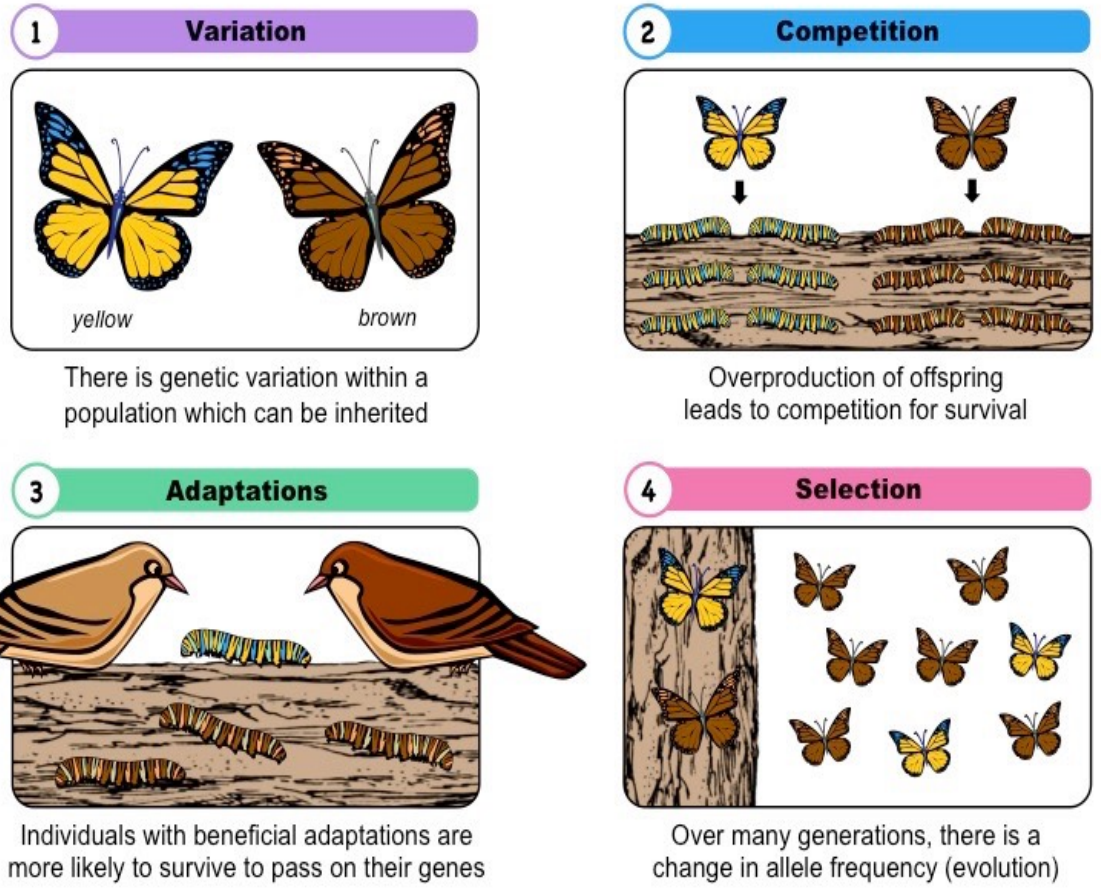
Population Genetics

Genetic Influence

Natural Selection Review

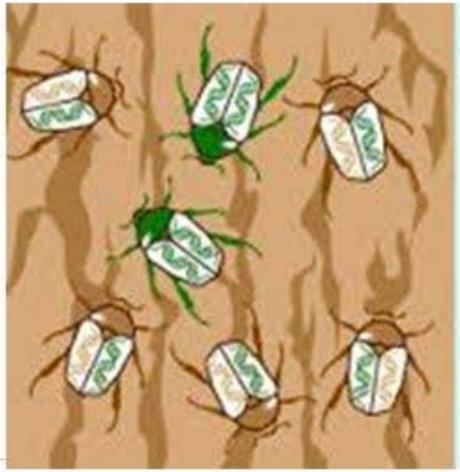
- Population
- Variation
- Time
- Survive
- Reproduce

Adaptation



Microevolution

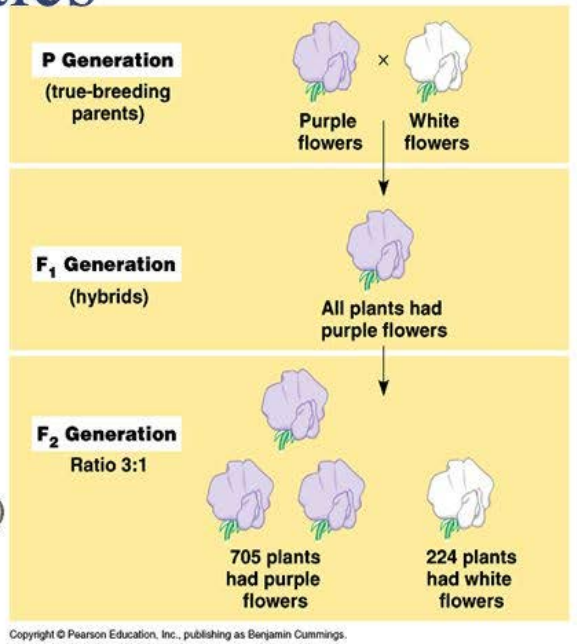
- The generation-to-generation change in frequencies of alleles within a population is called **microevolution**. Its evolution on the smallest scale.
- Mechanisms of microevolution:
  - Natural Selection
  - Sexual Selection
  - Artificial Selection
  - Genetic Drift
  - Gene Flow



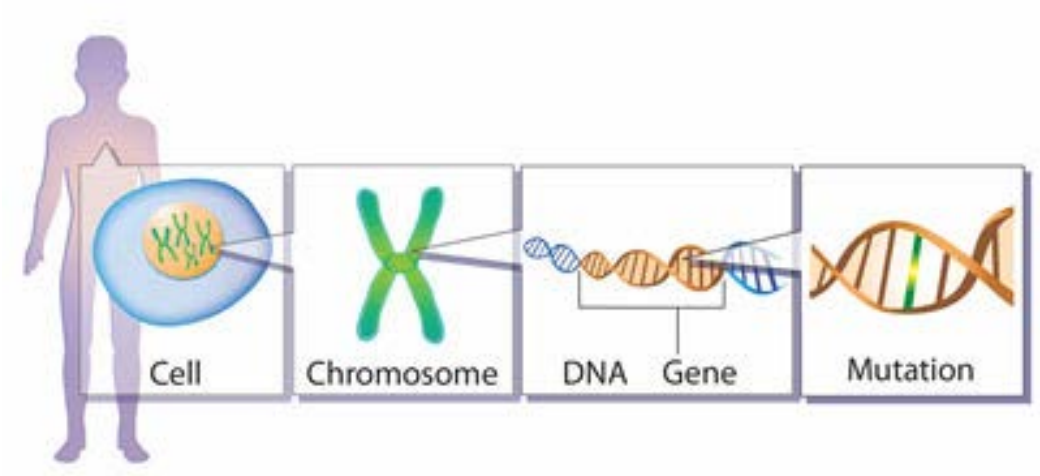
Gregor Mendel

Mendelian genetics

- **Character**
  (heritable feature, i.e., fur color)
- **Trait**
  (variant for a character, i.e., brown)
- **True-bred**
  (all offspring of same variety)
- **Hybridization**
  (crossing of 2 different true-breds)
- **P generation** (parents)
- **F1 generation** (first filial generation)

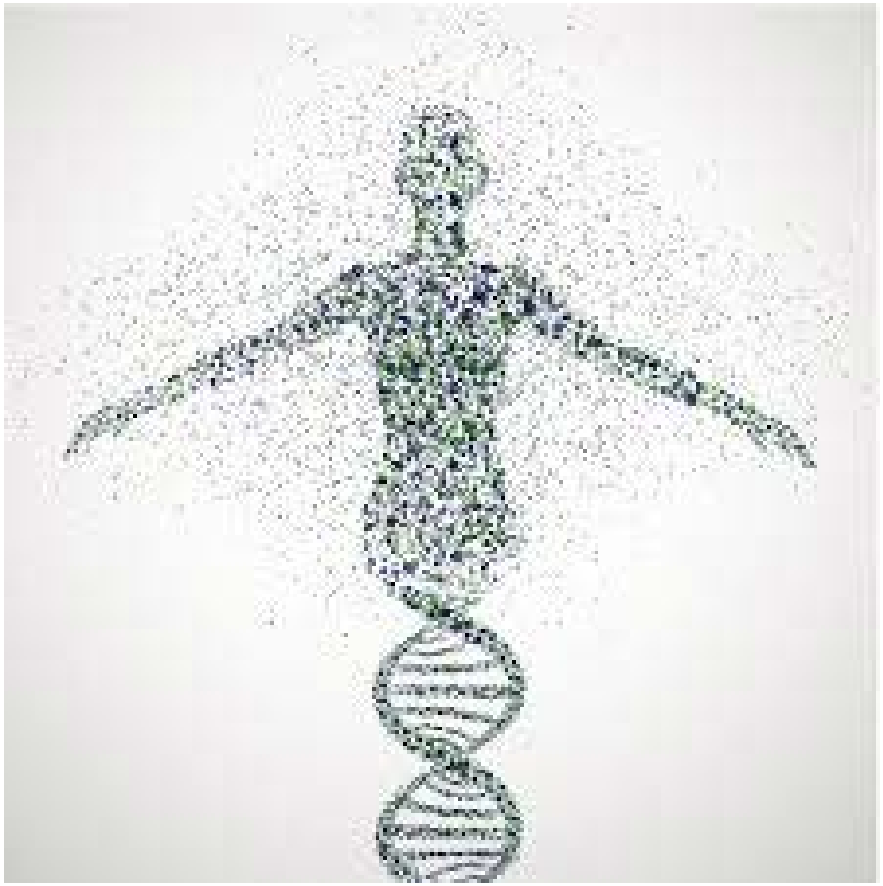


What does inheritance mean?



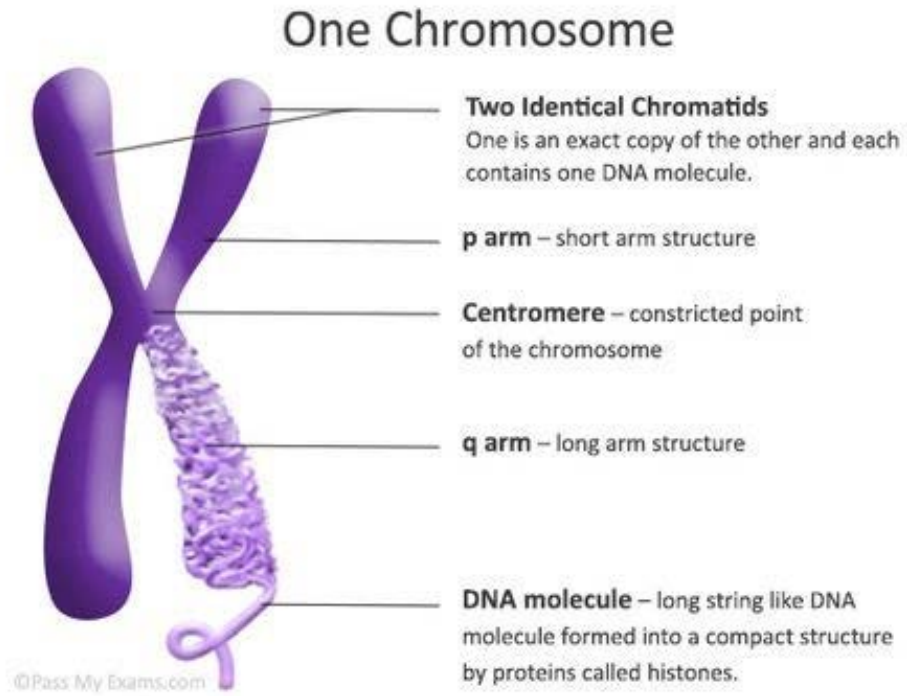
Genomics

- Chromosome Structure
- DNA
- Genes
  - Variation
  - Expression
- Central Dogma
- Human Genome Project
- Applications
- Current Research
- Epigenetics
- What Next

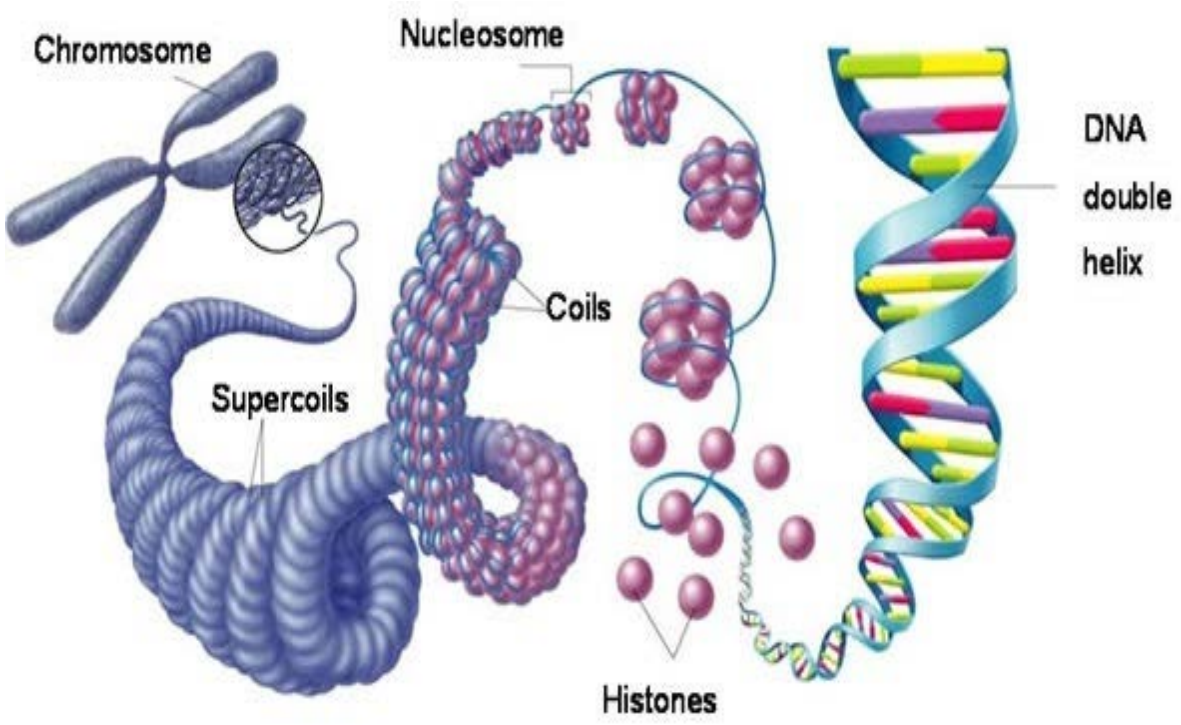


Chromosome

- Karyotyping
- Structure
- Number
- Bands
- Location
- Processes
- Problems



DNA



- Location
- Structure
- Base Pair
- Replication
- Protein Synthesis
- Regions
  - Exons
  - Introns
  - Transposons
  - Telomeres

Human Genome Project (HGP)

What were the goals of the Human Genome Project

- Project goals were to
- *Identify* all the approximately 20,000-25,000 genes in human DNA,
- *Determine* the sequences of the 3 billion chemical base pairs that make up human DNA,
- *Store* this information in databases,
- *Improve* tools for data analysis,
- *Transfer* related technologies to the private sector, and
- *Address* the ethical, legal, and social issues (ELSI) that may arise from the project.
- The Project also
- aimed to sequence the genomes of several other organisms that are important to medical research, such as the mouse and the fruit fly.

Benefits of Human Genome Project research

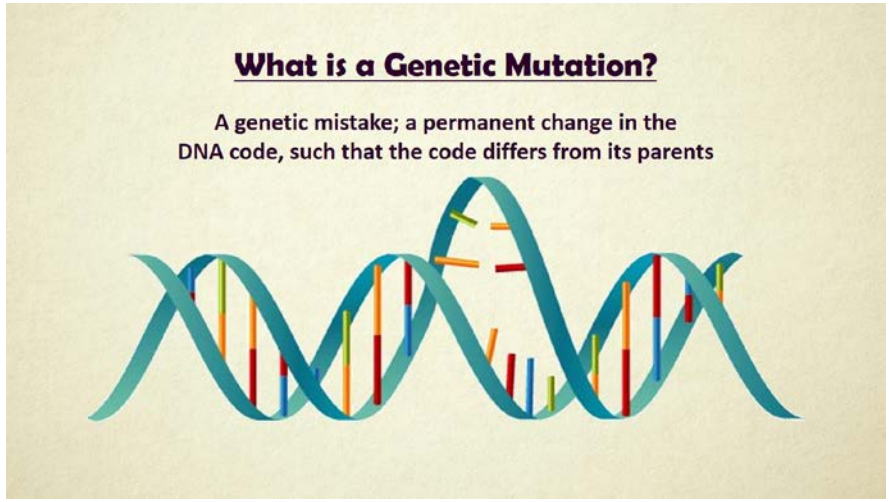
- improvements in medicine.
- microbial genome research for fuel and environmental cleanup.
- DNA forensics.
- improved agriculture and livestock.
- better understanding of evolution and human migration.
- more accurate risk assessment.

www.sliderbase.com

International Research Effort

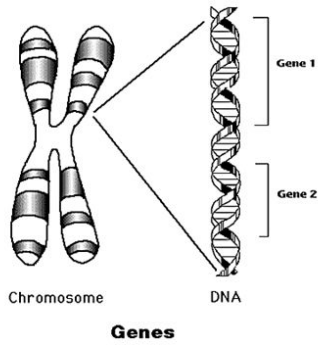
Mutations

- Define
- Organism involved
  - Eukaroyotes: Plants, Animals
  - Prokaryotes: Bacteria vs. Virus
- Chromosomes involved
- Causes
- Rate
- Chromosome changes
- End Results
  - =
  - +
  - -

