HIV

October-06-12
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Pre Lecture

1. The general mechanisms by which vaccines protect against diseases.
   - They create a catch of "weapons" for your body's immune system to use when needed
   - When a person gets a viral infection, it may take days or weeks for your body to fight back at full strength
   - When said person is pre-immunized there are forces in the body pre-trained to recognize and fight off certain viruses

2. Why developing a vaccine against HIV is relatively challenging, compared to other diseases.
   - They are always changing
   - Mutates furiously
   - Decoys to evade immune system
   - Attacks the cells trying to fight it
   - Hides itself in your genome

3. Why people are encouraged to get a flu vaccince each year (as opposed to one time only)
   - They virus changes all the time and therefor one certain antibody cannot be used
   - A best guess is taken at what the most prevalent strain of virus will be and the vaccine is issued

Lecture

Epidemic- A widespread occurrence of an infectious disease in a community at a particular time

Pandemic- When the infectious disease hits goes global

The fatalities and number of people living with HIV and AIDS is beginning to no longer increase, in the case of AIDS, descend

The Tree of Life

-After 30 years there is still no cure for HIV

-Viruses do not a have a place on the tree of life because they are not living organisms

-they cannot reproduce without a host

-they are obligate parasites: they cannot live without a host

-they have no metabolic processes

-they have no cells

-Anti-viral therapy has severe side effects

-cannot kill the virus without damaging host cells

-Viruses such as HIV store their information on RNA, not DNA

-must go through reverse transcription which has a high rate of error which cause mutations

-Reverse transcription RNA à DNA

-Retro viruses use reverse transcription

-HIV focuses on immune cells in the human body

HIV Lifecycle

-HIV fuses to host cell and injects information into host cell

-RNA is reversed transcribed into DNA

-reverse transcriptase

-Splices DNA into host DNA
-Transcription, translation, new viruses assemble and bud off or lyse out
-The immune system collapses and host will succumb to a secondary virus

AZT mimics Thymidine and inhibits reverse transcriptase

-AZT attempts to stop reverse transcription
-AZT mimics thymidine and inhibits reverse transcription
-AZT will attach to a DNA chain and will cause a stop
-AZT resistance began and is now completely resistant to the drug
-the virus has changed and AZT is now recognized and avoided
-in addition to a high mutation rate there is also a high reproduction rate

Humans have evolved too

-some people have not contracted the disease despite repeated exposure
-they have a deletion of a set of amino acids of a protein
-1 copy = slightly protected
-2 copies = completely protected
-the strange geographical distribution could be due to:
    -possible selection pressure by HIV
    -forward in N. Europe due to historical epidemics (plague, small pox)
    -chance and history?

Origins

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Pre Lecture

1. characteristics shared by all life.
   All life:
   1. Displays order
   2. Harnesses and utilizes energy
   3. Reproduces
   4. Responds to stimuli
   5. Exhibits homeostasis
   6. Grows and develops
   7. Evolves

2. in what way properties of life are "emergent".
   - The properties of life are considered "emergent" because they emerge from many simpler interactions that, in themselves, do not have the properties found at higher more complex levels.
   - Ex. The ability to harness and utilize energy is not a property of molecules or proteins or biological membranes in isolation; rather the ability emerges from the interactions of all three of these as parts of a metabolic process.

3. characteristics of the "habitable zone" of a solar system.
   - A position where heat from the sun allows for surface temperatures to be within a range that allows water to exist in a liquid state.

4. conditions of a primitive Earth.
   Atmosphere- probably contained an abundance of water vapour from the evaporation of water at the surface, as well as large quantities of Hydrogen (H_2), Carbon dioxide (CO_2), ammonia (NH_3), and methane (CH_4). Almost a complete absence of oxygen (O_2).
   No ozone layer (O_3)- allowed UV light to reach the lower atmosphere and drive the formation of biologically important molecules.

