

# Please sign up for presentations and debates

1. Presentations to the class

2. Debate (1 more needed)

"To know or not to know (Breast Cancer, Alzheimer's, ALS, Paternity)."

# Reading for Wed. Apr. 6

nature  
genetics

## Euan Ashley

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Large-scale association analysis identifies 13 new susceptibility loci for coronary artery disease

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### Clinical assessment incorporating a personal genome



*Euan A Ashley, Atul J Butte, Matthew T Wheeler, Rong Chen, Teri E Klein, Frederick E Dewey, Joel T Dudley, Kelly E Ormond, Aleksandra Pavlovic, Alexander A Morgan, Dmitry Pushkarev, Norma F Neff, Louanne Hudgins, Li Gong, Laura M Hodges, Dorit S Berlin, Caroline F Thorn, Katrin Sangkuhl, Joan M Hebert, Mark Woon, Hersh Sagreiya, Ryan Whaley, Joshua W Knowles, Michael F Chou, Joseph V Thakuria, Abraham M Rosenbaum, Alexander Wait Zaranek, George M Church, Henry T Greely, Stephen R Quake, Russ B Altman*

\*Look up your genotype at 13 susceptibility loci at [gene210.stanford.edu](http://gene210.stanford.edu)

# Workshop

## Monday April 4

- Input height data
- Earwax GWAS explanation (Konrad)
- lactose, alcohol, eye, asparagus GWAS problems (class)
- Minor alleles have information (Stuart)
- Height vs parents height (Konrad/Rob)

# Class GWAS

Trait	SNP	P value	OR
Earwax	17822931	3.4E-5	13.3
Eye	7495174	1.95E-5	Undef (26.2)
Bitter	713598	.00148	6.2
Asparagus	4481887	.2	2.03
lactose	4988235	.15	5

# GWAS of the future?

- Consider a locus with alleles A and a, and genotypes AA, Aa and aa
- Suppose aa has a recessive disease phenotype
- Suppose allele frequency of a is 0.10

# GWAS of the future

	normal	disease	
AA	780	20	800
Aa	185	5	190
aa	1	9	10
	966	34	1000

# GWAS of the future

	normal	disease	
AA	780	20	.800
Aa	185	5	.190
aa	1	9	.010
	.966	.034	1000

# GWAS of the future

	normal	disease	
AA or Aa	965	25	.990
aa	1	9	.010
	.966	.034	1000



Chi squared = sum of  $\frac{(\text{observed} - \text{expected})^2}{\text{expected}}$

	normal	disease	
AA or Aa	.966 x .990	.034 x .990	.990
aa	.966 x .010	.031 x .010	.010
	.966	.034	1000

Chi squared = sum of  $\frac{(\text{observed}-\text{expected})^2}{\text{expected}}$

	normal	disease	
AA or Aa	.966 x .990 956	.034 x .990 33.6	.990
aa	.966 x .010 9.66	.031 x .010 .31	.010
	.966	.034	1000

Chi squared = sum of  $\frac{(\text{observed}-\text{expected})^2}{\text{expected}}$

	normal	disease
AA or Aa	$\frac{(965-956)^2}{956}$	$\frac{(25-33.6)^2}{33.6}$
aa	$\frac{(1-9.66)^2}{9.66}$	$\frac{(9-.31)^2}{.31}$

Chi squared = sum of  $\frac{(\text{observed}-\text{expected})^2}{\text{expected}}$

	normal	disease
AA or Aa	.085	2.20
aa	7.76	243



This is the really informative class – aa with disease

-Suppose you wanted to verify the results in a second study

-Suppose you wanted to test whether aa had a phenotype different than AA or Aa

Plan A – do the same study by genotyping 1000 individuals

Plan B - If you knew the genotypes of people, search for aa cases and compare to AA or Aa controls.

# GWAS of the future

	normal	disease	
AA	78	2	80
Aa	18	1	19
aa	1	9	10
	97	12	109

# GWAS of the future

	normal	disease	
AA	96	3	99
aa	1	9	10
	97	12	109

# GWAS of the future

	normal	disease	
AA	96	3	90.8
aa	1	9	9.2
	.89	.11	109



# Expected results

	normal	disease	
AA	88	10.88	.908
aa	8.9	1.1	.092
	.89	.11	109

# Chi squared results

	normal	disease	
AA	.727	5.7	.908
aa	7.0	56.7	.092
	.89	1.1	109

-Suppose you wanted to verify the results in a second study

-Suppose you wanted to test whether aa had a phenotype different than AA or Aa

Plan A – do the same study by genotyping 1000 individuals.

Chi squared  $\sim 250$ ; 1000 cohort

Plan B - If you knew the genotypes of people, search for aa cases and compare to AA or Aa controls.

Chi squared  $\sim 68$ ; 109 cohort