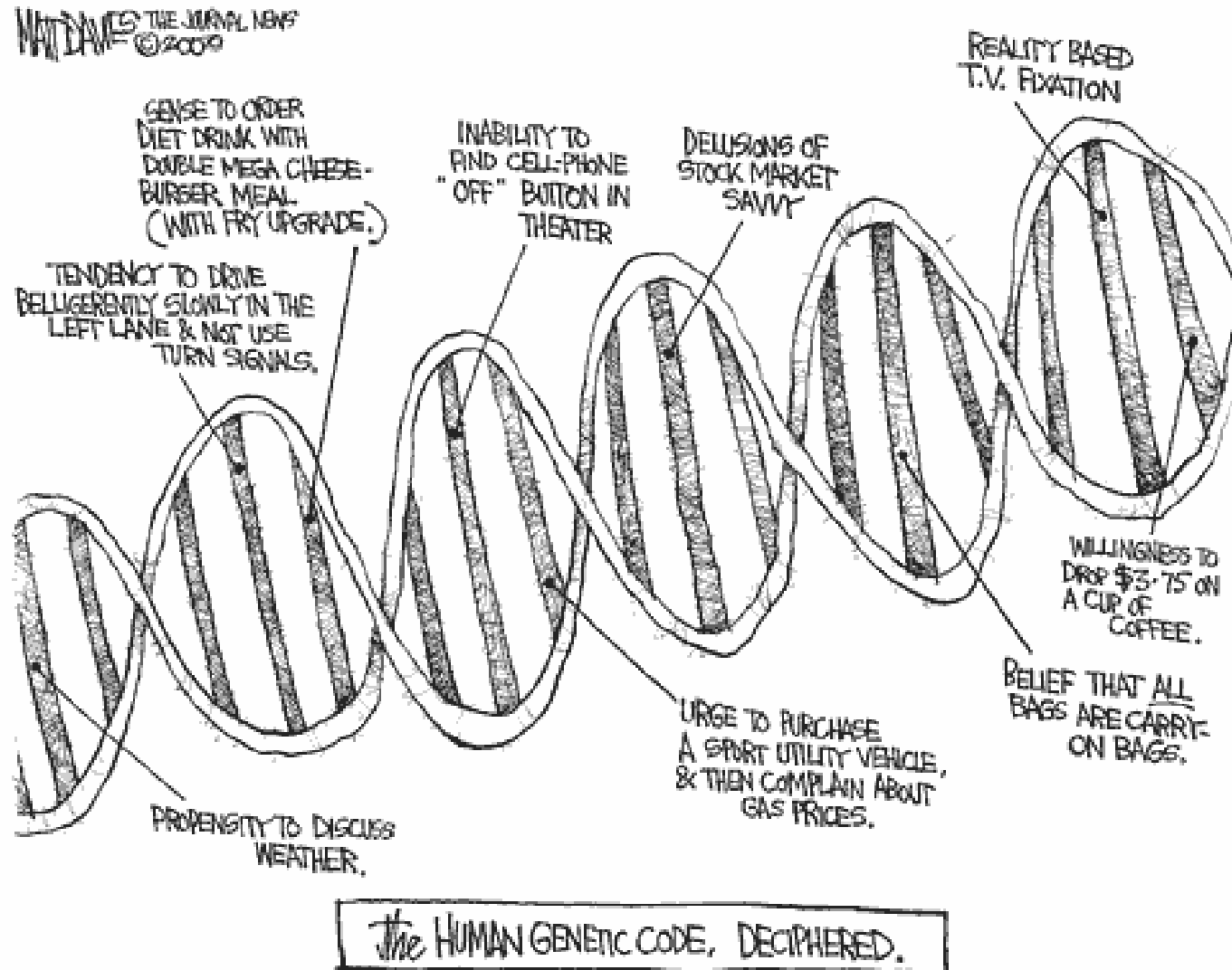


Epidemiology 217

Molecular and Genetic Epidemiology I



Outline

- **Course structure**
- Overview of genetics
- Overview of genetic epidemiology and the rest of the course

Course Goals

- Develop a framework for interpreting and incorporating genetic information in your research
- **Learn:**
 - Common genetic measures.
 - Some population genetics.
 - Approaches to search for disease-causing genes:
 - **Association** (key aspect of course)
 - Linkage
 - Admixture

Course Details

11 Tuesdays from 01/08/2013 – 03/19/2013, 1:10-3:00 pm, CB6702 (China Basin)

Course Directors:

Thomas Hoffmann, HoffmannT@humgen.ucsf.edu

John Witte, WitteJ@humgen.ucsf.edu

Lecturers:

Joe Wiemels, joe.wiemels@ucsf.edu

Eric Jorgenson, eric.jorgenson@kp.org

Neil Risch, rischn@humgen.ucsf.edu

Teaching Assistant:

Kirsten Kangelaris, kkangelaris@ucsf.edu

website:

<https://courses.ucsf.edu/course/view.php?id=901>

(Lectures, homework assignments, and answers)

Assignments

- **Problem sets (50%)**

Due at noon on Mondays to Kirsten Kangelaris, kkangelaris@ucsf.edu

- **Reading / class participation (20%):**

Genetic Epidemiology: Methods and Applications, by Melissa A. Austin.
CABI, 2013. ISBN: 978-1780641812.

Books may be purchased either through the publisher or a variety of commercial venues (e.g., Amazon.com), where you can also read the beginning of the first chapter.

Students may be called upon during class to answer questions about the assigned chapters.

- **Final project (design study)**

- 30% of grade (due Friday, 3/15 at Noon)
- Present to class

Syllabus - <https://courses.ucsf.edu/course/view.php?id=901>

Date	Topic / Content	Lecturer	Required Reading (pre-lecture)	Assignment Due (Monday @ noon)
01/07/2014	Introduction: The Big Picture The process of genetic epidemiology; general approaches to assess the genetic basis of disease.	T Hoffmann	Austin Chapter 1	
01/14/2014	Population Genetics, Modeling Genetic Inheritance Basics of population genetics; Hardy-Weinberg Equilibrium; aggregation; heritability.	T Hoffmann	Austin Chapter 2	Assignment 1 (Due 1/13 at Noon)
01/21/2014	Mendel's Laws and Molecular Genetics Mendel's laws (segregation, assortment); molecular measures; genotyping; arrays; sequencing.	J Wiemels	Austin Chapter 3	Assignment 2 (Due 1/20 at Noon)
01/28/2014	Family-based Studies Linkage analysis, Family-based association studies, TDT, FBAT	T Hoffmann	Austin Chapter 4	Assignment 3 (Due 1/27 at Noon)
02/04/2014	Genetic Association Studies General principles; candidate gene studies.	J Witte	Austin Chapter 5	Assignment 4 (Due 2/03 at Noon)
02/11/2014	Genome-wide Association Studies (GWAS) Agnostic searches across genome for associated SNPs; multiple testing; Imputation; Consortia.	J Witte	Austin Chapter 6	Assignment 5 (Due 2/10 at Noon)
02/18/2014	Gene-Environment Interactions and Epistasis Interactions; pharmacogenetics; less common & rare variants	J Witte	Austin Chapter 7	Assignment 6 (Due 2/17 at Noon)
02/25/2014	Non-mendelian genetics Mitochondrial (MT), De novo, Parent-of-origin, Methylation	E Jorgenson	Austin Chapter 8	Assignment 7 (Due 2/24 at Noon)
03/04/2014	Next Generation Sequencing Full genome and exome sequencing studies. Software for genetic analysis.	E Jorgenson	Austin Chapter 9	Assignment 8 (Due 3/03 at Noon)
03/11/2014	Admixture Analysis Population substructure, admixture mapping.	N Risch	Winkler et al., Admixture mapping comes of age, Ann Rev Genom Human Genet 2010 11:65-89, read through the "Admixed populations" section.	
03/18/2014	Putting it all Together: Incorporating Molecular and Genetic Measures into Your Research Final Project presentations	T Hoffmann, J Witte	Austin chapters 10 and 11	Final Project Due Friday 3/14 @ noon

Molecular & Genetic Epidemiology

Distinction

- Molecular: molecular, cellular, and other biologic measurements, on disease [e.g., biomarkers - selenium in toe nails, proteins, hormones]
- Genetic: role of inherited factors in disease (encompassed within molecular)

Genetic Epidemiology

Focus of course

- Genetic epidemiology
 - Initially studied single gene disorders
 - Now more complex genetic disorders and environment
- Many designs same as epidemiology (e.g., case-control)
- Some specialized analysis methods.
- Population genetics increasingly important

Aims

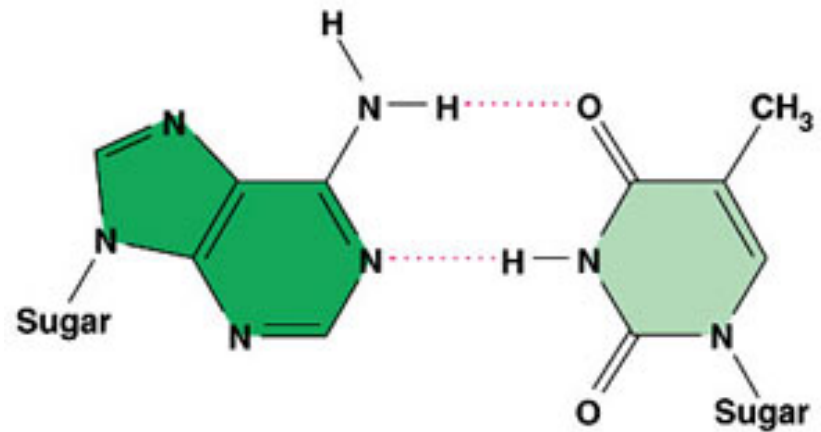
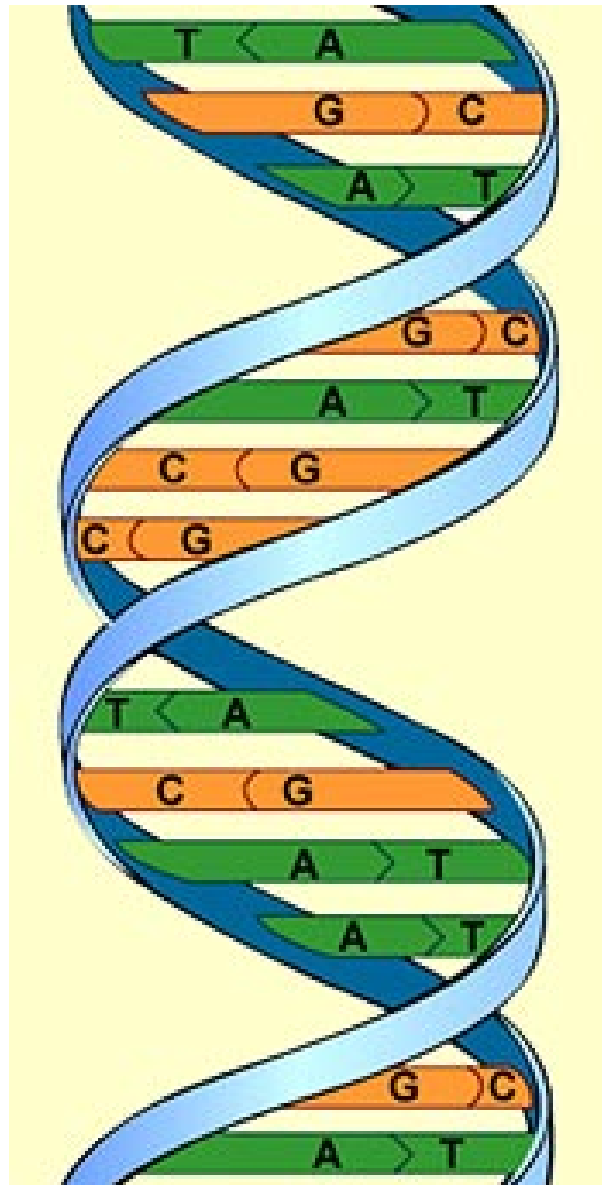
- Detect genetic causes of disease
- Understand biological process
- Prevention strategies, lifestyle intervention
- Improved therapeutic strategies, personalized medicine

	Genetics	Epidemiology
Origins	Biological science of inheritance Experimental/breeding	Methodological sciences / public health Observational/analytic studies
Focus	Mechanisms of inheritance, often on rare diseases	Etiologic factors, primarily on common diseases
Tools	Family studies Laboratory methods Statistical models Population models	Observational studies Case-control studies Cohort designs Clinical trials
Goals	Understand mechanisms of inheritance	Understand distribution etiology, and progression of diseases
Overlap	Diseases of interest Population studies Ultimate goal of disease prevention	

Outline

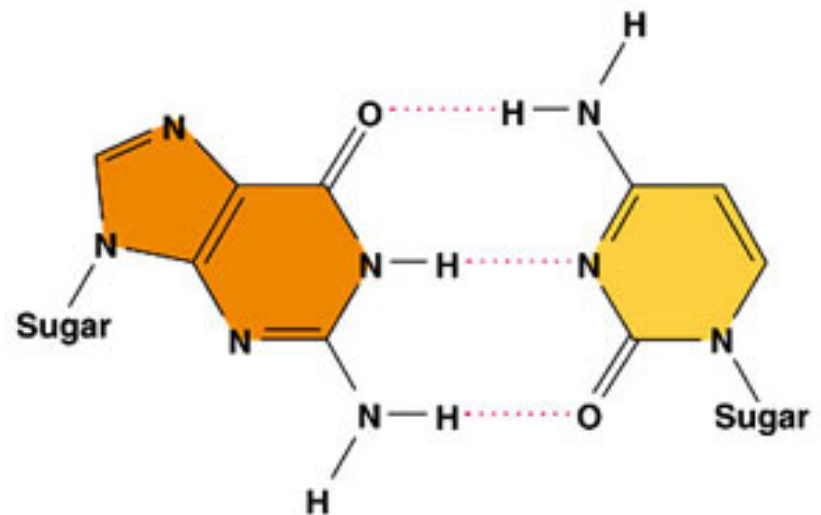
- Course structure
- **Overview of genetics**
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DNA