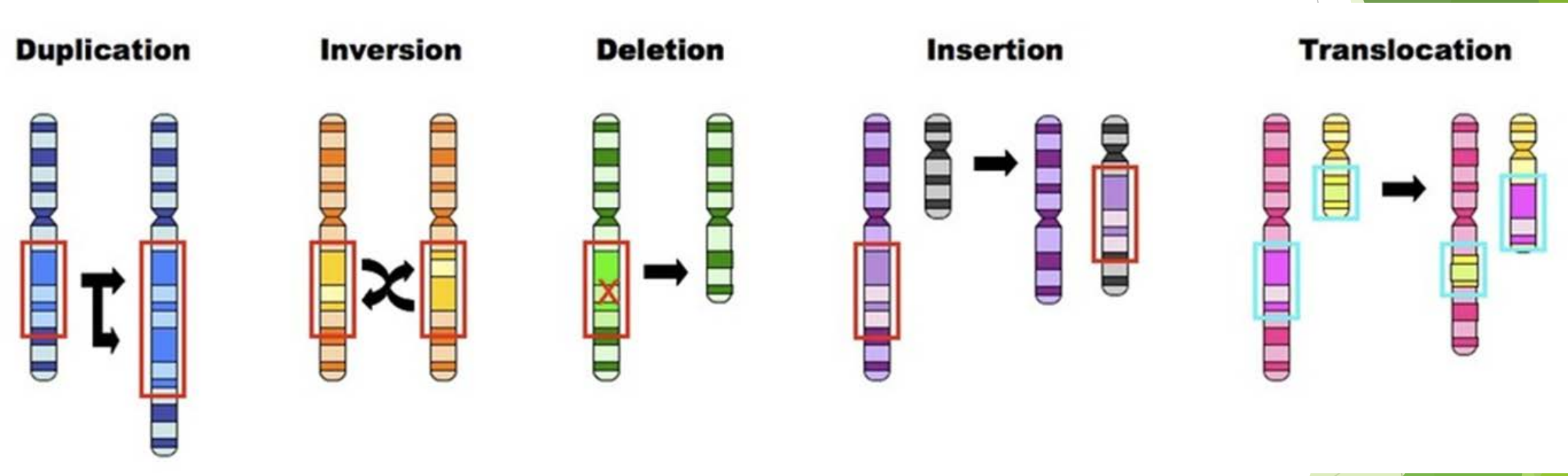


Mutations …

- are changes in the genetic material
- can be good or bad
- can be on a single gene or the whole chromosome



Mutation Types

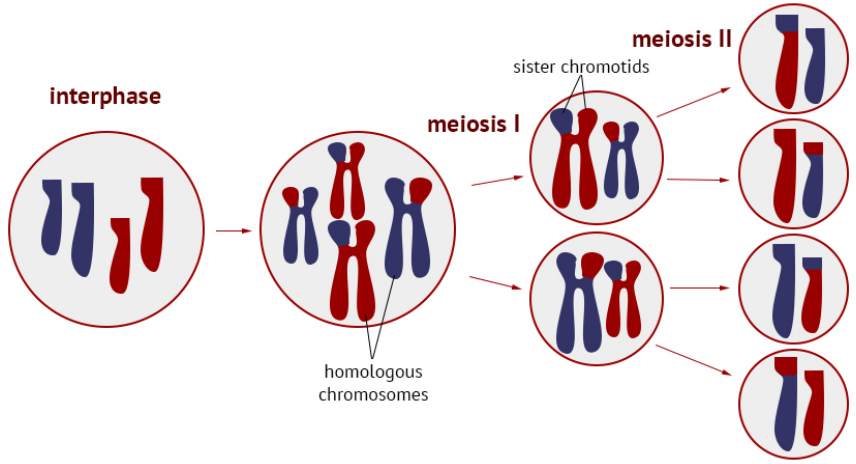


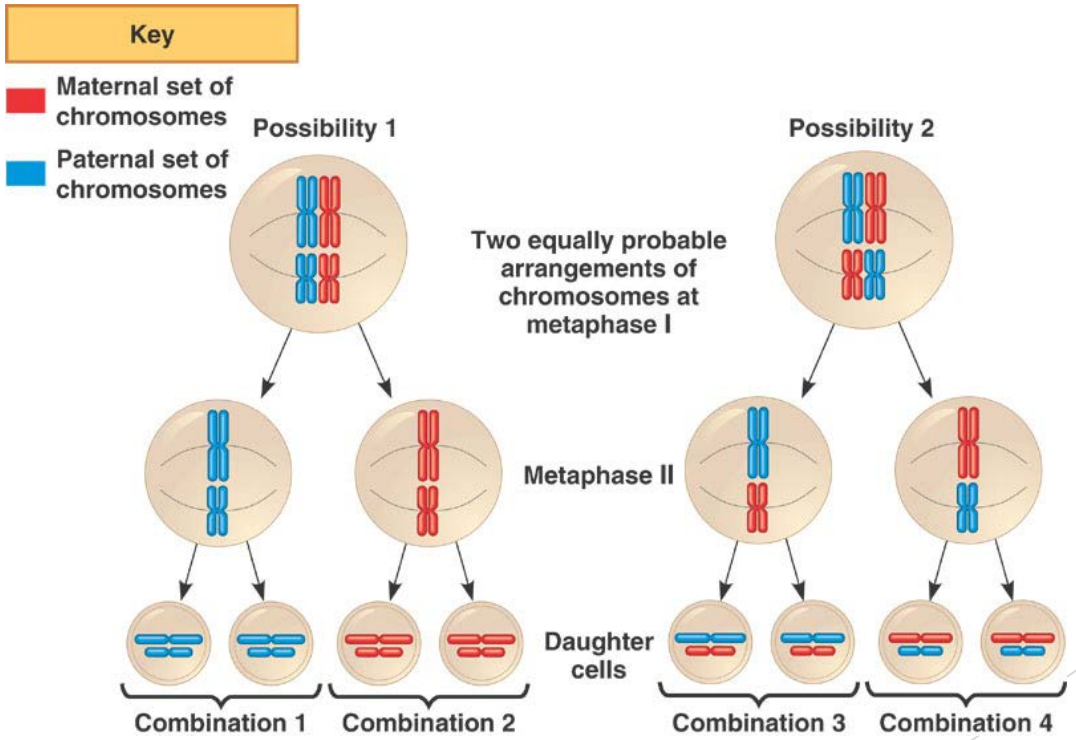
Reproductive Changes

Crossing Over

Independent Assortment

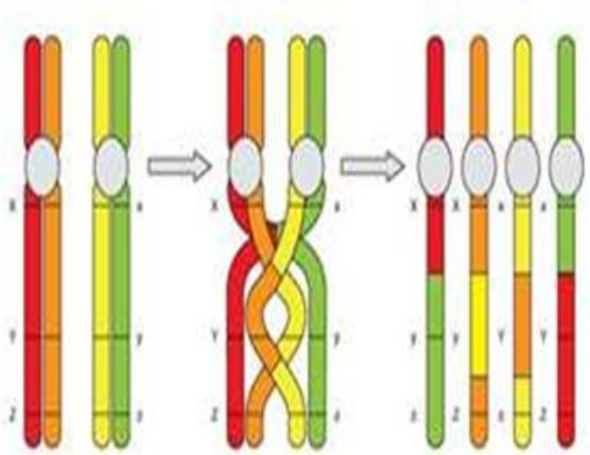
Fertilization





Significance of Meiosis:

- Genetic Variation caused by the possible combinations of chromosomes during "Crossing Over" in Meiosis 1.
- Crossing over increase genetic diversity as the genes on the chromosomes combine in number of ways.



- An alteration in the DNA structure during meiosis cause mutations.
- In most cases mutations are maladaptive and the new cell dies.
- A small number of mutations are viable ----- the cell survives. If the mutant gamete combines with another gamete to produce an offspring ---- the mutation can be passed to the next generation.

Structural vs. Numeric

Variation

- Define term
- Genetic
  - Homozygous %
  - Heterozygous %
  - Examples
    - Gene
    - Nucleotide
- Geographic
  - Environment
  - Isolation

Data Sets

Table 1.1 Examples of types of data	
Quantitative	
Continuous	**Discrete**
Blood pressure, height, weight, age	Number of children Number of attacks of asthma per week
Categorical Qualitative	
Ordinal (Ordered categories)	**Nominal (Unordered categories)**
Grade of breast cancer Better, same, worse Disagree, neutral, agree	Sex (male/female) Alive or dead Blood group O, A, B, AB

Genetic Variation

Discrete Characters

- Differences in a defined form
- One characteristic
- Have trait or not (either / or)
- Single gene, different phenotypes
  - examples

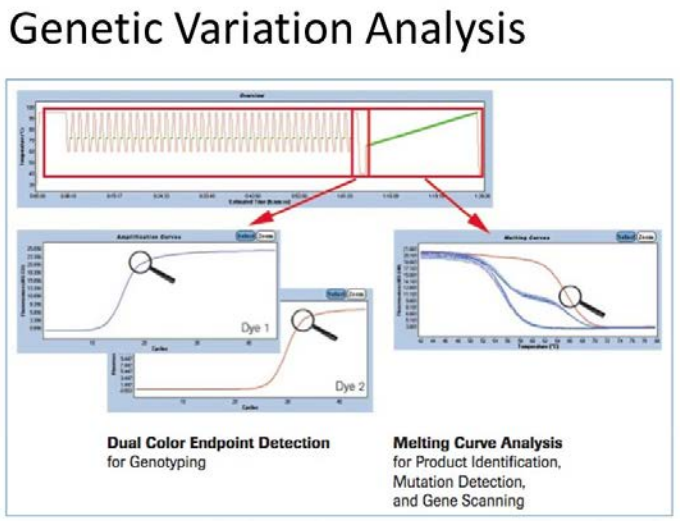
Quantitative Characters

- Differences in range of forms
- Not one or the other
- Influences of several genes on a characteristic
  - examples

Determining variations

Gene

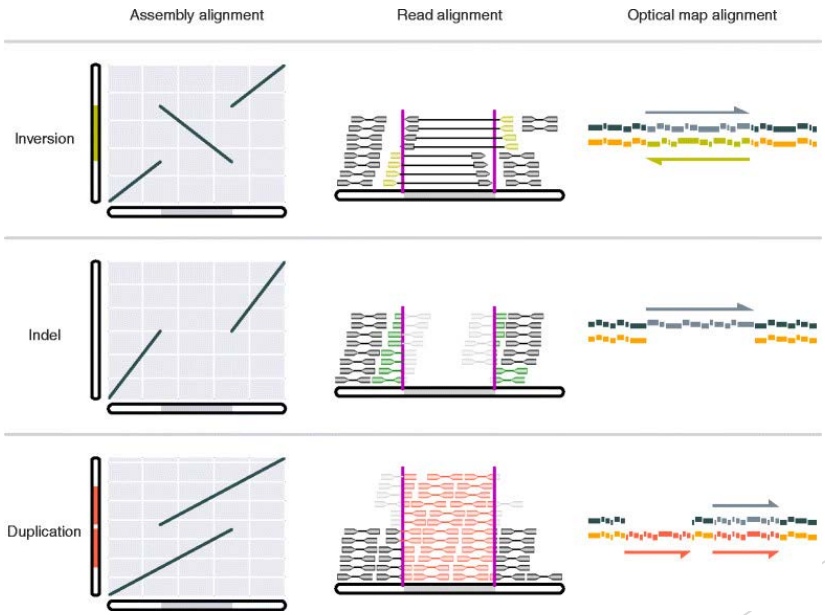
- PCR



Different genotyping methods analyze fluorescent signals from different parts of a Real-Time PCR run.

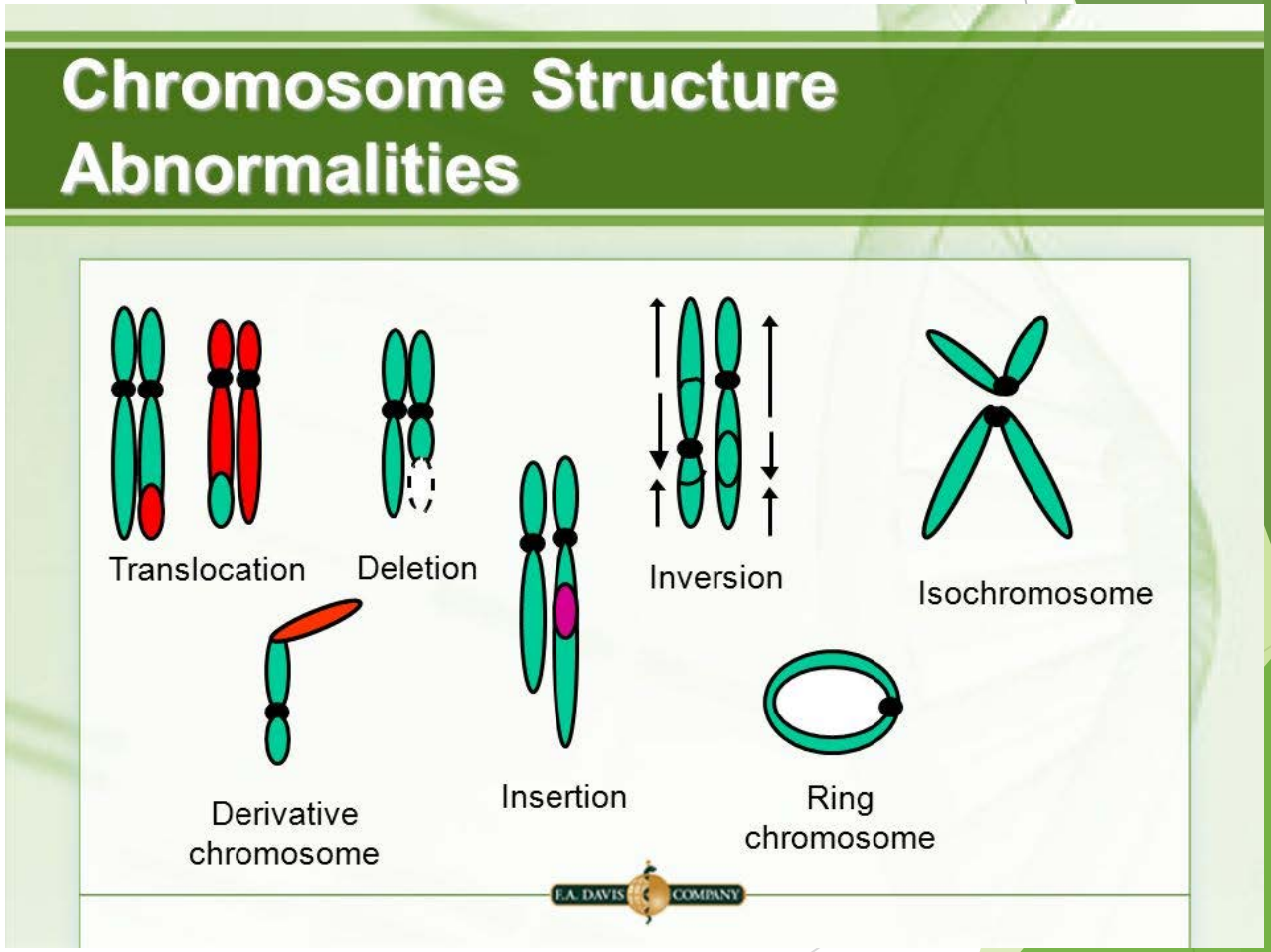
Nucleotide

- DNA sequencing



Genomic *Evolution*

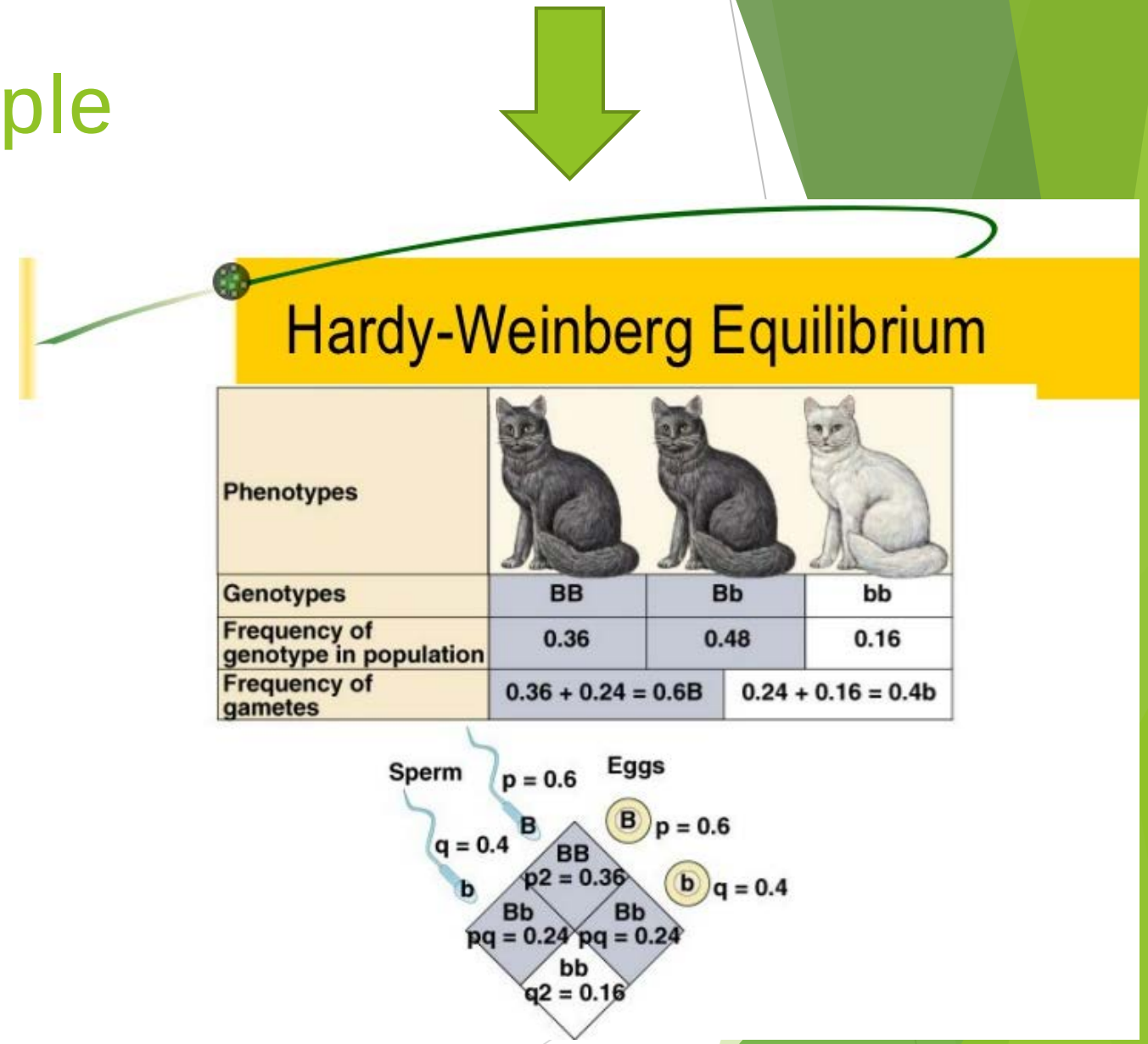
- Comparative Analysis
  - Shared characteristics
  - Explains Divergence
  - Phenotype differences
- Mutations
  - Define
  - Types
  - Results (=, -, +)
- Meiosis Mistakes
  - Duplication
  - Inversions
  - Breaks



