Workshop Overview

Genotype 2 Phenotype 4 Non-biologists "G2P4NB"

- Purpose: provide introductory material on genetics and genomics for non-biologists interested in applying their data science skills to the Genotype to Phenotype field
- Anticipated that this ***cannot*** be a replacement for course in genetics, but that this will serve to give you a view of the field that can help you understand questions of interest to genetics as well as the complexity present in biological samples

Workshop Schedule

- <u>Day 1, March 18 2021:</u>
  - Overview
  - Molecules
- <u>Day 2, March 25 2021:</u>
  - Genetics, alleles, and linkage
  - Quantitative measurements
- <u>Day 3, April 1 2021:</u>
  - Epigenetics/Epitranscriptomics
  - Systems biology and networks
- <u>Day 4, April 8 2021:</u>
  - Ethics and social considerations
  - Current challenges and research topics

Workshop Overview

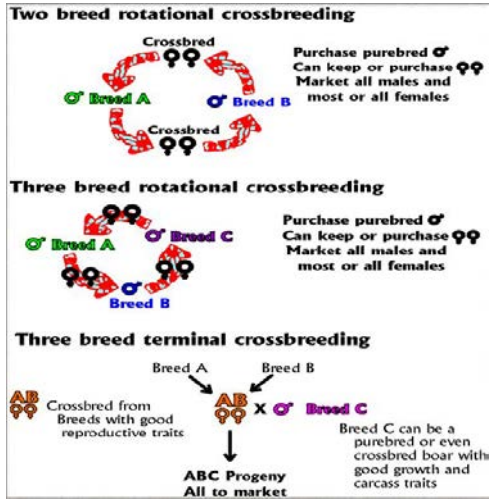
- Time 11-1pm Pacific and 2-4pm Eastern
- Workshop series will use:
  - Zoom to meet & create breakout sessions
  - General format of:
    - 30 min lecture, 15 minutes breakout questions, 15 minutes of discussion as a group
  - Zoom chat: used to ask questions about content from the 30 minute presentations
  - HackMD.io will be used for breakout sessions to answer questions

A quick demonstration of HackMD.io

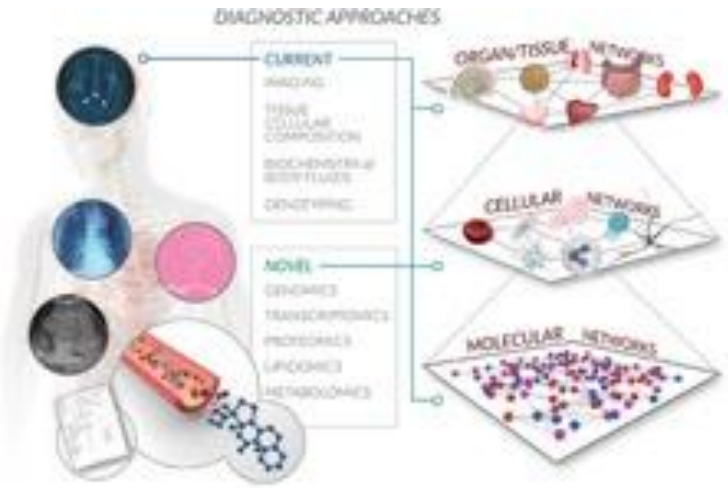
Link to our page is in Zoom chat

Genetics is the study of how information flows in biology

- To understand genetics, we need to discuss many concepts on several levels because biological information is embedded into many levels of biology



Chapter 19 Opener
Introduction to Genetic Analysis, Tenth Edition
© 2012 W. H. Freeman and Company



- Populations
  - Individuals
    - Tissues
      - Cells
        - Molecules

- Genetics is complex and demands your attention!

Genes to messenger to proteins

DNA ⟶ mRNA ⟶ Protein

Biological information flow

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Session 2

Clifford Weil

Molecules, Central Dogma and Phenotypes

- Cells and organisms are busy, complex, 4D places — lots going on, short timelines, routine business AND response to changing situations-- need clear instructions, a lot of communication and coordination
- DNA → RNA → PROTEIN
- "Genotype" is the complete set of genetic information within a cell or organism; "Phenotype" is any outward manifestation of that genotype

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Session 3

Clifford Weil

Alleles, Inheritance, Linkage

An allele is a form of a gene; geneticists often use mutant alleles to tell us a gene's function.

In organisms with two copies of every chromosome (diploids), chromosomes segregate from one another at meiosis so that only one allele of each gene ends up in each sperm or egg.

Alleles of genes located near one another on the same chromosome are likely to be inherited together ("linked"). Alleles of genes on different chromosomes are inherited independently of one another ("unlinked").

