SISG 2022 - Module 2

Introduction to Genetics and Genomics

What is a gene?

11:20am EDT, Monday, July 11th

Joe Lachance and Greg Gibson

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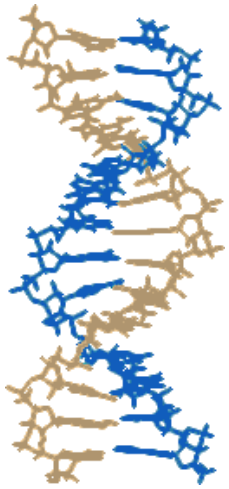


Instructors

Greg Gibson

Joe Lachance

Georgia Institute of Technology

Date	Time (PDT)	Time (EDT)	Topic	Instructor
Monday, July 11	8:00 – 8:20	11:00 – 11:20	Introductions	
	8:20 – 9:05	11:20 – 12:05	What is a Gene ?	JL
	9:05– 9:20	12:05 – 12:20	Break	
	9:20 – 10:15	12:20 – 1:15	Heritability	GG
	10:15 – 10:45	1:15 – 1:45	Q&A Discussions	
Monday, July 11	11:45 – 12:45	2:45 – 3:45	Quantitative Genetics	GG
	12:45 – 1:00	3:45 – 4:00	Break	
	1:00 – 2:00	4:00 – 5:00	Molecular Biology	JL
	2:00 – 2:30	5:00 – 5:30	Q&A Discussions	
Tuesday, July 12	8:00 – 9:00	11:00 – 12:00	Genome-Wide Association Studies	GG
	9:00 – 9:15	12:00 – 12:15	Break	
	9:15 – 10:15	12:15 – 1:15	Molecular Evolution	JL
	10:15 – 10:45	1:15 – 1:45	Q&A Discussions	
Tuesday, July 12	11:45 – 12:45	2:45 – 3:45	Gene Expression Profiling	GG
	12:45 – 1:00	3:45 – 4:00	Break	
	1:00 – 2:00	4:00 – 5:00	Population Genetics	JL
	2:00 – 2:30	5:00 – 5:30	Q&A Discussions	
Wednesday, July 13	8:00 – 9:00	11:00 – 12:00	Genomic Medicine	GG
	9:00 – 9:15	12:00 – 12:15	Break	
	9:15 – 10:15	12:15 – 1:15	Genetic Ancestry	JL
	10:15 – 10:45	1:15 – 1:45	Q&A Discussions	

Format

- Lectures will be recorded and posted online. Please remind us we accidentally forget to hit the record button on Zoom!
- Student microphones will be muted during each lecture, but please use the chat feature – the more questions you ask, the more you will learn
- Every few minutes we check to see if there are any questions in chat
- After each block of lectures, we will form small breakout rooms so that classmates can get to know each other via chat or video
- We will also hold open question and answer sessions (these informal "office hours" will not be recorded)

What is a gene?

- How would you define a gene?

- Which matters more, structure or function?

Terminology

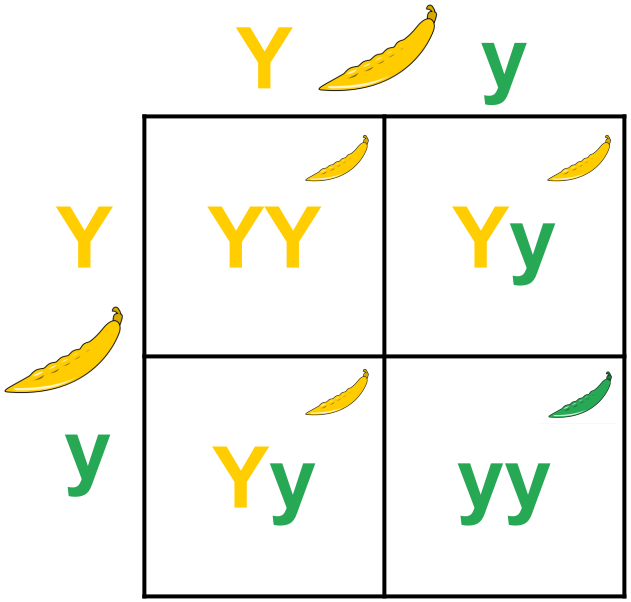
- **Genes**: DNA sequences that encode a functional protein or RNA molecule
- **Allele:** one of two or more alternative forms of a gene
- **Genotype:** the genetic makeup of an individual
- **Phenotype:** the observable characteristics and traits of an organism
- **Genome**: the complete set of genetic material in a cell or organism
- **Haplotype**: closely linked DNA sequencies on the same chromosome that are co-inherited

