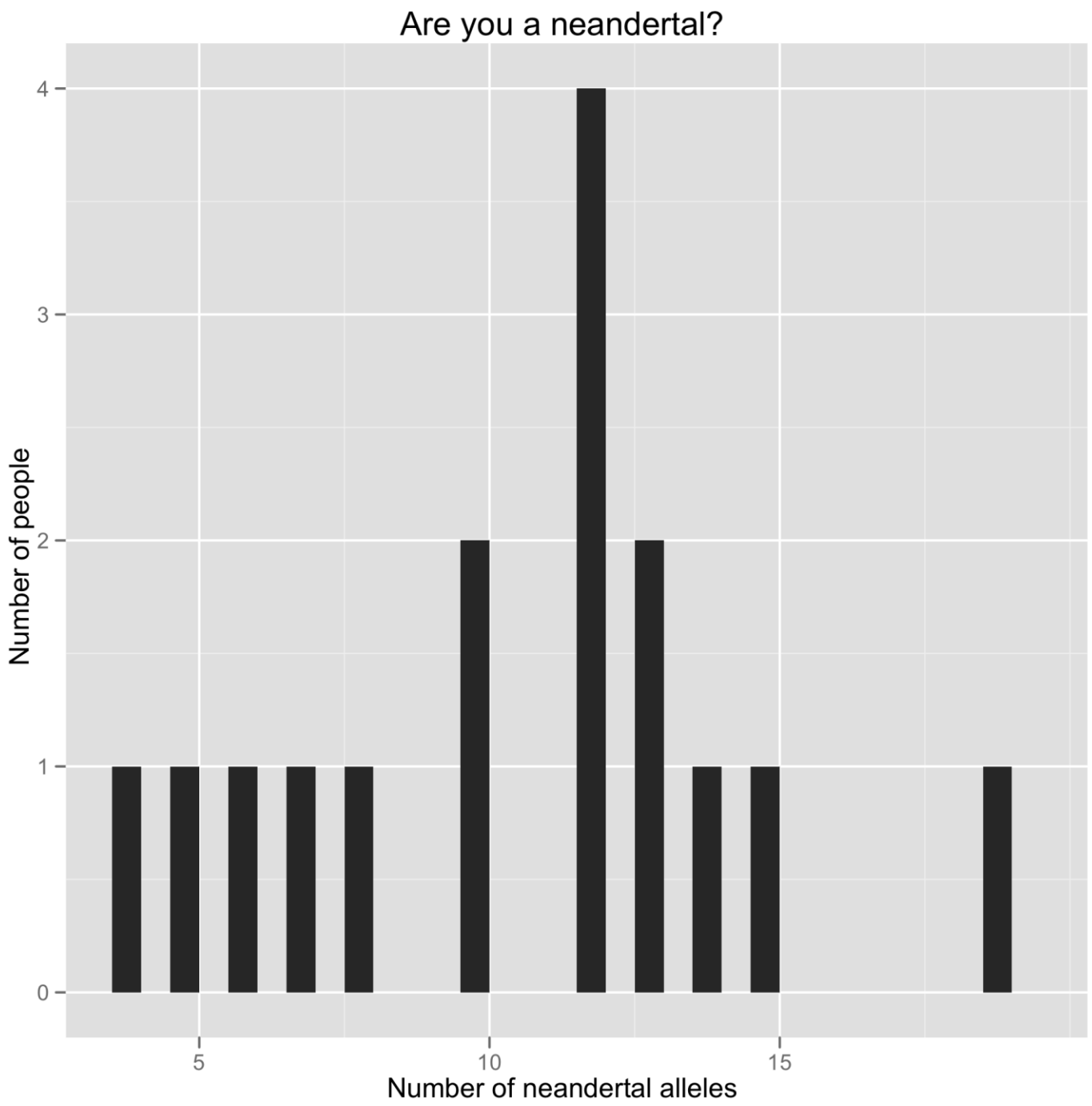
Height prediction



How much Neanderthal are you?

Neanderthal

George Church,
Harvard Geneticist


Are you a neandertal?
Number of people
0
1
2
3
4
5
10
15
Number of neandertal alleles

History

Joint Genotyping Task Force

Charles Prober Dean
Russ Altman Genetics
Pat Brown Biochem.
Mike Grecius Neur.
Carlos Bustamente Gen.
Ralph Horwitz Psych
Anne James Legal Counsel
Stuart Kim Dev. Bio.
Phil Lavori HRP
Kelly Ormond Genetics
Mike Snyder Genetics
Keyan Salari Med. School

Hank Greely Law School
Clarence Braddock Med School
Gil Chu Biochem
Sean David Med. School
Harry Greenberg Dean
Louanne Hudgins Epidemiology
Jesse Karmazin Med. School
Mark Krasnow Biochem
David Magnus Cen. BME
Alan Schatzberg Psych.
Atul Butte BMI
Mildred Cho Pediatrics

Personal Genotyping

- Voluntary. You can use a public genome file instead of your own.
- Confidential – instructors will not know who opted to be genotyped.
- Private – You will not be asked to reveal your own private DNA information.
- Counseling - genetic counseling via 23andMe and medical/psychological counseling via Dr. Alan Schatzberg (Psychology, Stanford).