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Session 4

Ryan Bartelme

Quantitative Methods in Genomics and Phenotyping - Main Points

- We can quantify differences in genomes by analyzing single nucleotide polymorphic (SNP) data
- We can use SNP data in genome-wide association studies to estimate correlations between DNA sequence information and observed phenotypes
- Cellular and organismal responses to the environment can be quantified with gene expression studies

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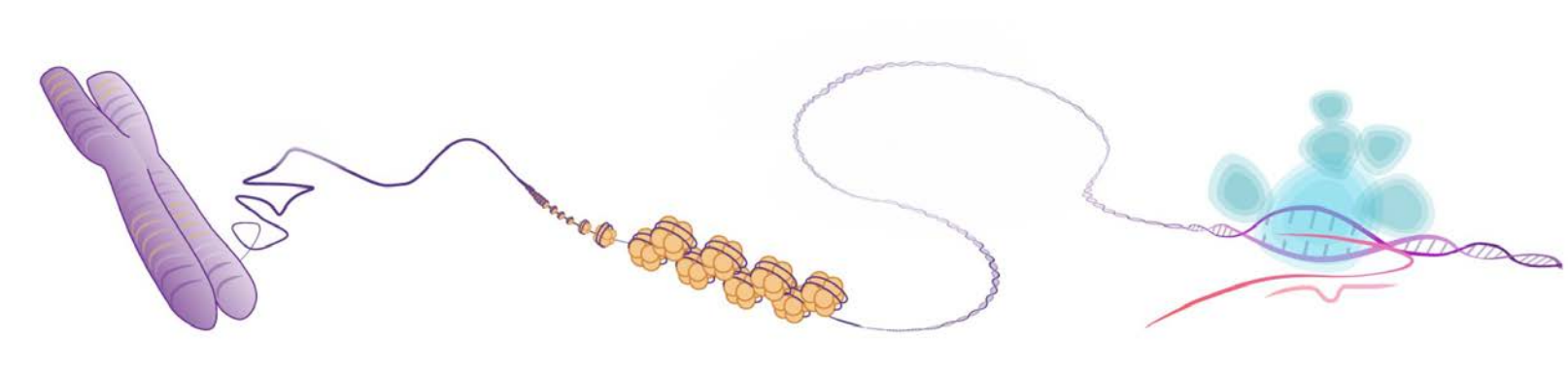
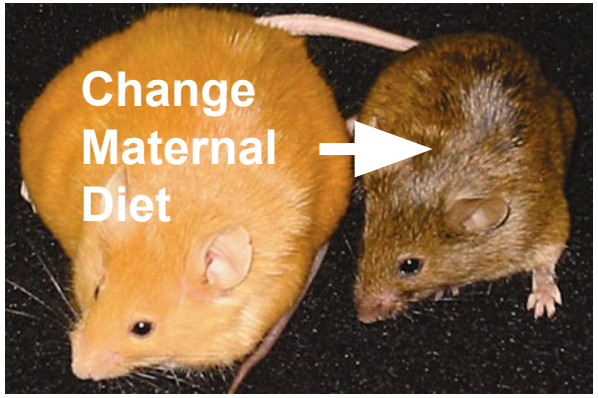
Session 5

Chris Tuggle

Epigenetics and Epitranscriptomics

- Study of epigenetics: how the genome functions across cells, tissues, and environments.
- Epi- “above or upon” so epigenetics is study of heritable *phenotypic* variation that does not involve changes to the DNA sequence.
- Reversible molecular changes to the chromosome or RNA molecule that affect biological function- often due to environment changes.





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Session 6

Ryan Bartelme

Network and Systems Biology in Genomics & Phenotyping - Main Points

- Biological networks vary in scope (ex. cellular vs. organismal vs. ecosystem)
- These networks are scale free
- Microorganisms and microbiomes create a diverse metabolic network inside and outside hosts

Session 7 Ellen Goddard

Ethical and Societal Considerations

How did societal disinterest in traditional plant and animal breeding become a global debate about GMOs?

As technology advances (gene editing) are we facing new opposition or acceptance?

Why are views of different applications of the technology so divergent?

- Human applications – genetic diseases
- Plant and animal applications – productivity, disease and drought resilience,
  - plant applications - *bananas, corn, cotton, chestnut trees*
  - animal applications – *dairy cattle, pigs, chickens, cheese*

What are the ethical considerations about the use of this technology ?
Are the views of scientists aligned with the views of the public ? Should they be?

What is the role of data, science and science communication in the use of new and possibly controversial technologies?

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Session 8

Eric Lyons

Current challenges and research topics in AG2PI

- AG2PI members to present short talks on their current work
- Participants propose topics/questions for which they would like additional information
- Opportunity for open discussion to facilitate future collaborations

Questions on Workshop structure?