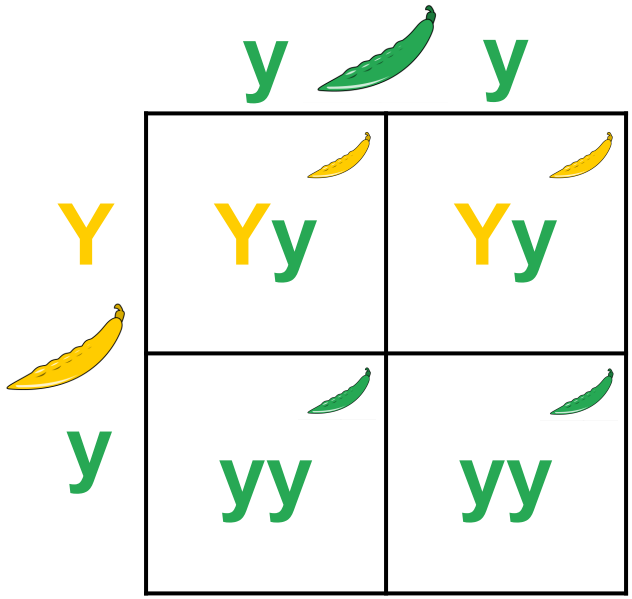
Mendel's laws of inheritance

- Law of segregation (1st law)
  - Parental pairs of alleles separate during gamete formation
- Law of independent assortment (2nd law)
  - Pairs of alleles for different traits segregate independently
- Law of dominance (3rd law)
  - Heterozygotes manifest the trait associated with the dominant allele
- *These rules are often broken!*

Image source: Wikipedia

Mendelian ratios

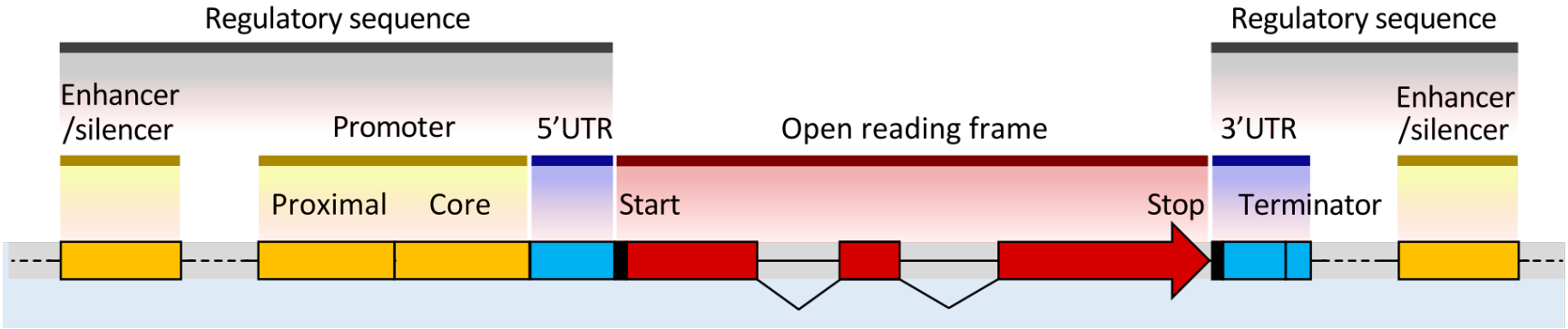




- Punnett squares can be used to predict the products of breeding
- Genetics is not always this simple!

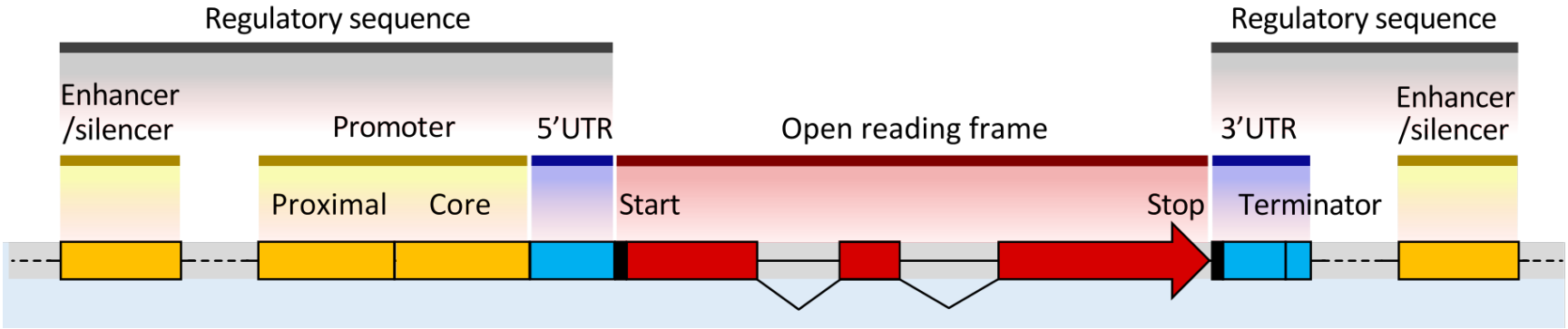
	Prokaryotes	Eukaryotes
Internal structures	No organelles	Organelles
DNA	Circular No introns DNA in cytoplasm	Linear Introns DNA in nucleus
Genome size	Tend to be < 5Mb	10Mb-100,000Mb
Chromatin	No histones	Histones
Ploidy	Haploid	Usually diploid
Reproduction	Asexual (binary fission)	Asexual (mitosis) and sexual (meiosis)

The structure of (protein coding) genes



- Exons: nucleotide sequence not removed by splicing (coding DNA)
- Introns: nucleotide sequence removed by splicing (noncoding DNA)
- Cis-regulatory elements
  - Enhancers: increase the likelihood of transcription when bound to activators
  - Silencers: decrease likelihood of transcription when bound to repressors
  - Promoters: region of DNA where transcription is initiated
- UTRs: untranslated regions