Adenine (A)

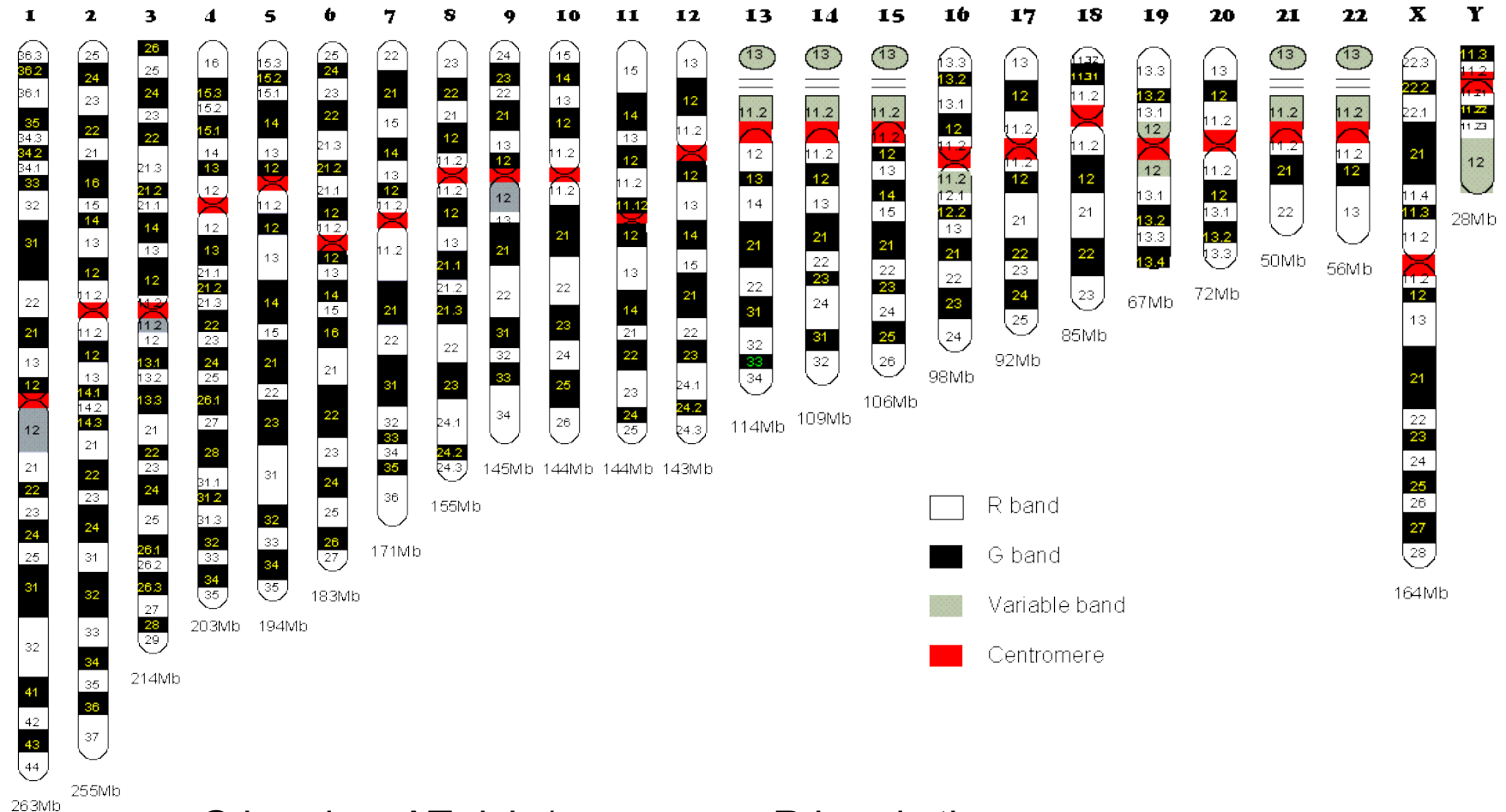
Thymine (T)



Guanine (G)

Cytosine (C)

Human Chromosomes



- G bands – AT rich / gene poor; R bands the reverse
- Look for broad structural abnormalities from these stains

Human Chromosome 21

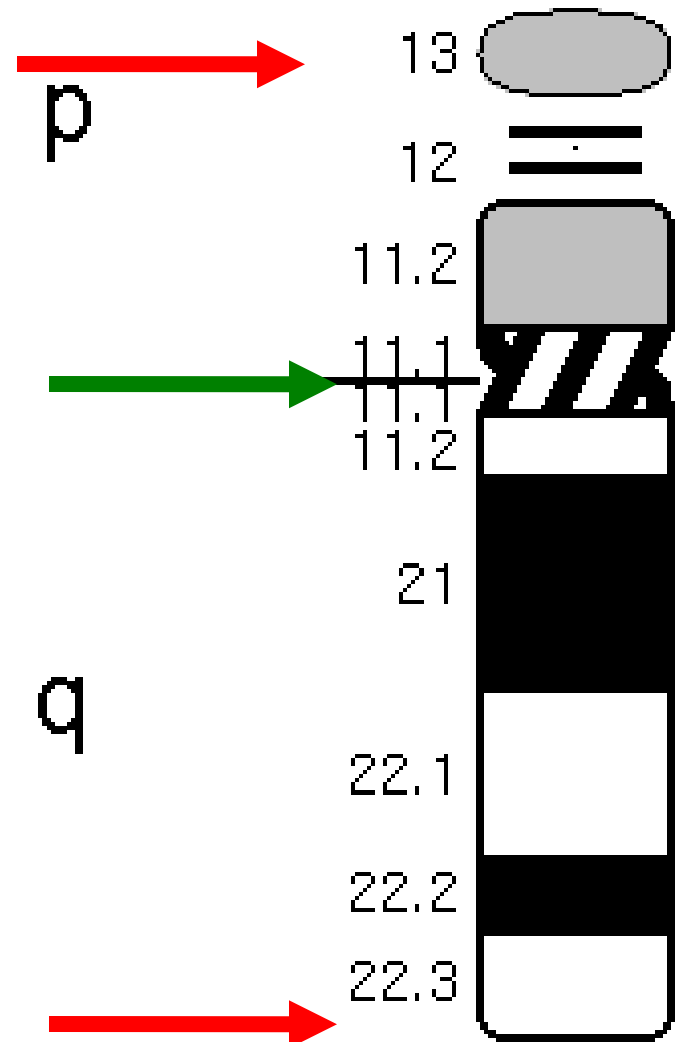
Telomeres

Centromere

p: petit arm

q: queue (tail) or long arm

21q22.1 is pronounced
twenty-one q two two
point one



Chromosome Bands

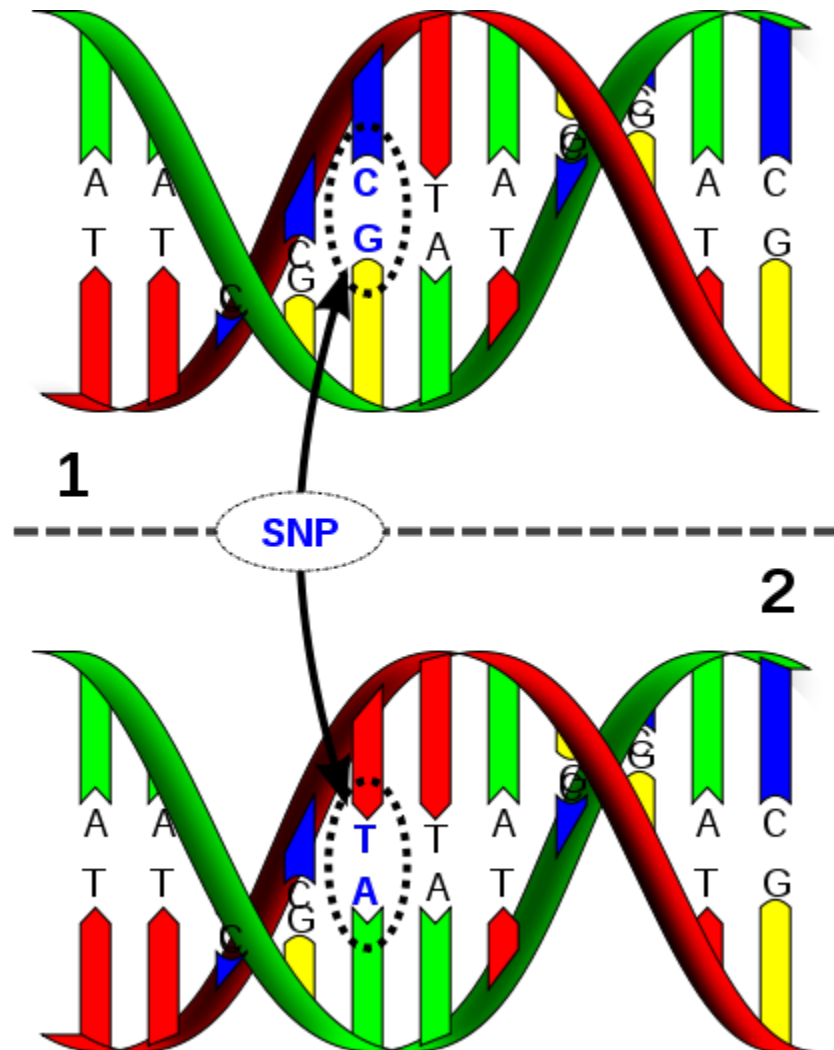
- Stain chromosomes so they can be seen by microscope
 - e.g., Giesma stain (G-banding).
- Appear as alternating bands
 - e.g., dark/G-band and light band.
 - Specific to phosphate groups of DNA.
 - Attaches to DNA regions with high adenine-thymine (A-T) bonding.
- With low resolution, few bands seen:
 - ... p2, p1 centromere q1, q2, ... (count out from centromere).
- With higher resolution sub bands seen:
 - ... p12, p11 centromere q11, q12 ...

Variation in Genome

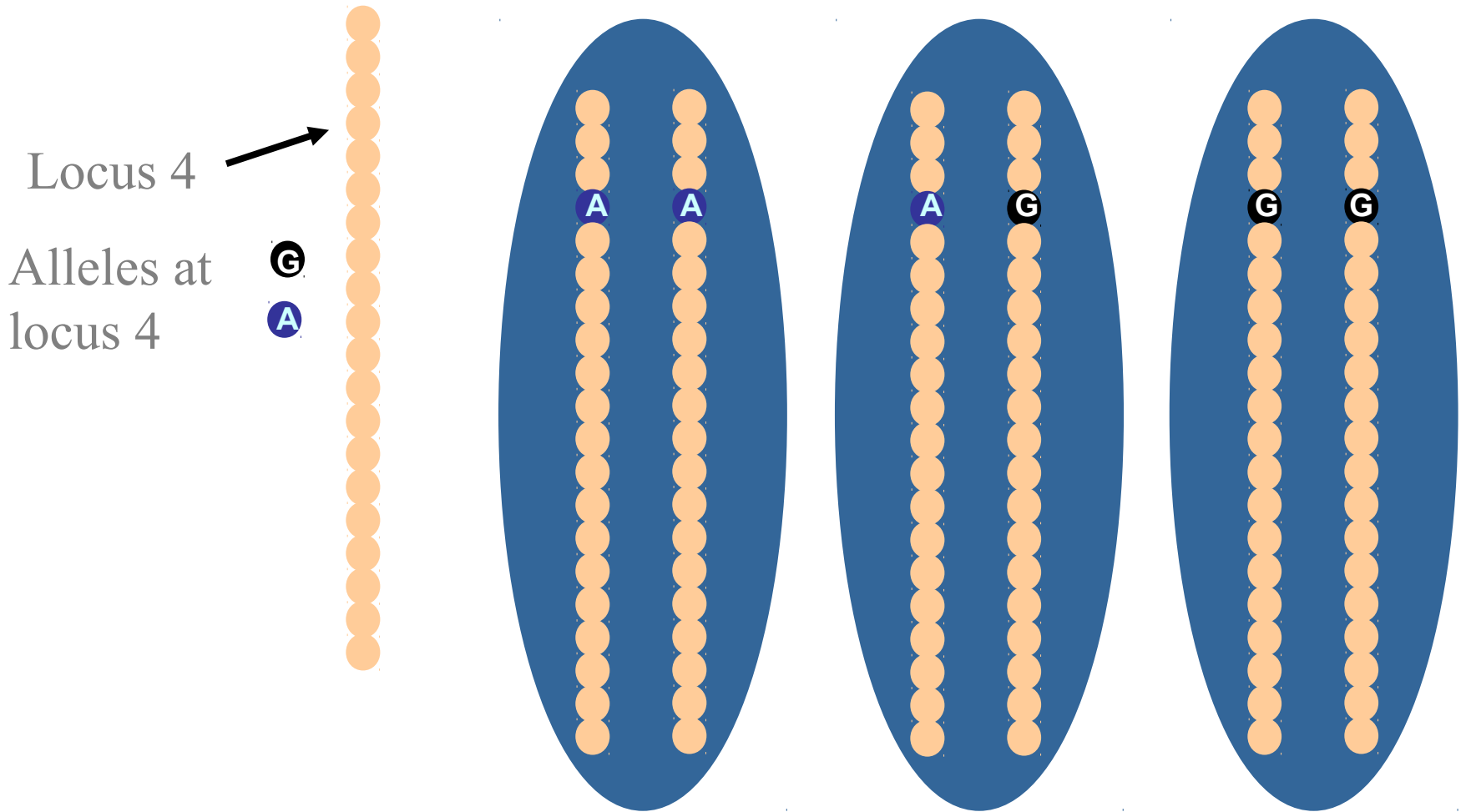
- Mutation
 - When event first occurs in an individual:
 - genetic change due to internal events (e.g., copy errors during cell division) or external agents (e.g., radiation, mutagens).
 - Can end with one generation, or be passed on (germline mutations)
- Polymorphism
 - Means “many forms”
 - Minor allele frequency (MAF) $> 1\%$
 - Generated by old mutations (random, or fitness benefit).