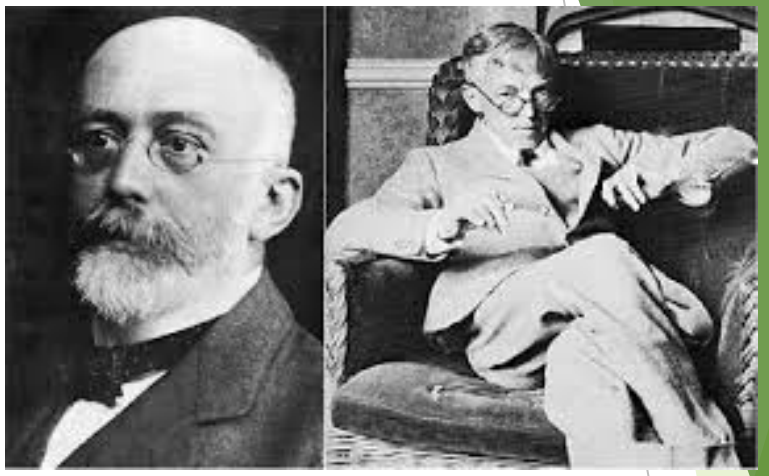
Hardy-Weinberg Principle

- Population
- Allele/Gene frequency
- Constant
- No influences

		Females	
		A (p)	a (q)
Males	A (p)	AA (p2)	Aa (pq)
	a (q)	Aa (pq)	Aa (q2)



H-W Equilibrium

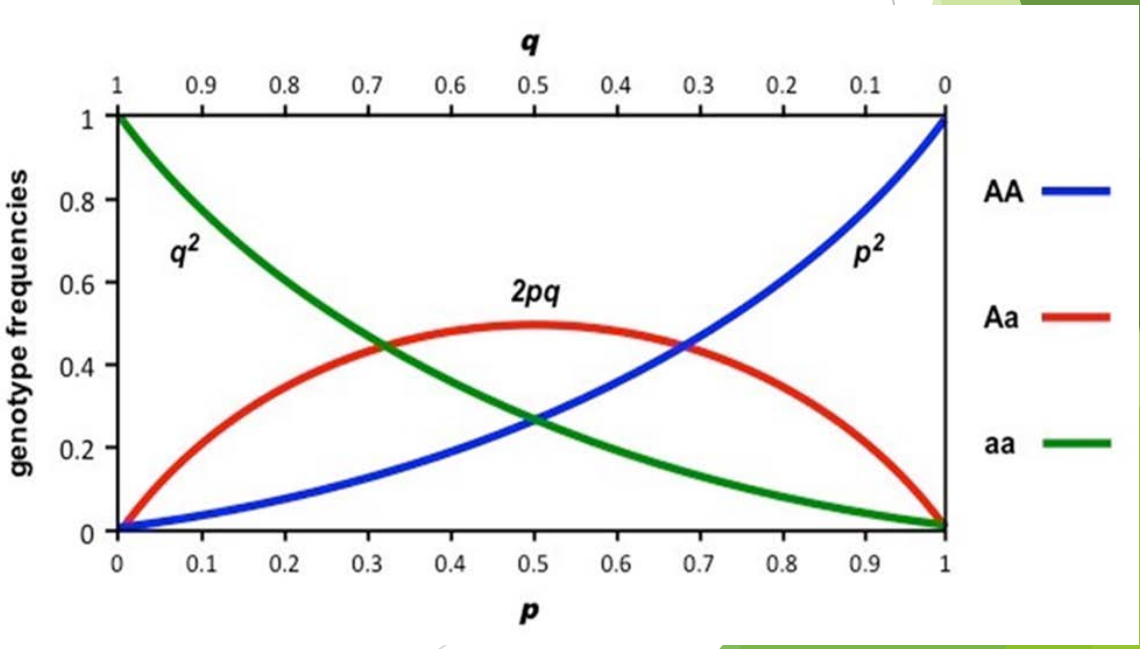


Hardy-Weinberg Principle

The original proportion of genotypes in a population remains constant

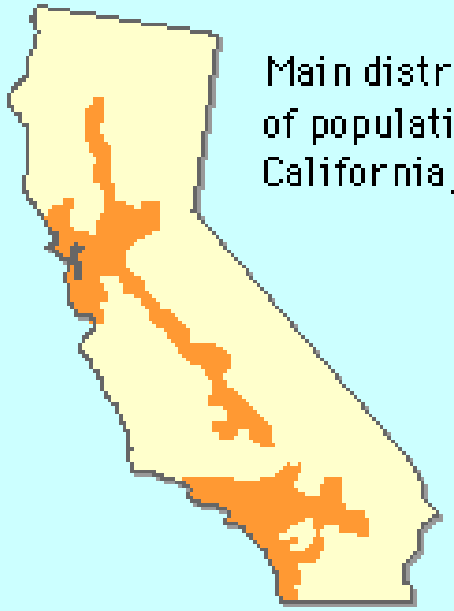
if

- population size is large
- random mating is occurring
- no mutations
- no genes are introduced or lost
- no selection occurs
  - means: all genotypes can survive and reproduce equally well



Large Breeding Population

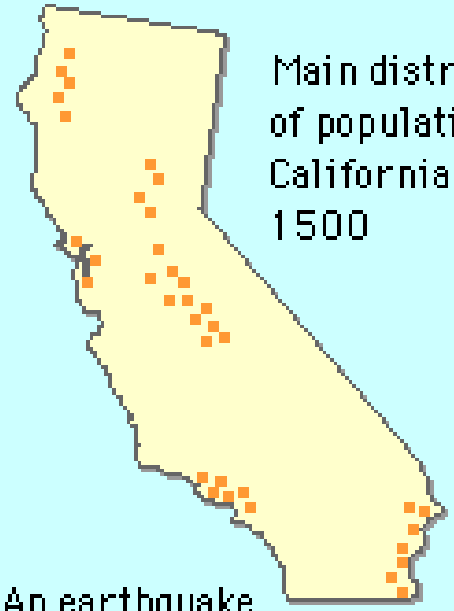
LARGE BREEDING POPULATION



Main distributions of population in California, 1997

An earthquake that kills three people out of a population of 10 million has little effect on the composition of the gene pool.

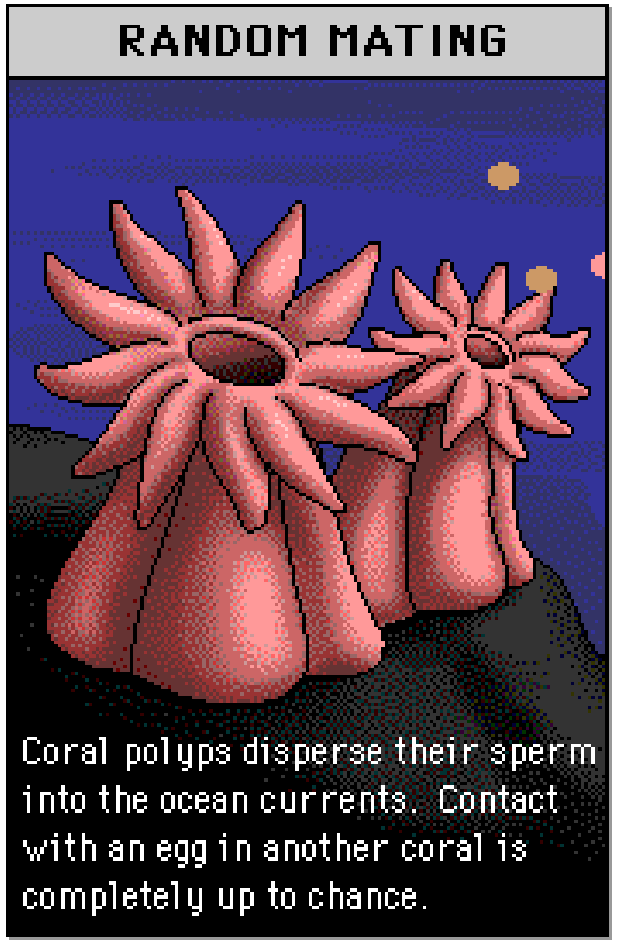
SMALL BREEDING POPULATION

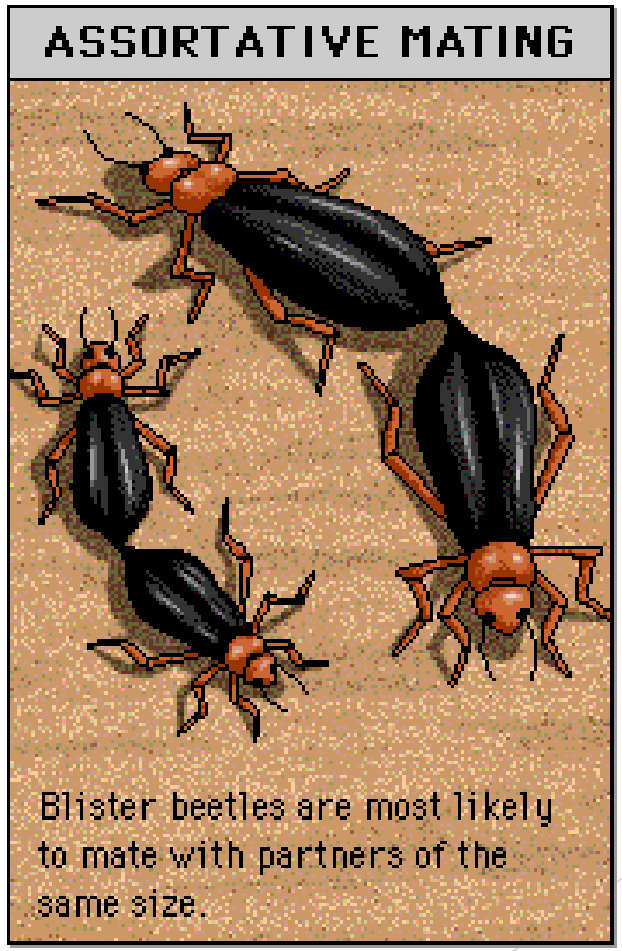


Main distributions of population in California, before 1500

An earthquake that kills three people out of a band of 20 individuals has a significant effect on the composition of the gene pool.

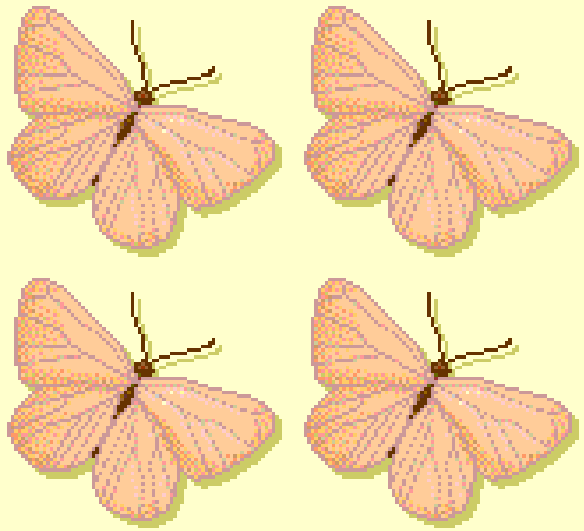
Random Mating





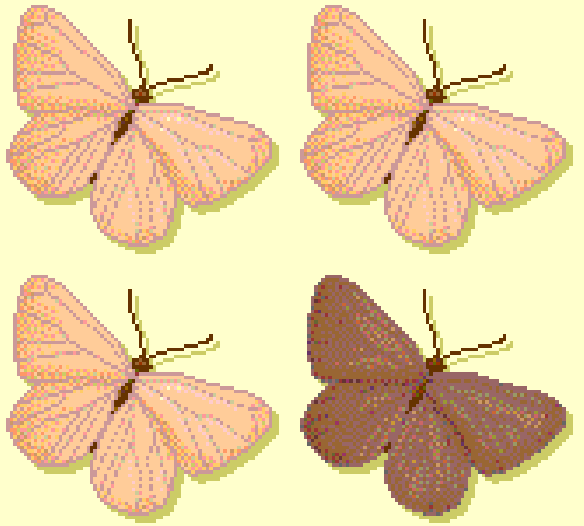
No allele frequency changes due to mutations

NO MUTATIONS



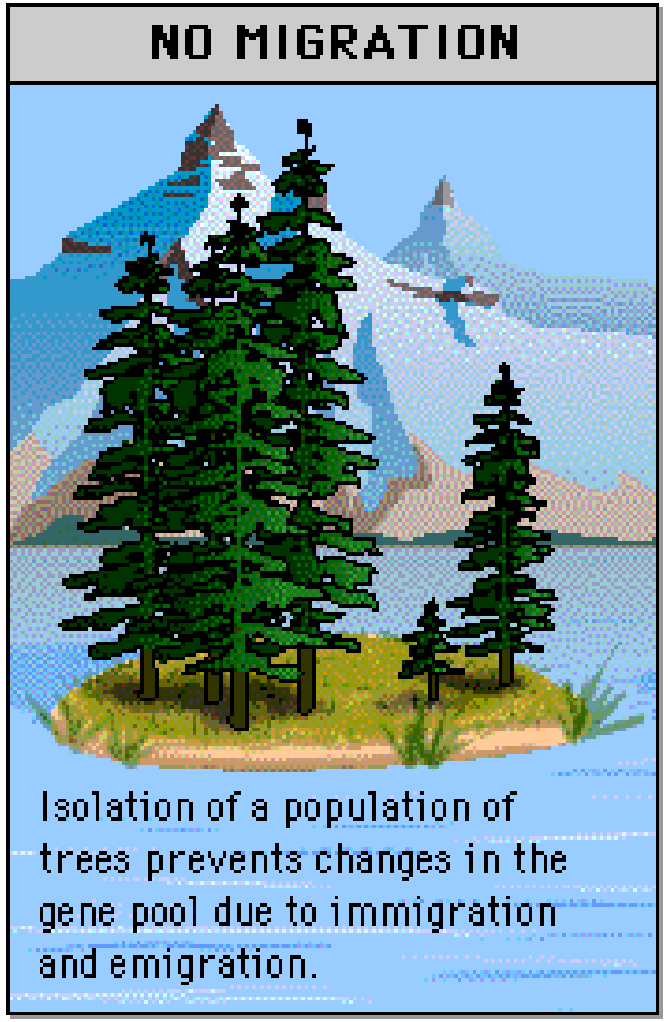
With no mutations, the composition of the gene pool remains the same generation after generation, if the other conditions for Hardy-Weinberg equilibrium are also met.

MUTATIONS

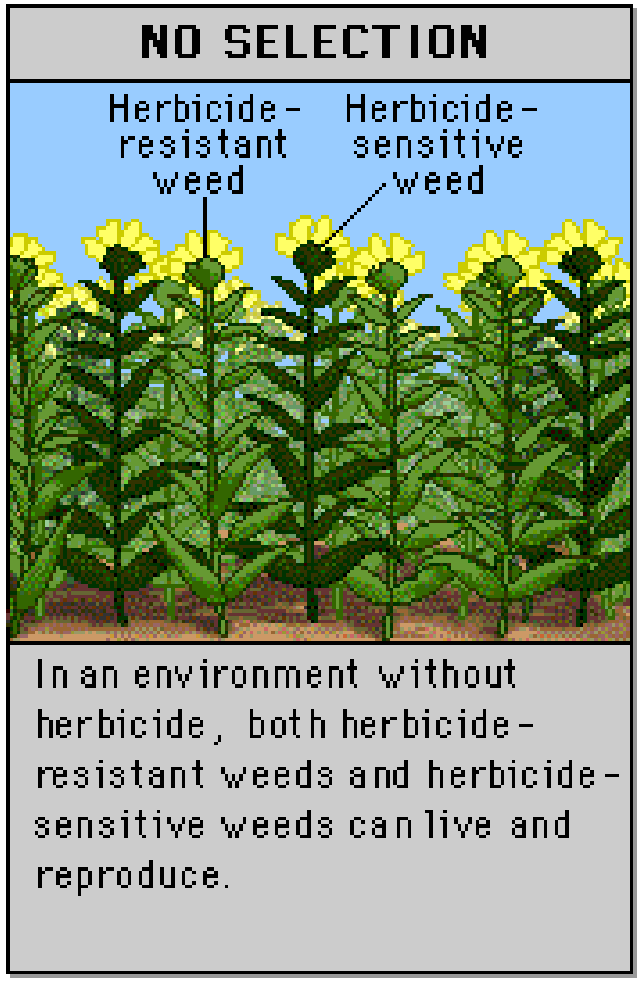


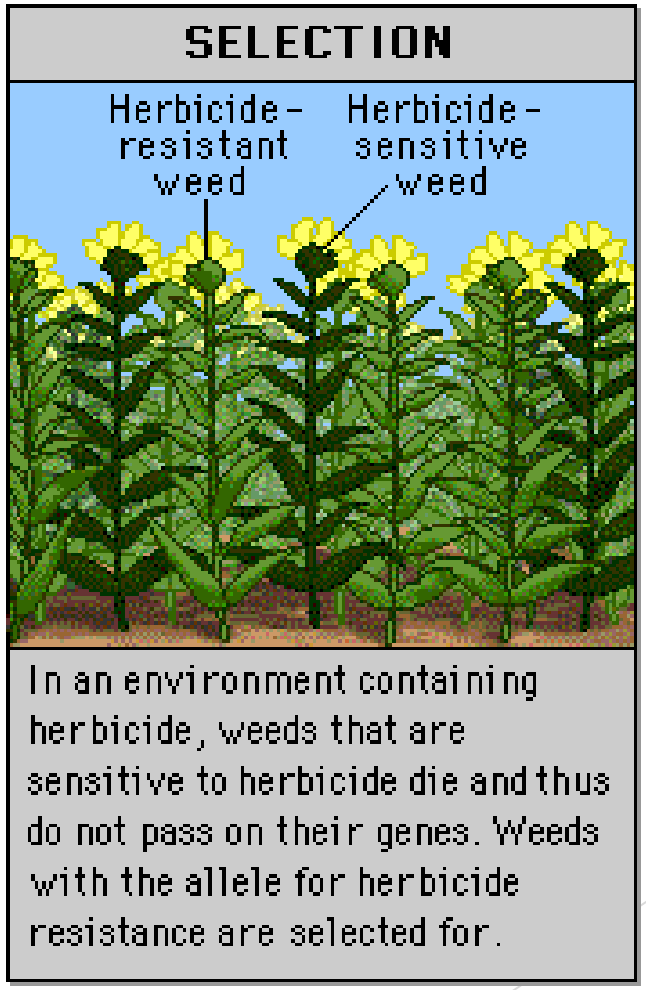
Mutations change the composition of the gene pool. New alleles are introduced, and allelic frequencies change.