5. types of molecules that were, and were not, synthesized by the Millar-Urey experiment.
   Molecules that were synthesized:
   - Urea
   - Amino acids
   - Lactic, formic and acetic acids

   Molecules not synthesized with the addition of Hydrogen Cyanide (HCN) and Formaldehyde (CH_2O)
   - Building blocks of complex biological molecules
     - Amino acids
     - Nucleic acids
     - Sugars
     - Phospholipids

6. importance of liposomes in evolution of first cells.
   - Early protobionts (a group of abiotically produced organic molecules that are surrounded by a membrane or membranelike structure) were similar to liposomes (a lipid vesicle in which the lipid molecules form a bilayer very similar to a cell membrane).
   - Clay catalyzed the polymerization of nucleic acids and accelerated the formation of lipid vesicles.
   - Clay became encapsulated in these vesicles, which would provide catalytically active surfaces

within membrane vesicles upon which key reactions could take place.

7. characteristics of mimivirus that suggest it should be considered to be alive.
   - The fact that it can get sick makes it more alive

8. characteristics of virophage.
   - A virophage infects a mamavirus (slightly larger than a minivirus) and uses its machinery to replicate
     - Produces fewer and often more deformed mamavirus particles which makes the virus less effective

Lecture

According to the Oparin–Haldane hypothesis, what was the composition of the primordial atmosphere?
A: molecular hydrogen (H2), water, ammonia, and methane

What was the main conclusion of the now famous Miller-Urey experiment?
A: Simple "building block" molecules can be created under abiotic conditions.

Some scientists argue that viruses are not living. Which of the following statements is true and supports the argument that viruses are, therefore, not alive?
A: Viruses do not contain ribosomes, therefore they are not alive.

Life Developed Early
-Life on earth developed quite early, shown through geological evidence, shown through stromatolites (3.5 bya)
-Earth is 4.6 billion years old
-Cyanobacteria are very sophisticated so they were therefor they are most likely not the first form of life

LUCA (Last Universal Common Ancestor)
-Using the tree of life to show what is living, we can determine that viruses are not living
-Humans are derived from the last universal common ancestor (the main stem of the tree of life)
-Characteristics of the living things on the tree of life
-Genetic system based on DNA
-everything has ATP
-they all share proteins (central dogma)
-cells are made up of lipids
-common system of protein assembly
-glucose and glycolysis

What Came Before LUCA
The last universal common answer
-does not mean that everything came from the exact same form of life
-there was most likely many forms of early life
-it was the last common ancestor that survived that created the tree of life

Prokaryotes do not exist on the tree of life
-they are not a single group of organisms
-bacteria and archaea do not share anything in common and they cannot be grouped into prokaryotes
-the pro would assume that they came before, which they did not
-also suggests that evolution moves from simpleàcomplex which is not always true
simple to complex ....misconception

Reductive evolution

They stream lined themselves
Why would they remove the characteristics of eukaryotes ?
Faster reproduction
Extremophiles: they can reproduce in extreme conditions

BioDiversity

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Pre Lecture

1. The approximate times by which the first cells, and the first eukaryotic cells, had appeared.
   - Prokaryotic cells existed 3.5-3.8 Bya
   - Eukaryotic cells had diversified 2.5-2.8 Bya

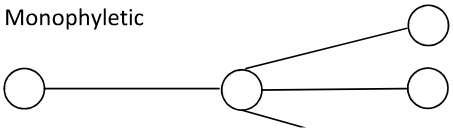
2. The two-kingdom, five-kingdom and three-kingdom (three domain) systems for classifying living things.
   a. Two Kingdom
      - Plants and Animals
        - Determined by structure and function, type of metabolism, movement
      - Eukaryote and Prokaryote
        - Eukaryotes: multicellular, plant and animal and fungi
          - Presence of any internal membranous networks such as a nuclear membrane, organelles or cytoskeleton
          - Presence of endoplasmic reticulum, Golgi apparatus and mitochondria
          - Reproduce by mitotic cell division
        - Prokaryotes: single celled
          - Absence of any internal membranous networks such as a nuclear membrane, organelles or cytoskeleton
          - Absence of endoplasmic reticulum, Golgi apparatus and mitochondria
          - Reproduce by binary fission
   b. Five Kingdom
      - Prokaryotes and 4 domains of Eukaryotes
      - 4 domains: protists, fungi, plants and animals
   c. Three Kingdom
      - Eubacteria and Archaea (prokaryotes) and Eukarya (eukaryotes)
        - Eubacteria: major forms of bacteria and cyanobacteria
        - Archaea: unicells with cell walls made of different molecules than those found in Eubacteria. Often live in more rigorous environmental conditions
        - Eukarya: includes some unicellular organisms and the three groups of multicellular organisms (plants, animals, fungi)