Single Nucleotide Polymorphism (SNPs)

- Change a single DNA letter
- Most frequent genetic variant
- 1 per 300 base pairs
 - Common (MAF>5%)
 - Less common (1-5%)
 - Rare 'variants' (<1%)
 - “SNV”



Genotypes



Locus: chromosomal location that's polymorphic.

Alleles: different variants @ locus

- Each somatic cell is diploid (two copies of each autosome)
- Thus 3 genotypes at locus 4 (use only one strand, often forward): AA, AG, GG

Types of Variants in Genes

- ♦Noncoding

- ♦Coding

- Synonymous = no change in amino acid
- Nonsynonymous/nonsense = change to stop codon
- Nonsynonymous/missense = change amino acid

e.g., **MTHFR C677T SNP**

Normal ('wild-type') allele

Gene sequence	GCG	GGA	GCC	GAT.....
Protein Sequence	Ala	Gly	Ala	Asp.....

Variant allele

Gene Sequence	GCG	GGA	GTC	GAT.....
Protein Sequence	Ala	Gly	Val	Asp

Human Genome Statistics

- 3,283,984,159 basepairs
- 20,442 known protein coding genes
- 649,964 exons
- Short variants (SNPs, indels, somatic mutations):
41,113,446
- Mutation rate $\approx 10^{-8}$ per bp per generation
- In each person:
 - 65 new mutations expected
 - 1 variant per 1,331 basepairs
 - 2,444,055 variants
- Most variants are old

Course Goals – Please Fill out

Name: Tom Hoffmann

Department/Program: Epidemiology and Biostatistics, and
Institute for Human Genetics

Background in Genetics: Undergraduate classical
genetics course (Snustad & Simmons), many statistical
genetics courses

Background in Statistics: PhD in Biostatistics

Research Interests: Methods for and analysis of the
underlying genetic architecture of many diseases, esp.
age-related hearing impairment.

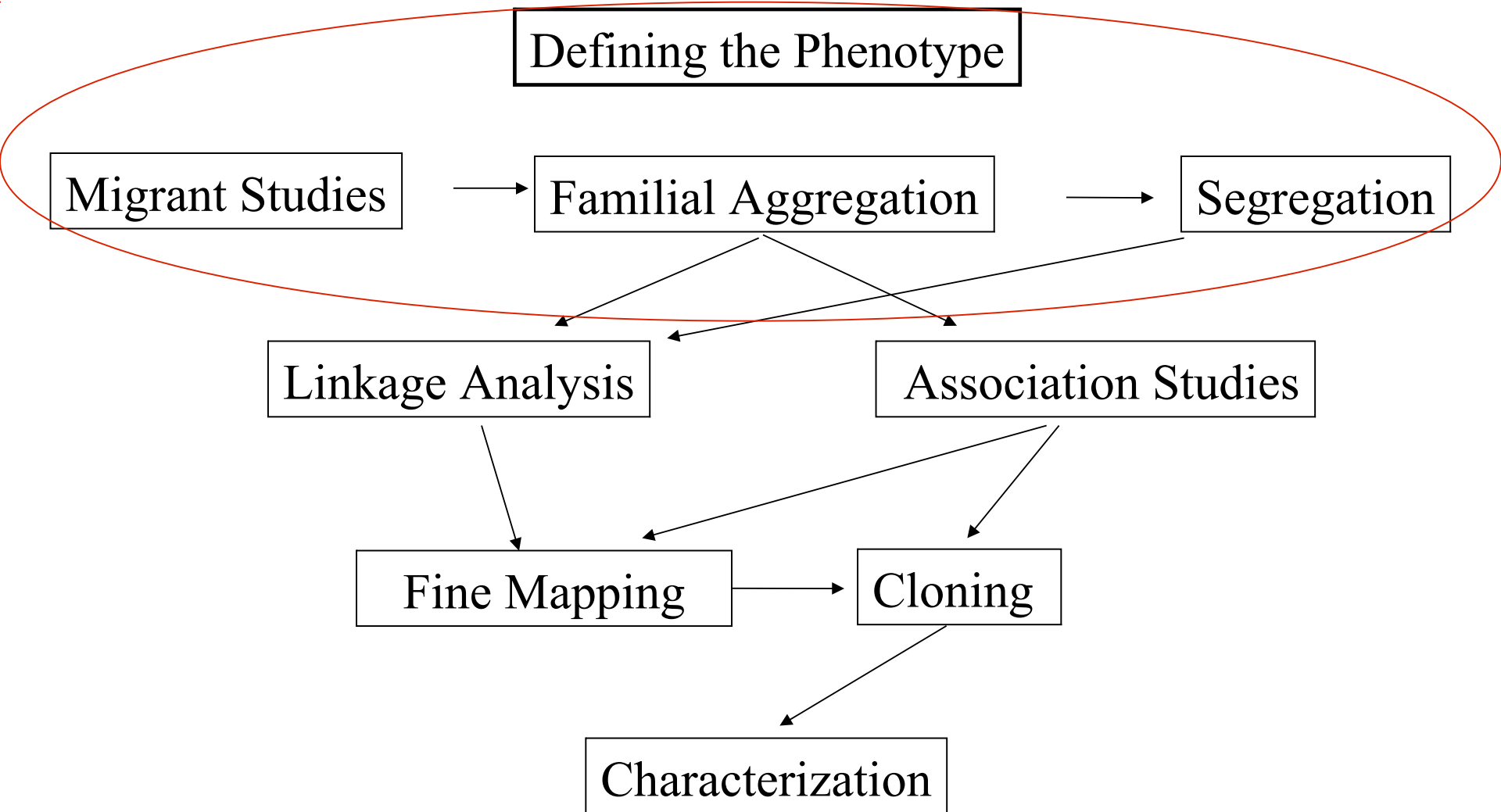
What do you want to get out of this course?

Be able to use genetic information in my research.

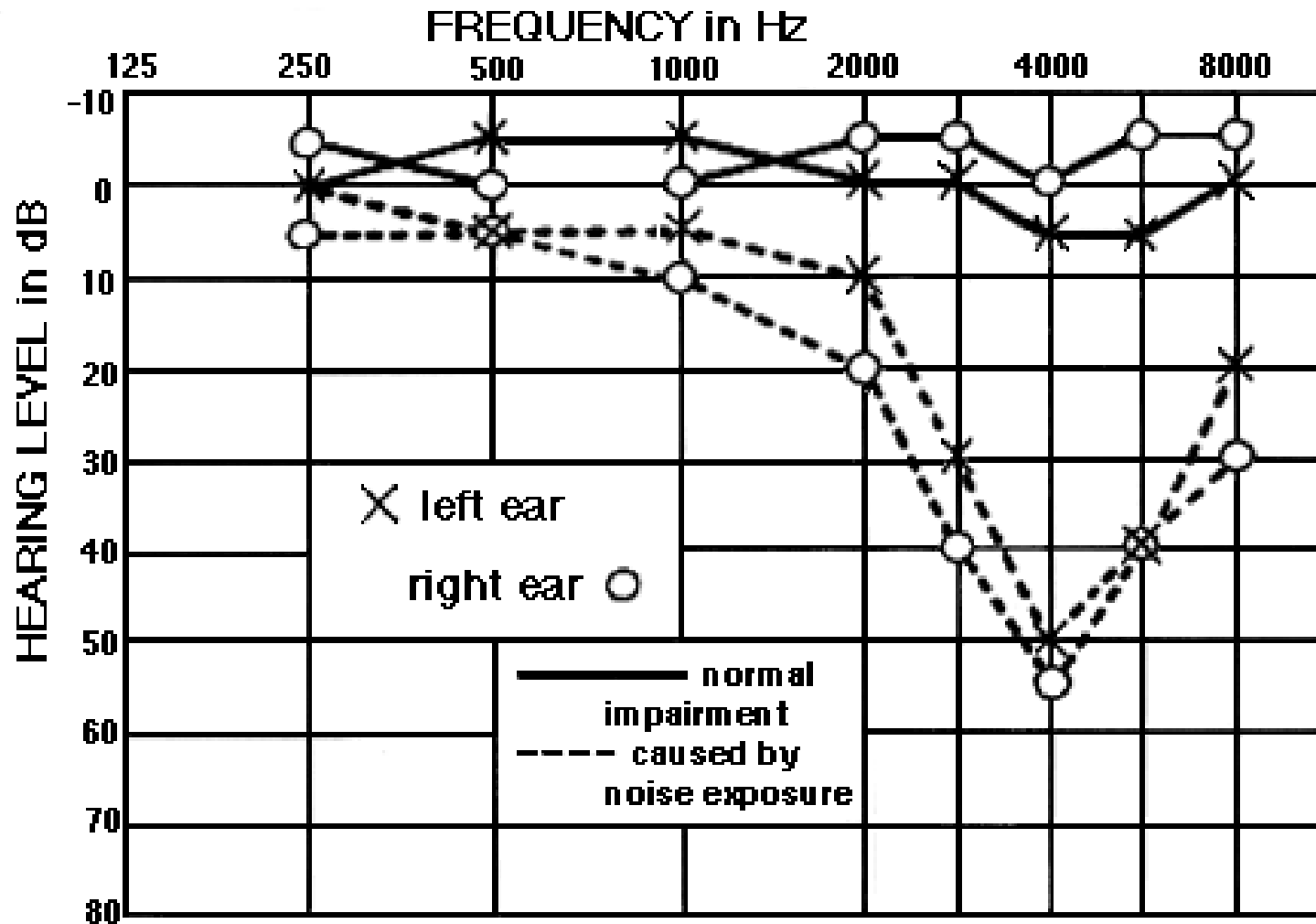
Outline

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- **Overview of genetic epidemiology and the rest of the course**

Process of Genetic Epidemiology



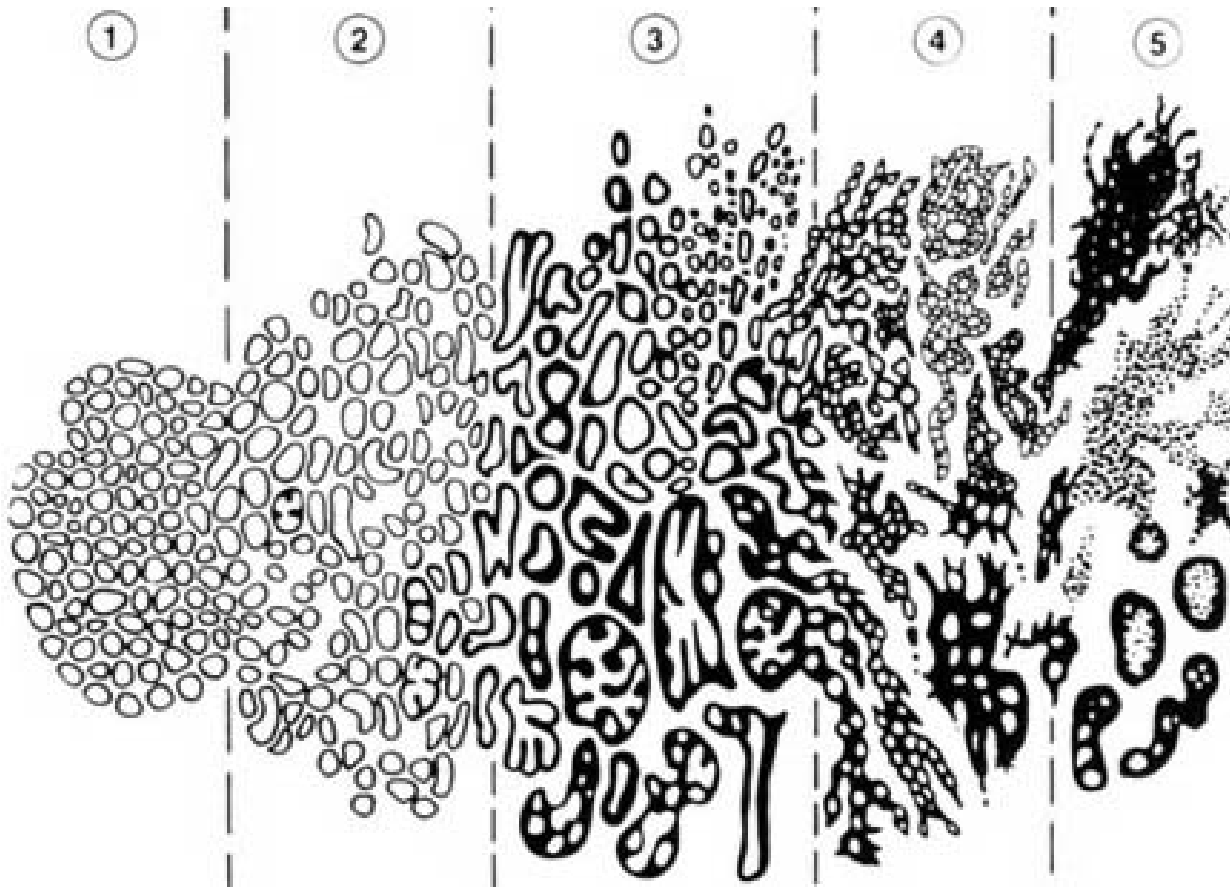
First: Define the Phenotype!



You'll be doing this in your first homework some...

