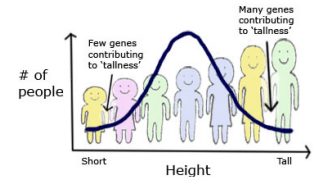


Module – Complex Trait (Quantitative) Genetics

Student Assessment Exercise starts at 08h55



202 Lecture 14 — Heritability and tools for finding the genes underlying complex traits

1. QTL analysis wrap-up (Ch19 Section 5)
 2. Genome-Wide Association Studies (GWAS) (Ch19 Section 6)
- Note: We do not have time to cover narrow sense heritability

PRIMERS—Quantitative Genetics
Reading: **Ch 19: 19.5, 19.6**

Textbook Questions : See myCourses.

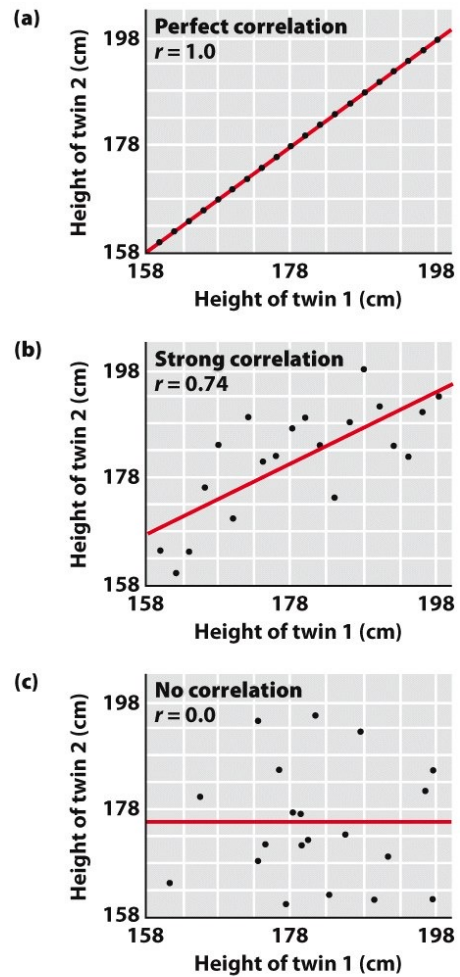


Figure 19-4
Introduction to Genetic Analysis, Tenth Edition
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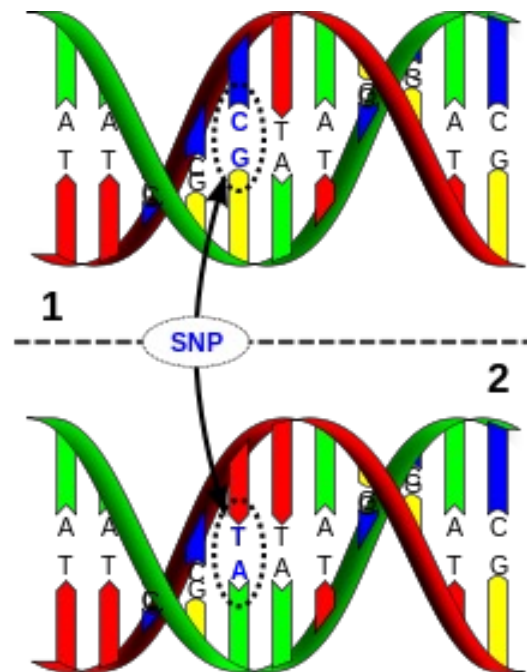


Twin Sisters Separated at Birth Reunite

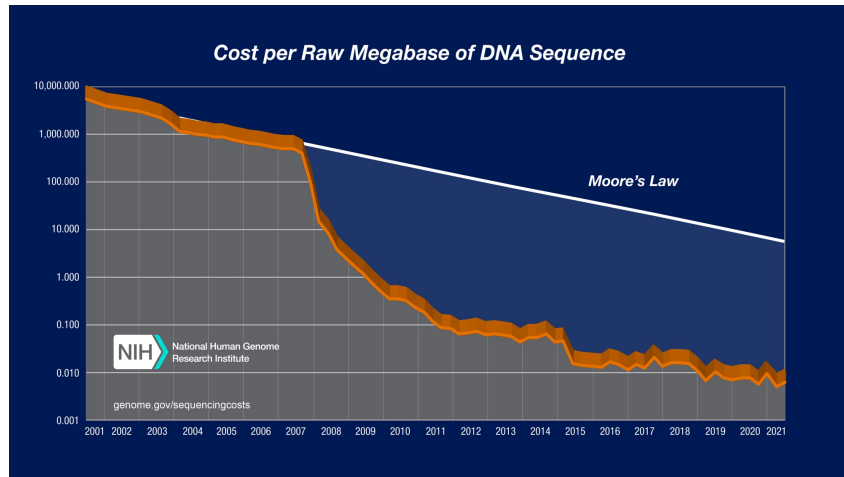
[Visit](#)