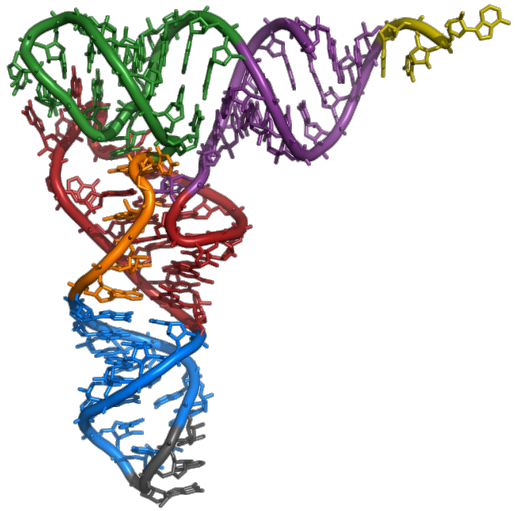
The structure of (protein coding) genes



- Which parts would you consider to be part of a gene?

RNA genes

- DNA sequences which encode function non-coding RNA are called RNA genes
- Transfer RNAs (tRNAs)
- Ribosomal RNAs (rRNAs)



- Different types of small RNAs (e.g., microRNAs, siRNAs)

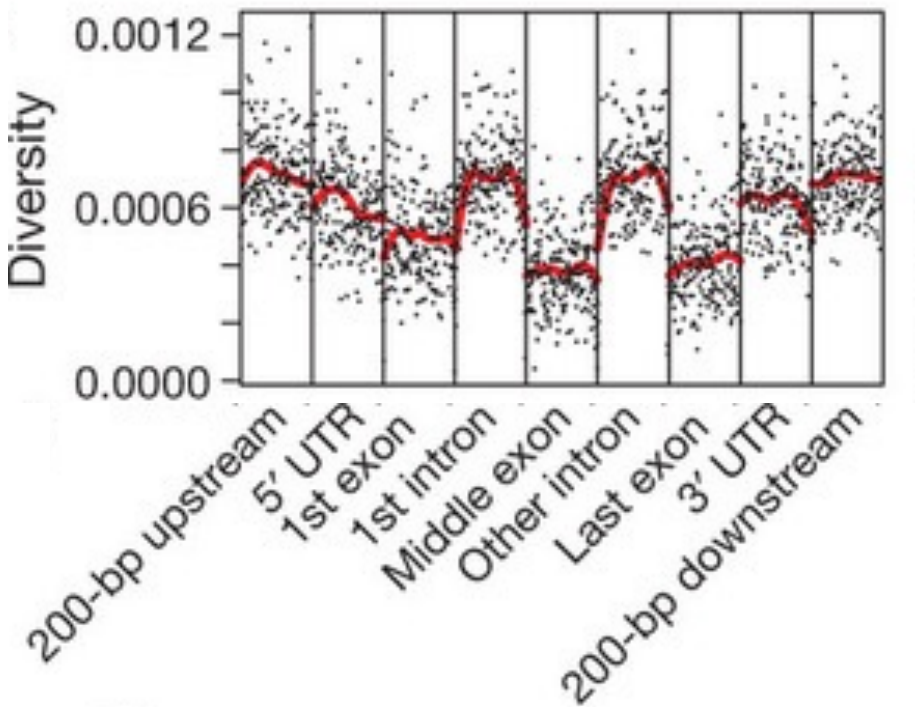
The locus of evolution

- What sort of genetic changes underlie morphological adaptations?

- Hopi Hoekstra and Jerry Coyne
  - Protein-coding DNA matters

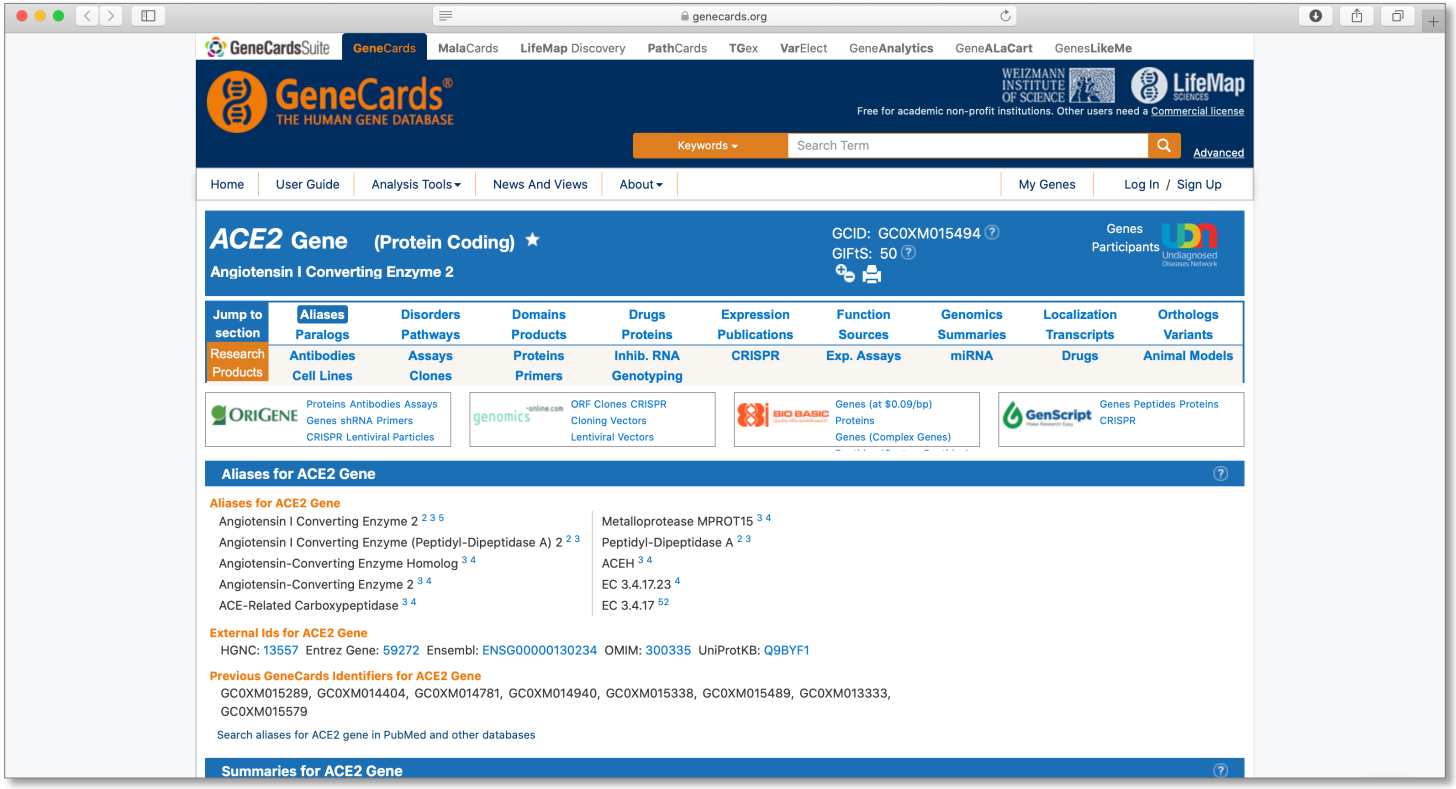
- Sean Carroll
  - It's all about regulatory DNA