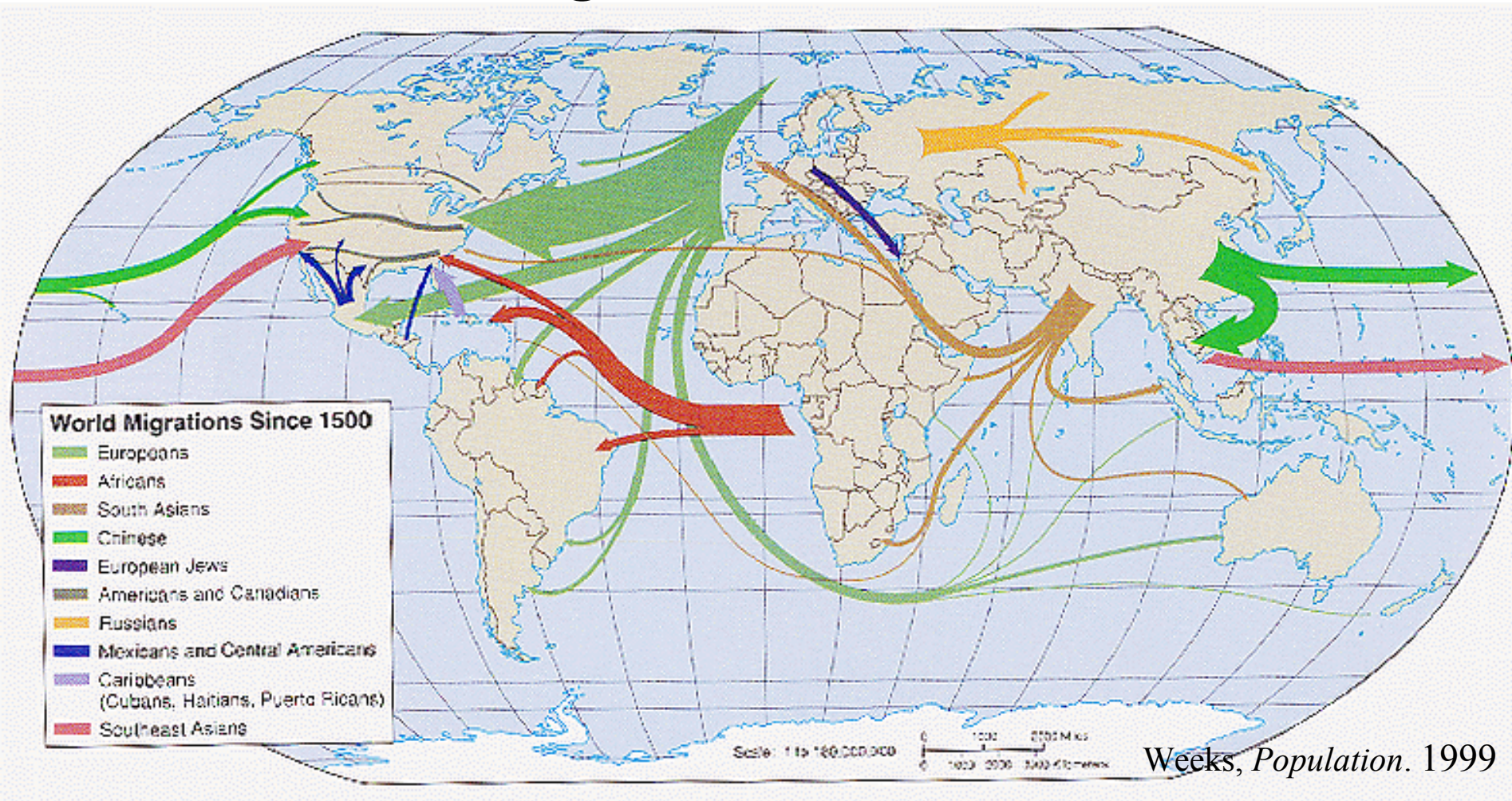
<http://www.sfu.ca/sonic-studio/handbook/Audiogram.html>

First: Define the Phenotype!



Gleason DF. In Urologic Pathology: The Prostate. 1977; 171-198.

Migrant Studies

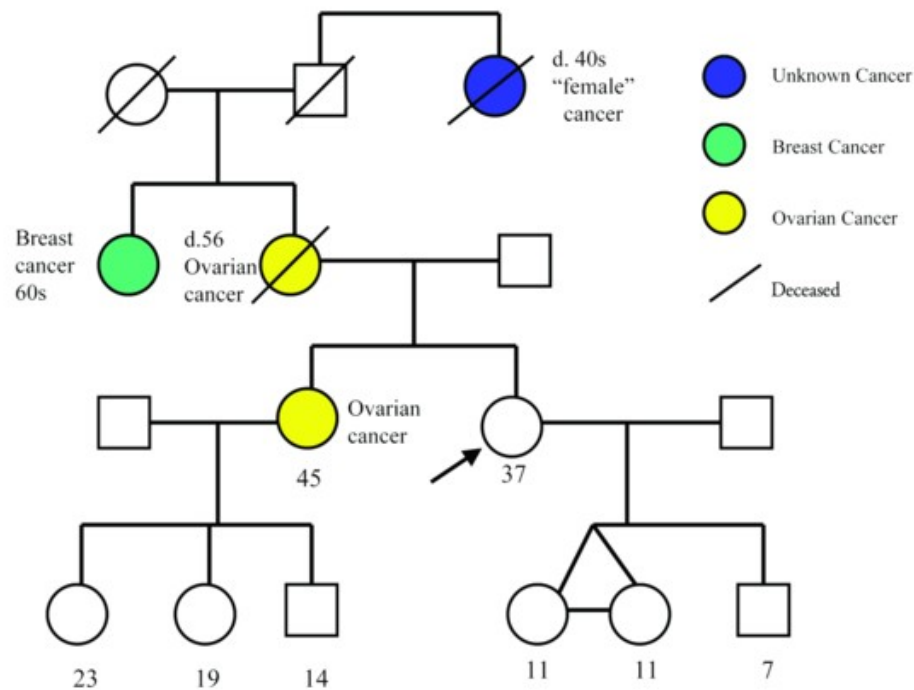


Studies based on the assumption that migrants carry a risk that reflects their country of origin, rather than the host country.

"Migrant Studies". Encyclopedia of Biostatistics, John Wiley and Sons 2005.

Familial Aggregation

- Does the phenotype tend to run in families?



Analysis of Twin Studies



- Compare the disease concordance rates of MZ (identical) and DZ (fraternal) twins.

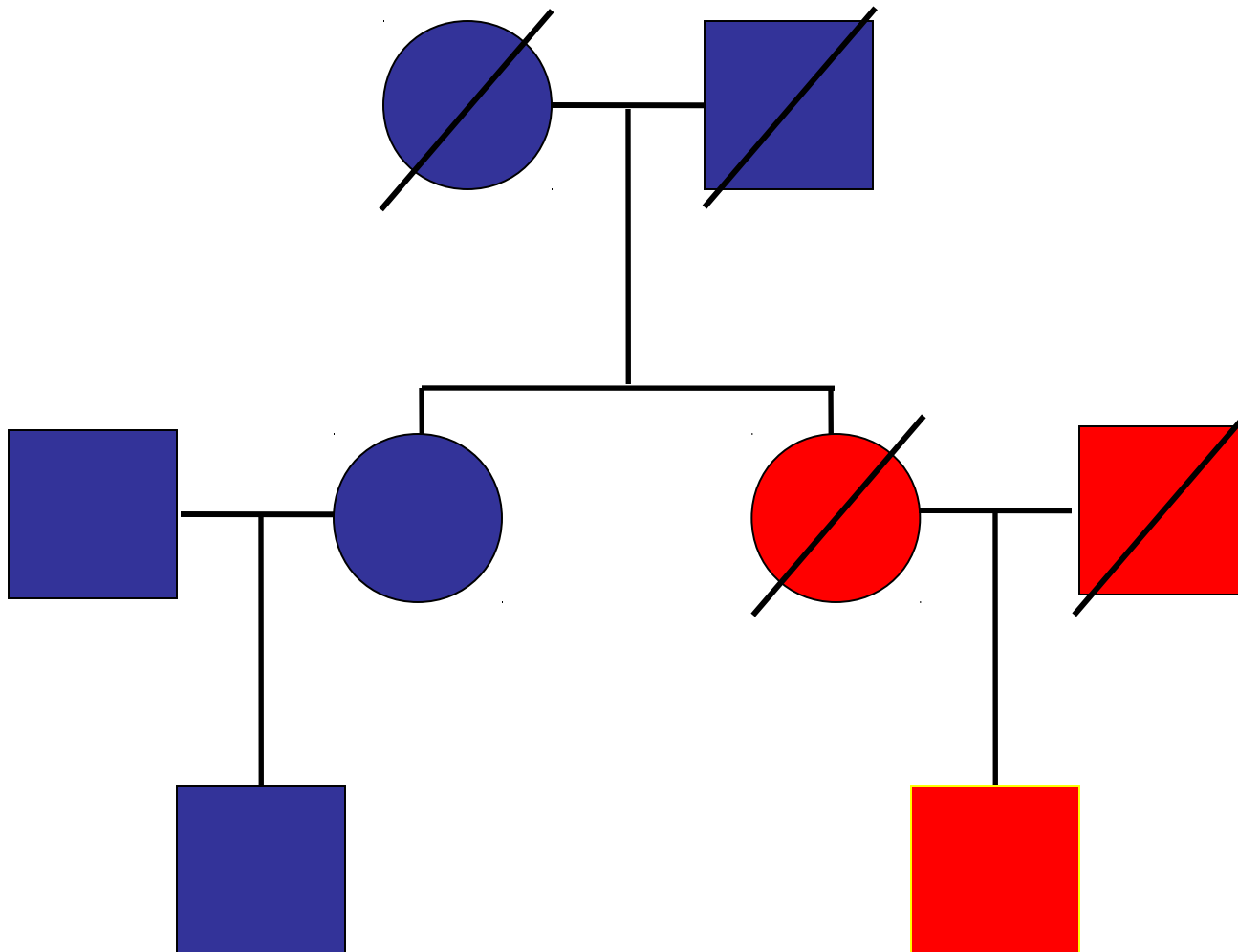
		Twin 1		Concordance = $2A/(2A+B+C)$
Twin 2	Disease	Yes	No	
	Yes	A	B	
	No	C	D	

Then one can estimate heritability of a phenotype.

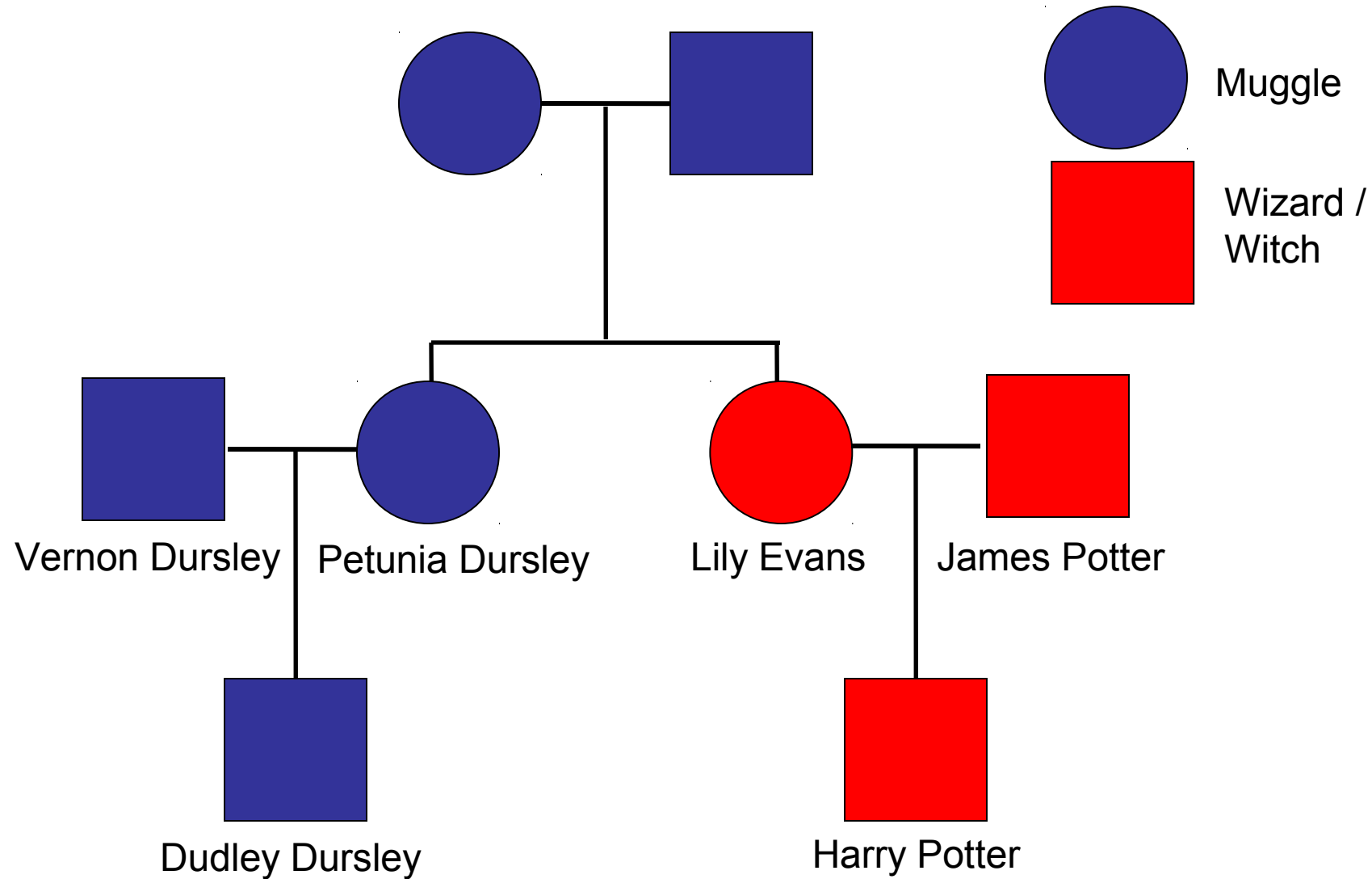
Models of Genetic Susceptibility

- Study families.
- Estimate 'mode of inheritance' & what type of genetic variant might be causal.
- Determine whether the disease appears to follow particular patterns across generations.
- Estimate whether variants are rare or common, etc.