TWIN STUDIES:
 $r = \text{Correlation} =$
Broad Sense Heritability (H^2)

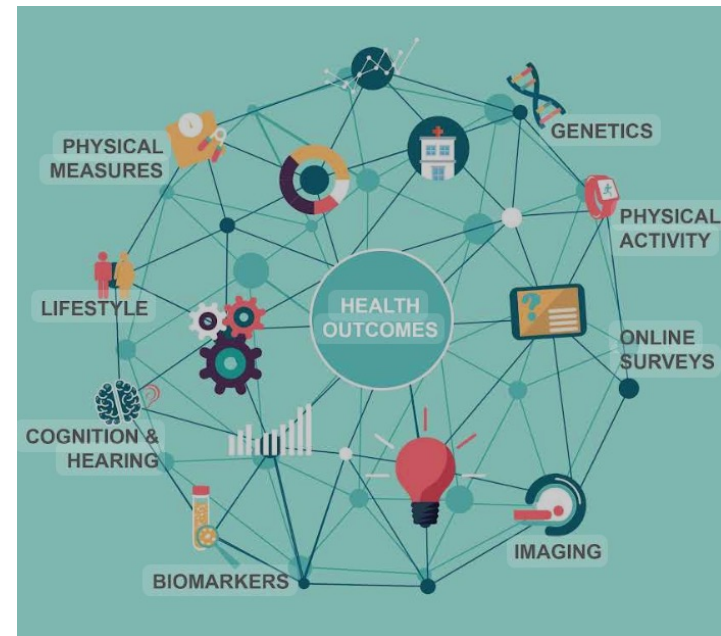
Quantitative Trait Locus mapping (QTLs and the genetic architecture of complex traits)



Genome-Wide Association Approach to Common and Complex Diseases



Low sequencing costs



*Lots of data in "Biobanks" including
sequence data*

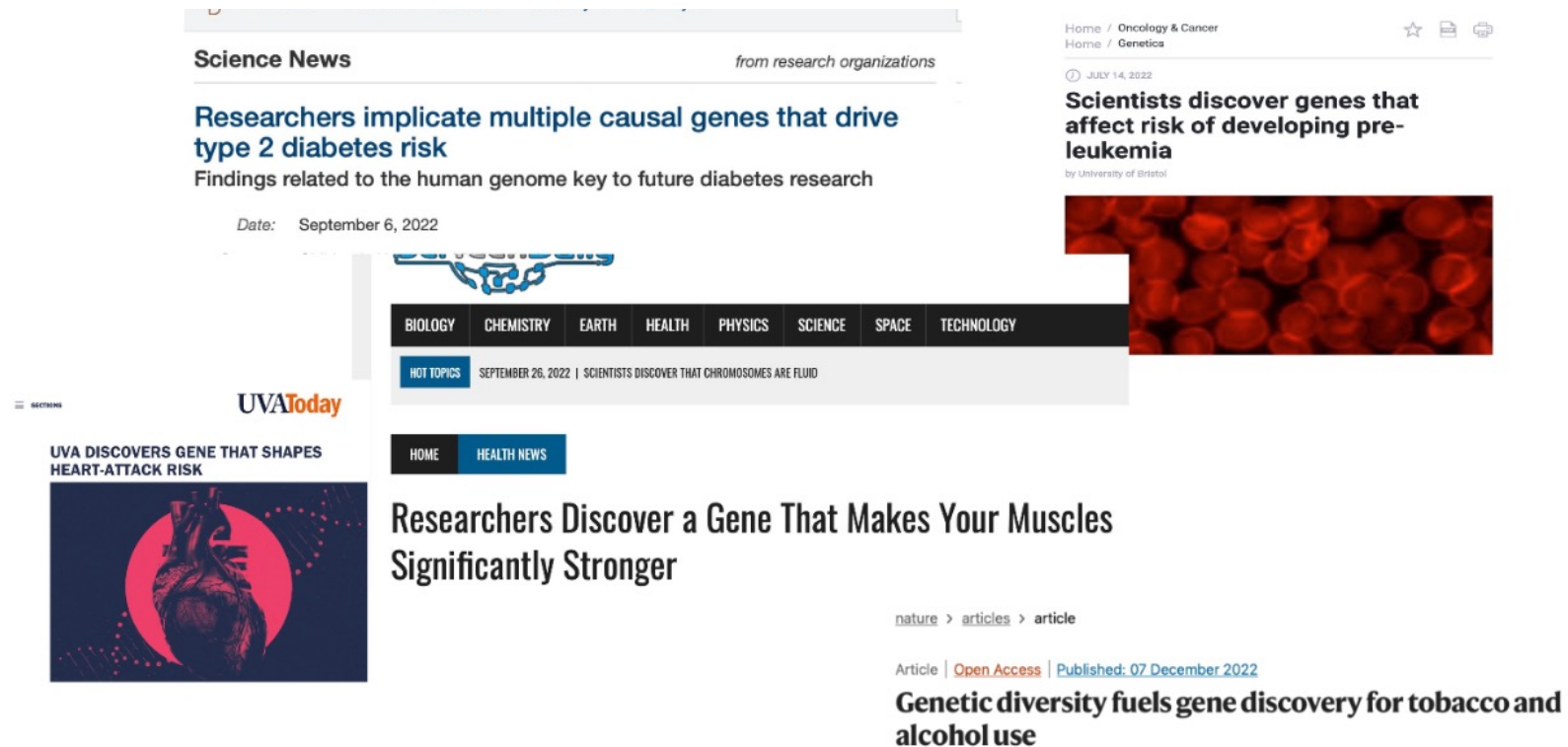
Genetic architecture of complex traits. Two basic approaches:

- **QTL mapping**...resembles classical mapping approaches (controlled crosses used to locate genes that influence the quantitative trait)
- ★ **Association mapping or genome-wide association studies (GWAS)**...relies on **population surveys** (controlled crosses *not* used) to locate genes that influence the quantitative trait

Genetic architecture of complex traits. Two basic approaches:

- **QTL mapping**...resembles classical mapping approaches (controlled crosses used to locate genes that influence the quantitative trait)
- ★ • **Association mapping or genome-wide association study (GWAS)**...relies on population surveys (controlled crosses not used) to locate genes that influence the quantitative trait

GWAS had been important in finding genetic risk factors for major diseases and other complex traits



The collage consists of four distinct news snippets. The top-left snippet is from 'Science News' and features a headline about researchers implicating multiple causal genes in type 2 diabetes risk, dated September 6, 2022. The top-right snippet is from a genetics website, dated July 14, 2022, reporting on the discovery of genes affecting the risk of developing pre-leukemia, with a background image of red blood cells. The bottom-left snippet is from 'UVA Today' and reports on the discovery of a gene that shapes heart-attack risk, accompanied by an image of a heart. The bottom-right snippet is from 'nature' and reports on genetic diversity fueling gene discovery for tobacco and alcohol use, published on December 7, 2022.

Science News *from research organizations*

Researchers implicate multiple causal genes that drive type 2 diabetes risk
Findings related to the human genome key to future diabetes research

Date: September 6, 2022

UVA Today

UVA DISCOVERS GENE THAT SHAPES HEART-ATTACK RISK

Scientists discover genes that affect risk of developing pre-leukemia
by University of Bristol