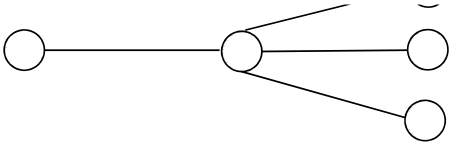
3. Main characteristics distinguishing members of the Eubacteria, Archaea, Eukaryote domains of life.
   Eubacteria: lack of histone proteins, contains genes coding for histones
   Eukarya: includes photosynthetic and non-photosynthetic protozoans and algae, multicellular plants, animals and fungi. Eukarya share mechanisms of cell division and protein synthesis, almost all are aerobic.

4. Meaning of horizontal gene transfer and why this makes it challenging to recreate the universal tree of life.
   - The transfer and incorporation of one organism's or species DNA into the DNA of a different organism or species
   - Horizontal gene transfer has occurred between prokaryote lineages and from prokaryotes to eukaryotes
   - Due to a great amount of gene exchange occurring between prokaryotes, recreating the tree of life for prokaryotes becomes very difficult

5. Monophyletic vs. polyphyletic groupings of organisms
   - In monophyletic (one origin) evolution only a single reptilian group served as ancestor to the mammalian radiation
     - Monophyletic is used for a lineage of organisms that share a single common ancestor
   - In polyphyletic (many origins) evolution two or more reptilian groups served as ancestor to the mammalian radiation
     - Polyphyletic is used for groups that have more than one common ancestor

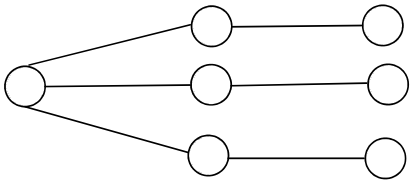
Monophyletic





Reptiles

Polyphyletic



Reptiles

Lecture

Why is the traditional classification of prokaryote vs. eukaryote not very useful in modern biology?
A: Neither of these groups is monophyletic; each group contains organisms that are not very closely related to one another.

From the time of Aristotle until the 1950s, most naturalists classified living things into two groups. What were these groups?
A: Plants and Animals

Baker's yeast is a unicellular eukaryote.
Which of the following characteristics would you expect this organism to show?
A: Division by mitosis (eukaryotes replicate using mitosis)

- Prokaryotes use binary fission: The process whereby a cell divides asexually to produce two daughter cells

Charles Darwin: idea that every species was originated from on common universal ancestor

Estimates anywhere from 3mil to 100mil species
Most of the species on earth have not been described although it is obvious that there are many more

What do we call that single common ancestor? That's LUCA (Last Universal Common Ancestor)

- Everything in the tree of life has some sort of commonality
- All life on earth has certain traits in common
- There is something in every organism on earth that has something in common
    - Storing genetic information in DNA

For any group of organisms we can ask what was the most recent common ancestor

- Starting with present day humans following the evolutionary tree to find the last universal common ancestor

All humans have a common ancestor
The point where the human family tree converges
Approximately 3000 years ago there was one direct common ancestor to all humans today

End-cretaceous mass extinction marks the end of the age of the dinosaurs and the beginning of the age of the mammals

5-6000 years ago we would have been very closely related to chimps
We did not descend from chimps, we simply share a common ancestor
Next MRCA of African great apes

Meteor hitting earth cause the distinction of half of the species on earth
Painted the way for the age of the mammal
Over 40% of all species of mammals are rodents