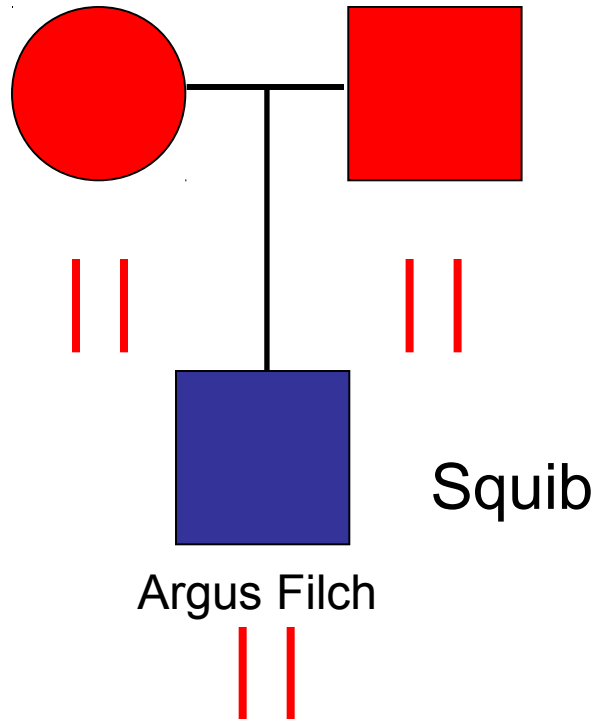
Segregation



Segregation: Harry Potter's Pedigree



Filch?



Segregation Analysis

- What is the best model of inheritance for observed families?
 - Dominant
 - Recessive
 - Additive
 - Disease allele frequency?
 - Magnitude of risk?
- Fit formal genetic models to data on disease phenotypes of family members.
- The parameters of the model are generally fitted finding the values that maximize the probability (likelihood) of the observed data.
- This information is useful in parametric linkage analysis, which assumes a defined model of inheritance.

Process of Genetic Epidemiology

Defining the Phenotype

Migrant Studies

Familial Aggregation

Segregation

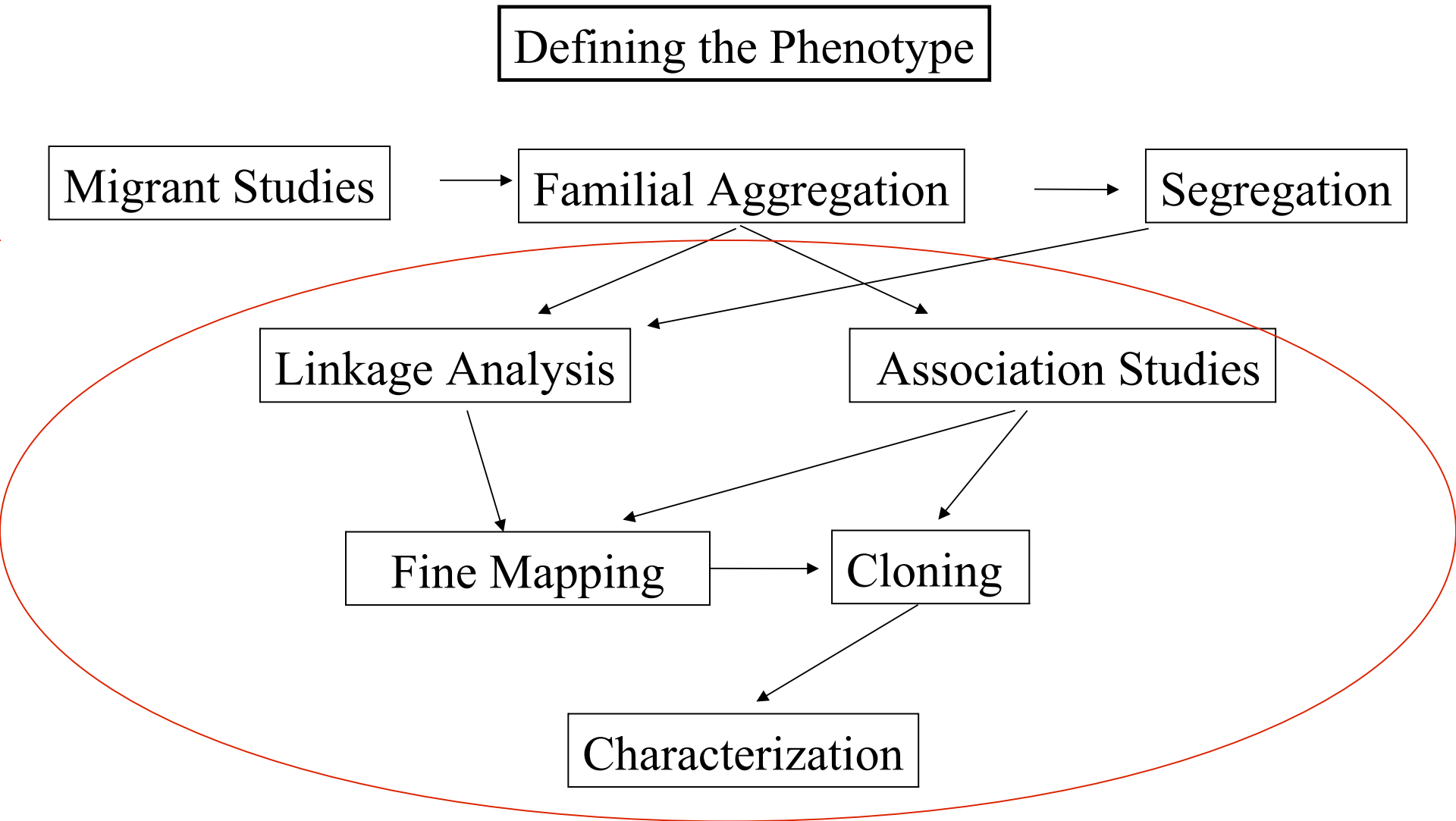
Linkage Analysis

Association Studies

Fine Mapping

Cloning

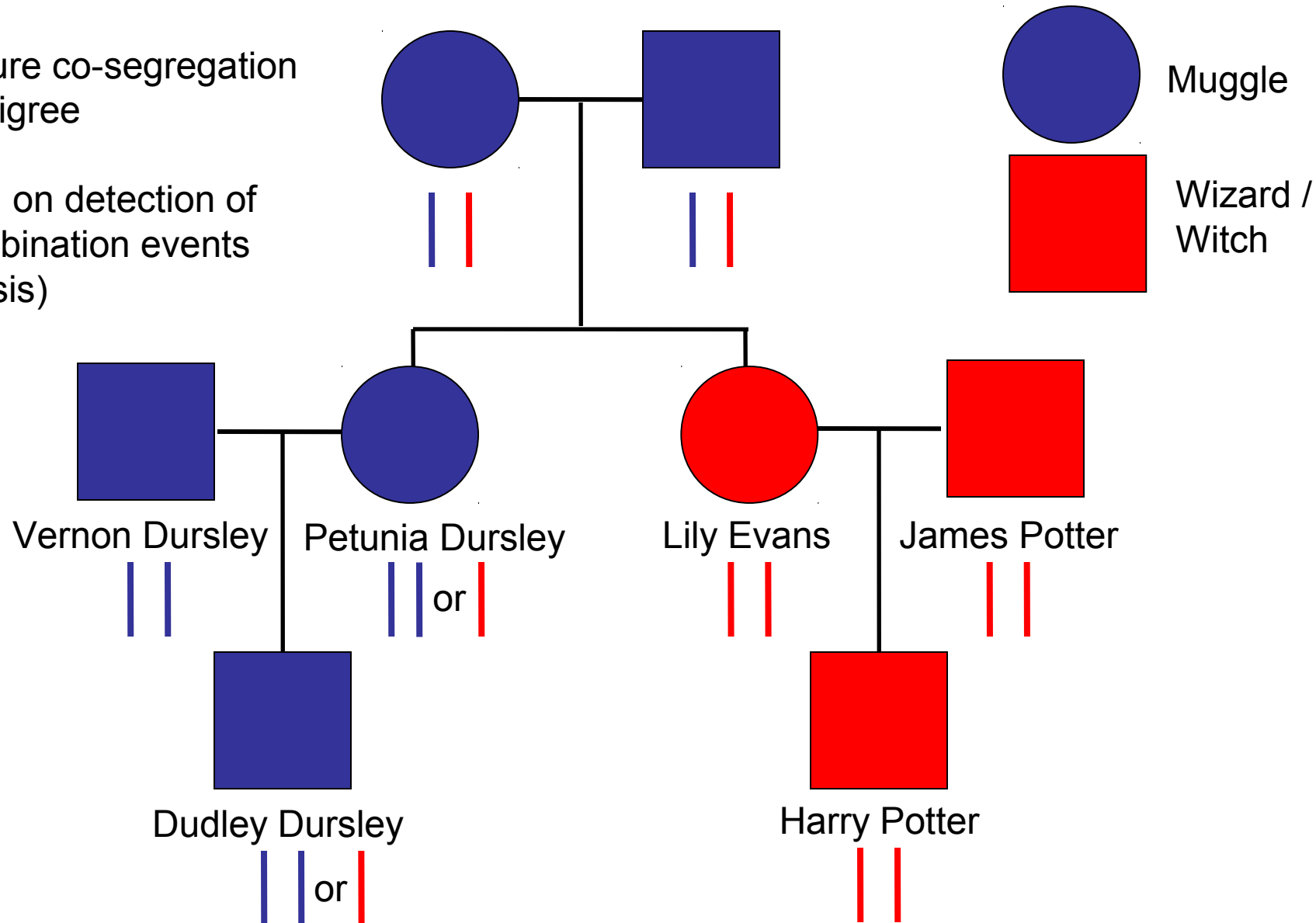
Characterization



Linkage: Harry Potter's Pedigree

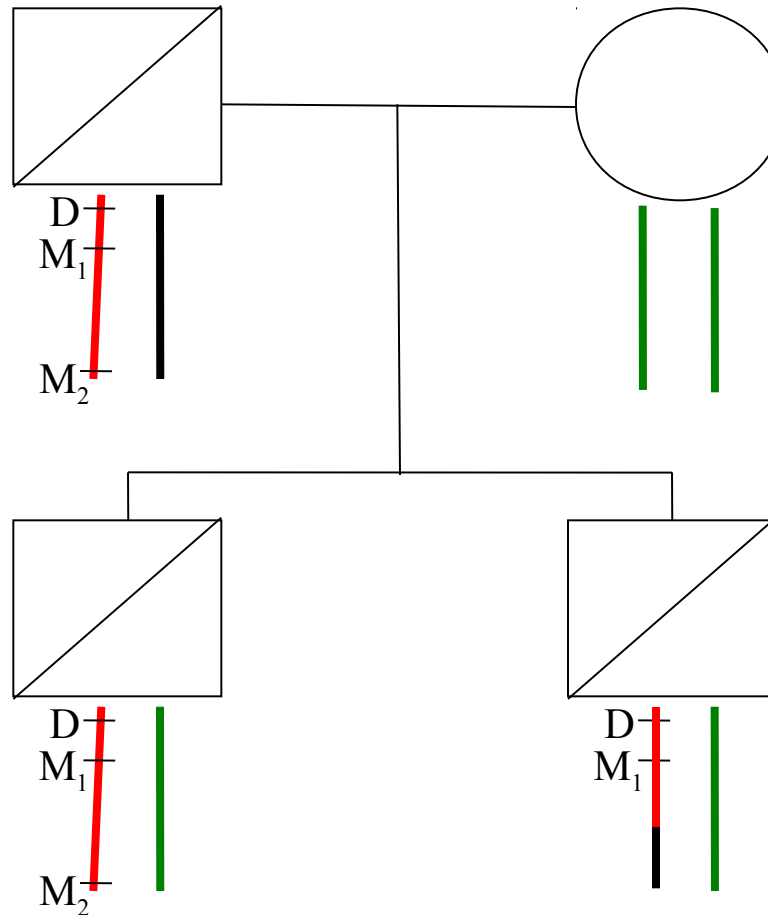
Measure co-segregation
in pedigree

Based on detection of
recombination events
(meiosis)

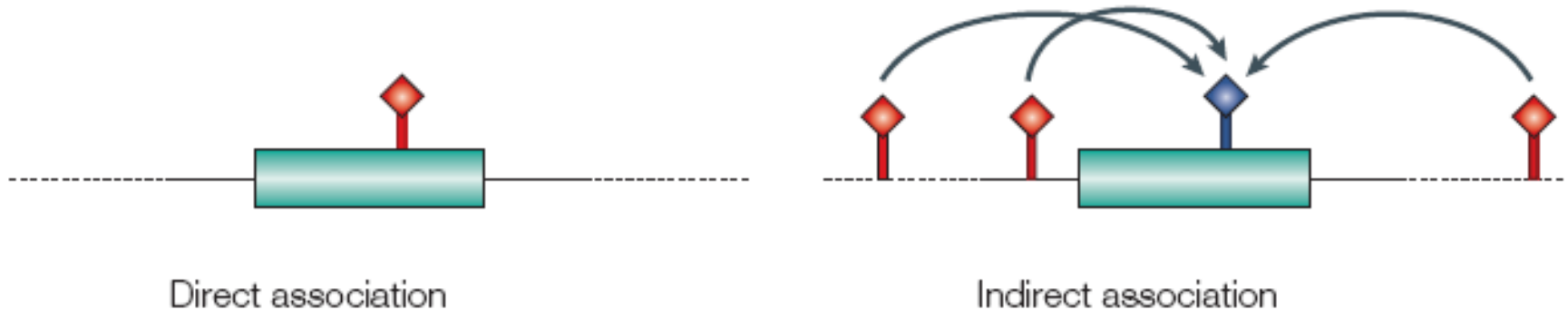


Covered more in Austin Ch 4 & Lecture 4: Family-based studies

Affected sib-pair Linkage



Linkage Disequilibrium

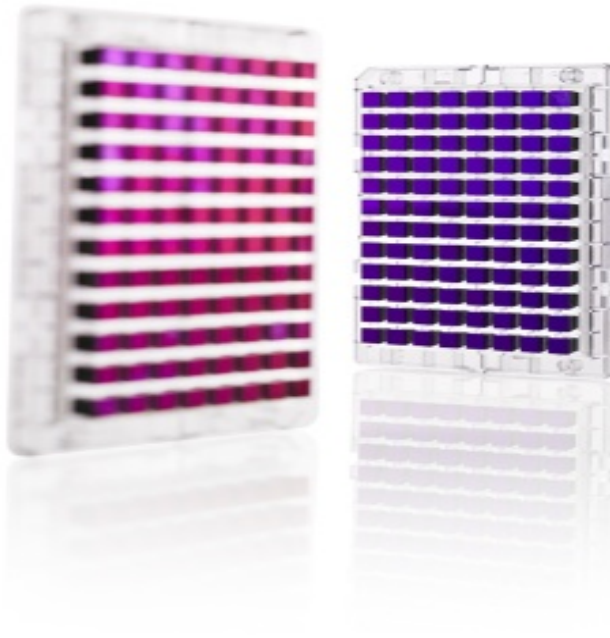


important fundamental concept will come up repeatedly and be explained further in course