Home / Oncology & Cancer
Home / Genetics

JULY 14, 2022

Researchers Discover a Gene That Makes Your Muscles Significantly Stronger

nature > articles > article

Article | [Open Access](#) | Published: 07 December 2022

Genetic diversity fuels gene discovery for tobacco and alcohol use

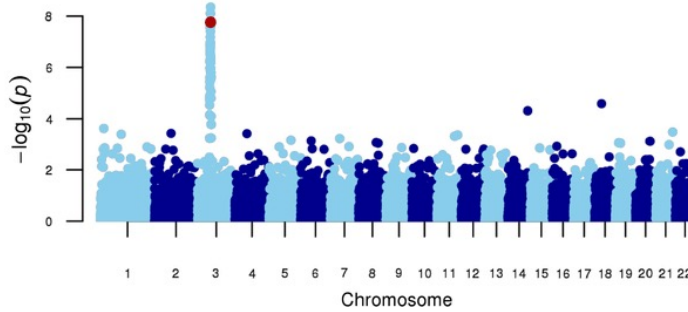
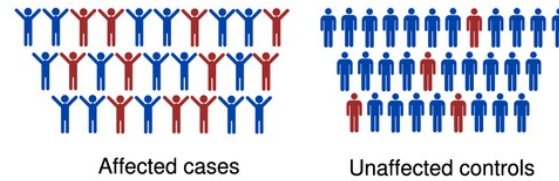
Using SNPs to Track Predisposition to Disease and other Genetic Traits

Sequence Variation

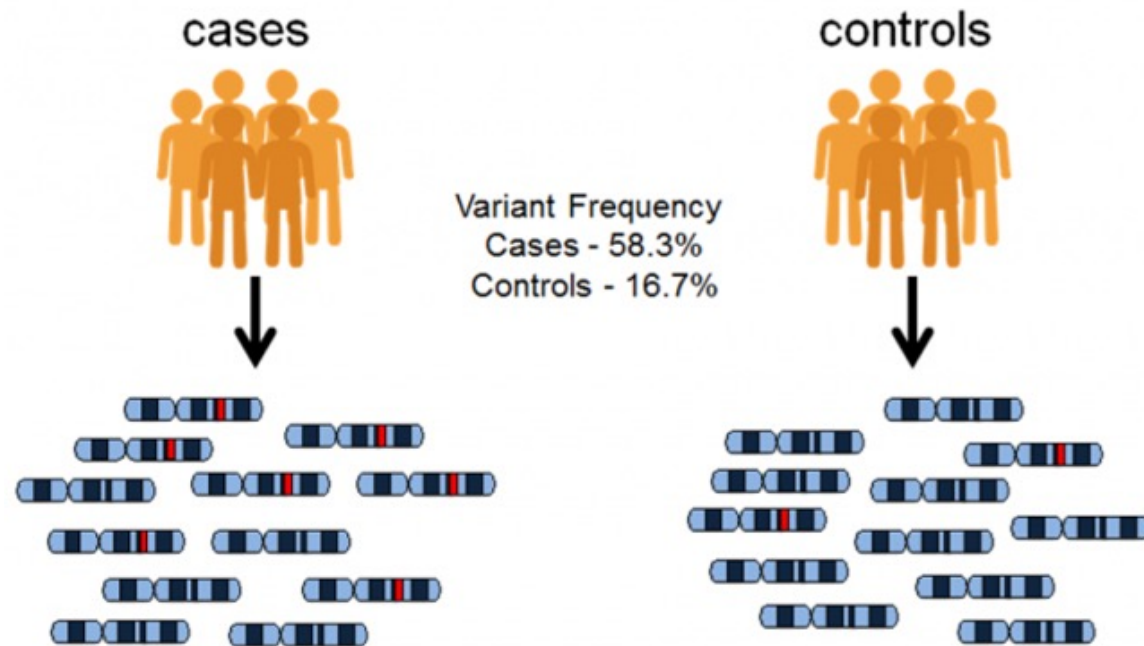
ATGCCAGTGTTTCAAGATGCTTGGCCAGCTGGACGAGGGCGATGAC
ATGCCAGTGTTTCAAGATG**T**TGGCCAGCTGGACGAGGGCGATGAC