How to get genotyping kits

1. Attend both informations sessions or watch them on the internet (Jan. 18 and 25).
2. Fill out form
3. Bring form and check to Kathy in Beckman B300.
4. Make check $49 to Stanford.
5. Bring samples back to Flora or Kathy B300
6. We will ship the group of samples back to company Monday 4pm Jan 30 by FEDEX
7. Results in 6-8 weeks.
8. Class starts Tuesday April 3, 2012.

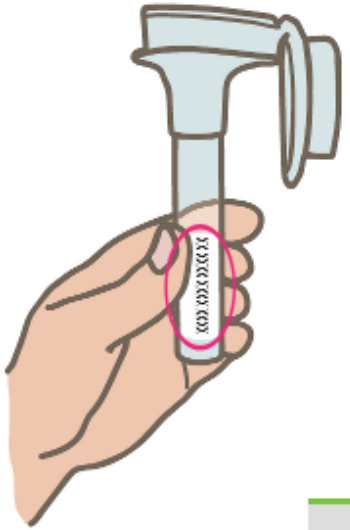
23andMe genetics just got personal.

Search 23andMe Go | Log in | Register Your Kit | Blog | Help | Cart

welcome | ancestry | health | how it works | store

register your kit

1 enter barcode 2 terms of service 3 consent 4 add a profile



Please enter the barcode found on your DNA collection tube.

Each person's barcode only needs to be entered once. If you have already entered the barcode for a given kit, you can just log in to your account.

Barcode on Tube:

Security Check: SNJAH I can't read them.

Type the letters you see in the picture above.

Register

https://www.23andme.com/user/claim/

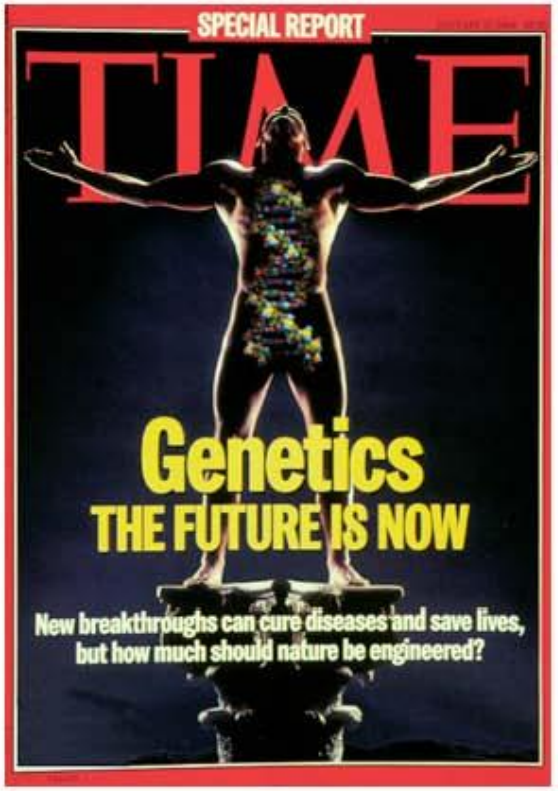
Informed Consent for Personal Genotyping

Approximately 3,000 genetic counselors and 1,100 medical geneticists in pediatrics, obstetrics, cancer genetics, neurogenetics, cardiogenetics…

The "new" genetics of today and tomorrow

- Complex genetics 101
  - All the genetic rules are less clear
  - Addressing common conditions of adulthood
  - Involves both genetic and lifestyle components
  - Genome wide testing via SNPs and exome/genome sequencing

- Testing available for more and more conditions, but good prediction still a long way off for most common complex disease



health and traits: complete list

Your 23andMe scan includes genetic analysis on all of the following diseases, traits, and conditions. This list grows every month as new research is published.

Clinical Reports (30)

Clinical Reports give you information about conditions and traits for which there are genetic associations supported by multiple, large, peer-reviewed studies. Those associations must also have a substantial influence on a person's chances of developing the disease or having the trait. Because these associations are widely regarded as reliable, we use them to develop quantitative estimates and definitive explanations of what they mean for you.