In population genetics, linkage disequilibrium is the non-random association of alleles at two or more loci, that descend from single, ancestral chromosomes.

http://en.wikipedia.org/wiki/Linkage_disequilibrium

Genotyping technologies

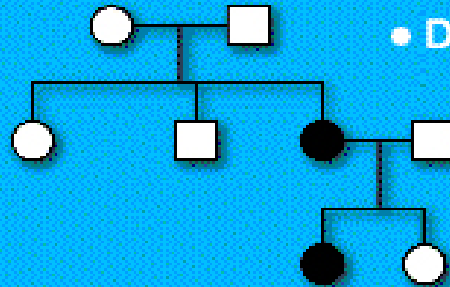


Covered more in Austin Ch 3 & Lecture 3: Mendel's laws and Molecular Genetics

Association Studies

Approaches to Identifying Susceptibility Genes for Common Diseases

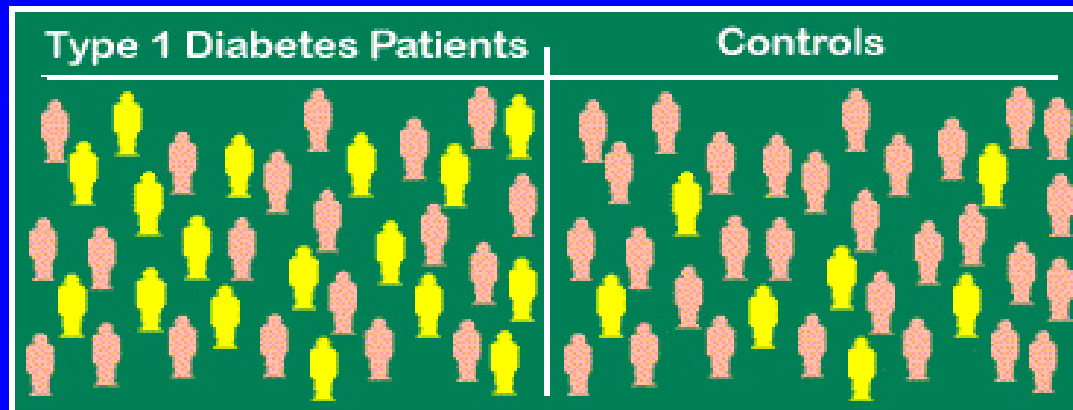
Linkage Studies:



- A relation between loci
- Done within families

Association Studies:

- A relation between alleles
- Done in populations



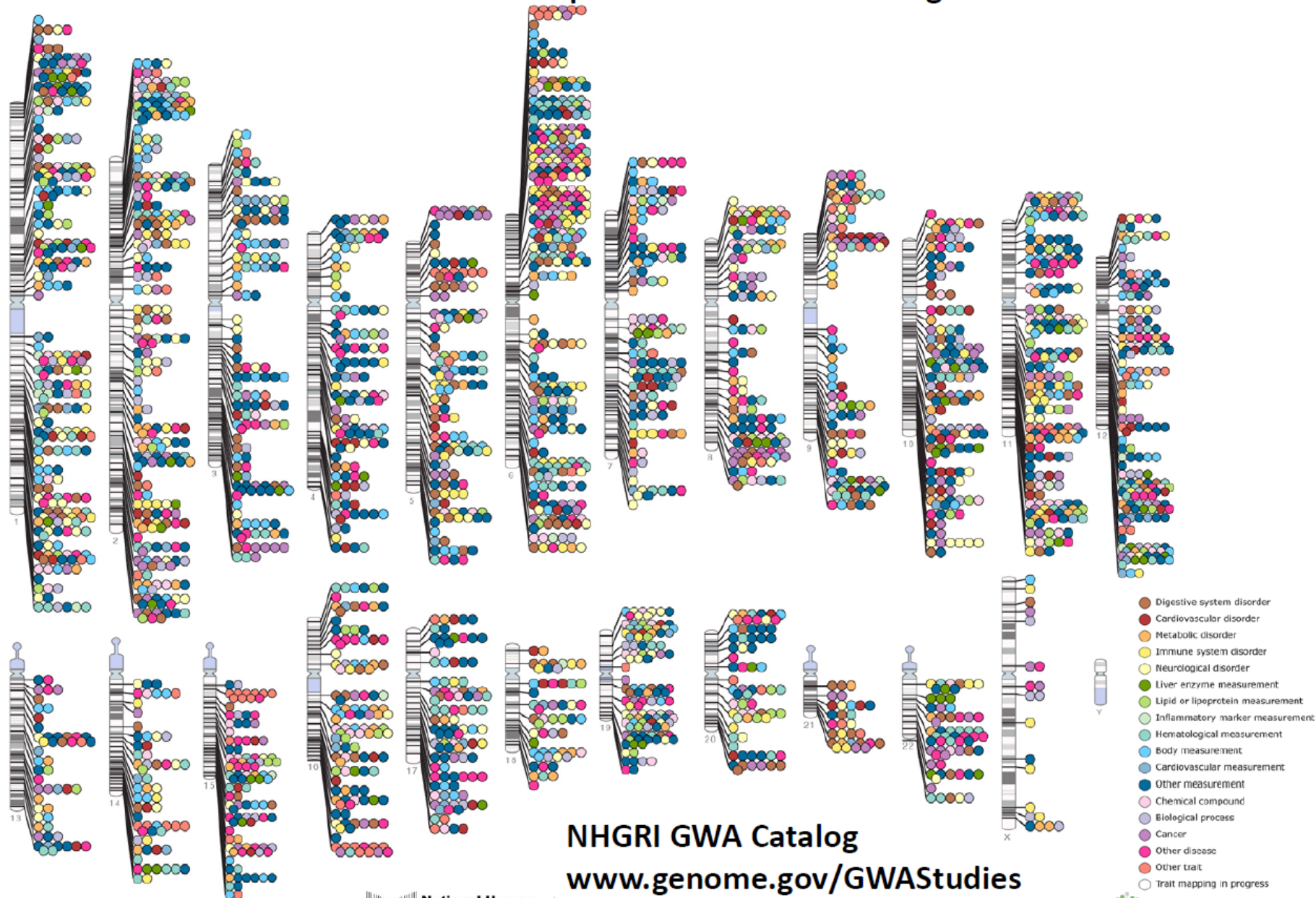
Genome-wide Association Studies



Covered more in Austin Ch 5-7 & Lecture 5-7, Genome-wide Association Studies (GWAS)+

Published Genome-Wide Associations through 07/2012

Published GWA at $p \leq 5 \times 10^{-8}$ for 18 trait categories



NHGRI GWA Catalog

www.genome.gov/GWASStudies

www.ebi.ac.uk/fgpt/gwas/

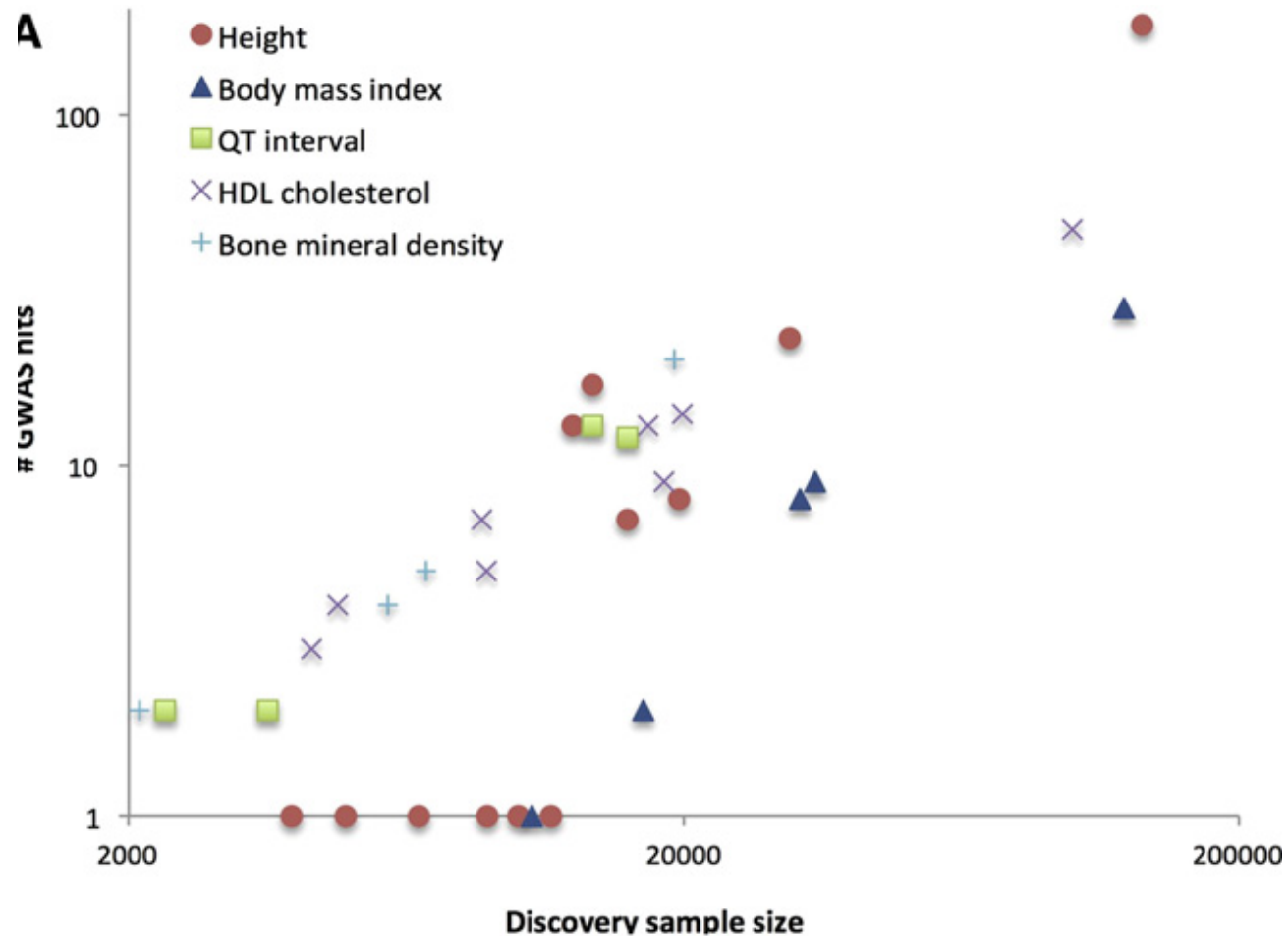


EMBL-EBI



Size matters

- Why?
- Consortia



Admixture Mapping

- Potentially powerful approach to searching for disease-causing genes
- Requires:
 1. Two populations with naturally occurring phenotypic and genetic differences.
 2. Recent gene flow between the populations (e.g., within 10 generations).
- Markers in the vicinity of the trait locus will also show excess ancestry from the population with the higher allele frequency