Disease

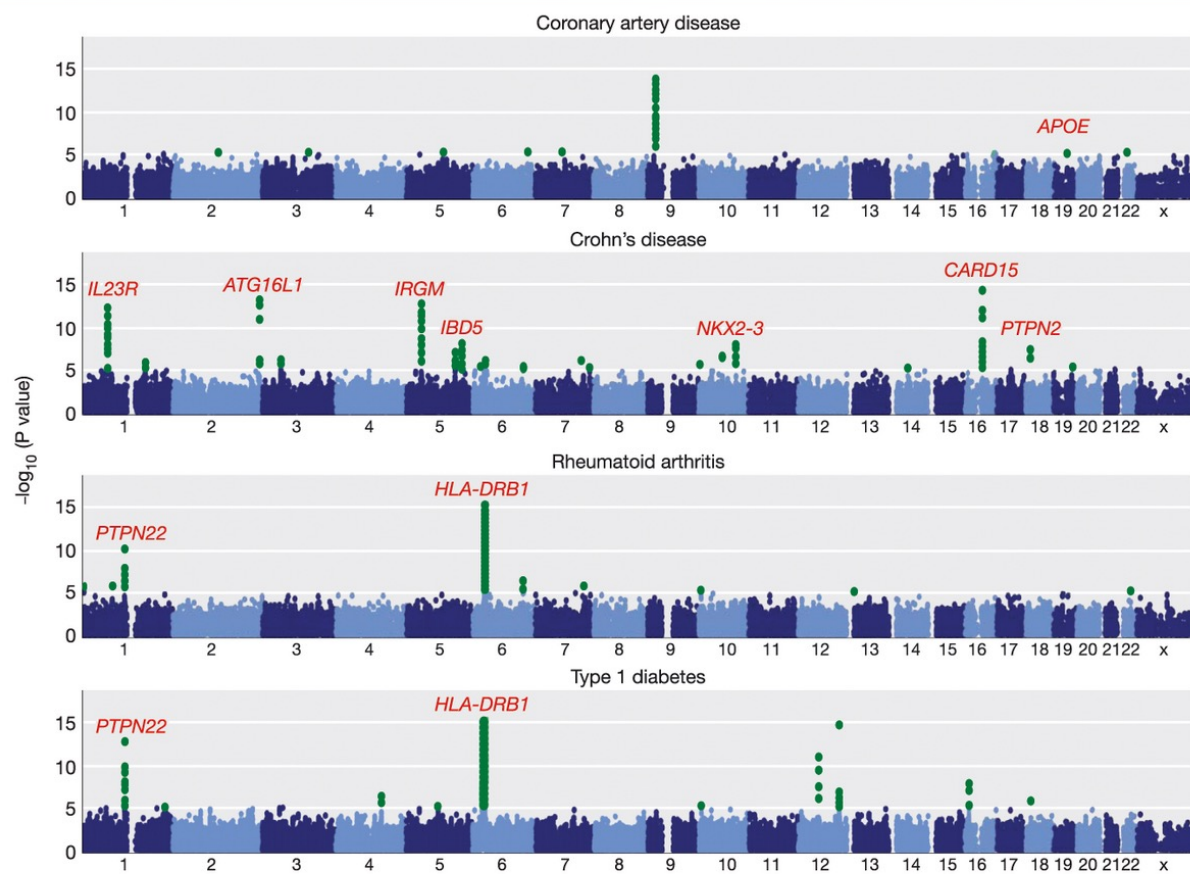
GWAS



Using SNPs to Track Predisposition to Disease and other Genetic Traits



Association mapping identifies genes for disease susceptibility



Clinical Genetic Testing Direct to Consumer

23andMe genetics just got personal. [sign in](#) | [claim codes](#) | [blog](#) | [help](#)

Search 23andMe

[our service](#) [genetics 101](#) [for the experts](#) [store](#) [about us](#)

[order now](#) [try a demo](#)

1869: Gregor Mendel discovers the laws of inheritance.
200,000 years ago: Homo sapiens walks the Earth.
2003: The Human Genome Project maps a single person's genome.

2007: 23andMe introduces the first Personal Genome Service.
Unlock the secrets of your own DNA. Today.

175,000 years ago: The mother of all present-day humans is born in Africa.
1953: Watson and Crick uncover the double-helix structure of DNA.

Welcome to 23andMe, a web-based service that helps you read and understand your DNA. After providing a saliva sample using an at-home kit, you can use our interactive tools to shed new light on your distant ancestors, your close family and most of all, yourself.

[Sign up for our Email Newsletter](#)

Gene Journal

What do your genes say about you?

Family Inheritance

Do you have your mother's sense of taste?

Ancestry

Who were your ancient ancestors?

Genome Labs

Would you like to search your genome?

What's new at 23andMe

Apr 23, 2008: 23andMe redesigns its Personal Genome Service and adds two new Gene Journal topics. Try a demo or order our service today!