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Session 1: Overview

Fundamental Concepts

Major divisions in Genetics

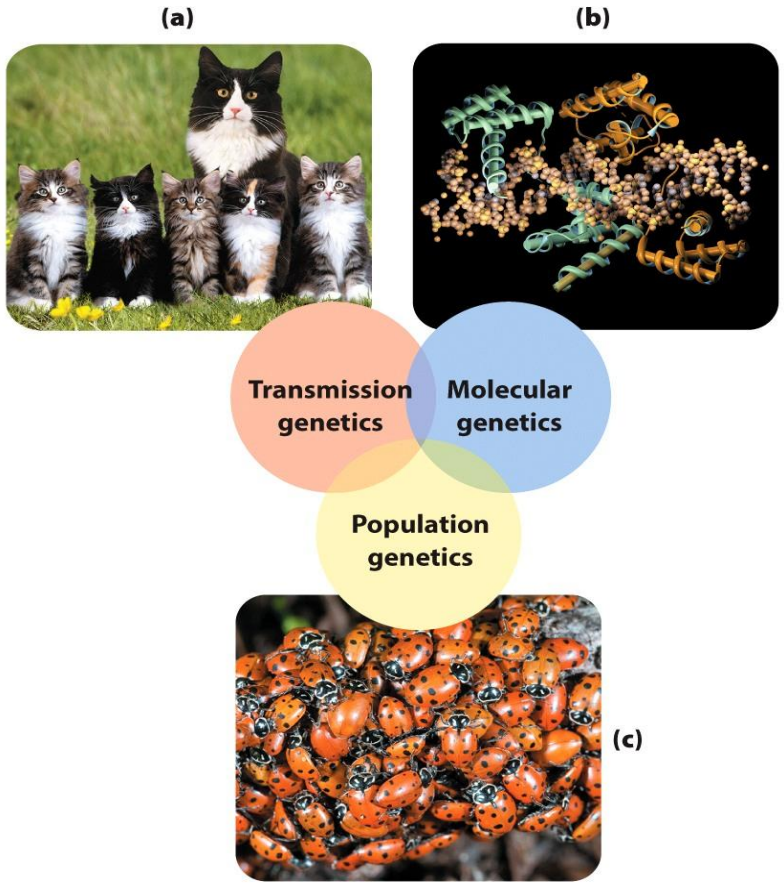

Figure 1.6
Genetics: A Conceptual Approach, Fifth Edition

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Session 1: Overview

Fundamental Concepts

Genes are the fundamental units of heredity

Genes come in multiple forms called alleles

Genes confer phenotypes

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Session 1: Overview

Fundamental Concepts

Genetic information is carried in DNA and RNA

Genes are located on Chromosomes

Chromosomes separate through processes of Mitosis and Meiosis

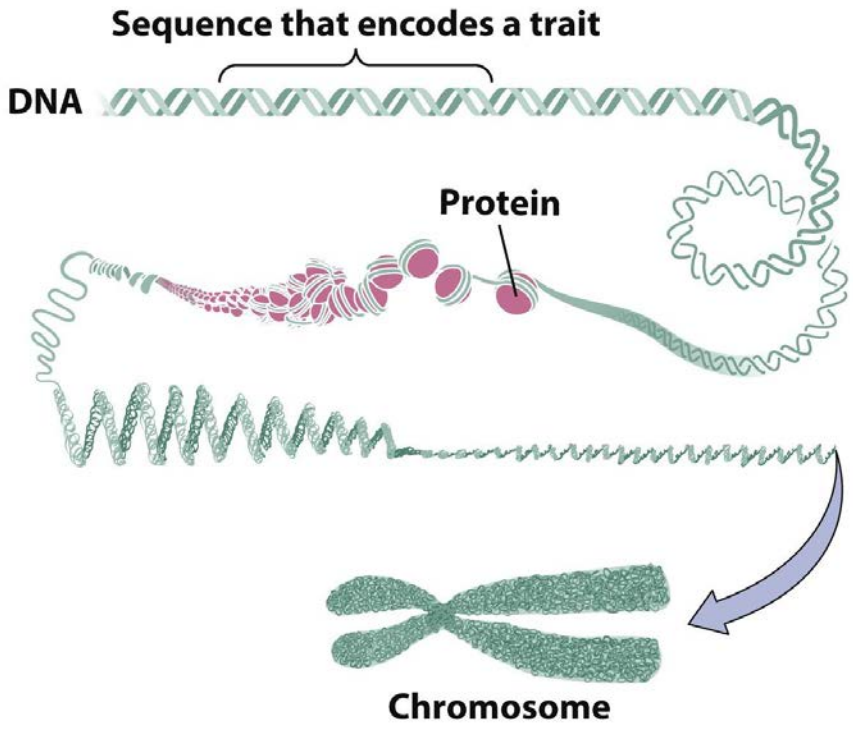

Figure 1.14
Genetics: A Conceptual Approach, Fifth Edition

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Session 1: Overview

Fundamental Concepts

Genetic information is transferred from DNA to RNA to Protein

Mutations are permanent changes in genetic material- that can be transferred from cell to cell or parent to offspring