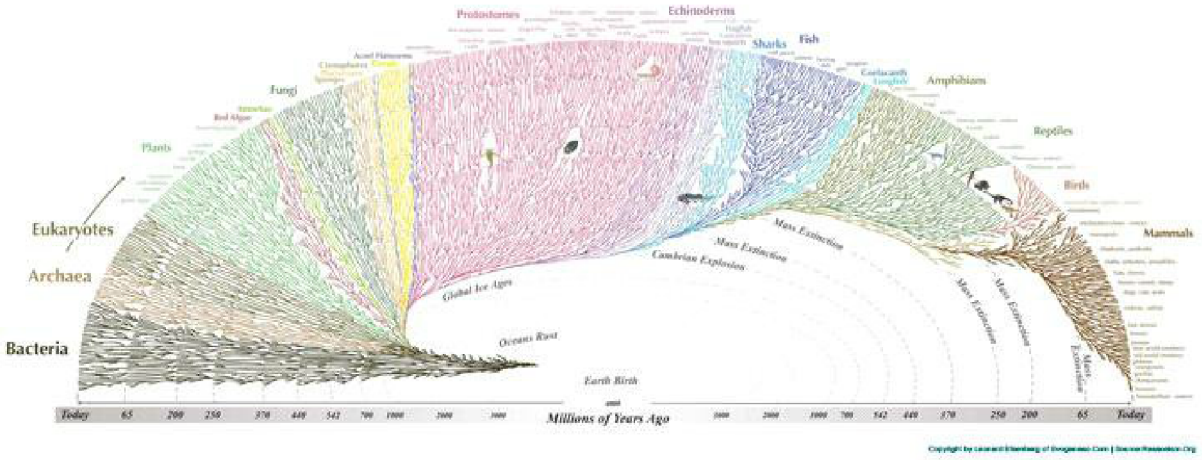
Monotremes- egg laying mammals

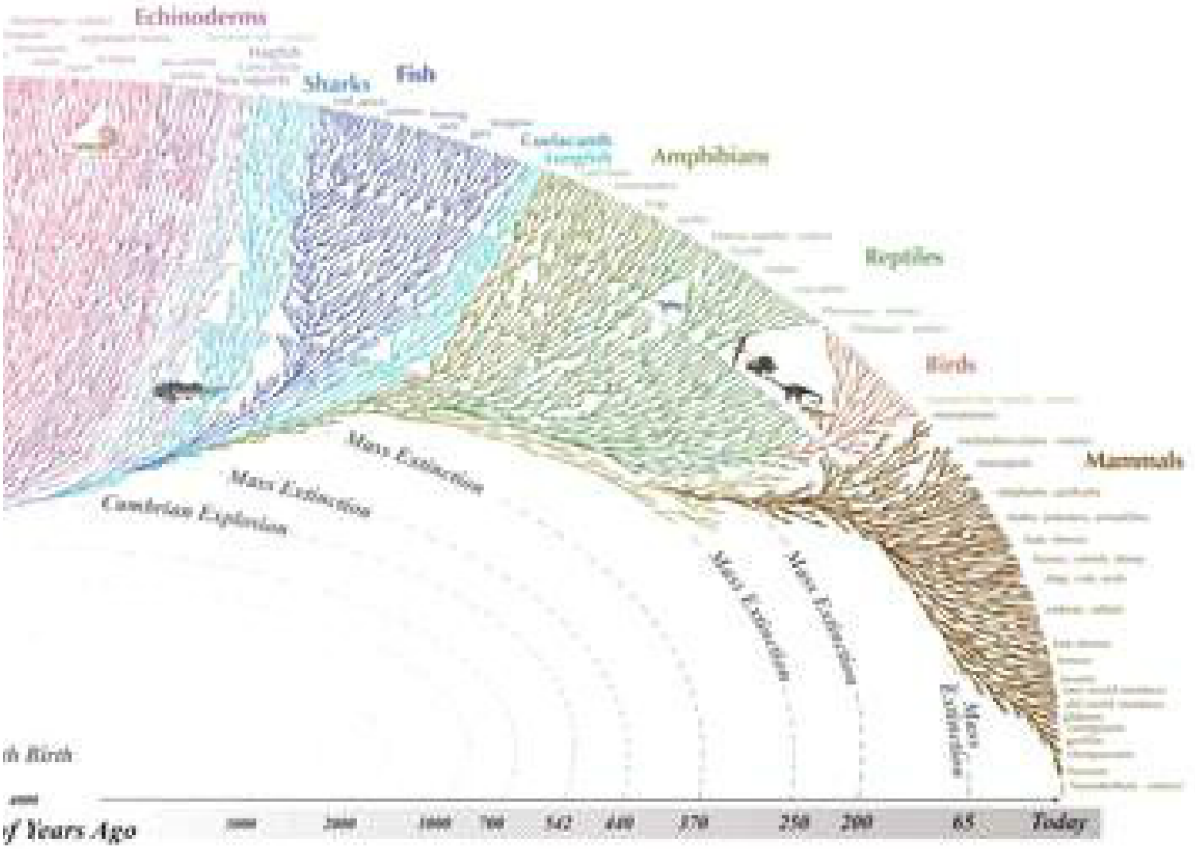
Rendezvous 17: Amphibians
MRCA of all tetrapods 340 mya