DNAdirect Clinical Genetic Testing Online

[PROFESSIONALS](#) [Register](#) [Login](#)

Enter search terms... [Go!](#)

ORDER A TEST **FREE TESTING ADVICE** **CONSULTING SERVICES**

[Our Services](#) [Tests We Offer](#) [Genetics & You](#) [About Us](#)

New! 3 Gene Panel for Drug Response
When it comes to medications, one size doesn't fit all. Our 3 Gene Drug Response Panel can predict how you respond to many of the most commonly prescribed drugs. [Learn More >>](#)

Family History
If it runs in your family it doesn't have to be your destiny. Find out if genes are really involved - and what you can do about them. [Learn More >>](#)

DNAarchive
preserving genetic history for the future
Home DNA Storage based on revolutionary new technology

Fertility & Pregnancy
Looking for carrier screening? Having difficulty getting pregnant? [Learn More >>](#)

Signs & Symptoms
Do you have a chronic, undiagnosed condition? It could be genetic. [Learn More >>](#)

Ethnic Risks
Are you more or less likely to carry certain disease-related genes? [Learn More >>](#)

Lifestyle Issues
If you carry certain genes, you can take steps to live longer and healthier. [Learn More >>](#)

5 Questions You Should Ask
The National Society of Genetic Counselors recommends you ask 5 important questions before genetic testing. DNA Direct can help you answer them. [Learn More >>](#)

Senate Passes GINA
The Genetic Information Non-Discrimination Act was passed on April 24, 2008. When signed into law, consumers will be reassured that their genetic information is protected against misuse by employers and insurance companies. [Learn More >>](#)

MEDICAL GENETIC TESTING

- Alpha-1 Antitrypsin Deficiency
- Ashkenazi Jewish Carrier Screening
- Blood Clotting Disorders
- Breast & Ovarian Cancer
- Colon Cancer Screening
- Cystic Fibrosis
- Diabetes Risk - deCODE T2™
- Hemochromatosis (Iron Overload)
- Infertility
- Recurrent Pregnancy Loss

DRUG RESPONSE TESTING

- 2D6, 2C9 & 2C19 Gene Tests
- Warfarin Response
- Tamoxifen 2D6

ANCESTRY, ETHNICITY & PATERNITY

- Ancestry & Ethnicity Testing
- Paternity Testing

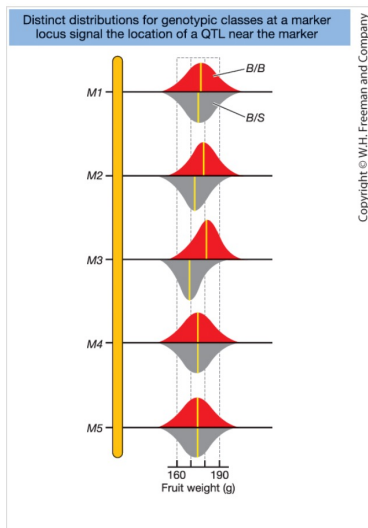
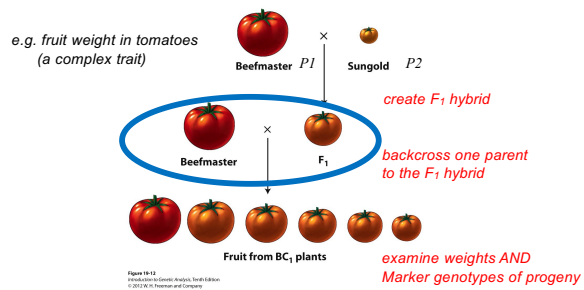
HOME DNA STORAGE

- DNA Archive™

PERSONAL GENOME COUNSELING

- Genome Scans
- Whole-Genome Sequencing

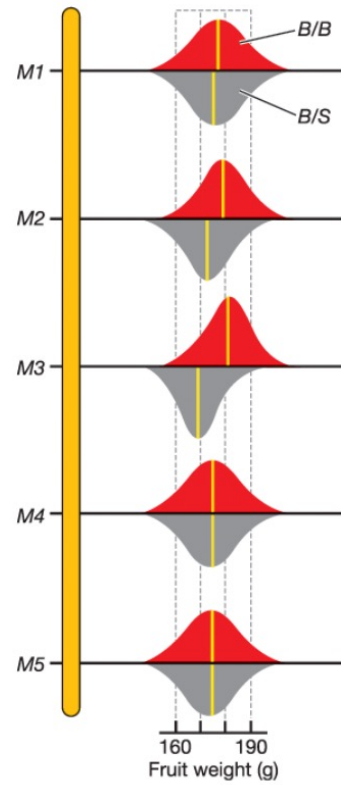
QTL mapping begins with crosses of two inbred lines
(that differ in the trait of interest and their molecular marker genotypes)