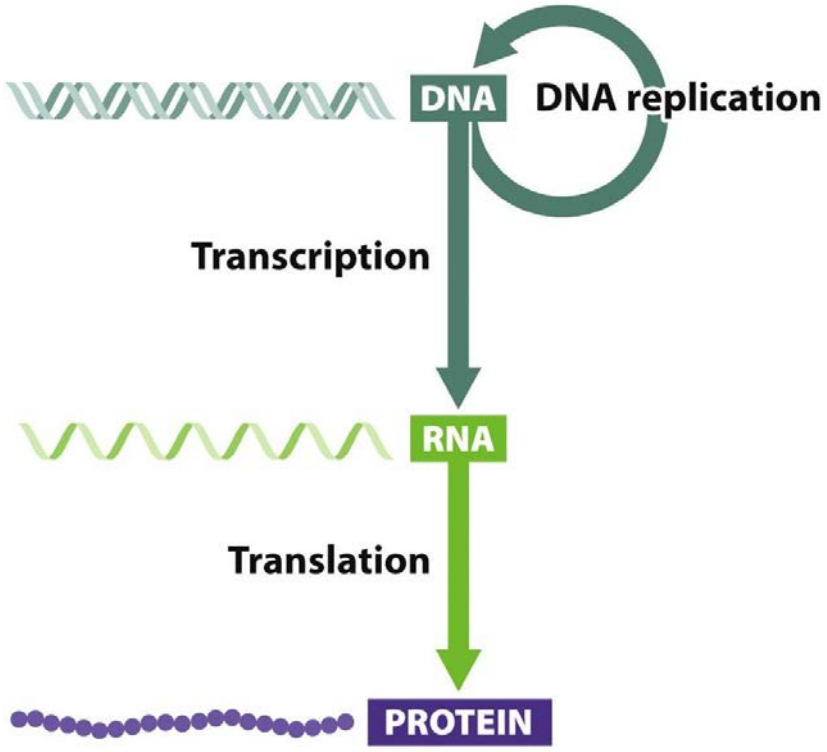

Figure 10.16a
Genetics: A Conceptual Approach, Fourth Edition

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Session 1: Overview

Fundamental Concepts

Some traits are controlled by only 1 or a few genes- "simple" or Mendelian genetics

Some traits are affected by many genes and environmental factors

"complex" or quantitative genetics

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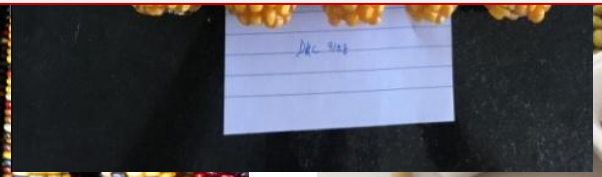
Why the emphasis on "simple" and "complex" genetics?

Few large gene effects: simple to predict P from G
Many small effects: complex to predict P from G

Most economically important traits are complex and affected by many genes- predicting G2P is ***hard***



http://www.poultryhub.org/species/fancy-chicken-breeds/

Simple genetics directly affects patient lives

Using Genetic testing to make *informed* medical decisions and
change a likely future phenotype

LOS ANGELES — "TWO years ago I wrote about my choice to have a preventive double mastectomy. A simple blood test had revealed that I carried a mutation in the BRCA1 gene. It gave me an estimated 87 percent risk of breast cancer and a 50 percent risk of ovarian cancer. I lost my mother, grandmother and aunt to cancer." *Angelina Jolie – predicting her future*

One test on one gene variant with a very large effect on risk of breast cancer (normal risk is 12%)

G2P: Does this mean that BRCA1 is the only gene controlling the cancer phenotype?

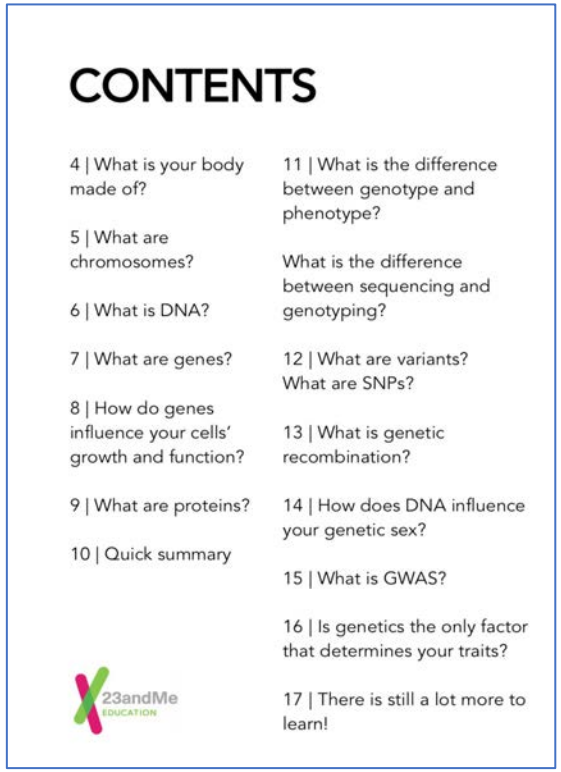
http://www.nytimes.com/2015/03/24/opinion/angelina-jolie-pitt-diary-of-a-surgery.html?_r=0

Linking Genotype to Phenotype

Tons of resources for **G2P** in humans....