No migration: imigration or emigration



No Natural Selection





Hardy-Weinberg “Rules”

- 2n
- Sexual reproduction
- Non-overlapping generations
- Mating is random
- Large population size
- Allele frequencies are = in sexes
- No influences…

- Influences
  - Genetic Drift
  - Genetic Flow
  - Mate Choice/Sexual Selection
  - Mutation
  - Natural Selection
  - Meiotic Drive
  - Bottleneck
  - Founder Effect
  - Inbreeding

To estimate the frequency of alleles in a population, we can use the Hardy-Weinberg equation. According to this equation:

p = the frequency of the dominant allele (represented here by *A*)

q = the frequency of the recessive allele (represented here by *a*)

For a population in genetic equilibrium:

$p + q = 1.0$ (The sum of the frequencies of both alleles is 100%.) Allele frequency

$(p + q)^2 = 1$

so

$p^2 + 2pq + q^2 = 1$

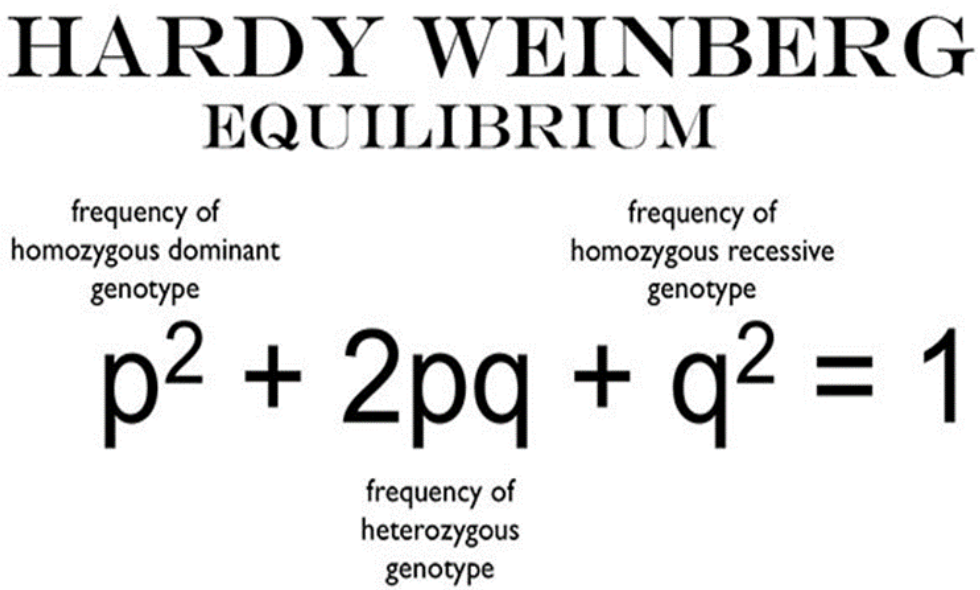
The three terms of this binomial expansion indicate the frequencies of the three genotypes: Genotypes

p^2 = frequency of *AA* (homozygous dominant)

$2pq$ = frequency of *Aa* (heterozygous)

q^2 = frequency of *aa* (homozygous recessive)

Equation for Genotypes



$(p + q)^2 = p^2 + 2pq + q^2 = 1$

Where:

p = the frequency of allele A

q = the frequency of allele a

p^2 = the frequency of individual AA

q^2 = the frequency of individual aa

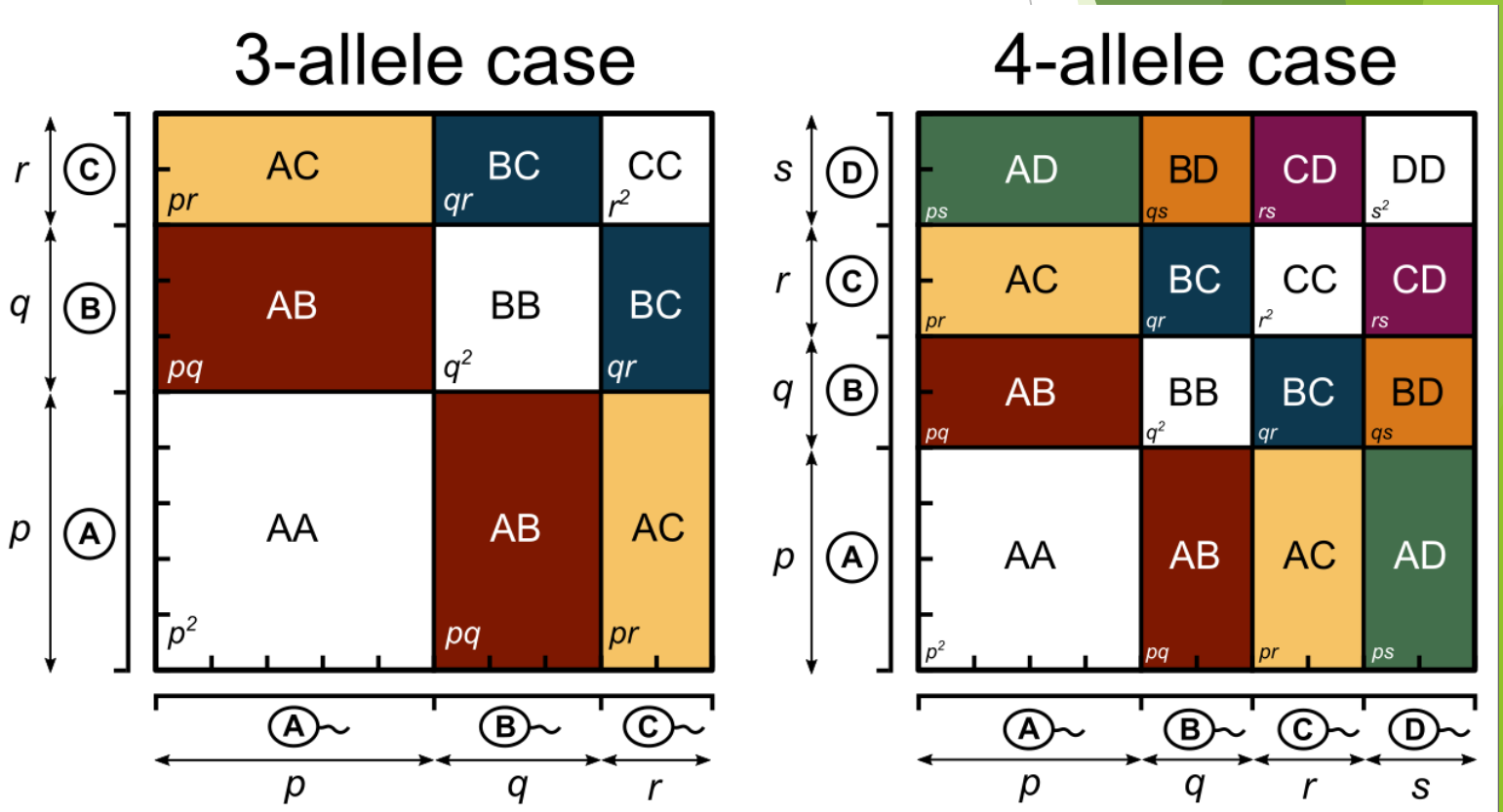
2pq = the frequency of individual Aa

Frequency of alleles

Frequency of genotypes

What about extra allele frequency?

- 3 alleles
  - $(P + Q + R)^2 =$
  - $p^2 + q^2 + r^2 + 2pq + 2pr + 2qr$
- 4 alleles
  - $(P + Q + R + S)^2 =$
  - $p^2 + q^2 + r^2 + s^2 + 2pq + 2pr + 2qr + 2ps + 2qs + 2rs$



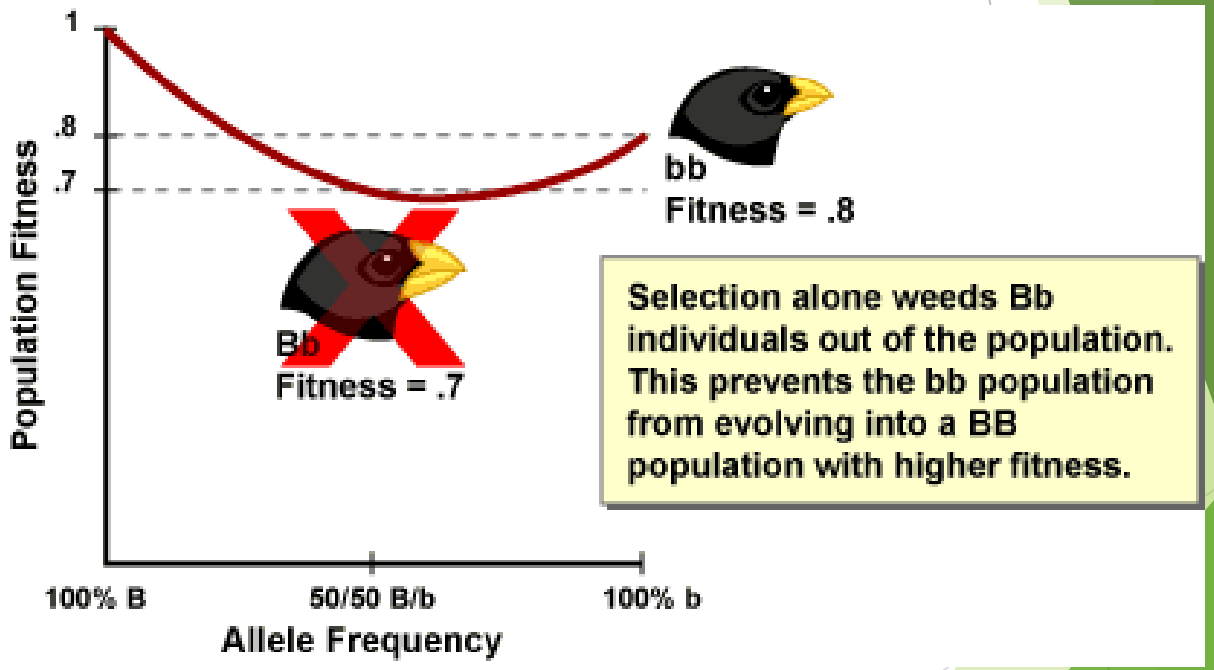
In Reality…

The conditions for Hardy-Weinberg equilibrium are **never** met in nature.

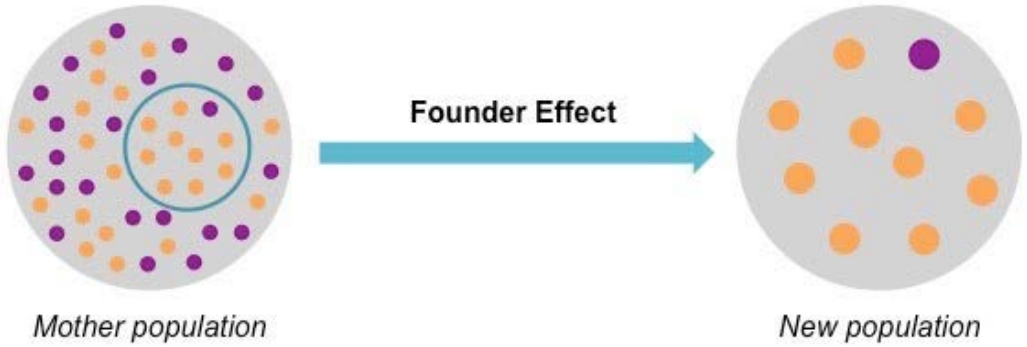
- There are always some disturbing influences in nature
- Hardy-Weinberg equilibrium can be approximated in the lab
- It has usefulness as a model for studying real populations

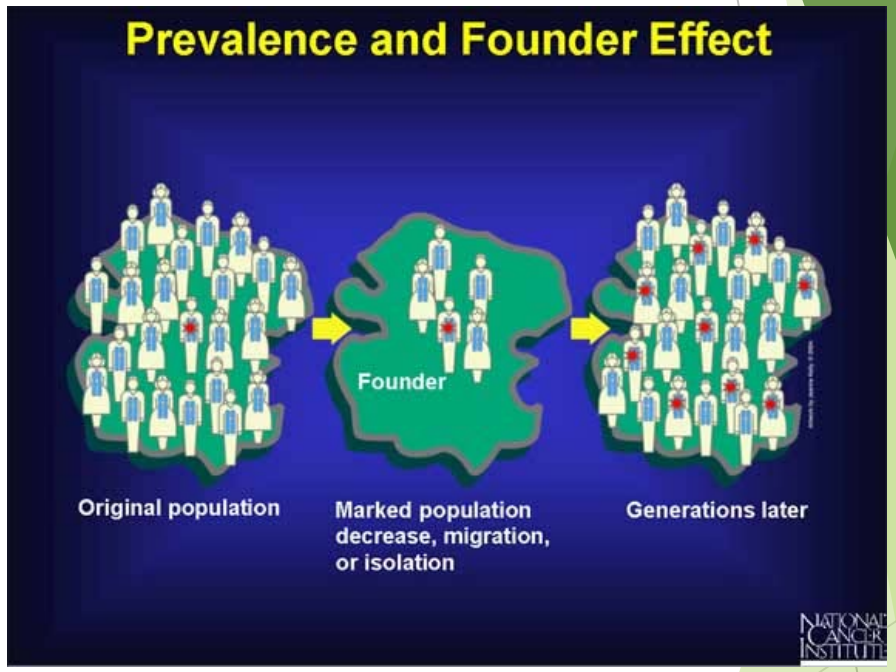
Genetic Drift

- Small populations
- Loss of genetic variation
- Decreased offspring
- Increase frequency of harmful alleles
- Examples
  - Founder Effect
  - Bottleneck



Founder Effect

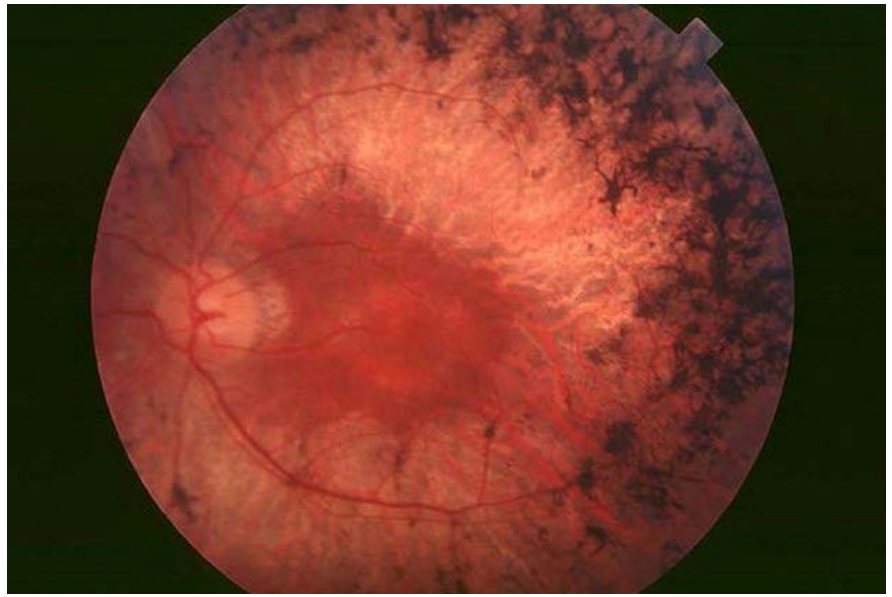


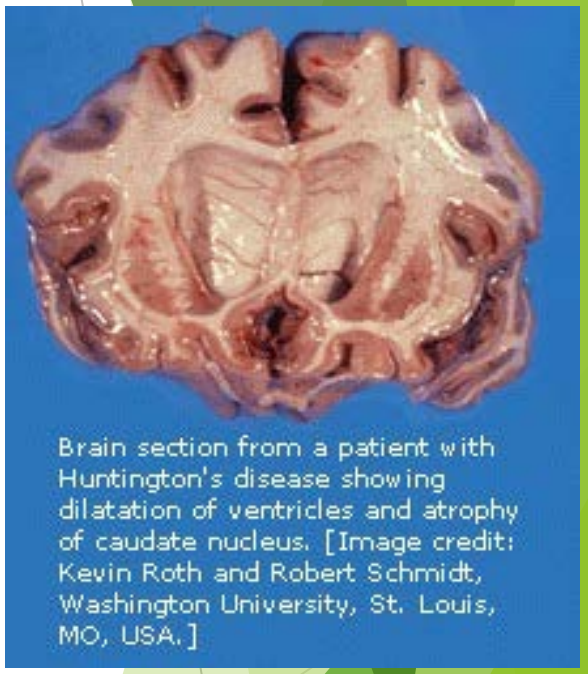


Small population, Isolation

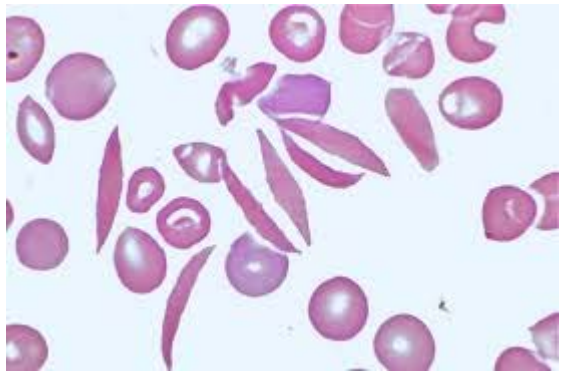
Human Diseases related to the Founder effect

- Sickle Cell Anemia
- Meleda (plantopalmar keratoderma)
- Ellis-van Creveld syndrome
- Fumarase Deficiency
- Huntington’s Disease
- Retinitis Pigmentosa
- Deafness
- Tay-Sachs
- Maple Syrup Urine Disease (MSUD)



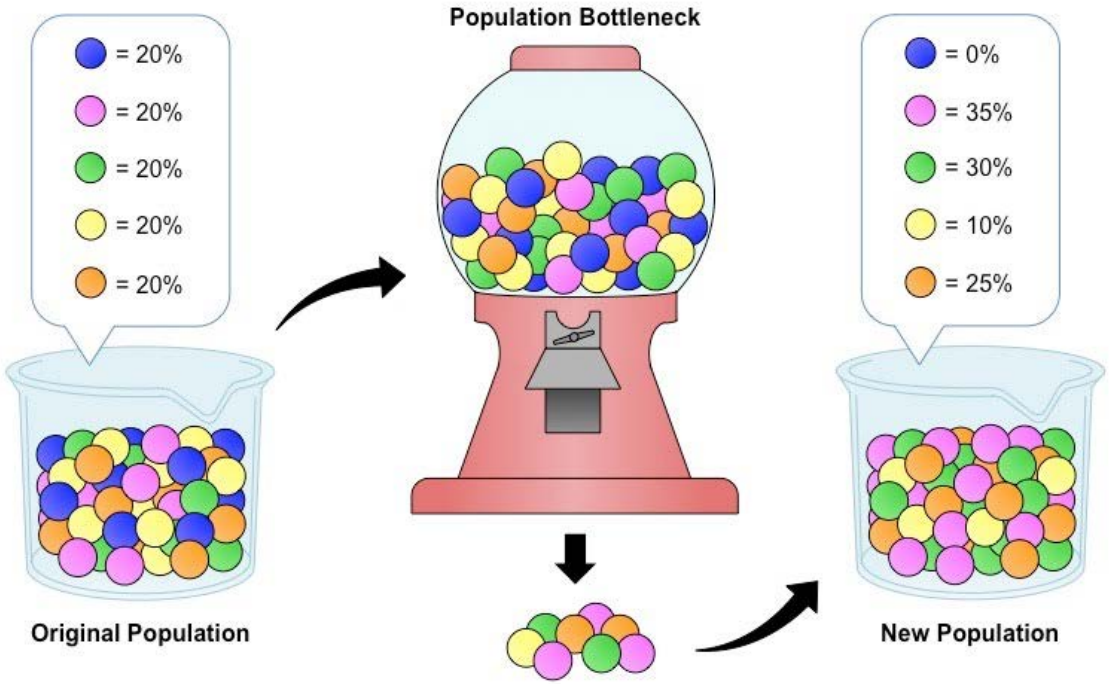


Brain section from a patient with Huntington's disease showing dilatation of ventricles and atrophy of caudate nucleus. [Image credit: Kevin Roth and Robert Schmidt, Washington University, St. Louis, MO, USA.]