Admixture Mapping

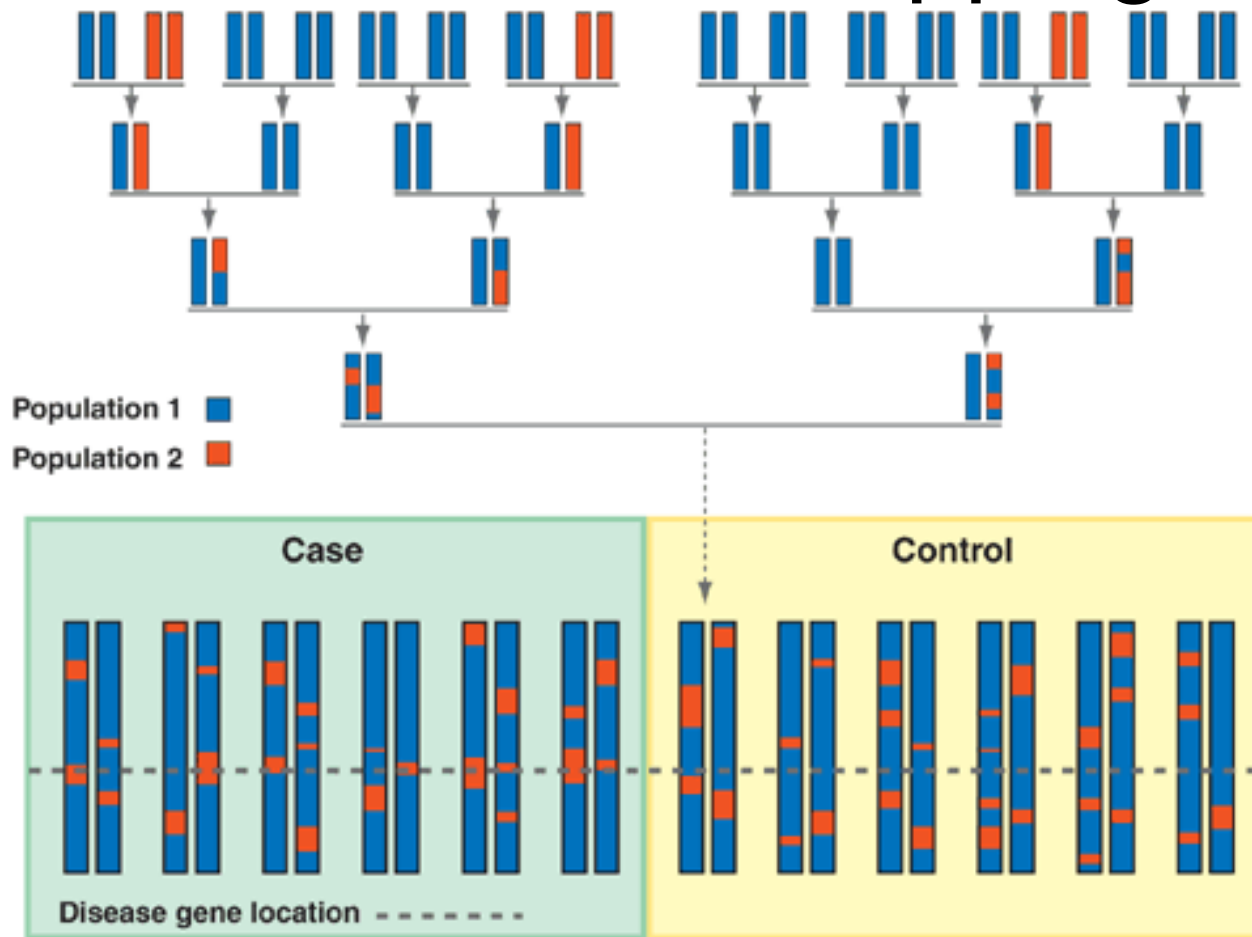


Figure 1 Schematic of one chromosome pair from each of several individuals in an admixed population. A group of cases (for a given disease) and a group of controls are separately presented at the bottom left and the bottom right, respectively. For one of the control individuals (arrow), a schematic presentation of all its ancestors in the last four generations is shown in the upper part of the figure. Admixture mapping can be ideally applied if population 1 (blue) and population 2 (red) carry a different allele at the disease locus (dashed line). Whole-genome scanning under the admixture mapping strategy consists of scanning the genome and identifying the regions with an excess of 'red' ancestry in the cases versus the controls, assuming that the 'red' population carries the predisposition allele. The size of the blocks from different ancestors will depend on the number of generations since the populations were mixed.

Summary of Main Mapping Approaches

	Linkage Analysis	Admixture	Association Study
Power*	Low	Moderate/High	High
# SNPs required for scan	Low	Low	High
Sensitivity to genetic heterogeneity	Low	Moderate	High
Mapping resolution	Poor	Intermediate	Good

Cloning a Gene

- Showing that it is clearly causal for disease.
- Generally requires experiments beyond those undertaken by a genetic epidemiologist.

Re-Sequencing Genomes (Ozzy Osbourne?)

Scientists to map Ozzy Osbourne's genetic code to find out how he survived so much substance abuse

NICK KLOPSIS
JILLY NEWS WRITER

Monday, June 14th 2010, 1:39 PM



Sayles/AP

Ozzy Osbourne has had many issues relating to drug and alcohol abuse, so scientists are mapping out his genetic code to find out how his body can take it.

You can't kill rock and roll, but it's not usually this hard to kill a rocker.

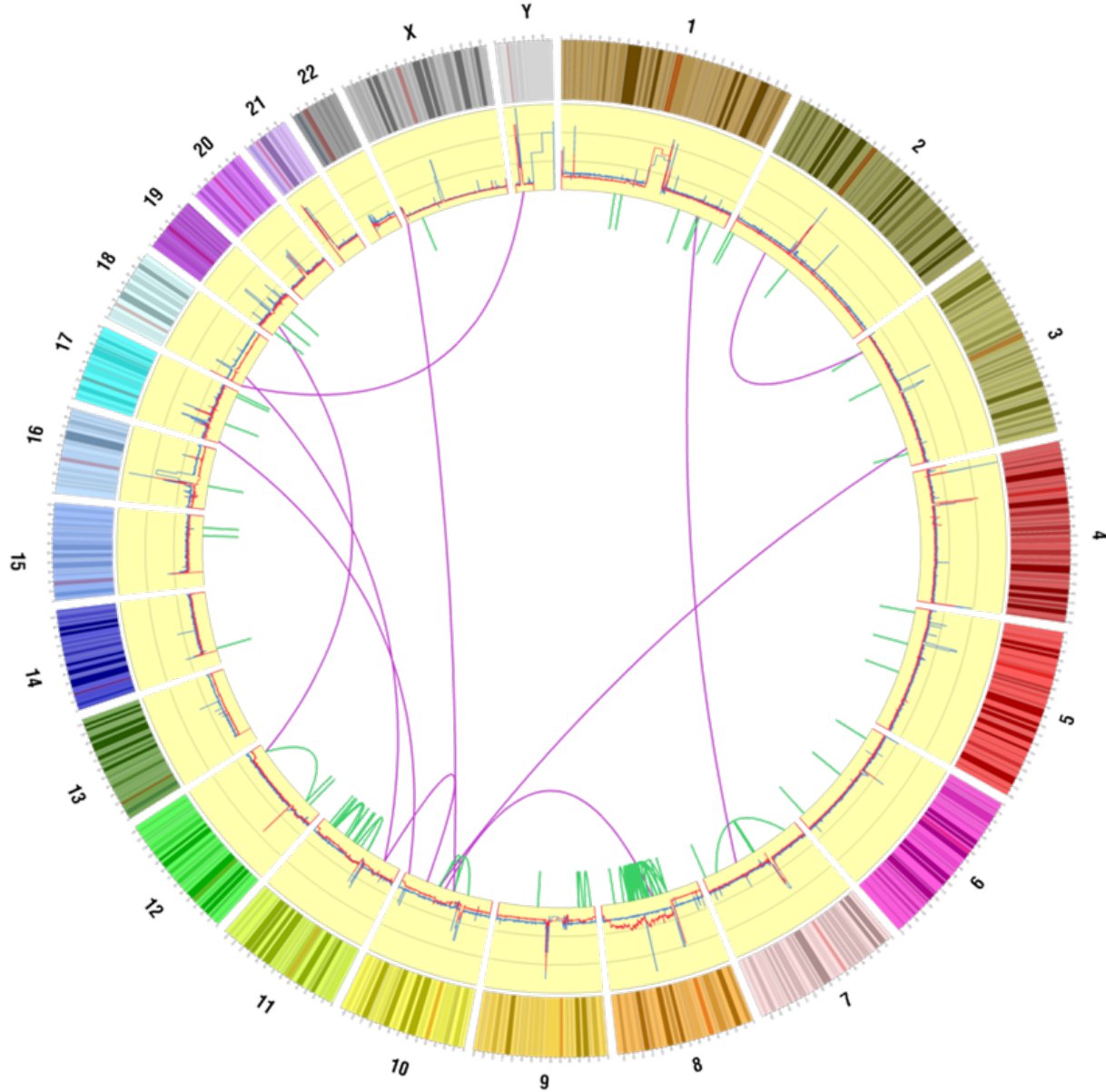
RELATED NEWS

[Covered more in Lecture 9: Next-generation sequencing](#)

"Sequencing and analysing individuals with extreme medical histories provides the greatest potential scientific value."

Nathan Pearson,
Director of Research
Knome

Circos Plot: Tumor – Normal



Remi Kazma

Characterization

- Once genes are identified, molecular methods are used to determine the structure of the gene, identification of regulatory elements, etc.
- Use epidemiologic studies to distinguish public health implications:
 1. Determine frequencies of causal alleles; and
 2. Characterize their effects—and interacting environmental factors—on disease rates.

Genetic Testing?



THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Cumulative Association of Five Genetic Variants with Prostate Cancer

S. Lily Zheng, M.D., Jieli Sun, Ph.D., Fredrik Wiklund, Ph.D., Shelly Smith, M.S.,
Pär Stattin, M.D., Ph.D., Ge Li, M.D., Hans-Olov Adami, M.D., Ph.D.,
Fang-Chi Hsu, Ph.D., Yi Zhu, B.S., Katarina Bälter, Ph.D.,
A. Karim Kader, M.D., Ph.D., Aubrey R. Turner, M.S., Wennuan Liu, Ph.D.,
Eugene R. Bleecker, M.D., Deborah A. Meyers, Ph.D., David Duggan, Ph.D.,
John D. Carpenter, Ph.D., Bao-Li Chang, Ph.D., William B. Isaacs, Ph.D.,
Jianfeng Xu, M.D., D.P.H., and Henrik Grönberg, M.D., Ph.D.

About Crestani

1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017, 2018, 2019, 2020, 2021, 2022, 2023, 2024, 2025, 2026, 2027, 2028, 2029, 2030, 2031, 2032, 2033, 2034, 2035, 2036, 2037, 2038, 2039, 2040, 2041, 2042, 2043, 2044, 2045, 2046, 2047, 2048, 2049, 2050, 2051, 2052, 2053, 2054, 2055, 2056, 2057, 2058, 2059, 2060, 2061, 2062, 2063, 2064, 2065, 2066, 2067, 2068, 2069, 2070, 2071, 2072, 2073, 2074, 2075, 2076, 2077, 2078, 2079, 2080, 2081, 2082, 2083, 2084, 2085, 2086, 2087, 2088, 2089, 2090, 2091, 2092, 2093, 2094, 2095, 2096, 2097, 2098, 2099, 2100, 2101, 2102, 2103, 2104, 2105, 2106, 2107, 2108, 2109, 2110, 2111, 2112, 2113, 2114, 2115, 2116, 2117, 2118, 2119, 2120, 2121, 2122, 2123, 2124, 2125, 2126, 2127, 2128, 2129, 2130, 2131, 2132, 2133, 2134, 2135, 2136, 2137, 2138, 2139, 2140, 2141, 2142, 2143, 2144, 2145, 2146, 2147, 2148, 2149, 2150, 2151, 2152, 2153, 2154, 2155, 2156, 2157, 2158, 2159, 2160, 2161, 2162, 2163, 2164, 2165, 2166, 2167, 2168, 2169, 2170, 2171, 2172, 2173, 2174, 2175, 2176, 2177, 2178, 2179, 2180, 2181, 2182, 2183, 2184, 2185, 2186, 2187, 2188, 2189, 2190, 2191, 2192, 2193, 2194, 2195, 2196, 2197, 2198, 2199, 2200, 2201, 2202, 2203, 2204, 2205, 2206, 2207, 2208, 2209, 2210, 2211, 2212, 2213, 2214, 2215, 2216, 2217, 2218, 2219, 2220, 2221, 2222, 2223, 2224, 2225, 2226, 2227, 2228, 2229, 2230, 2231, 2232, 2233, 2234, 2235, 2236, 2237, 2238, 2239, 2240, 2241, 2242, 2243, 2244, 2245, 2246, 2247, 2248, 2249, 2250, 2251, 2252, 2253, 2254, 2255, 2256, 2257, 2258, 2259, 2260, 2261, 2262, 2263, 2264, 2265, 2266, 2267, 2268, 2269, 2270, 2271, 2272, 2273, 2274, 2275, 2276, 2277, 2278, 2279, 2280, 2281, 2282, 2283, 2284, 2285, 2286, 2287, 2288, 2289, 2290, 2291, 2292, 2293, 2294, 2295, 2296, 2297, 2298, 2299, 2300, 2301, 2302, 2303, 2304, 2305, 2306, 2307, 2308, 2309, 2310, 2311, 2312, 2313, 2314, 2315, 2316, 2317, 2318, 2319, 2320, 2321, 2322, 2323, 2324, 2325, 2326, 2327, 2328, 2329, 2330, 2331, 2332, 2333, 2334, 2335, 2336, 2337, 2338, 2339, 2340, 2341, 2342, 2343, 2344, 2345, 2346, 2347, 2348, 2349, 2350, 2351, 2352, 2353, 2354, 2355, 2356, 2357, 2358, 2359, 2360, 2361, 2362, 2363, 2364, 2365, 2366, 2367, 2368, 2369, 2370, 2371, 2372, 2373, 2374, 2375, 2376, 2377, 2378, 2379, 2380, 2381, 2382, 2383, 2384, 2385, 2386, 2387, 2388, 2389, 2390, 2391, 2392, 2393, 2394, 2395, 2396, 2397, 2398, 2399, 2400, 2401, 2402, 2403, 2404, 2405, 2406, 2407, 2408, 2409, 2410, 2411, 2412, 2413, 2414, 2415, 2416, 2417, 2418, 2419, 2420, 2421, 2422, 2423, 2424, 2425, 2426, 2427, 2428, 2429, 2430, 2431, 2432, 2433, 2434, 2435, 2436, 2437, 2438, 2439, 2440, 2441, 2442, 2443, 2444, 2445, 2446, 2447, 2448, 2449, 2450, 2451, 2452, 2453, 2454, 2455, 2456, 2457, 2458, 2459, 2460, 2461, 2462, 2463, 2464, 2465, 2466, 2467, 2468, 2469, 2470, 2471, 2472, 2473, 2474, 2475, 2476, 2477, 2478, 2479, 2480, 2481, 2482, 2483, 2484, 2485, 2486, 2487, 2488, 2489, 2490, 2491, 2492, 2493, 2494, 2495, 2496, 2497, 2498, 2499, 2500, 2501, 2502, 2503, 2504, 2505, 2506, 2507, 2508, 2509, 2510, 2511, 2512, 2513, 2514, 2515, 2516, 2517, 2518, 2519, 2520, 2521, 2522, 2523, 2524, 2525, 2526, 2527, 2528, 2529, 2530, 2531, 2532, 2533, 2534, 2535, 2536, 2537, 2538, 2539, 2540, 2541, 2542, 2543, 2544, 2545, 2546, 2547, 2548, 2549, 2550, 2551, 2552, 2553, 2554, 2555, 2556, 2557, 2558, 2559, 2560, 2561, 2562, 2563, 2564, 2565, 2566, 2567, 2568, 2569, 2570, 2571, 2572, 2573, 2574, 2575, 2576, 2577, 2578, 2579, 2580, 2581, 2582, 2583, 2584, 2585, 2586, 2587, 2588, 2589, 2590, 2591, 2592, 2593, 2594, 2595, 2596, 2597, 2598, 2599, 2600, 2601, 2602, 2603, 2604, 2605, 2606, 2607, 2608, 2609, 2610, 2611, 2612, 2613, 2614, 2615, 2616, 2617, 2618, 2619, 2620, 2621, 2622, 2623, 2624, 2625, 2626, 2627, 2628, 2629, 2630, 2631, 2632, 2633, 2634, 2635, 2636, 2637, 2638, 2639, 2640, 2641, 2642, 2643, 2644, 2645, 2646, 2647, 2648, 2649, 2650, 2651, 2652, 2653, 2654, 2655, 2656, 2657, 2658, 2659, 2660, 2661, 2662, 2663, 2664, 2665, 2666, 2667, 2668, 2669, 2670, 2671, 2672, 2673, 2674, 2675, 2676, 2677, 2678, 2679, 2680, 26

For months, the Republicans are unrelentant in New York and New Jersey, marshaling nearly as much negative news coverage as Clinton. The bottom line seems to be that they were confident would be more than pay's measure for president.