Population between Two Inbred Tomato Lines—Beefmaster and Sungold

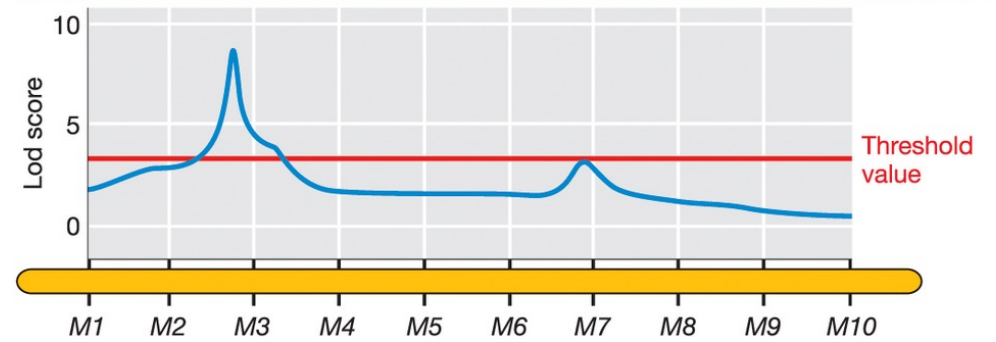
| Plant | Fruit wt. (g) | Markers | | | | |
|-------------|---------------|---------|-------|-------|-------|-------|
| | | M1 | M2 | M3 | M4 | M5 |
| Beefmaster | 230 | B/B | B/B | B/B | B/B | B/B |
| Sungold | 10 | S/S | S/S | S/S | S/S | S/S |
| BC_1-001 | 183 | B/B | B/B | B/B | B/S | B/S |
| BC_1-002 | 176 | B/S | B/S | B/B | B/B | B/B |
| BC_1-003 | 170 | B/B | B/S | B/S | B/S | B/S |
| BC_1-004 | 185 | B/B | B/B | B/B | B/S | B/S |
| BC_1-005 | 182 | B/B | B/B | B/B | B/B | B/B |
| BC_1-006 | 170 | B/S | B/S | B/S | B/S | B/B |
| BC_1-007 | 170 | B/B | B/S | B/S | B/S | B/S |
| BC_1-008 | 174 | B/S | B/S | B/S | B/S | B/S |
| BC_1-009 | 171 | B/S | B/S | B/S | B/B | B/B |
| BC_1-010 | 180 | B/S | B/S | B/B | B/B | B/B |
| BC_1-011 | 185 | B/S | B/B | B/B | B/S | B/S |
| BC_1-012 | 169 | B/S | B/S | B/S | B/S | B/S |
| BC_1-013 | 165 | B/B | B/B | B/S | B/S | B/S |
| BC_1-014 | 181 | B/S | B/S | B/B | B/B | B/S |
| BC_1-015 | 169 | B/S | B/S | B/S | B/B | B/B |
| BC_1-016 | 182 | B/B | B/B | B/B | B/S | B/S |
| BC_1-017 | 179 | B/S | B/S | B/B | B/B | B/B |
| BC_1-018 | 182 | B/S | B/B | B/B | B/B | B/B |
| BC_1-019 | 168 | B/S | B/S | B/S | B/B | B/B |
| BC_1-020 | 173 | B/B | B/B | B/B | B/B | B/B |
| Mean of B/B | — | 176.3 | 179.6 | 180.7 | 176.1 | 175.0 |
| Mean of B/S | — | 175.3 | 173.1 | 169.6 | 175.3 | 176.4 |

Distinct distributions for genotypic classes at a marker locus signal the location of a QTL near the marker

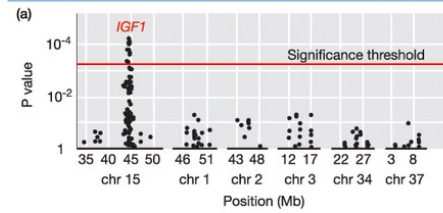


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Lod scores provide statistical evidence for QTL



Association mapping finds a gene for body size in dogs



(b)



Wrap-up

Midterm questions to be selected from the following topics:

Hardy-Weinberg theory

Inbreeding (including calculation of F from pedigrees)

**Forces that change allele frequencies in populations
(mutation, migration, drift, selection)**

**Quantitative genetic variation, heritability, response to
selection.**

**Tools for mapping the genes underlying complex traits
(GWAS)**