Bottleneck

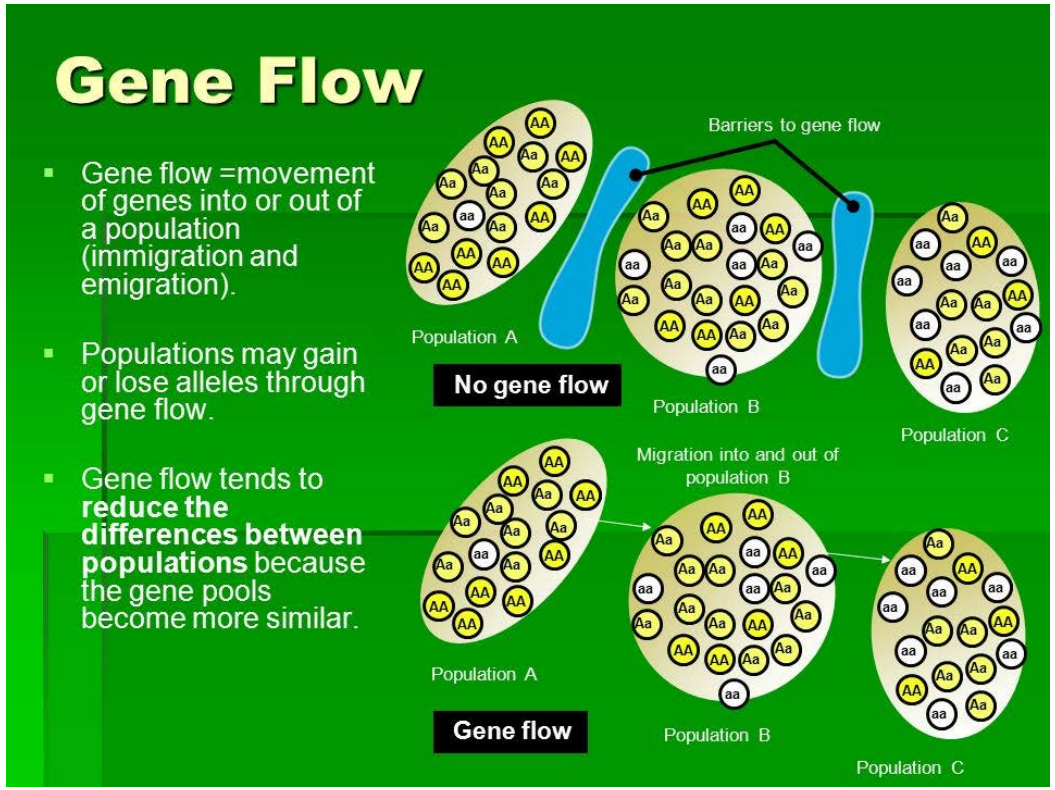
- Original population size reduced
- Decreases genetic diversity
- Causes
  - Habitat destruction
  - Predation
  - Environmental disaster

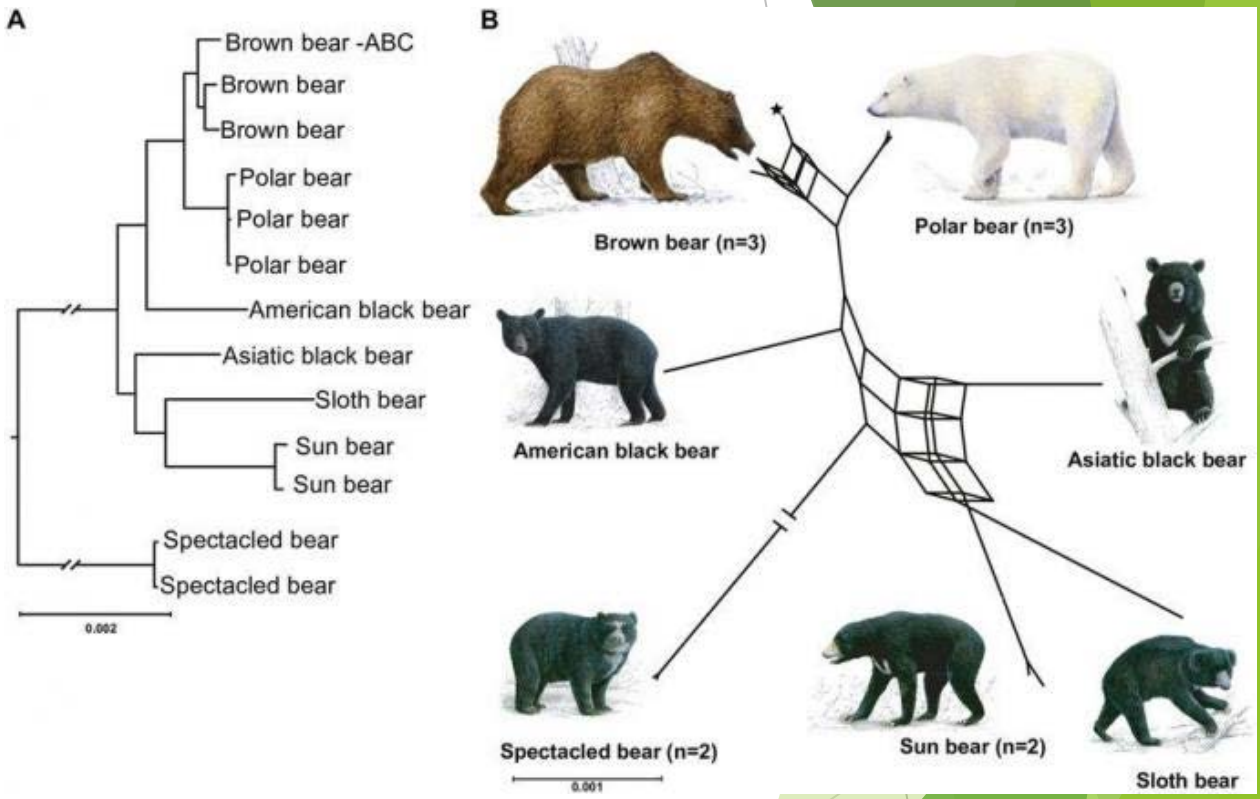


Bottleneck example

Northern Elephant Seals were heavily hunted by man in the early 19th century reducing their population size to about 20 individuals. Today the population has rebounded to over 30,000 but the effects of the bottleneck are evident in their DNA. There is little genetic variation among this population when compared to a population of Southern Elephant seals that were not heavily hunted.

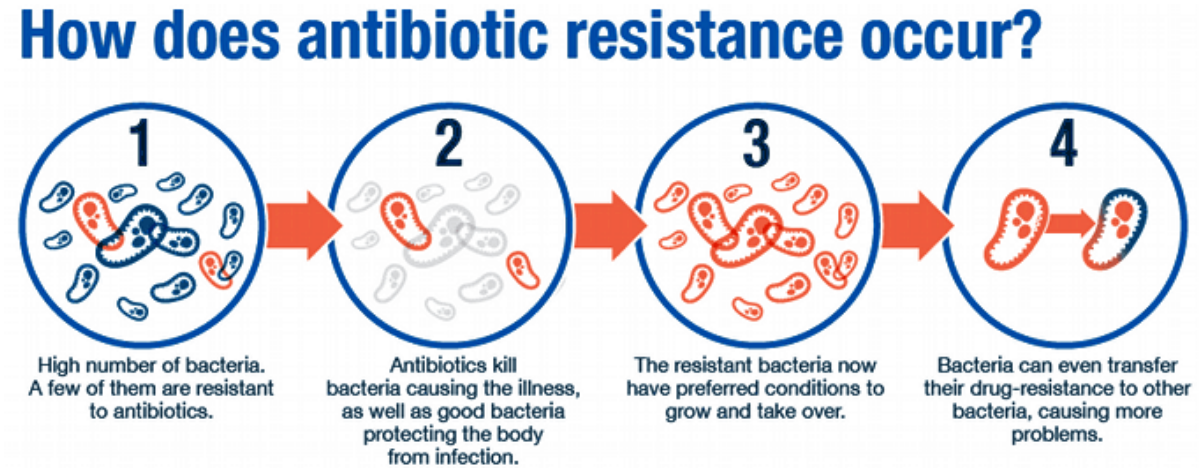
Gene Flow = Movement in or out

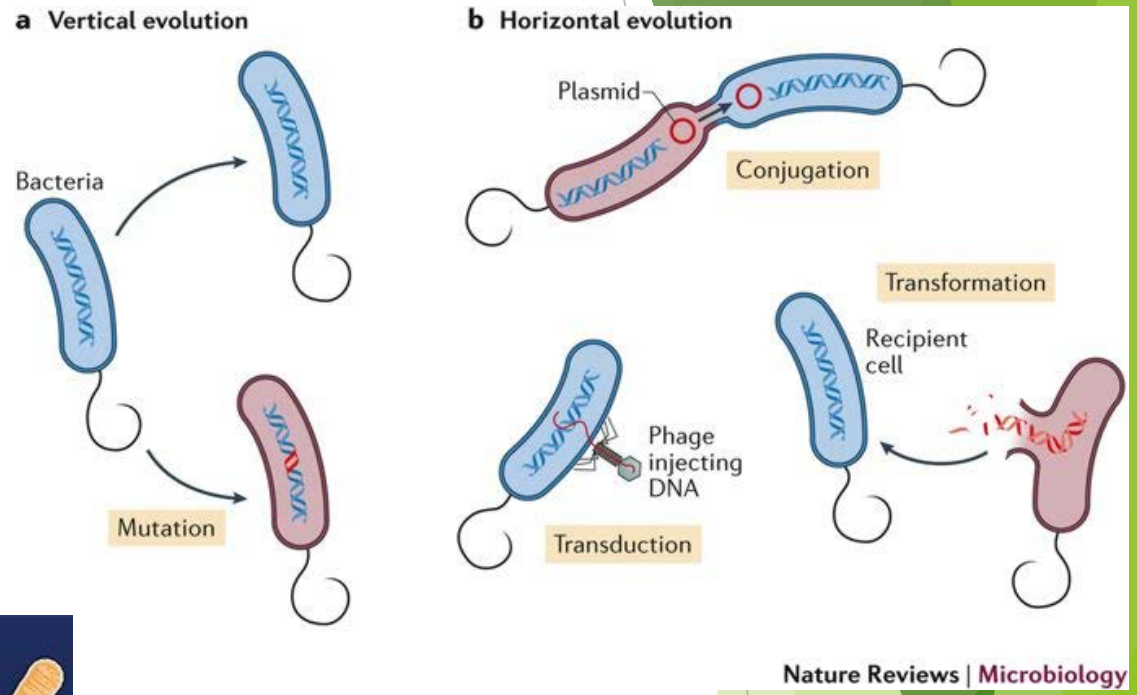




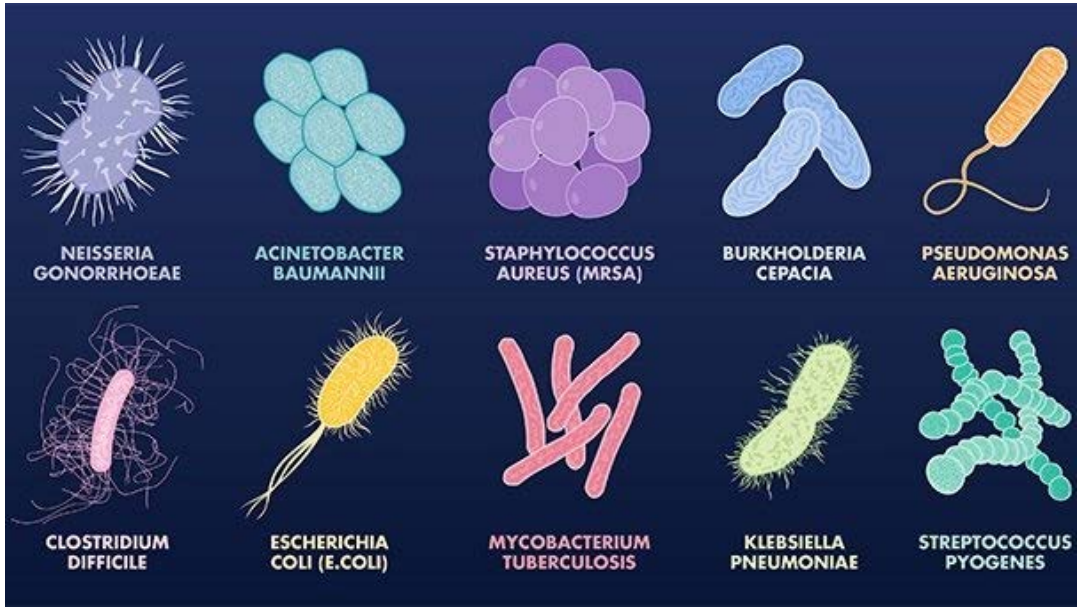
Transfer of alleles
Reduce genetic differences

Antibiotic Resistance





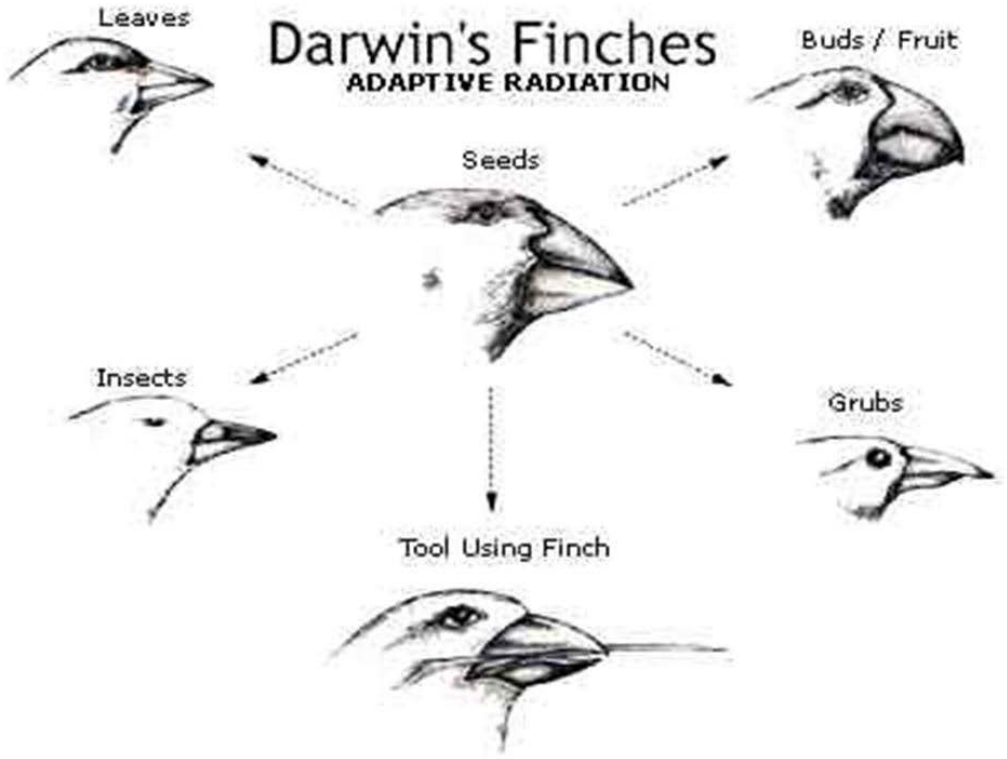
MRSA
VRSA
CRE




NATURAL SELECTION
SEXUAL SELECTION
ARTIFICIAL SELECTION
ECOLOGICAL SELECTION

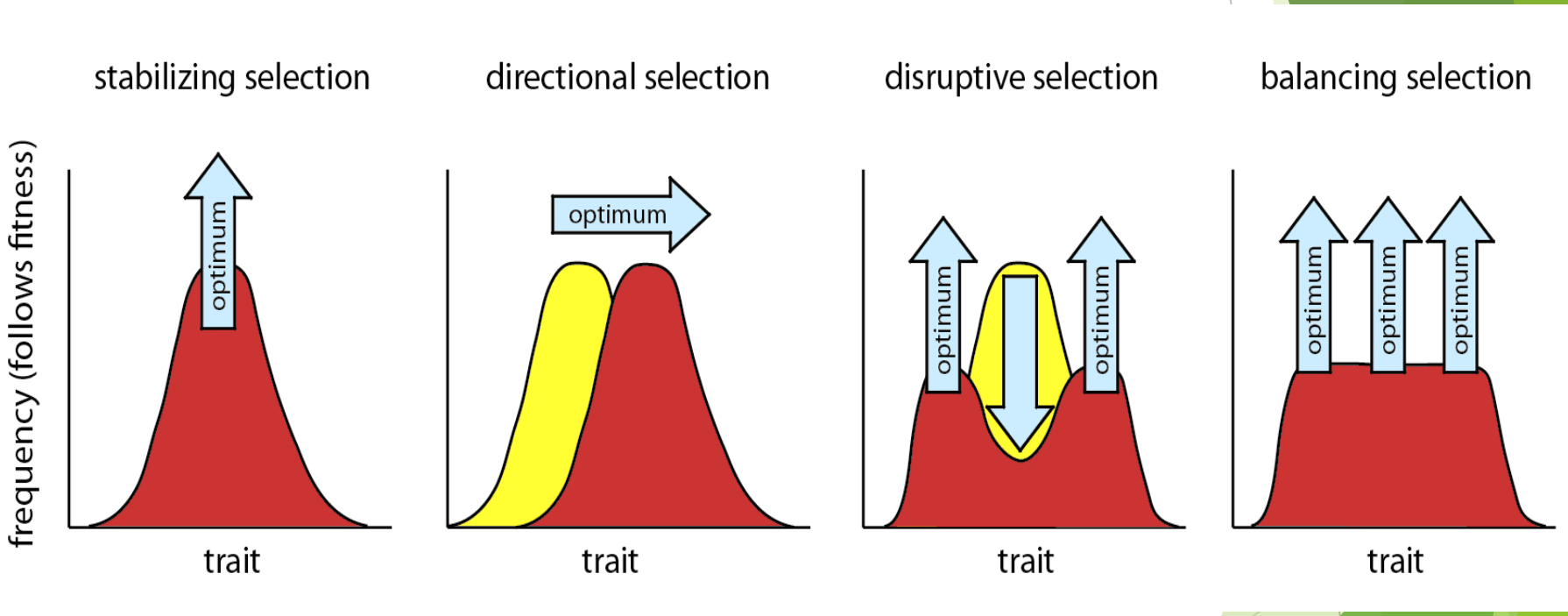
Natural Selection

- Adaptive Selection
  - Creation of new genes
  - Favors some alleles
- Reasons
  - Dynamic
  - Continuous
  - Relative Fitness



Natural Selection Types

- Directional
- Disruptive
- Stabilizing
- Balancing



Sexual Selection

Sexual Selection

- **Sexual selection** is natural selection for mating success.
- It can result in **sexual dimorphism**, marked differences between the sexes in secondary sexual characteristics.
- Male showiness due to mate choice can increase a male's chances of attracting a female, while decreasing his chances of survival.