THE FISHBURN, N.C. — Truismers walking outposts under for Governor Stuart McCarry in North Carolina last weekend noticed something odd: Four people remained silent at a community meeting for a project that they intended for McCarry to preside, because of his still distant from his first wife, Carol, who joined the couple's three children while Mr. McCarry was a prisoner of war in Vietnam.

By Tuesday afternoon, a group calling itself Vietnam Veterans

Lesson Learned

Although Mr. McLean, of New York, testified that the trials were open to the public, the New York Times reported that the trials were held in secret.

many more top political aides in attendance, were less than on hand to try to counter the attacks before there is major damage.

In 2000, author William Miller's anti-Soviet *Confessions of a Communist* syndicalist, "It was a far left thing in the Soviet communist world looking up at that big tower and seeing all these thousands of windows coming in to give and be-

those with less than five employees made up only 2 percent of the

Practices

Abstract

**\$300 to Learn
Risk of Cancer
Of the Prostate**

A New Test Is Raising Treatment Questions

Keywords: child sexual abuse; disclosure; self-blame

A combination of reasons and more variation in the regional culture could explain a lower rate of giving private money, researchers argued Wednesday.

A company formed by its members at White Forest University School of Medicine is expected to make the test available to a few smaller, rural Kentucky clinics, a White Forest spokesman claims. It should not be there long.

That is, some national experts say, a first wave of urbanization is projected to hit a combination of social and programming. The results, they agree, are that first the question in urban regions may be, and will become the subject of national development. Because the new land...

which will analyze DNA in blood or saliva samples and is to be directed by Professor Christiane Heide, current president, which may still get aggressive cancer, it could lead to more screening and an necessary surgery and complications. But, proponents say, it could also help men decide whether they want aggressive screening in the first place.

The researchers found that about 10 percent of the men in the study had one or more of the gene variants, and more than half had one or more. The cancer risk increased as the number of variants rose, and increased substantially only when men had four or five of the variants.

These will, based on their respective needs, represent 2 percent of the

Letter Comments[illegible]

**FED'S CHAIRMAN
IS SAID TO BACK
AID TO ECONOMY**

TRIPS WITH LANGUAGE

Special Support: Seven on Short-Term Package for Students

1. **Identify the main idea of the passage.**
 2. **Identify the supporting details.**

WASHINGTON — How to handle, chairman of the Federal Reserve, said today, is the question that he can support new cuts in spending measures to stimulate the economy, even if they increase the budget deficit, provided the measures are quick and temporary.

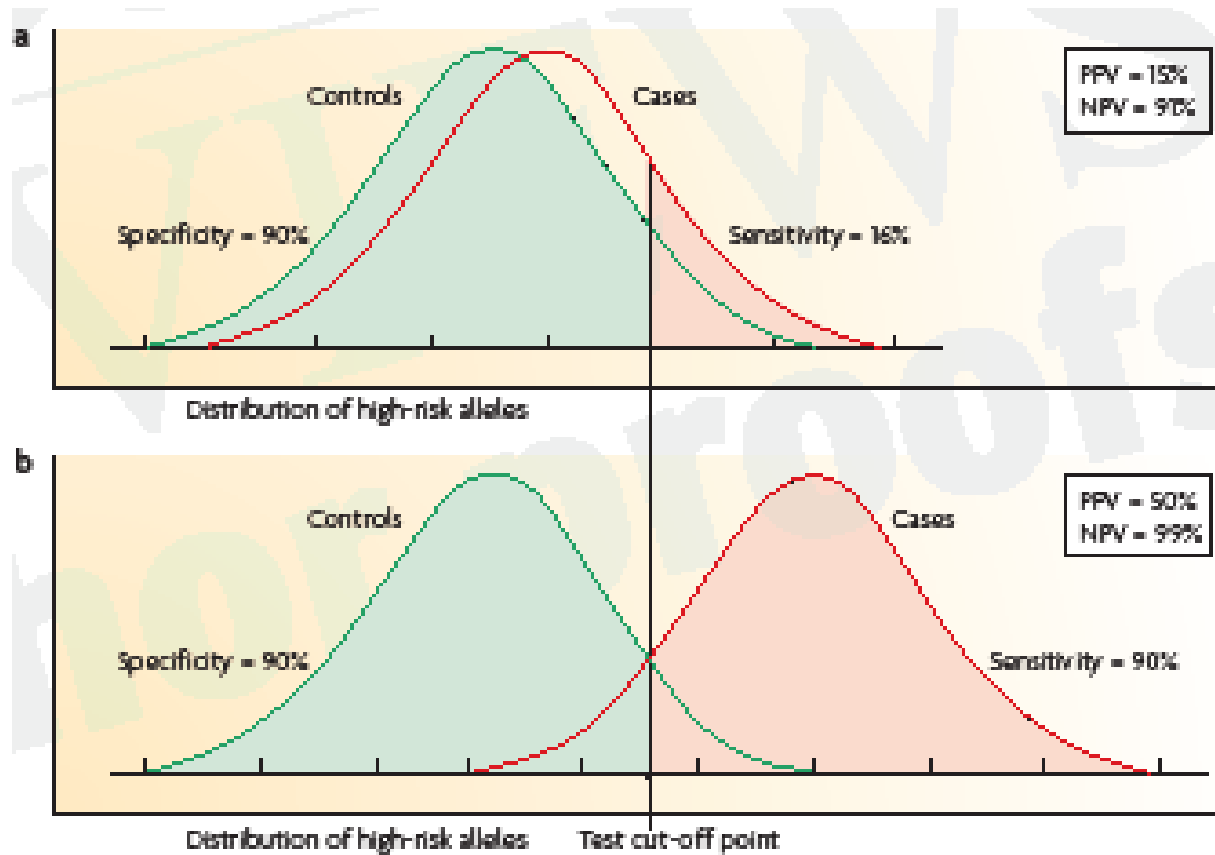
[illegible]

But, with growing evidence that the economy is slipping into a recession, Congress and the courts and President Bush are trying to come up with a package that would put more money in Americans' hands within the next few months.

The firm's willingness to give a nod to these attitudes is important. Many companies will not support claims without the client's blessing, and the direct issue of whether the Fed and Congress are considering such the authority is key word.

11.11.2014 **11.11.2014** **11.11.2014** **11.11.2014** **11.11.2014**

Large RR $\neq$ Good Prediction



Genetic Testing Based on GWAS?

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Please read the following statement below and click the "I understand" button to enter 23andMe.com.

Welcome to 23andMe.

At this time, we have suspended our health-related genetic tests to comply with the U.S. Food and Drug Administration's directive to discontinue new consumer access during our regulatory review process.

We are continuing to provide you with both ancestry-related genetic tests and raw genetic data, without 23andMe's interpretation.

If you are an existing customer please click the button below and then go to the health page for additional information, including information about refunds.

We remain firmly committed to fulfilling our long-term mission to help people everywhere have access to their own genetic data and have the ability to use that information to improve their lives.

Upon entering the site, please confirm you understand the new changes in our services.

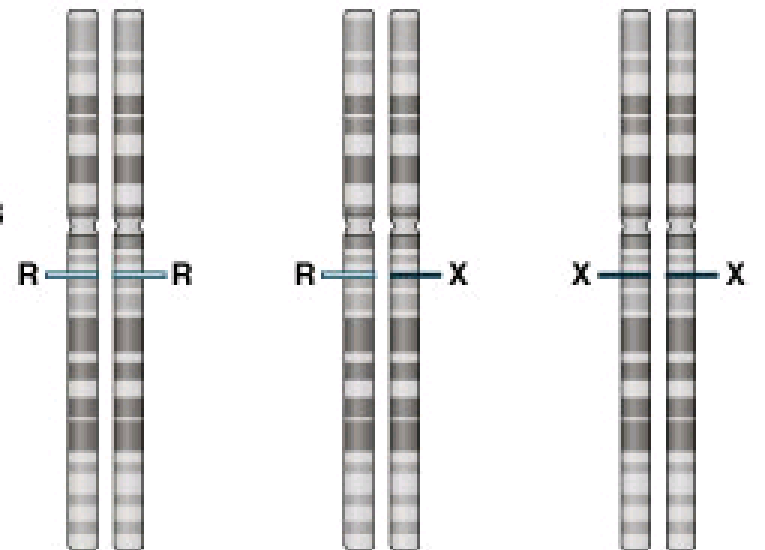
I understand that 23andMe only sells ancestry reports and raw genetic data at this time. I understand 23andMe will not provide health-related reports. However, 23andMe may provide health-related results in the future, dependent upon FDA marketing authorization.

Chromosome 11

Research suggests that elite athletes who rely on the power of fast-twitch fibers in their muscles, like sprinters, share a common genotype. These fibers contain a protein produced by the R allele (version) of the ACTN3 gene.

ACTN3

Possible variations (genotypes) of the ACTN3 gene.

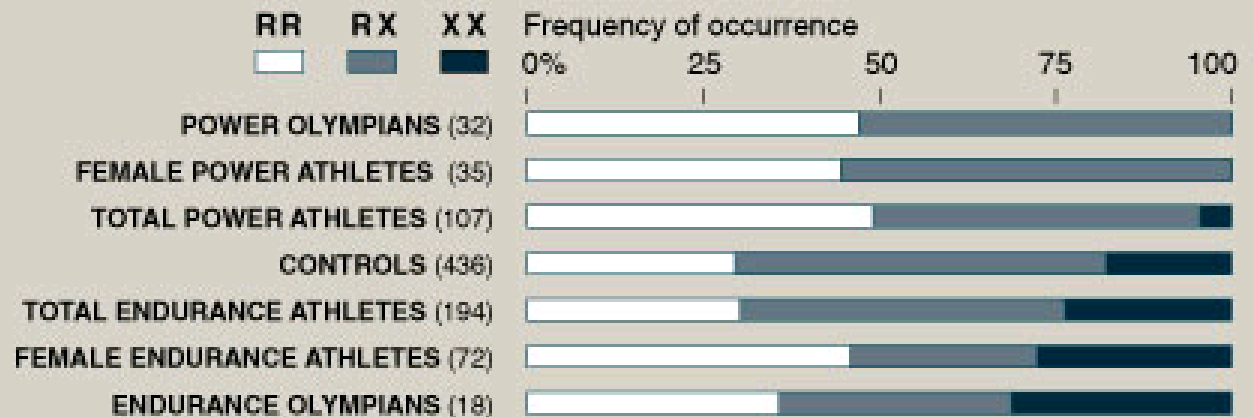


Beneficial for elite power and endurance athletes

Not beneficial for elite power athletes.

Genotype frequency among elite power/sprint athletes and elite endurance athletes.

Confidence intervals are 95%.





ATHLETIC TALENT LABORATORY ANALYSIS SYSTEM

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The New York Times -
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Description: Our *Atlas First* product is geared specifically at the youngest of athletes. Doing any type of performance based sport talent identification testing is very difficult below age 6 due to developmental levels of motor skills, strength and eye-hand coordination. *Atlas First* looks at only genetic markers, specifically the presence of ACTN3. Studies have found that individuals having the variant in both copies of their ACTN3 gene may have a natural predisposition to endurance events, one copy of their ACTN3 gene may be equally suited to for both endurance and sports/power event, neither copy of their ACTN3 gene may have a natural predisposition to sprint/power events. Knowing this information may be helpful, not in eliminating choices for sport activities but adding exposure to a host of team or individual sport events that may come easier to a young athlete.

The test is one of tool of many that can help children realize their athletic potential.

Other Products available through Atlas First

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- Weight monitoring charts
- BMI charts
- Height Prediction Calculator (not genetic)

\$149.00

Actress Vanessa Williams Explains How DNA Powers Her Family Tree

The following appeared in the Los Angeles Times, April 27, 2013.

Written by Jessica P. Ogilvie.

The world within Vanessa Williams
5 QUESTIONS

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Most of us are curious about our family lineage. For Vanessa Williams, who recently took part in the show "Who Do You Think You Are" and explored her family's history, the task was both surprising and informative. Here, she talks about what she learned and how she plans to use that information.

How did you become interested in finding out about your lineage?



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