23&Me:Genetics 101 Booklet

https://education.23andme.com/genetics-101-booklet/

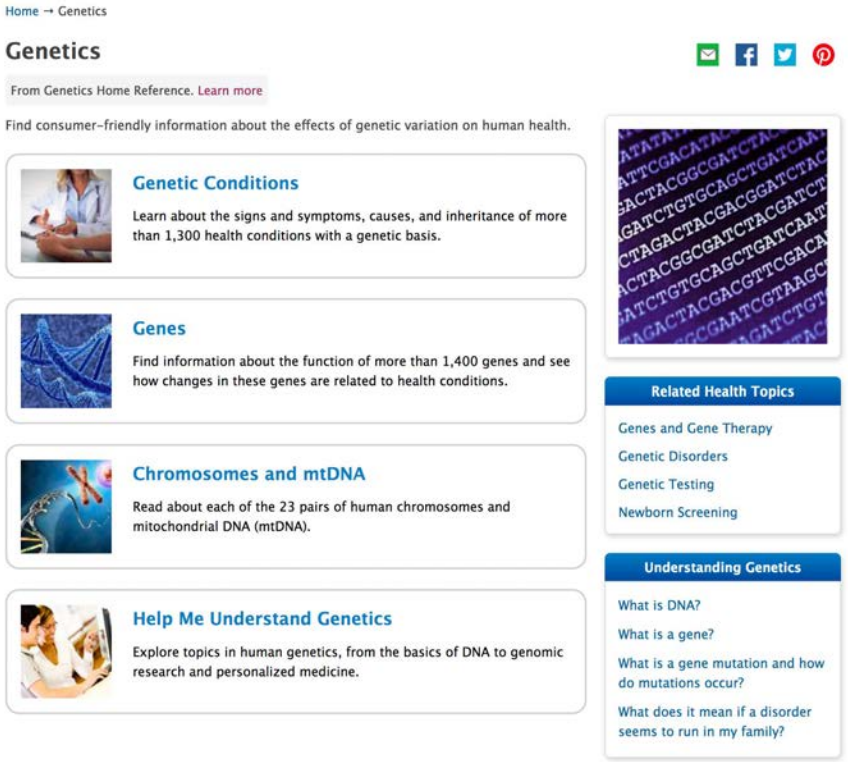


CONTENTS

23andMe EDUCATION

US Gov: Genetics Home Reference

https://medlineplus.gov/genetics/



Home → Genetics

Genetics

From Genetics Home Reference. Learn more

Find consumer-friendly information about the effects of genetic variation on human health.

Genetic Conditions

Learn about the signs and symptoms, causes, and inheritance of more than 1,300 health conditions with a genetic basis.

Genes

Find information about the function of more than 1,400 genes and see how changes in these genes are related to health conditions.

Chromosomes and mtDNA

Read about each of the 23 pairs of human chromosomes and mitochondrial DNA (mtDNA).

Help Me Understand Genetics

Explore topics in human genetics, from the basics of DNA to genomic research and personalized medicine.

Related Health Topics

- Genes and Gene Therapy
- Genetic Disorders
- Genetic Testing
- Newborn Screening

Understanding Genetics

- What is DNA?
- What is a gene?
- What is a gene mutation and how do mutations occur?
- What does it mean if a disorder seems to run in my family?

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Resources for G2P in agriculture?

Resources for known mutants with **large effects** on phenotype- “Mendelian or simple genetics”:

THE UNIVERSITY OF SYDNEY

OMIA - ONLINE MENDELIAN INHERITANCE IN ANIMALS

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WELCOME TO OMIA

Online Mendelian Inheritance in Animals (**OMIA**) is a catalogue/compendium of inh
261 animal species (other than human and mouse and rats, which have their own r
Associate Professor Imke Tammen of the University of Sydney, Australia, with help
stored in a database that contains textual information and references, as well as lin
and to OMIM and Ensembl.

OMIA is manually curated by a team of specialists. If you see an error or wish to su

To join the OMIA Support Group, register at OMIA Support Group.

From 1st September 2011, the OMIA ID is binomial, with the format OMIA xxxxxx-y
trait/disorder, and yyyy.. is the NCBI species taxonomy id (usually four digits, but so

Summary

	dog	cattle	cat	pig	sheep	horse	chicken	rabbit	goat	Other	TOTAL
TOTAL TRAITS/DISORDERS	787	556	363	286	258	242	223	103	90	691	3689
Mendelian trait/disorder	364	261	117	92	112	59	132	62	20	272	1556
Mendelian trait/disorder; likely causal variant(s) known	299	167	84	41	59	46	51	11	15	144	933
Likely causal variants	436	227	132	51	76	98	66	14	26	127	1271
Potential models for human disease	474	230	229	134	117	134	53	57	41	357	1859

April, neatly replicating the chronology of three of the most important discoveries in biology.