Rendezvous 18-22: Lungfish; Coelacanths; Ray-finned fish; Sharks; Jawless fish
these 'fish' are no more closely related to each other than they are to us
MRCA of all vertebrates 530 mya

Archaea
The sister group to the eukaryotes rather than to the bacteria
High temperature and concentration of chemicals, archaea are extremophiles

reconstructing patterns of relatedness, and even estimating numbers of species, is challenging
some similarities reflect shared ancestry; other traits similar due to convergence (eg eyes, sonar…)





Genomic Variation

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Pre Lecture

1. meaning of "C-value"
   - The term C-value refers to the amount of DNA contained within a haploid nucleus (e.g. a gamete) or one half the amount in a diploid somatic cell of a eukaryotic organism

2. "paradox" or "enigma" associated with C values
   - C-value enigma is the observation that genome size does not correlate with organismal complexity; for example, some single-celled protists have genomes much larger than that of humans.

3. meaning of haploid (n) and diploid (2n)
   Haploid: an organism or cell with only one copy of each type of chromosome in its nuclei
   Diploid: an organism or cell with two copies of each type of chromosome in its nuclei

4. relationship between C and n as measures of genome size.
   C-value: the amount of DNA in one genome, measured in grams or picograms, as well as bases or million bases Mb of one set of DNA

   n- The number of sets of chromosomes

5. proportion of the human genome that codes for protein
   - All protein coding sequences occupy less than 2% of the human genome

Lecture

Which of the following observations contributes to the C-value "paradox" (or "enigma")?
A: Members of the same group of organisms, say amphibians, have similar complexity but widely differing C values.

Immediately following the fertilization of a rhinocerous sperm and egg cell, the resulting zygote has two copies of every rhinocerous chromosome. The zygote is therefore diploid and the value of "n" is 2.
What is the value of "C".
A: 2.0

Many people assume that relatively little of the DNA sequence in their genome has some function other than coding for proteins needed in the structure and function of human cells.
How much of the human genome sequence is NOT coding for human proteins?
A: more than 75%
   - Only 2% of the genome sequence codes for human proteins

Difference that matter in evolution are usually difference in DNA, branches off the tree of life represent differences at the level of DNA and genomes

How many chromosomes do you have in any given skin cell?
   - There are x chromosomes in every cell of your body (1 or 2 depending on gender)

Genome: one copy of an entire set of chromosomes, when talking about nuclear DNA
   - There is DNA in other places such as in plants cells, DNA can be found in mitochondria, chloroplasts as well as in the nucleus

DNA polymerase: an enzyme that assembles complementary nucleotide chains during DNA replication

C-value: the amount of DNA in one genome, measured in grams or picograms, as well as bases or million bases Mb of **one** set of DNA

The genome size or C-value can vary considerably within a taxonomic group
- With Archaea and Eubacteria genome size is quite small but ranges