Polymorphism near genes



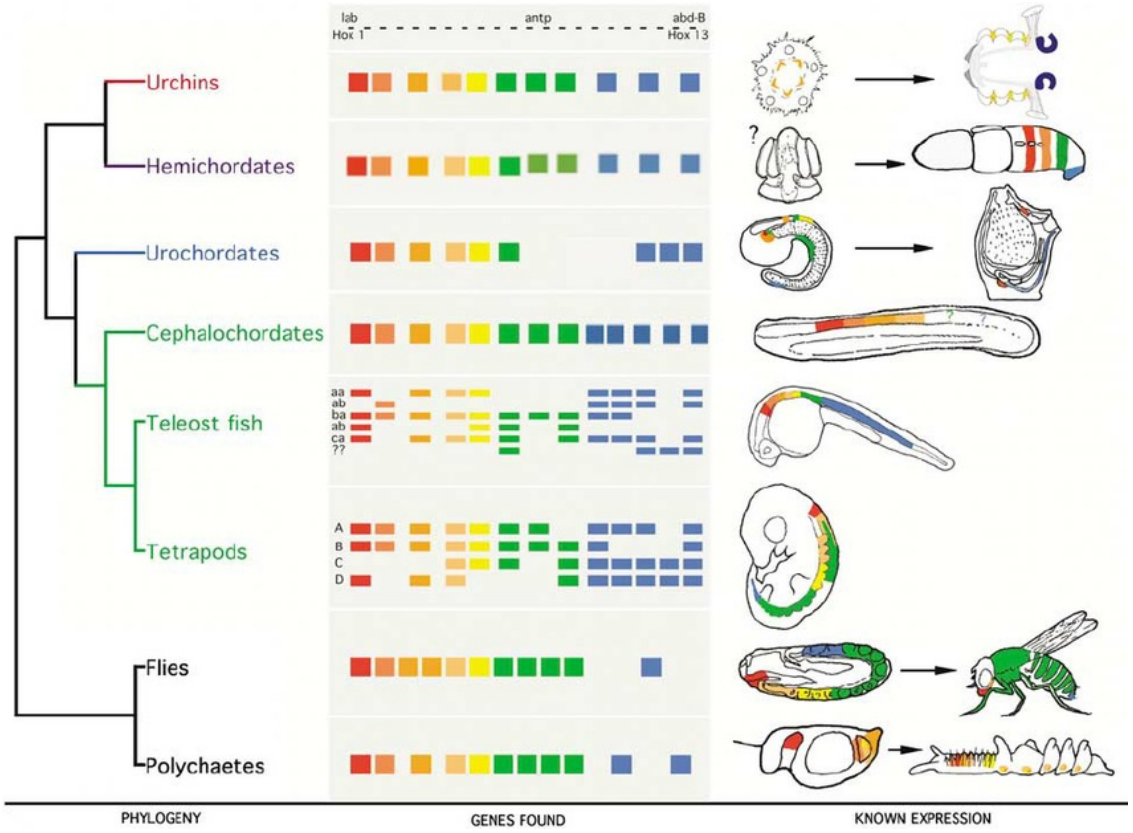
- Exons contain less genetic variation than non-coding DNA

GeneCards



- How to find more information about a particular gene?
- https://www.genecards.org