OMIA SUCCESSION PLAN: Although Frank Nicholas intends to continue working on OMIA while ever he can, a succession plan is needed. To this end, Imke Tammen, who will be known to many of

FAO | IAEA

Joint FAO/IAEA Programme
Nuclear Techniques in Food and Agriculture

Search Site

Home | Soil and Water | Plant Breeding | Livestock | Insect Pest Control | Food and Environment

eding and Genetics

eding and Genetics Section assists FAO and IAEA
s in the implementation of innovative and effective
g programmes using radiation induced mutation,
ection and pre-breeding technologies. This is done
arch and development (R&D), capacity development,
technology transfer and technical support and
assistance via Coordinated Research Projects (CRPs) and Technical Cooperation Projects (TCPs).

The overall aim is to enhance global food security through sustainable crop production using strategic fundamental and applied crops sciences research. Our work is driven by Member State demands, and the MSs are the recipients of technology transfer, capacity development, policy advice, materials and information. The major target is yield and yield stability, but this encompasses developing crops with greater resilience to climate change. Quality traits, especially nutritious foods, are also high on the agenda of Member States.

Mutation breeding is hugely successful. The wide use of mutation induction for crop improvement is documented in the FAO/IAEA Mutant Variety Database, which includes more than 3346 officially released mutant varieties from 228 different plant species in more than 73 countries throughout the world. Over 1,000 mutant varieties of major staple crops, cultivated on tens of millions of hectares enhance rural income, improve human nutrition and contribute to environmentally sustainable food security in the world.

- Training
- Knowledge Management

Publications

- Books & Proceedings
- Manuals, Guidelines & Protocols
- Newsletters & Annual Reports
- Scientific Papers

Meetings

- Forthcoming

Most economically important phenotypes are caused by *complex* genetics!

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You already know some complex genetics: human height

Chapter 19 Opener
Introduction to Genetic Analysis, Tenth Edition

- Height is an example of a <u>complex</u> trait because height is controlled by many genes
- "Genetic improvement" of tallness
- Parents interested in making basketball players…. Start with good genes- tall parents... Why?
- Is having "tall" genes enough? Do you expect the children of two tall parents to always be tall? Why or why not?

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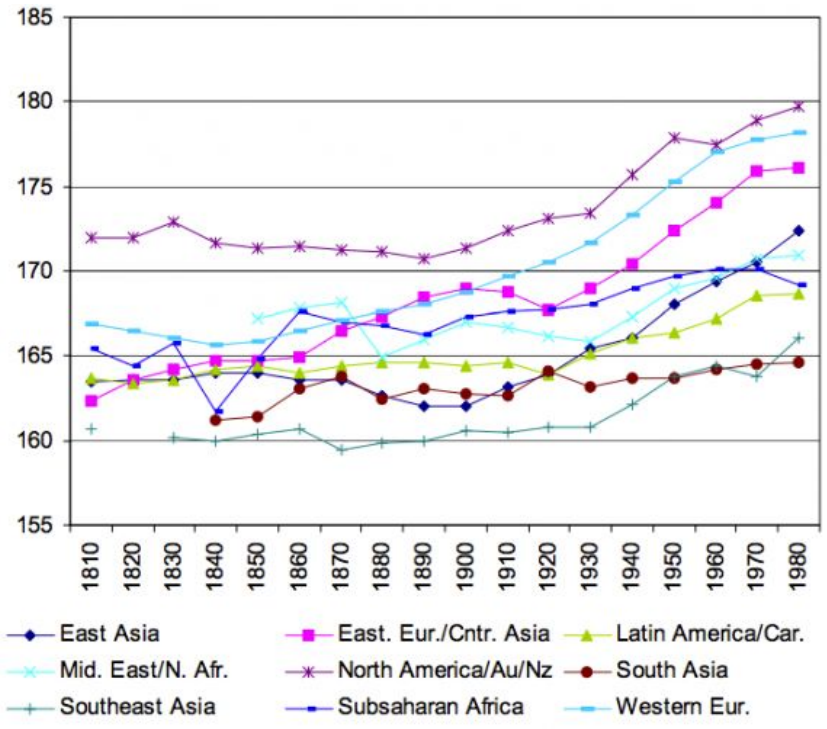
What else affects human height?