C-value enigma: Organism complexity is not directly correlated to genome size
One c-value is spread over an entire set of chromosomes

n- The number of sets of chromosomes
- Humans are diploid and therefor have an n-value of 2
- They have 23 pairs of chromosomes and therefor have a diploid number of 46 chromosomes (2n= 46)

Almost all Eukarya have linear chromosomes
Almost all Prokaryotes have circular chromosomes

Ploidy- the number of chromosome sets
Diploid- two sets of chromosomes
Triploid- three sets of chromosomes

What is the c-value of a triploid (3n) cell
- If one copy of DNA is C and you have 3 copies of DNA than you must be 3C
- 6C would also be acceptable during S phase where chromosomes replicate

DNA is would around proteins, wound around nucleosomes, made up of histone proteins
Each X shaped chromosome has two copies of DNA, they are replicated DNA
Once DNA is replicated it gives rise to chromatids, two sister chromatids created the X chromosome

Genome Projects:

- Sequencing a genome involves a replication reaction with a DNA template, a DNA primer, the four deoxyribonucleotides, and a mixture of four dideoxyribonucleotides, each labeled with a different fluorescent tag, and DNA polymerase. Replication stops at any place in the sequence in which a dideoxyribonucleotide is substituted for the normal deoxyribonucleotide. The lengths of the terminated DNA chains and the label on them indicate the overall sequence of the DNA chain being sequenced.
- The whole-genome shotgun method of sequencing a genome involves breaking up the entire genome into random, overlapping fragments, cloning each fragment, determining the sequence of the fragment in each clone, and using computer algorithms to assemble overlapping sequences into the sequence of the complete genome.

How human genome is different between races of people

55% of genome is composed of transposons, viruses and a few “dead genes” (junk)
Transposons and viruses do not code for humans
10% introns (junk)
25% is unknown
10% Essential (2% coding)

Each chromatid has one molecule of dsDNA (double stranded DNA)

Genomic Replication

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Pre-Lecture

1. purine and pyrimidine base-pairing in DNA/RNA
   Purine: nitrogenous base with 2 carbon-nitrogen rings (Adenine and Guanine)
   Pyrimidine: nitrogenous base with 1 carbon-nitrogen ring (Cytosine and Thymine)
   Purines pair with pyrimidines
   Complementary base pairs: Adenine + Thymine and Guanine + Cytosine

2. outcome of the classic Meselson and Stahl experiment
   To distinguish between parental and newly synthesized DNA they used a "heavy" isotope to tag the parental DNA.
   a. Bacteria was grown in a medium containing the heavy N15 isotope and incorporated into the nitrogenous bases of DNA
   b. They transferred the bacteria to a culture medium containing N14
   c. All newly synthesize DNA would therefor, contain N14. Before the transfer and after each round of replication a sample was taken
   d. DNA was mixed with cesium chloride (CsCl) and centrifuged the mixture
   e. The CsCl creates a density gradient and DNA double helices move to a position in the gradient where their density matches that of the CsCl. DNA of different densities is separated into bands with the densest DNA settling closer to the bottom

   Results:
   - DNA banding patterns matched those of semi-conservative replication

3. direction of movement of DNA polymerase on the template strand
   - DNA polymerase III adds DNA nucleotides to the RNA primer in the 5' --> 3' direction on the template strand
     - On the leading strand this is toward the replication fork
     - On the lagging strand this is away from the replication frok

4. meaning of semi-conservative, semi-discontinuous, leading and lagging strand
   - Semiconservative Replication: two strands of a parental DNA molecule unwind and each serves as a template for the synthesis of a complimentary strand.
   - Conservative Replication: each of the two strands of original DNA serves as a temple for new DNA.
   - Leading strand: a DNA strand assembled in the direction of DNA unwinding
   - Lagging strand: a DNA strand assembled discontinuously in the direction opposite to DNA unwinding

5. general action of proteins in Fig. 12.15.
   1) DNA helicase unwinds the DNA
   2) Primases synthesize short RNA primers in the 5' --> 3' direction
   3) Topoisomerase prevents twisting ahead of the replication fork
   4) DNA polymerase III adds DNA nucleotides to the RNA primer, continuing the 5' --> 3' direction
   5) Primase synthesizes a new RNA primer on the lagging strand template near the point of unwinding
   6) The primer is extended by the addition of DNA nucleotides by DNA polymerase III
   7) New DNA synthesis stops when the polymerase reaches the 5" end of the previous Okazaki fragment

8) DNA polymerase I removes the RNA primer of the previously synthesized Okazaki fragment one nucleotide at a time. It replaces the RNA nucleotides with DNA nucleotides. It leaves the template.