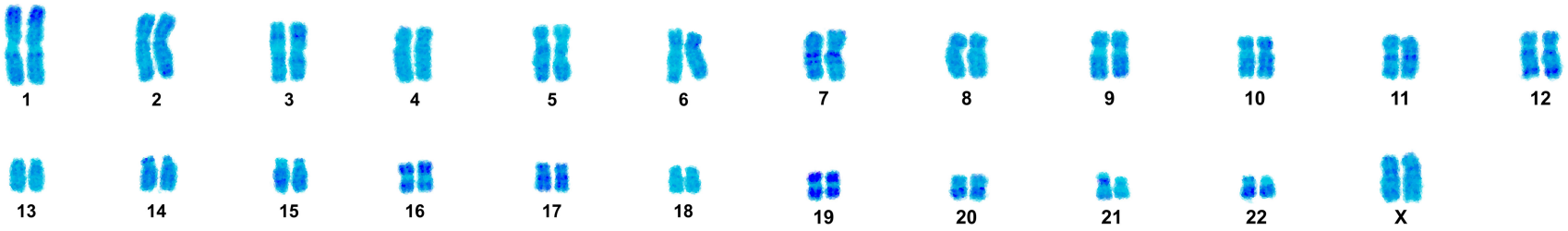
Different species share many of the same genes



- Homologous genes are two or more genes that descend from a common ancestral DNA sequences

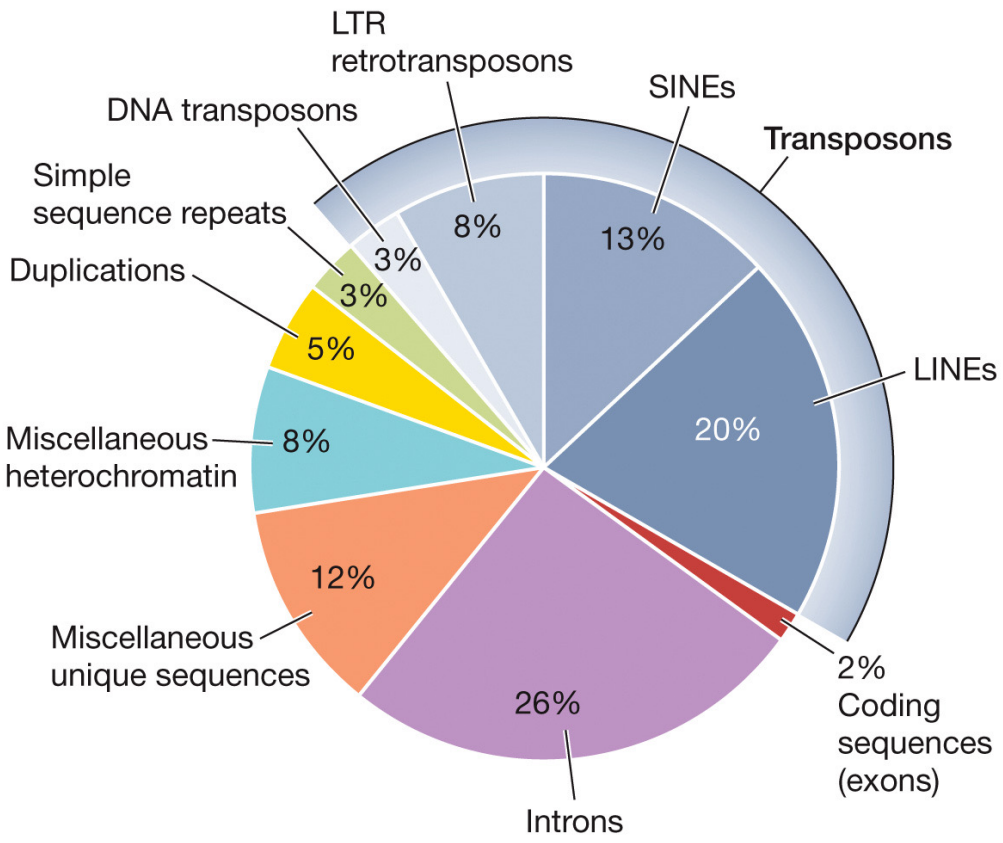
Figure from Swalla (*Heredity*, 2006)

Genes do not exist in isolation



- Genes are found on chromosomes
- DNA sequences that are close together on the same chromosome tend to be inherited together (**linkage**)
- Genes can interact with other genes (**epistasis**)

Genomic fractions



EVOLUTION 4e, Figure 14.14

- Most of the human genome is non-coding
- Transposons (selfish DNA) make up a large % of the human genome