Natural Selection

Favors traits that enhance survival, production of young, etc.

Sexual selection

Favors traits that enhance ability to mate.

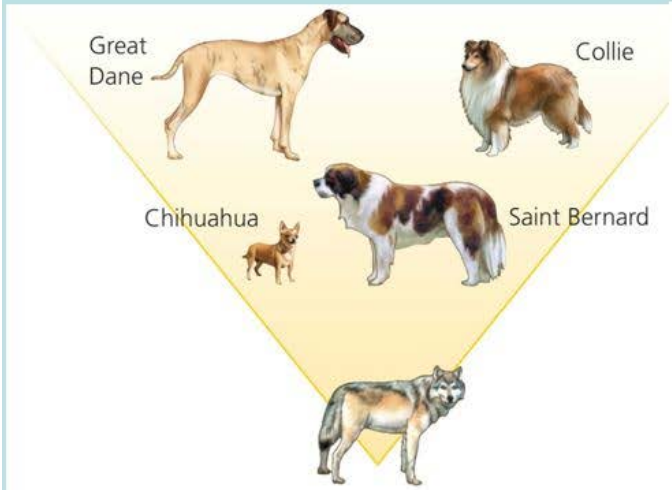
These traits may lead to lower **individual** survival

A subset of natural selection that acts through **inter- and intra-sexual interactions**

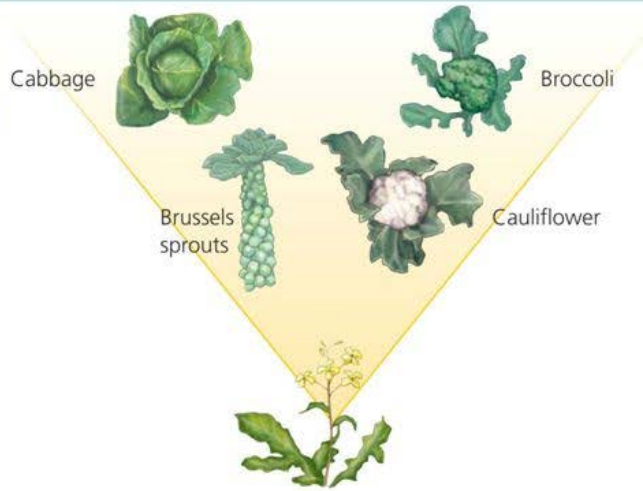
Artificial Selection

Artificial selection

- **Artificial selection**: the process of selection conducted under human direction
  - For example, by allowing only like individuals to breed, breeders have created the great variety of dog breeds and crop plants.



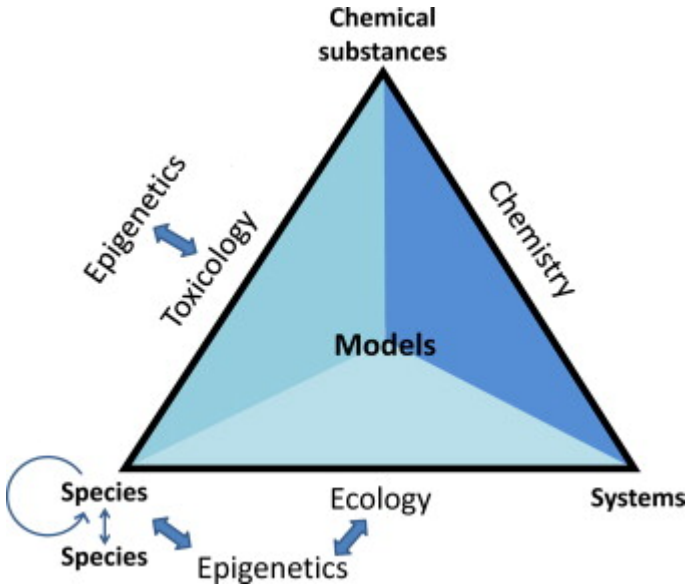
(a) Ancestral wolf and derived dog breeds

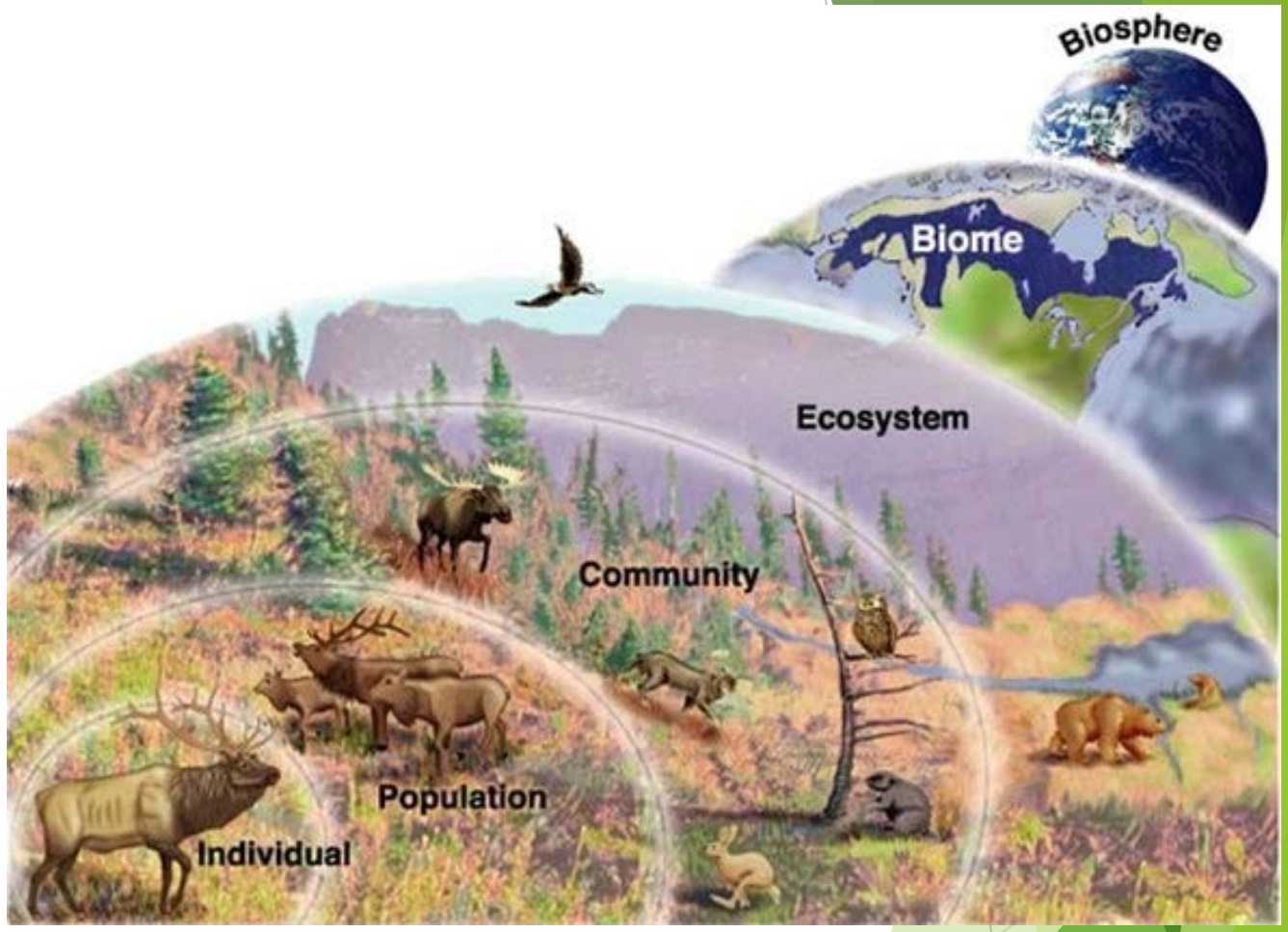


(b) Ancestral *Brassica oleracea* and derived crops

Ecological Selection

- Processes that act on inherited traits
- Environmental Pressures



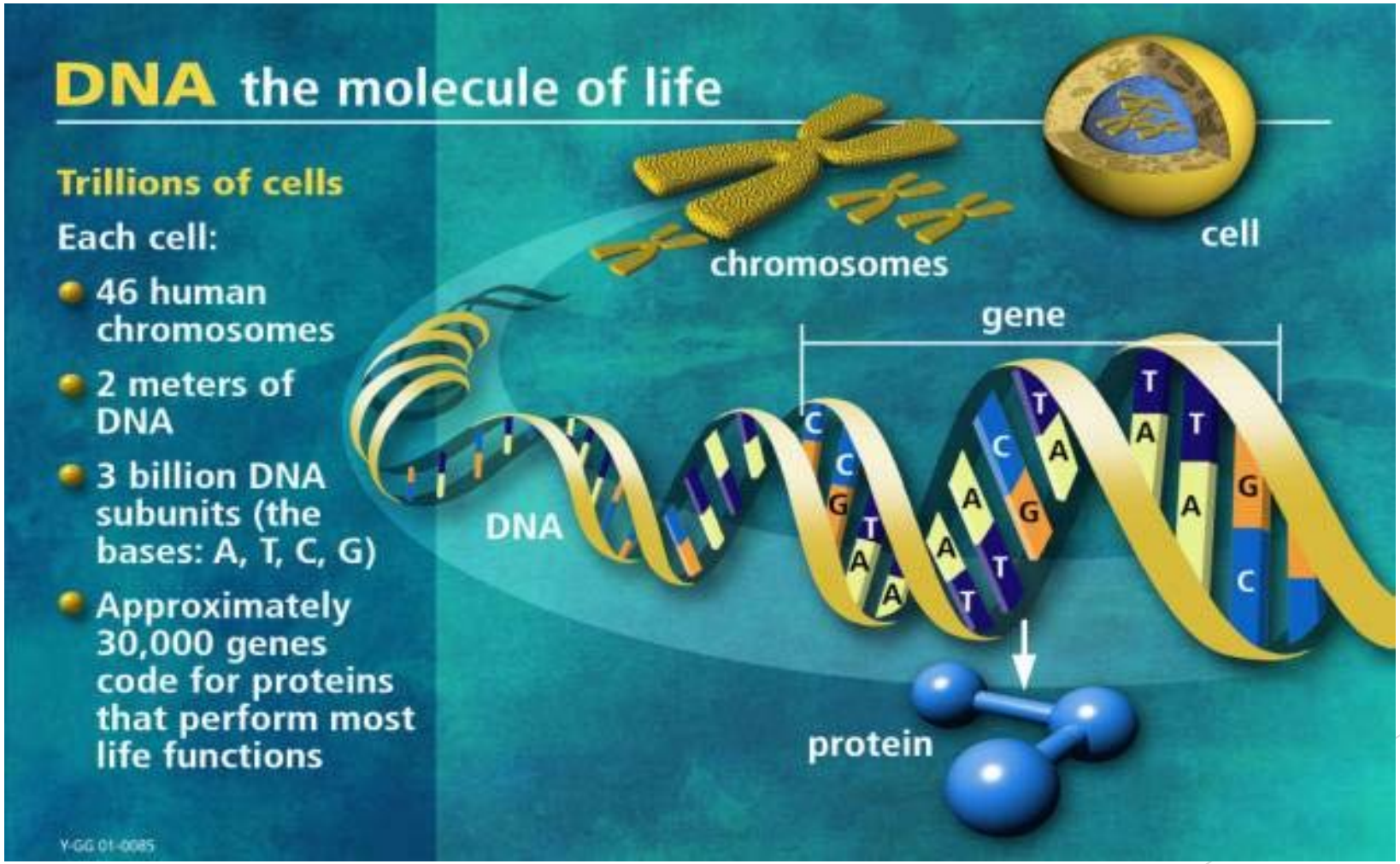


Smithsonian Study on
Decline of backyard bird populations

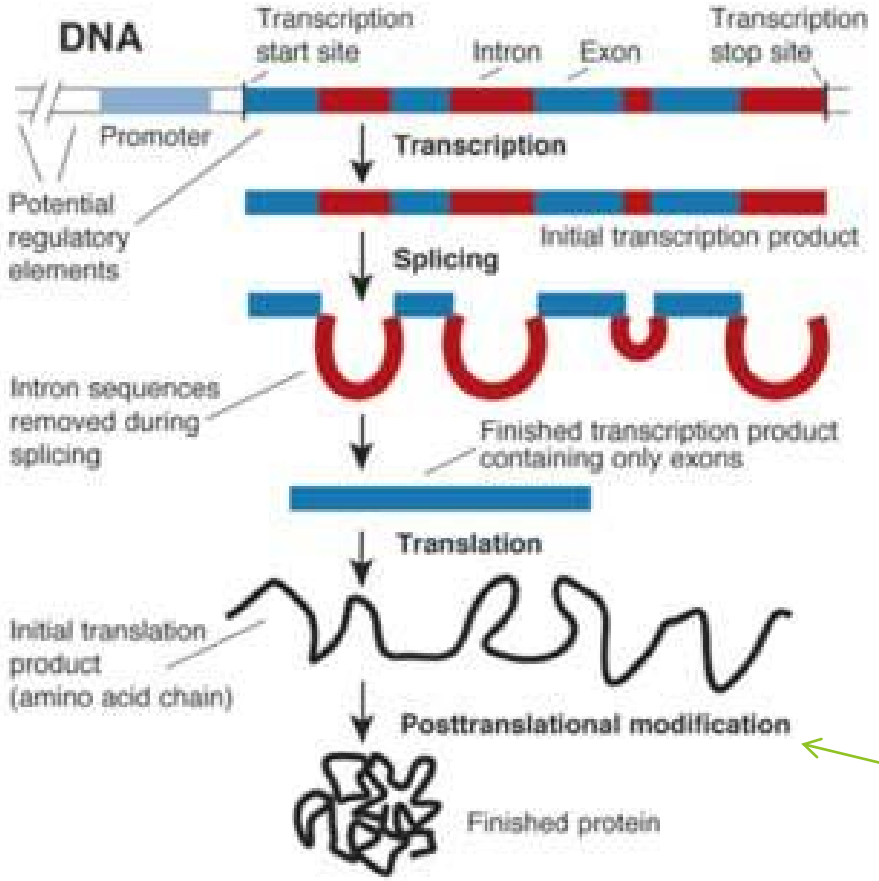
Population Genetics

- **Population genetics** refers to the study of evolution via the observation and modeling of allele frequencies and genetic change in populations of organisms.
- There are three parameters to keep in mind:
  - **allele frequency:** the proportion of a specific allele at a given locus, considering that the population may contain from one to many alleles at that locus.
  - **genotype frequency:** the proportion of a specific genotype at a given locus, considering that many different genotypes may be possible.
  - **phenotype frequency:** the proportion of individuals in a population that exhibit a given phenotype.