- Environment: Nutrition + medical technology
- Height is a <u>continuous trait affected by genes and the environment</u>
- But height is still “heritable”- what does this mean?
- Part of the variation can be measured as due to genetics

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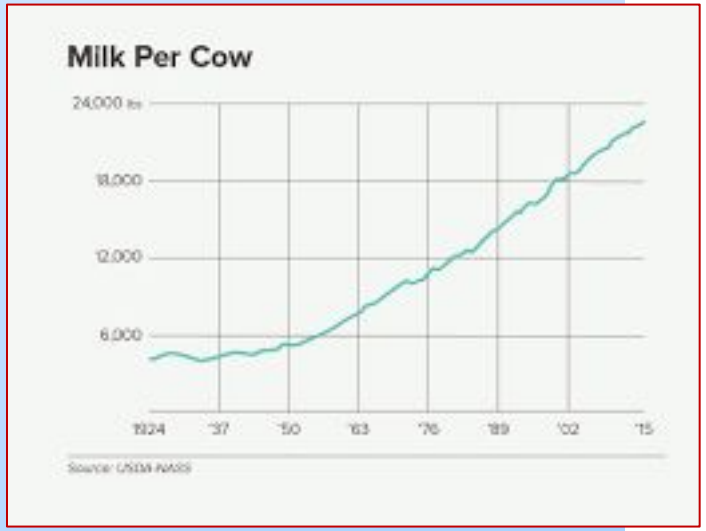
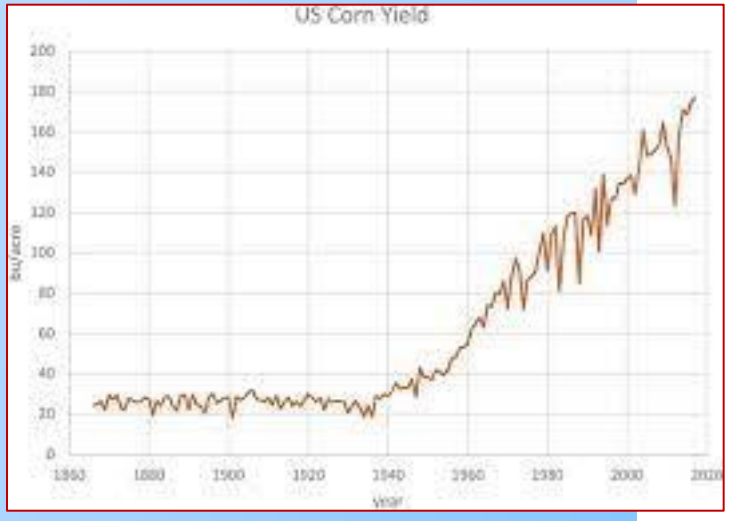
We can <u>predict</u> differences in heritable traits in future offspring!





We can observe the outcome of many crosses in offspring and learn to ***predict phenotypes*** □ change the population.

- ✔ Prediction is possible because there are clear rules that govern how genes move from parent to offspring, as well as how genes interact and control biological functions that we observe as specific phenotypes in traits.

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How else can we change traits in future offspring?

We can <u>use technology to mutate the genetic material in very specific ways</u> to generate new phenotypes—this is dependent on knowing exactly what part of the DNA structure to change practical application of knowing the exact genetic information in our animals and plants, hence a need for **genomics**

<u>Production of hornless dairy cattle from genome-edited cell lines</u>

Nature Biotechnology 34, 479–481 (2016) doi:10.1038/nbt.3560

CRISPr KO to prevent viral infection in pigs

http://parrottlab.uga.edu/SIVB/HTML/1997-3.html

The soybean at left expresses a Bt gene for resistance to caterpillars

Bowls of Golden and conventional rice. The golden color comes from ß-carotene, which the body converts to vitamin A.

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How about predicting and changing <u>our</u> future?

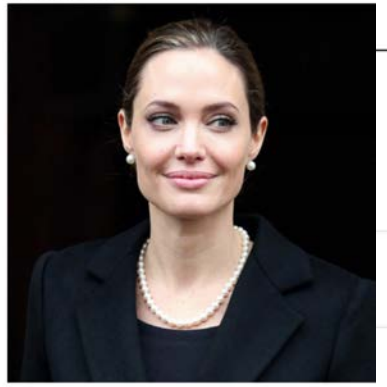
We can predict outcomes by knowing the function of the specific type of DNA molecules (gene alleles) and associating DNA variants with complex phenotypes we find □ using G2P information (lots of it)