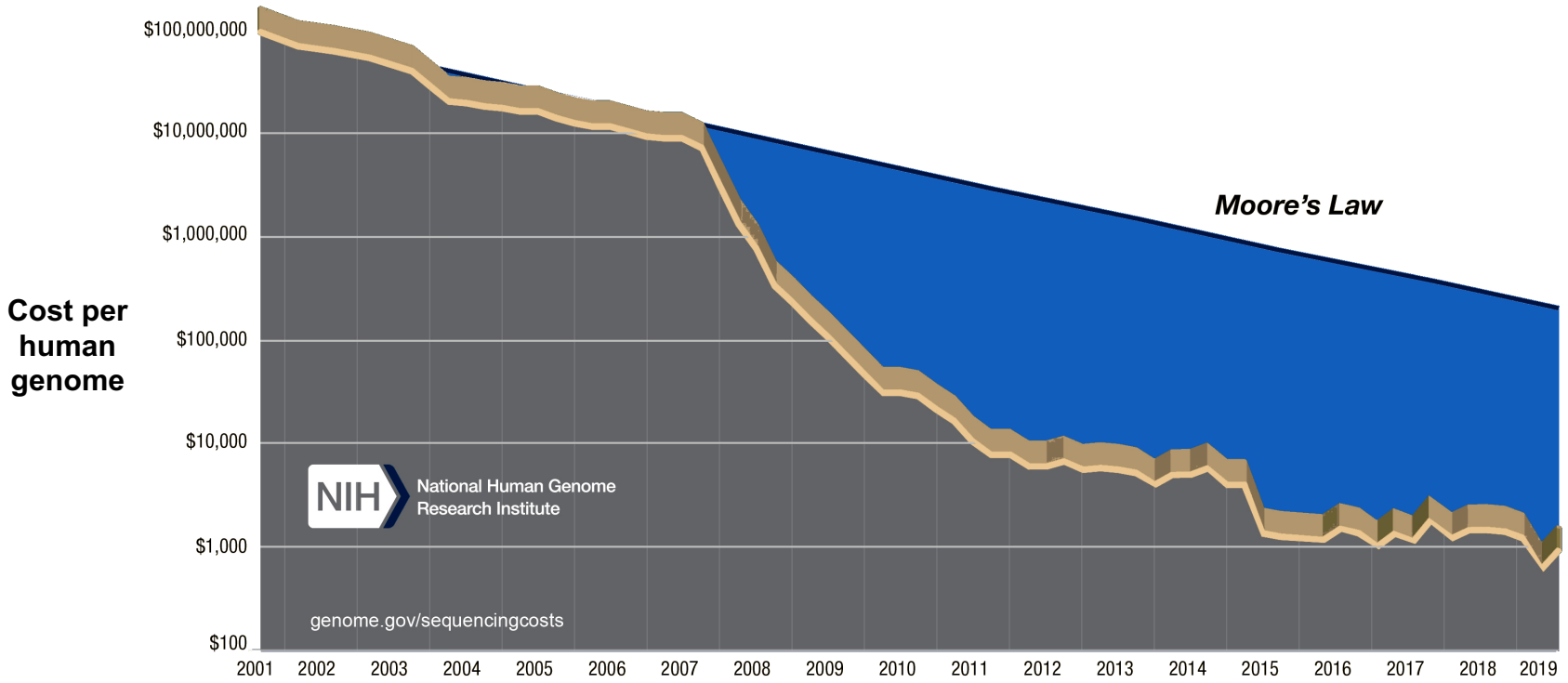
Whole genome sequencing (WGS)

- WGS is sometimes called next-generation sequencing
- Depth of coverage: average number of reads per base pair in a genome (low coverage = 5-10X, high coverage: >30X)
- One error per 100,000 base pairs (high coverage)
- Relatively expensive, but getting cheaper