Age-related Macular Degeneration
Alcohol Flush Reaction
Alpha-1 Antitrypsin Deficiency
BRCA Cancer Mutations (Selected)
Bitter Taste Perception
Bloom's Syndrome
Celiac Disease
Clopidogrel (Plavix®) Efficacy
Crohn's Disease
Cystic Fibrosis (Delta F508 mutation)
Earwax Type
Eye Color
G6PD Deficiency
Glycogen Storage Disease Type 1a
Hemochromatosis
Lactose Intolerance
Malaria Resistance (Duffy Antigen)
Muscle Performance
Non-ABO Blood Groups
Norovirus Resistance
Parkinson's Disease
Prostate Cancer
Psoriasis
Resistance to HIV/AIDS
Rheumatoid Arthritis
Sickle Cell Anemia & Malaria Resistance
Type 1 Diabetes
Type 2 Diabetes
Venous Thromboembolism
Warfarin (Coumadin®) Sensitivity

Research Reports (86)

About Breast Cancer

try a demo

Breast cancer can affect both sexes, but it is mainly a concern for women— one in eight will face the disease at some point in their lifetimes. Next to lung cancer, it is the second leading cause of cancer -related deaths in women. The good news is that the number of these deaths is steadily decreasing. Medicine is making great strides against the disease thanks to early detection and better treatments.

Learn more about the biology of Breast Cancer...
Major discoveries in Breast Cancer...

1 of 4. Having a regular mammogram can help detect breast cancer early, allowing more treatment options.

Example Genetic Data

Information for **Lilly Mendel (Mom)** assuming **European** ethnicity and an age range of 30-79

Lilly Mendel (Mom)

9.1 out of 100

women of European ethnicity who share Lilly Mendel (Mom)'s genotype will get Breast Cancer between the ages of 30 and 79.

Average

12.5 out of 100

women of European ethnicity will get Breast Cancer between the ages of 30 and 79.

What does the Odds Calculator show me?

Use the ethnicity and age range selectors above to see the estimated incidence of Breast Cancer due to genetics for women with **Lilly Mendel (Mom)**'s genotype. The 23andMe Odds Calculator assumes that a person is free of the condition at the lower age in the range. You can use the name selector above to see the estimated incidence of Breast Cancer for the genotypes of other people in your account.

The 23andMe Odds Calculator only takes into account effects of markers with known associations that are also on our genotyping chip. Keep in mind that aside from genetics, environment and lifestyle may also contribute to one's chances of developing breast cancer (if you are a woman).

Genes vs. Environment

27-40 %
Attributable to Genetics

The heritability of breast cancer is estimated to be 27-40%. This means that environmental factors contribute more to differences in risk for this condition than do genetic factors. Genetic factors that play a role in breast cancer include both unknown and known factors. Known factors include the rare but high-risk mutations in the BRCA1 and BRCA2 genes as well as the SNPs described here. Other factors that can increase your risk include being female, being older, a family history of breast or ovarian cancer, an abnormal breast biopsy, previous chest radiation, early menarche or late menopause, exposure to diethylstilbestrol (DES) in utero, not having children or having children after the age of 30, recent oral contraceptive use, long term post-menopausal hormone therapy

Questions you should think about…

- Why do you want to know?
- Why now versus at another time in your life?
  - As a medical student or graduate student, are knowing these risks going to make you more or less likely to worry about them?
  - How does your age, current health, relationship status and parenting status impact your decision?

- Have you told your family you are considering this? What do they think?
  - Is there external pressure to get tested? Is this a good or bad thing?

- With whom will you share your results?
  - Family? Partner? Doctor? Friends? Classmates? Teachers?

What are the potential benefits of personal genotyping

- You may have some validation that you are at increased risk for specific common disorders present in your family
- If you are found to be at elevated risk, this may help you decide to make some lifestyle or behavioral changes to decrease your risks, or to get screening at an earlier or more frequent age then otherwise
- If you are adopted and don't know your family medical history, this may provide you with some information

What are the potential "risks" to personal genotyping

- The emotional risks include:
  - You might learn that you have a high risk for something you were not previously aware of
    - Most risks from GWAS data are small odds ratios – this is not like testing for Huntington disease
    - 23andme does include BRCA1/2 Jewish founder mutations, which ARE highly penetrant
  - Depending on the test, you might learn about your risks for a condition like Alzheimer disease (Navigenics) or psychiatric illness risks for Bipolar or Schizophrenia (23andme)
    - In some cases you can opt out of learning this information if you don't want to learn it
  - You might learn something about your ancestry that makes you uncomfortable
  - If more than one person in your family gets tested, you might learn that family relationships are not what you expected

Are there any potential health risks?

- You might find out about an elevated health risk and decide to undergo an invasive screening test that wasn't really necessary, putting yourself at an increased risk for complications.

- You might find out about a decreased health risk and decide you no longer needed to undergo routine screening tests that are recommended to the general population, and there is always a chance you could still develop that condition (and have it detected at a later point, impacting prognosis).

What about GINA?

- Genetic information nondiscrimination act (signed 5/2008)
- Federal provisions to protect against genetic discrimination in the realms of health insurance (5/09) and employment (11/09)
- No protections for life, disability and long-term care insurance
- Few actual reports of discrimination on the basis of presymptomatic mutation status, but this federal bill will provide additional protections and, hopefully, help patients and families feel more confident undergoing testing
- http://www.genome.gov/10002328