The New York Times

The Opinion Pages | OP-ED CONTRIBUTOR

My Medical Choice

By ANGELINA JOLIE MAY 14, 2013

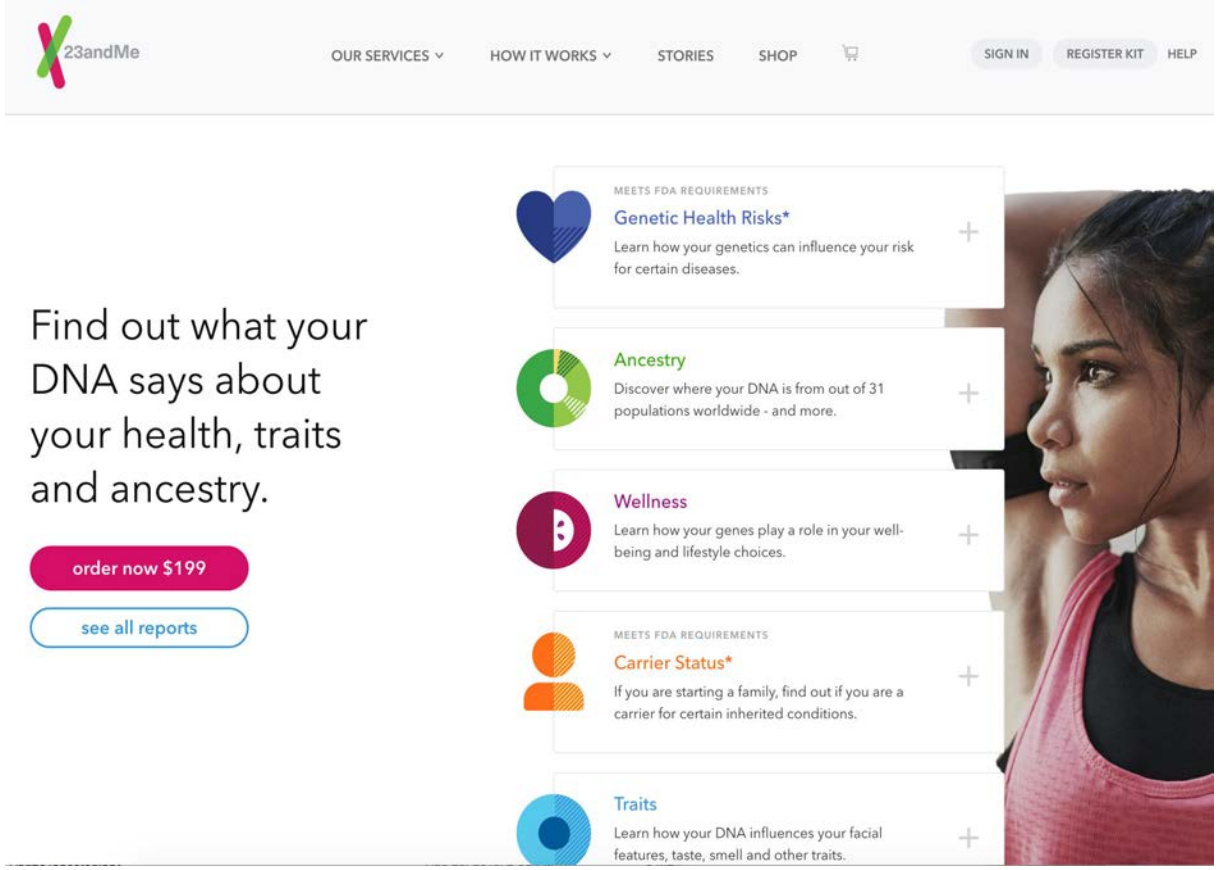


Angelina Jolie underwent a preventive double mastectomy.

LOS ANGELES

MY MOTHER fought cancer for almost a decade and died at 56. She held out long enough to meet the first of her grandchildren and to hold them in her arms. But my other children will never have the chance to know her and experience how loving and gracious she was.

We often speak of "Mommy's mommy," and I find myself trying to explain the illness that took her away from us. They have asked if the same could happen to me. I have always told them not to worry, but the



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Even "simple" genetic effects are not so simple

In 2015, she had a new scare– she had to decide on more surgeries….

"I did not do this solely because I carry the BRCA1 gene mutation, and I want other women to hear this."

She gathered <u>more biological information (Links between G and P)</u>

- **Inflammatory protein markers were high- linked to additional cancers**

In her case- Her mother, aunt and grandmother died of cancer (mother of ovarian cancer)… why is this family history important?
<u>More G2P information</u>

So she decided to have her ovaries and fallopian tubes removed immediately even though this would have major effects on her life..

She ends with "Knowledge is power"

Our hypothesis is this will be true for Agriculture as well!

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Albinism in Native American tribes: an example of environment (culture) changing a population's phenotype..

- Albinism rare in the world (1/20,000)- rare mutation that has poor health phenotype- sun sensitive, eye problems
- But incidence of albinism is 100x higher in the Hopi's ??
- Albino people are valued and given <u>special treatment in Hopi society- less work in the fields, no sun exposure</u>
  - This treatment decreases negative impacts
  - may increase the chance of passing on the allele ☺
- Example of artificial selection in human society

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Questions for Discussion in small groups

1. **Name a simple trait and a complex trait**
2. **What are the differences between traits with "simple" genetics from those with "complex" genetics?**
3. **How can we use genetics to predict a future phenotype in a plant or animal?**
4. **How can we change phenotypes?**