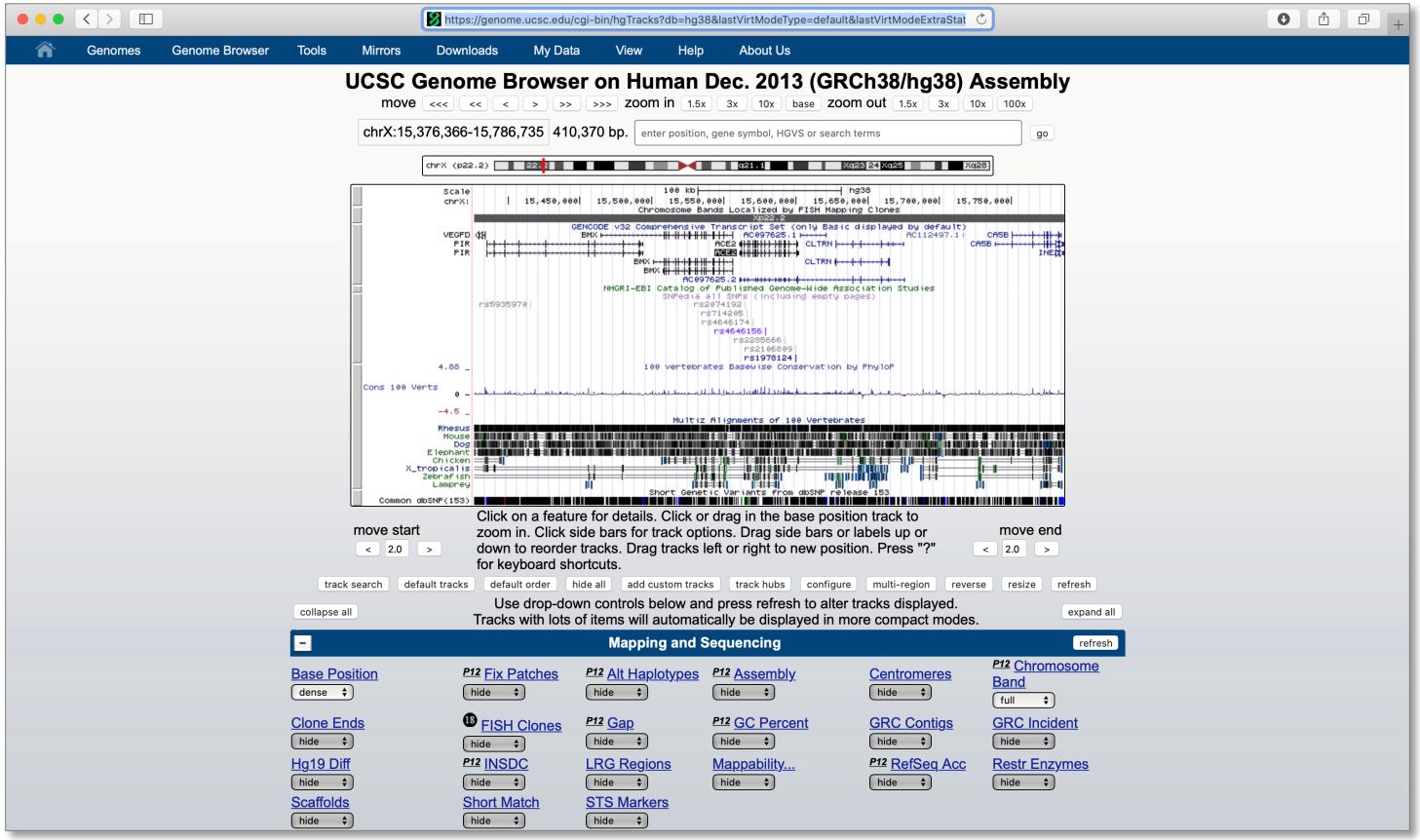
NovaSeq 6000

illumina

Declining sequencing costs



UCSC Genome Browser



- An online resource for exploring the human genome
- https://genome.ucsc.edu

Environmental context matters

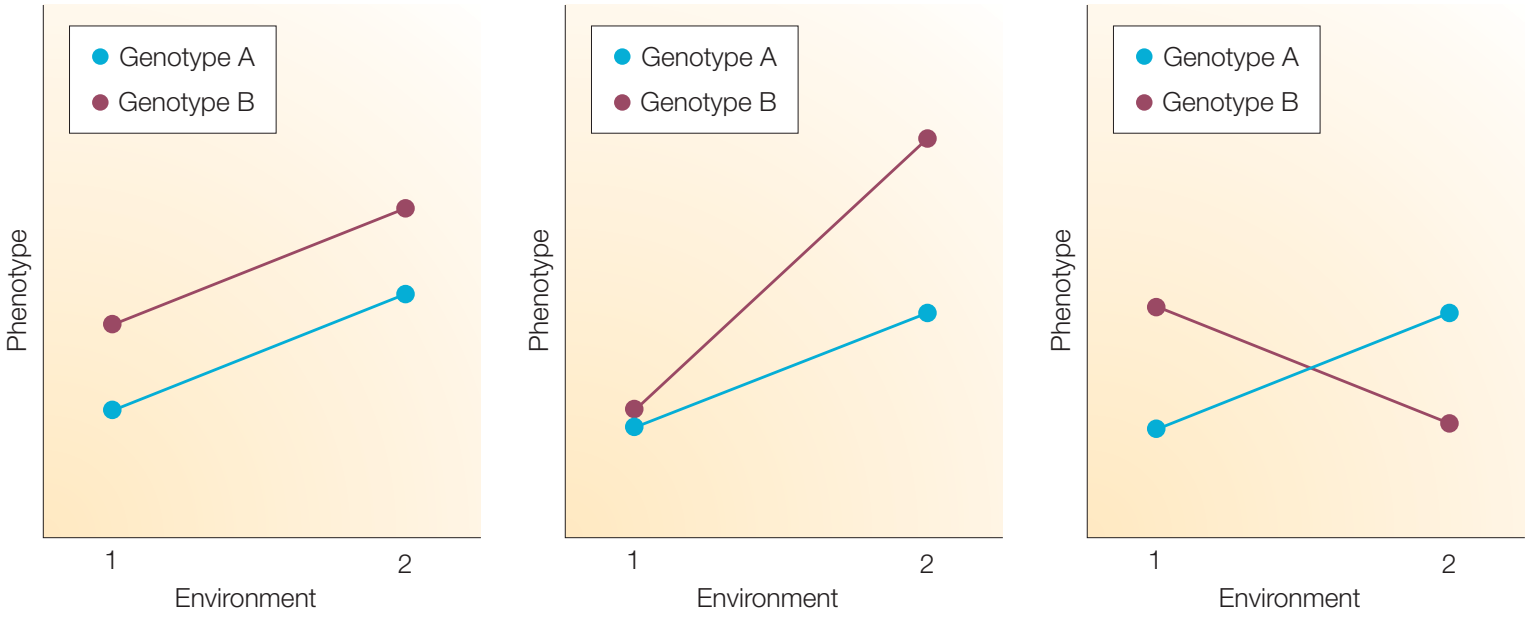
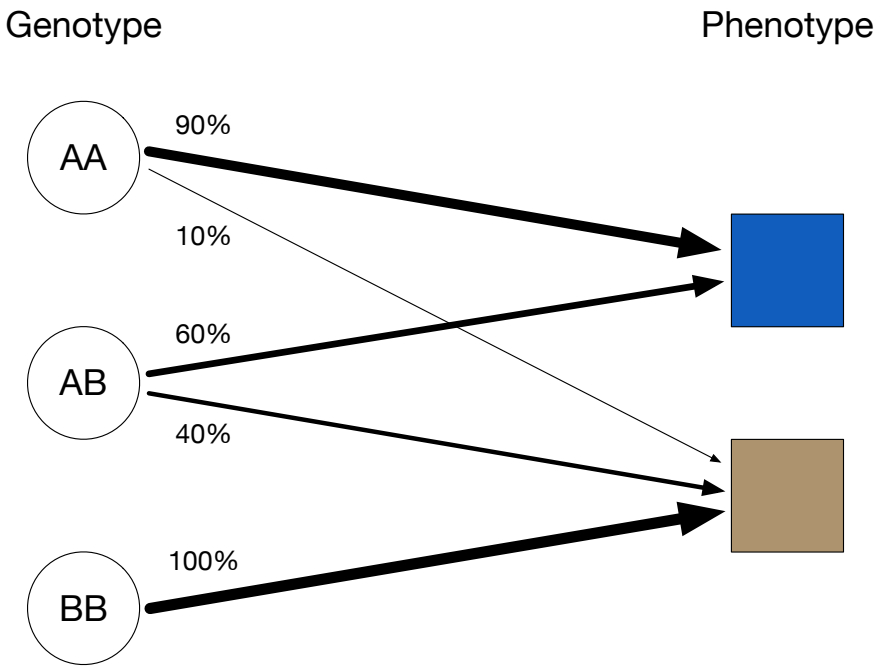