Central Dogma



Genes and Gene Expression

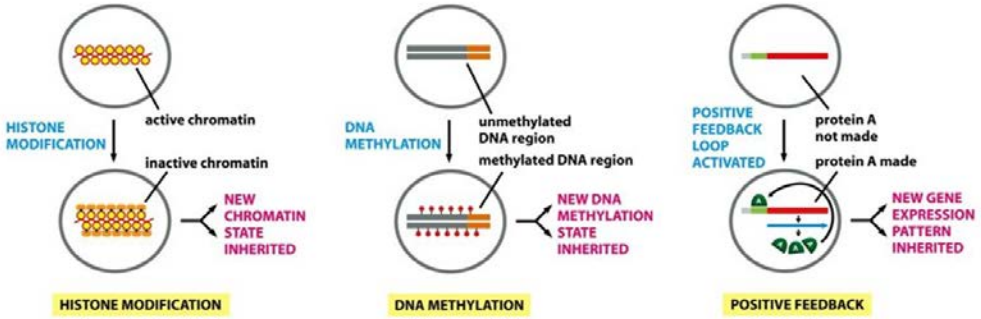


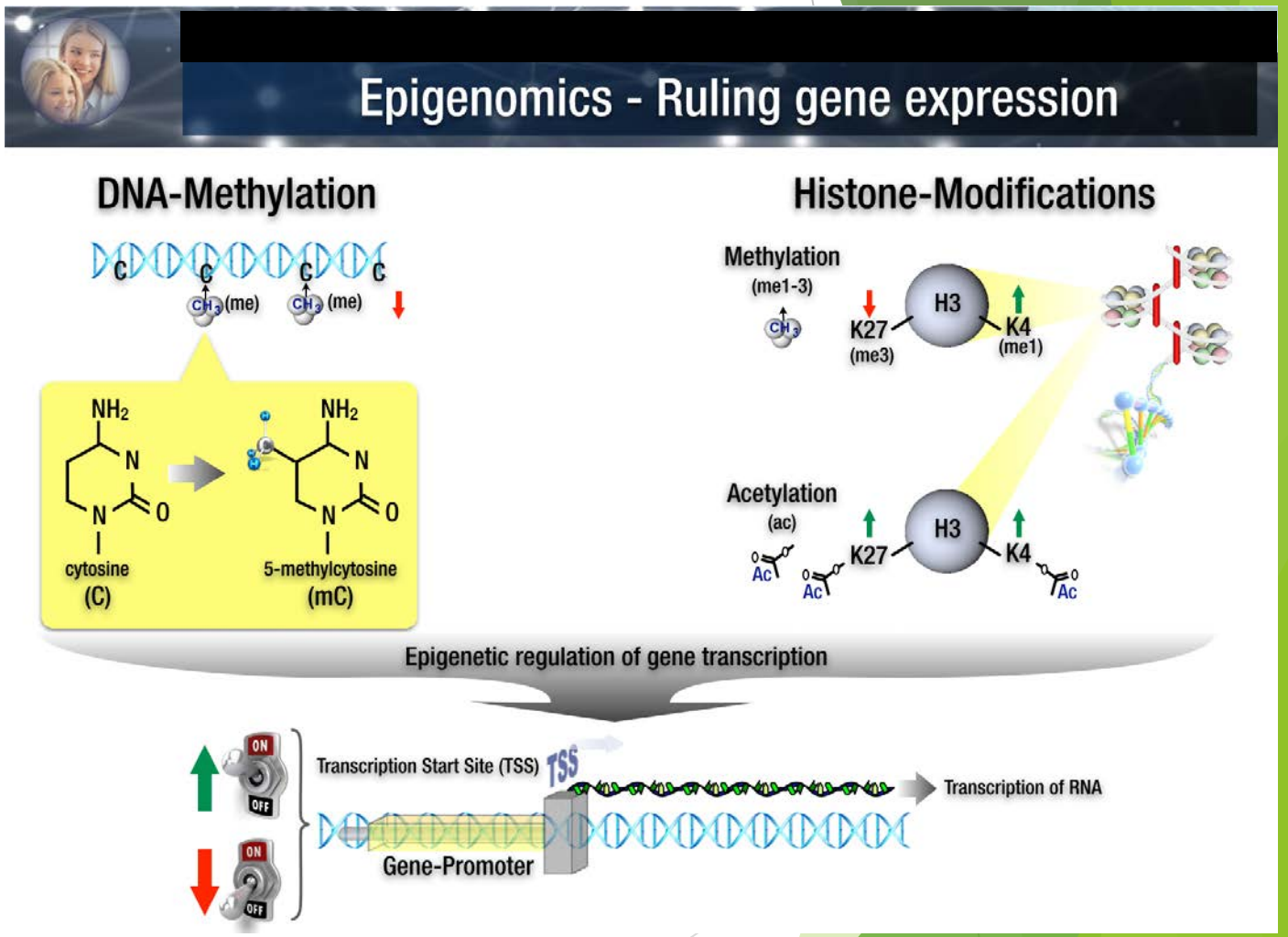
- Genetic Code Redundancy
- Highly Conserved Genes
- Number of Genes (e.g.)
  - Grains: 32,000-42,000
  - Nematodes 20,000
  - Humans 21,000
- Recent Discoveries
- New Fields
  - Evo-Devo
  - Proteomics

Epigenetics

Epigenetic Mechanisms

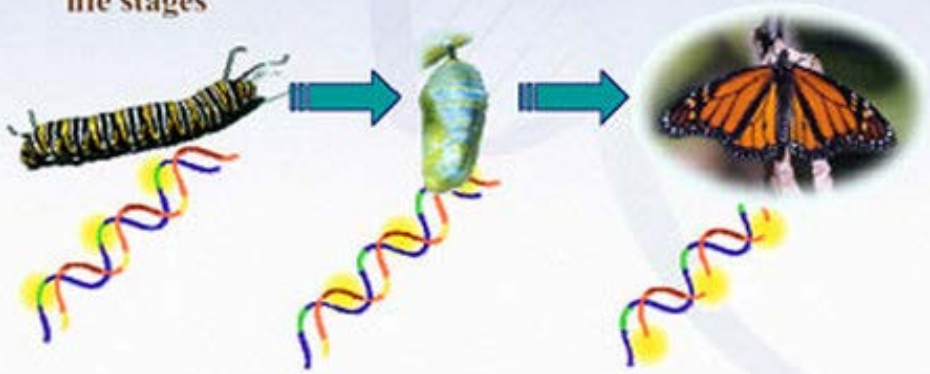
- Epigenetic inheritance- daughter cells maintain memory of gene expression pattern of parent cells
- Histone modifications, DNA methylation, and positive feedback loops contribute to epigenetic inheritance





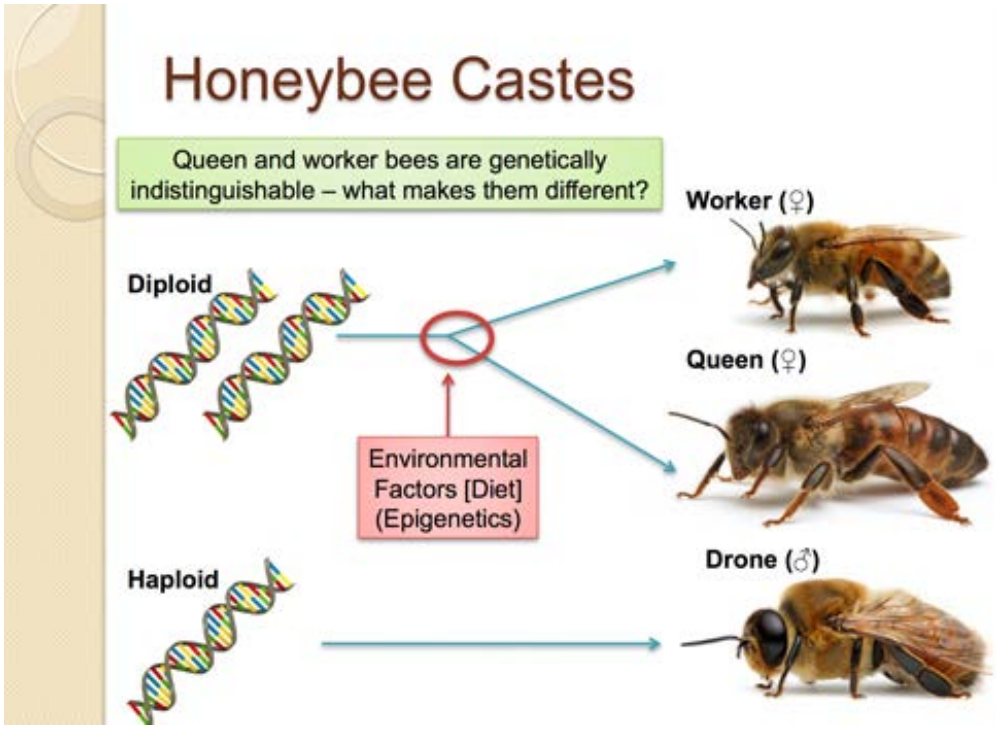
Epigenetics

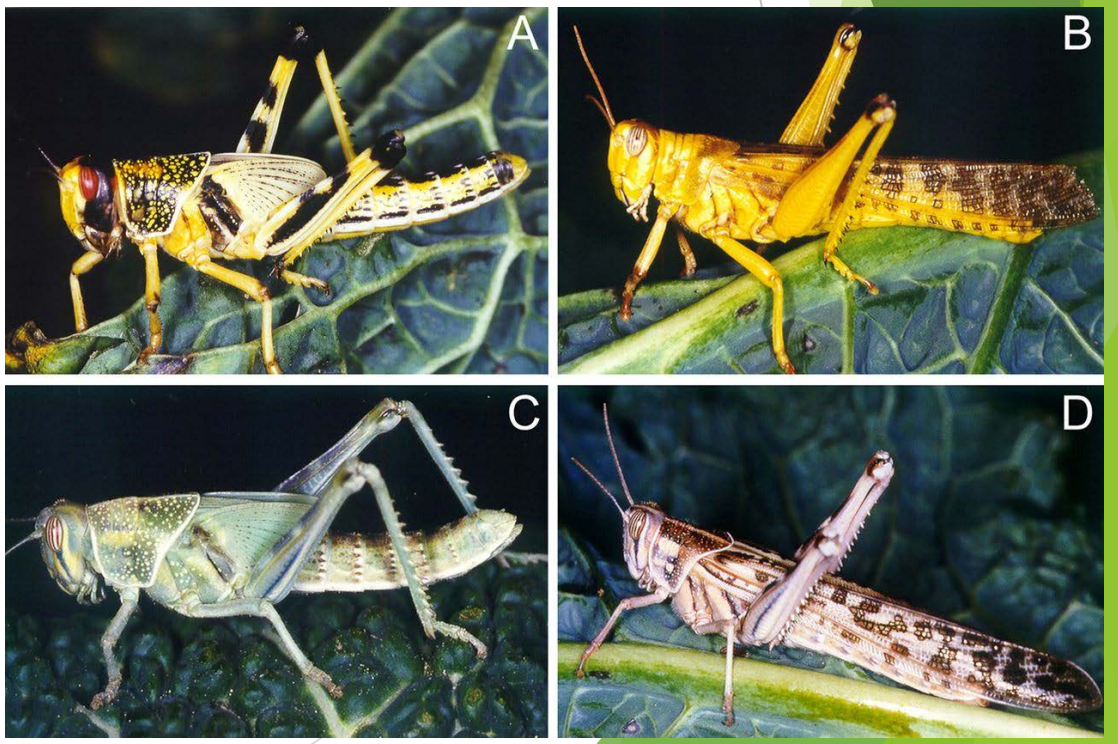
Epigenetics Regulation: the same set of genes but with expressions (structures) of those genes during different life stages



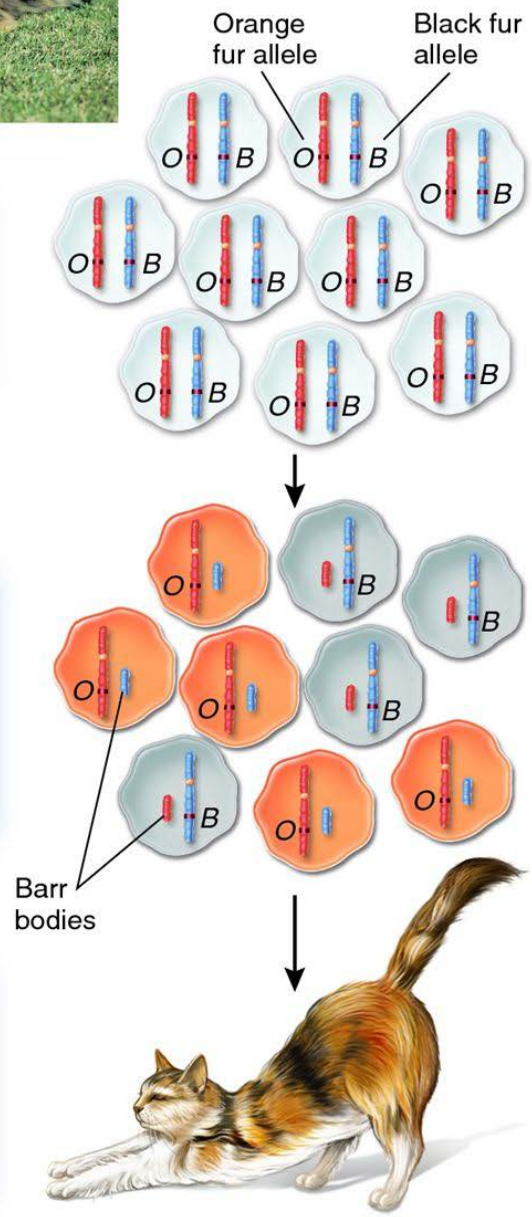
Honeybee Castes

Queen and worker bees are genetically indistinguishable – what makes them different?





(a) Calico cat



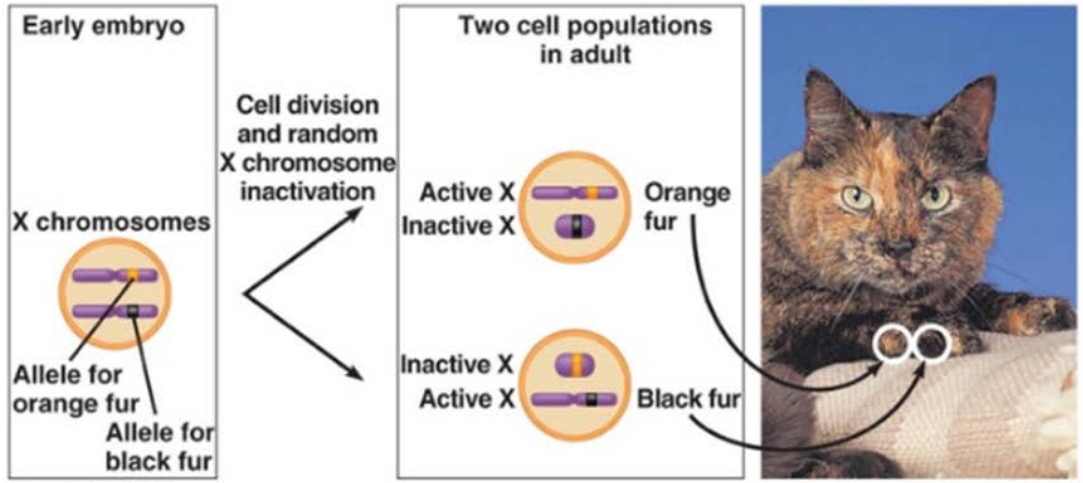
1 In the early embryo, all X chromosomes are initially active.

2 In each embryonic cell, random inactivation occurs for one of the X chromosomes, which becomes a Barr body.

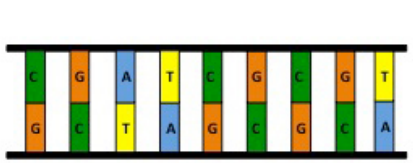
3 As development proceeds, the pattern of X inactivation is maintained during cell division.

(b) Process of X inactivation

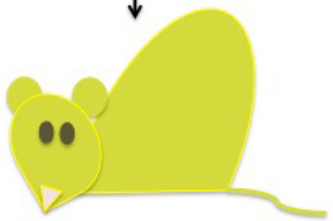
Epigenetics - example



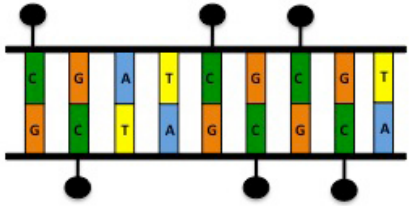
AGOUTI GENE



Unmethylated DNA



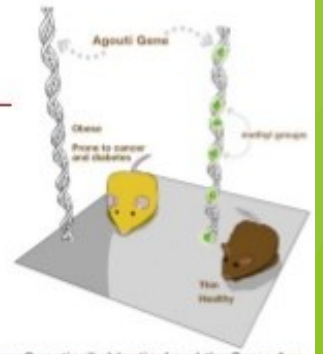
Yellow and obese mouse



Methylated DNA (Methyl group)

Thin and brown mouse

Maternal Diet in Pregnancy



Classic example of CH3-dependent Epigenetic Modification

- BPA ↓ methylation of agouti gene
- When mothers fed BPA their babies were yellow & obese
- When moms fed BPA + CH3-rich foods the offspring were brown & healthy
- Supplementation counteracted exposure
- Demonstrates how environmental exposure *in utero* can alter phenotypes in isogenetic pairs

These Two Mice are Genetically Identical and the Same Age

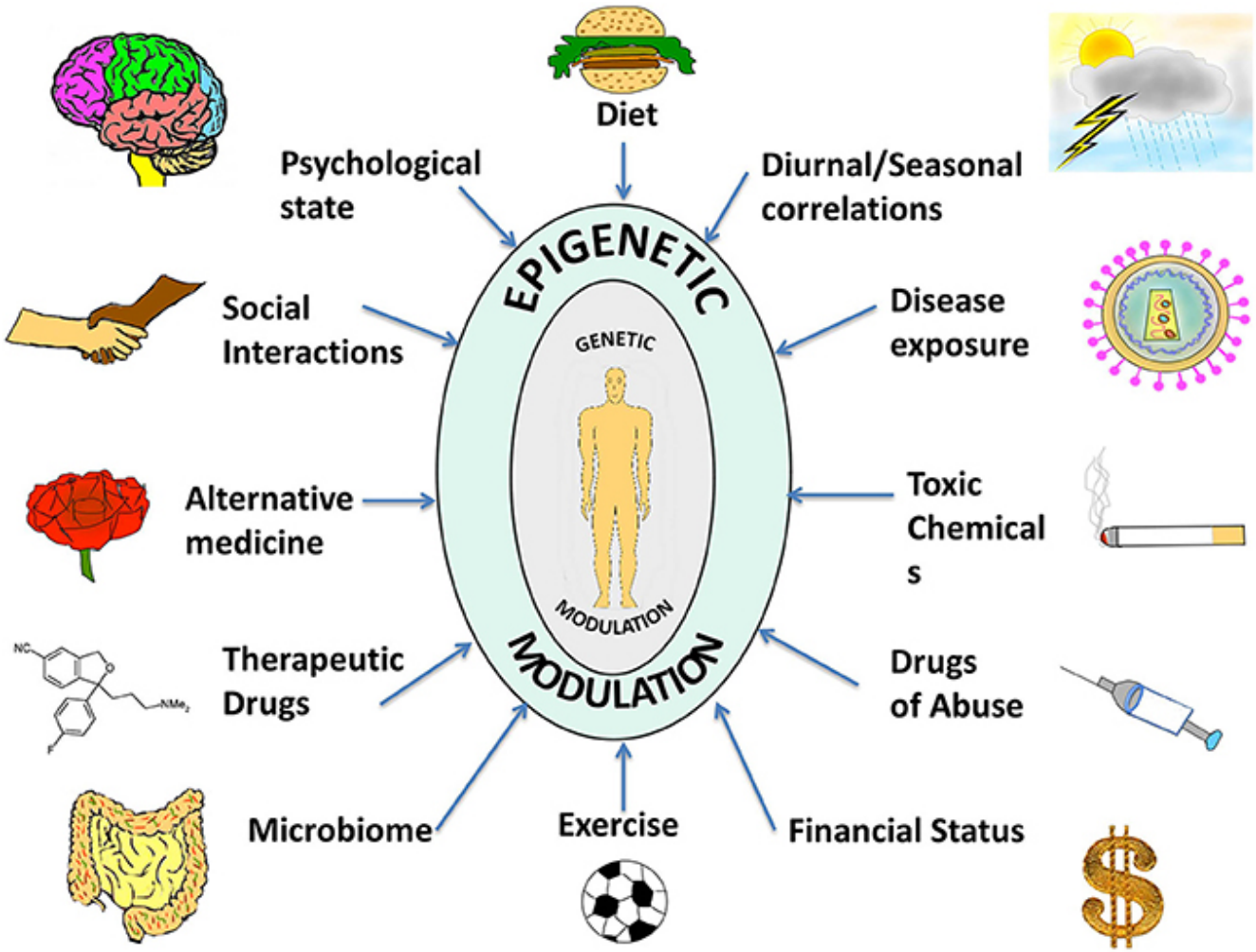
While pregnant, both of their mothers were fed Bisphenol A (BPA) but DIFFERENT DIETS:

The mother of this mouse received a **normal mouse diet**

The mother of this mouse received a diet **supplemented** with choline, folic acid, betaine and vitamin B12

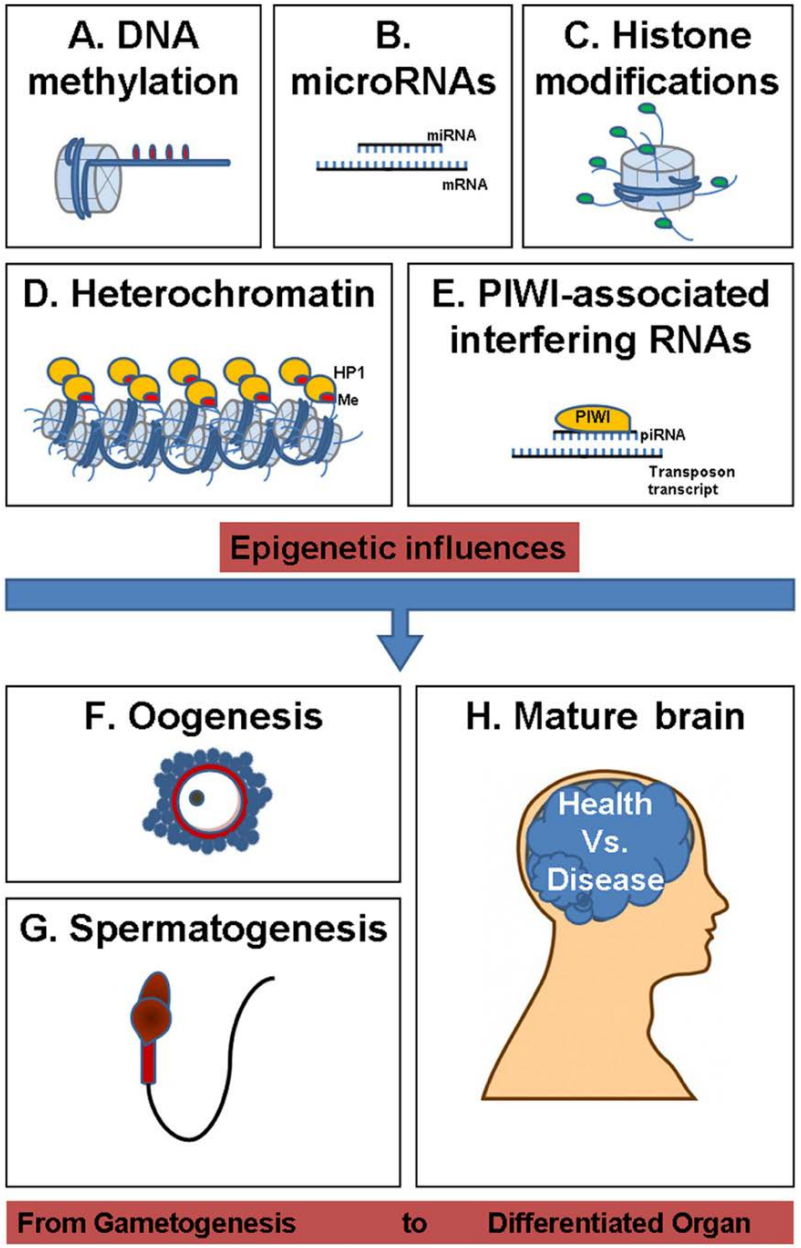
Waterland, Annu. Rev. Nutr. 2014;34:337–55
http://learn.genetics.utah.edu/content/epigenetics/nutrition/

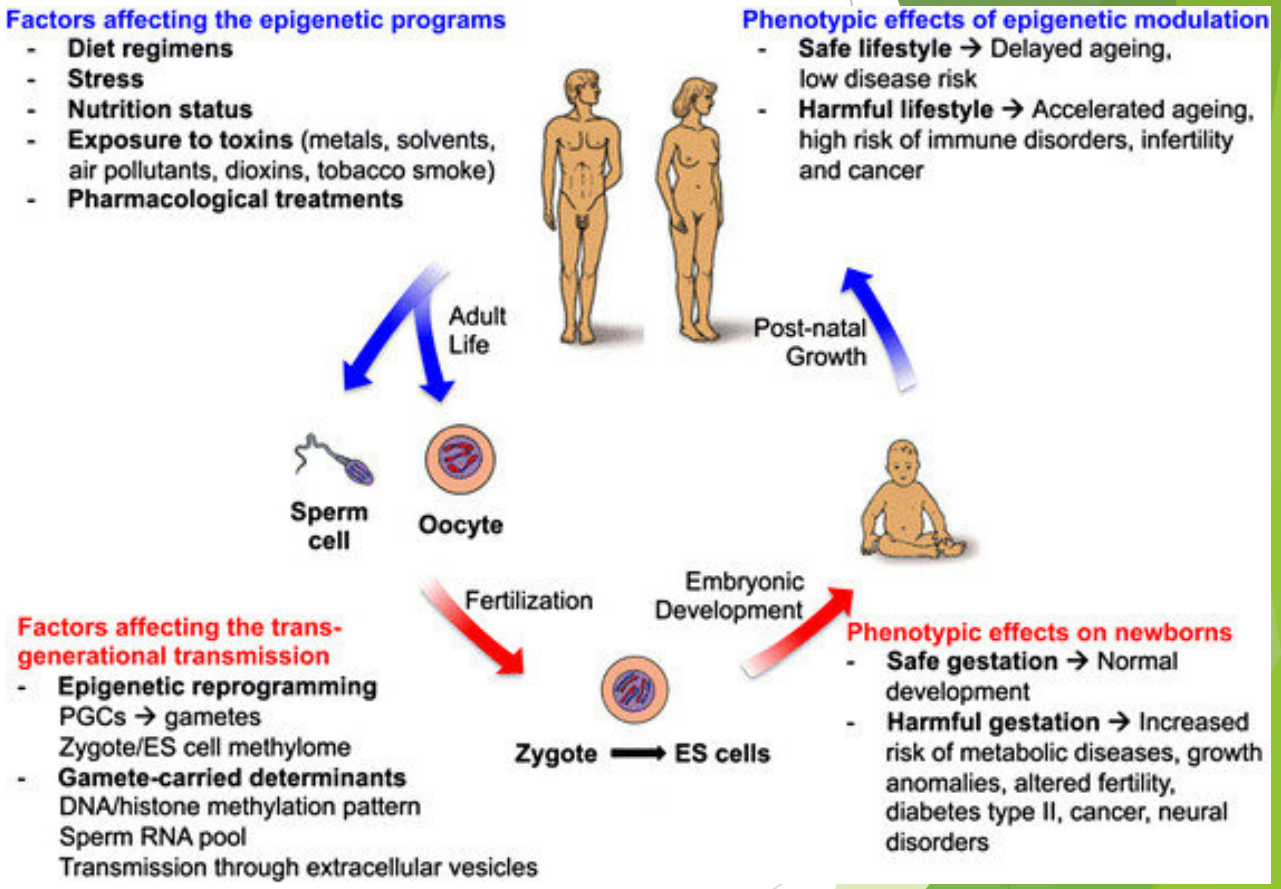
Epigenetics



Changes in genetic expression in response to environmental signals

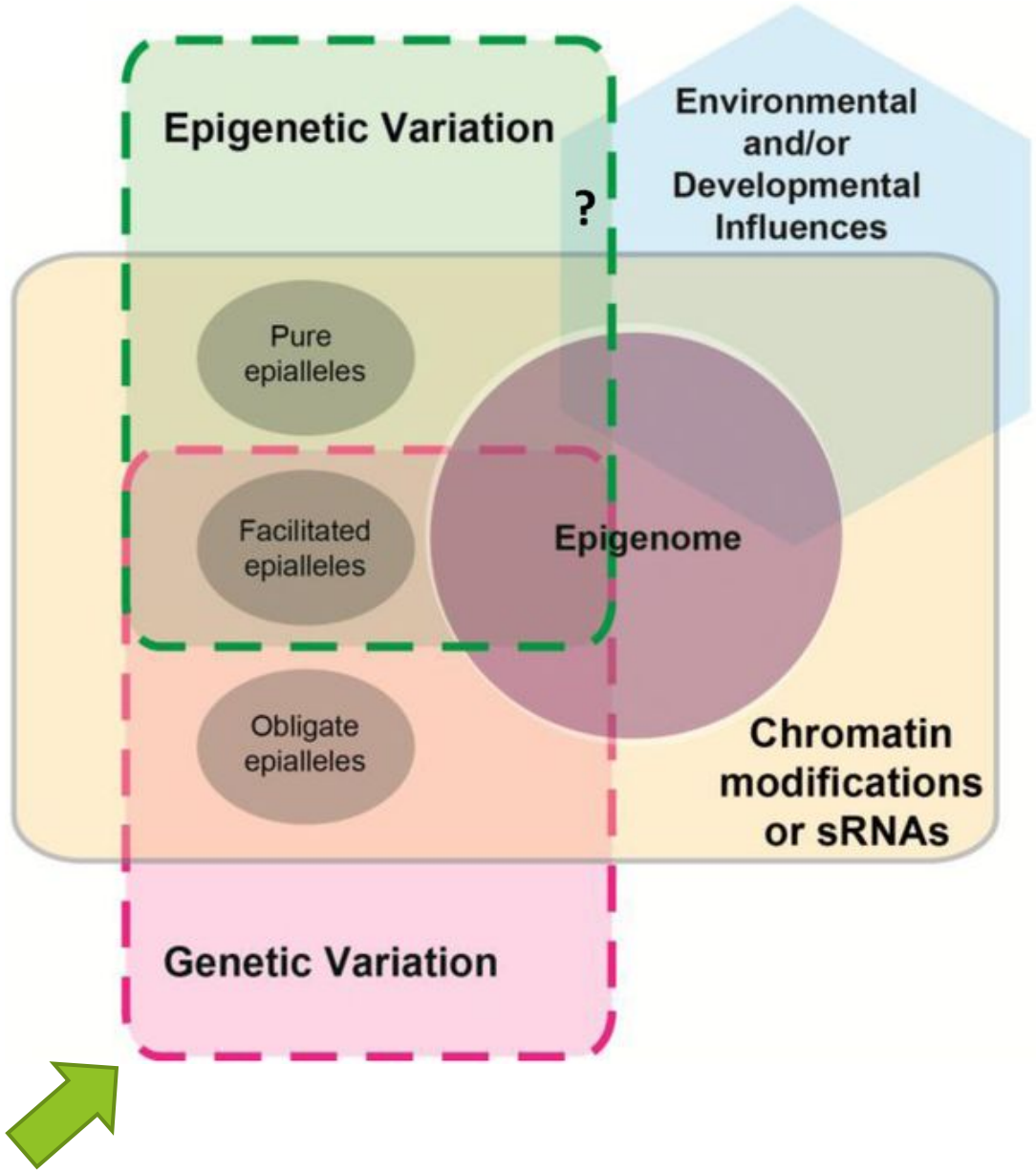
Influences Shaping Health and Disease





Article on epigenetic regulation

Summary



Epigenetic variation: Heritable differences that are independent of changes in DNA sequence

Chromatin modifications: Differences in the presence or types of histones (variants) and modifications of DNA (methylation) or histones (methylation, acetylation, etc) and small RNAs that are often associated with epigenetic variation but can be influenced by genetic variation or development / environment

Epigenome: The genome-wide distribution of chromatin modifications or DNA methylation patterns that may include non-heritable changes or genetically influenced patterns

Epialleles: Meiotically heritable allelic differences in chromatin state

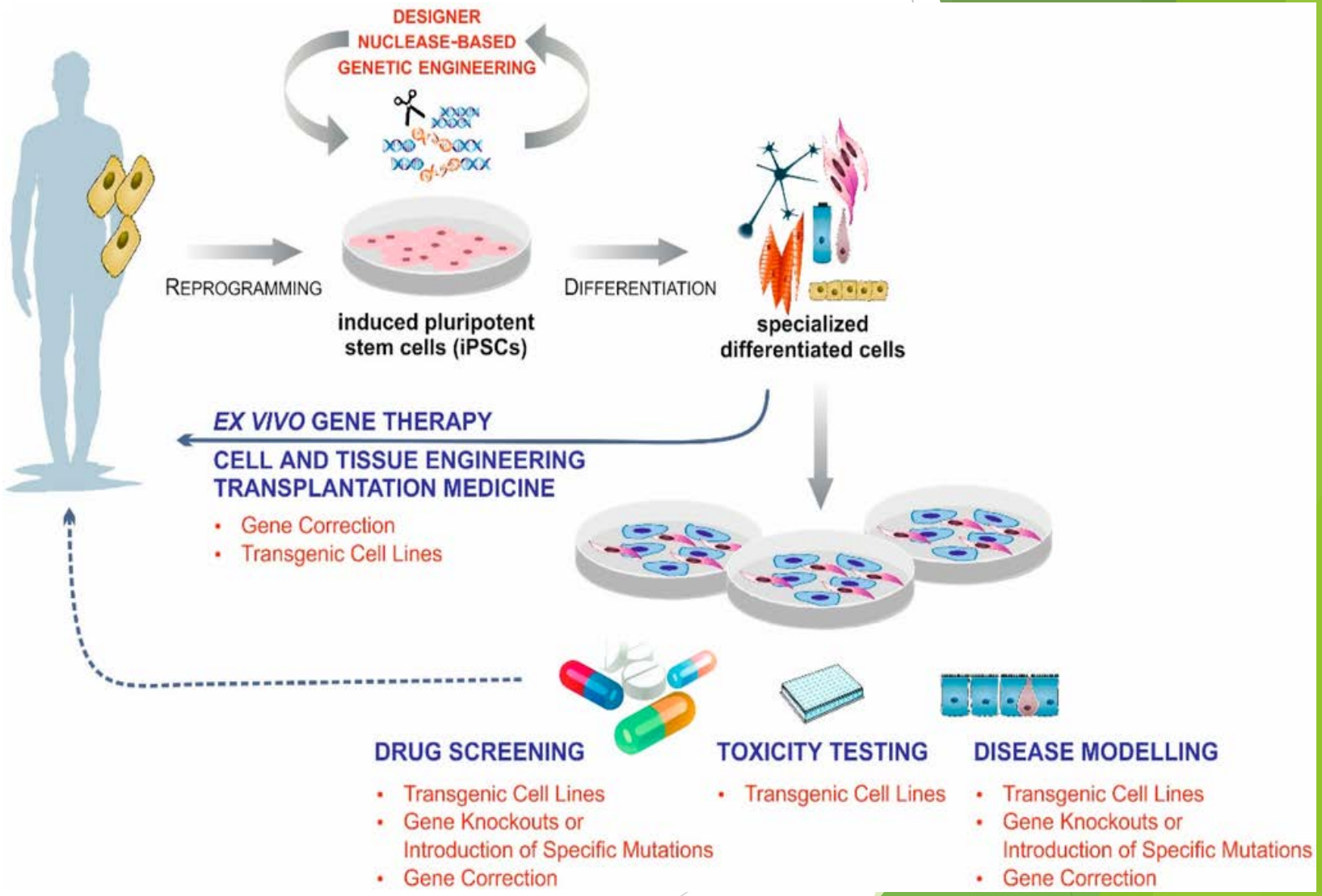
Pure epialleles: Epialleles that have differences in chromatin state that are independent of any genetic information

Facilitated epialleles: Epialleles for which a genetic difference (i.e. transposon insertion) leads to the potential to adopt alternate chromatin states

Obligate epialleles: Epialleles with altered chromatin state that is fully dependent upon genetic variants (either cis or trans-acting changes)

Applications

- Diagnostics
  - Cancer Genome Atlas
  - Congenital Disease
  - Alter Gene Expression
  - Stem Cell Research
  - Tumor Biomarkers
- Therapeutics
  - Targeted Gene Therapy
  - Transgenic Cell Lines
  - Pharmacogenomics



What about….

- Genetic Kits
  - Ancestry.com
  - 23&me
  - Helix
  - MyHeritage
  - Gene2Me
  - Vitagene
  - GeneLife
  - HomeDNA

vs

- DNA profiling (STR analysis)

Twins Ancestry kit link

Questions?


Population
Genetics
Search
Bern
Universität
diversity
study
populations
Institute
Institutes
University
Biology
Faculty
Faculties
Computational
Evolution
CMPG
molecular
Molecular
Menu
Contact
demographic
computer
Department
expansions
speciation
selection
genetic
Ecology
Map
also
Bioinformatics
Baltzerstrasse
theoretical
Media
Research
Constance
found
genomic
Impressum
Twitter
colleagues
colonisation
ecotypes
Africa
Science
Share
collaboration
instance
reconstruct
Notice
explore
humans
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Sciences
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genomics
evolutionary
discover
history
persisting
Swiss
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parameters
Jobs
adapt
E-Mail
Homepage
PloS
Recent
origin
Academy
effect
suggesting
Mutation
simulate
signatures
stage
developments
Central
paper
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genomes
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Proceedings