Image from Anholt and Mackay (*Nature Reviews Genetics*, 2004)

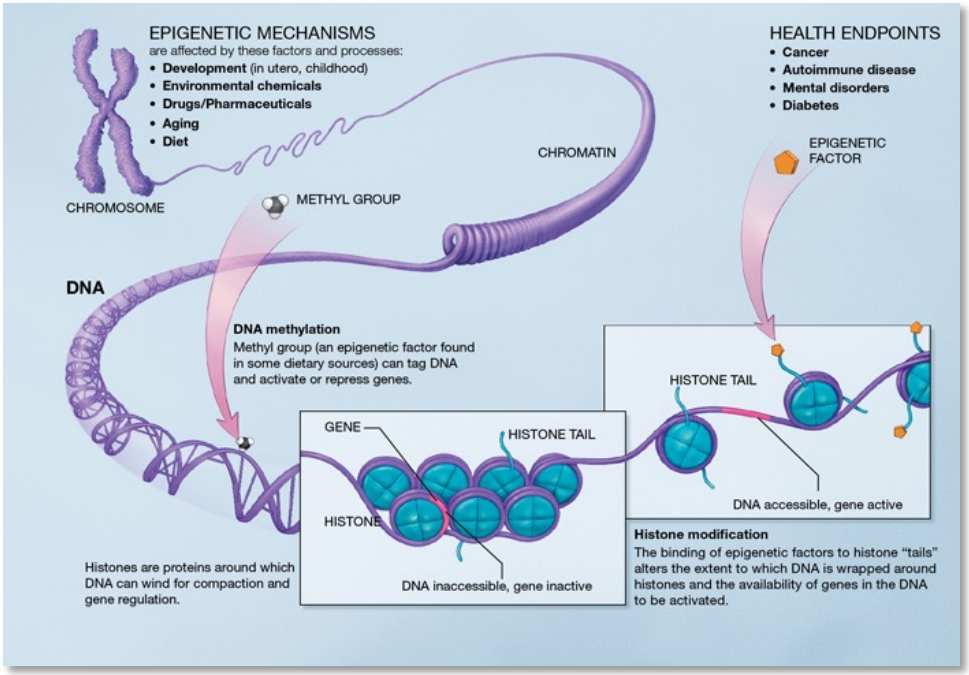
Incomplete penetrance



- Genotype-phenotype maps are not always one-to-one (e.g., some alleles increase your chances of getting hypertension)
- **Penetrance** refers to the proportion of individuals with a given genotype that show the expected phenotype

Epigenetics

- DNA methylation (methylated CpGs)
- Histone modification
- X-inactivation
- Genomic imprinting



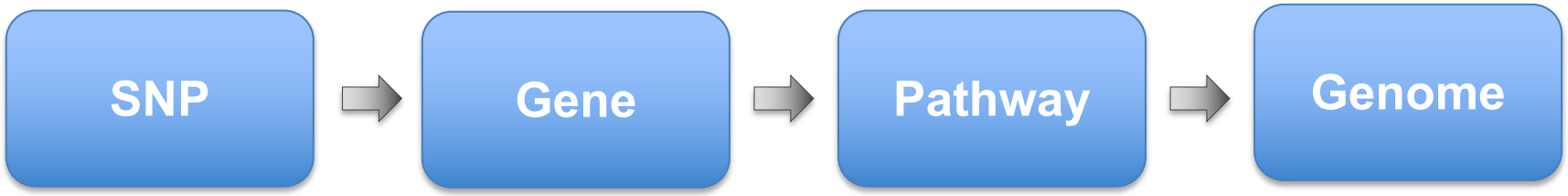
- Different people have different epigenetic marks
- Most of these epigenetic marks are erased each generation

Image from Wikipedia

Pleiotropy

- Be careful to avoid terminology like "cancer gene" or "height gene"
- This is because genes often contribute to multiple phenotypes (i.e., they are **pleiotropic**)
- Example: A mutation in the *Frizzle* gene results in feathers that curve outward, fewer eggs laid, and high body temperatures

Units of analysis in genetics



- Genetic data be analyzed on **population** as well as **individual** scales

- Sometimes we are more focused on **traits**...