9) DNA ligase seals the nicks between the two lagging fragments newly synthesized

Lecture

The cesium chloride gradient used by Meselson and Stahl allowed them to separate certain kinds of DNA from others. What kinds of DNA did they separate?
A: heavy DNA from light DNA

What is the role of the helicase enzyme in DNA replication?
A: unwinds the helix at the replication fork

When does the mass of DNA in an elephant cell increase during the cell cycle?
A: S phase

DNA runs antiparallel, the bases are connected through hydrogen bonds and each nucleotide base is connected by phosphodiester bonds- a bridging phosphate group between the 5' carbon of one sugar and the 3' carbon of the next sugar.

The 3' end has OH and the 5' end has a phosphate group

Each full turn of the double helix involves 10 base pairs and is 3.4 nm

DNA Replication:

- Dispersive Replication: neither parental molecule remains intact; both chains of each replicated double helix contain old and new segments.
- Helicase: unwinds the DNA
  Primase: synthesizes an RNA primer used as a starting point for nucleotide assembly by DNA polymerase
  DNA polymerase: assembles nucleotides into a polymer in a sequence complimentary to the sequence in the template. Then removes the primers and fills in the resulting gaps
  DNA ligase: closes remaining single-strand nicks
- Discontinuous replication: the DNA strand is synthesized in short lengths in the direction toward the replication fork; occurs because DNA must synthesize in the 3'à5' direction.
  Continuous replications: replication of one strand in the 3'à5' direction away from the replication fork
- Telomerase: adds telomere repeats to the end of linear chromosomes
  - Provides a buffer against chromosome shortening during replication
    Telomeres must be added to both ends of the replicated DNA strand

Interphase:

G1: period of cell growth before replication
S: period when DNA replicates and chromosomal proteins duplicate
G2: period after DNA replicates, cell prepares for division

Inheritance of Sameness

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Pre Lecture

More specifically, in multiple choice format, identify the . . .

1. stages and main characteristics of the stages of mitosis.
   Prophase: DNA condenses into chromosomes
   Prometaphase (late prophase): nuclear envelope dissolves and spindle fibres attach to chromosomes
   Metaphase: chromosomes are pulled by spindle fibres and aligned in the mid line of the cell
   Anaphase: cohesin dissolves and spindle fibres begin to pull sister chromatids to opposite poles
   Telophase: nuclear envelopes reforms and chromosomes recondense and in most cells cytokinesis forms the daughter cells

2. stage of cell division, given a micrograph of a dividing cell.
   Interphase:
   DNA is stranded and has not condensed into chromosomes
   G1: period of cell growth before replication
   S: period when DNA replicates and chromosomal proteins duplicate
   G2: period after DNA replicates, cell prepares for division

Mitosis:
   DNA condenses and coils around proteins called histones
   Cell division into to identical daughter cells

3. role and mechanism of the mitotic spindle.
   The spindle is the structure that moves chromosomes during cell division. In mitosis, spindles have two spindle poles, one for each resulting daughter cell. Spindles are made up of microtubules that radiate outward from microtubule organizing centres. The spindle microtubules can rapidly grow, shrink, and attach to kinetochores on chromosomes.

   Spindle fibres attach to kinetochores: protein on a chromosome that attaches to a spindle microtubule, they are usually but not always located near the centromere

4. role of cell cycle check points.
   - This causes the cell to divide properly
   - If not all the chromosomes are properly lined in the middle of the cell the cell will wait to ensure proper cell division

   - Located: G2 --> M
     Metaphase --> Anaphase
     G1 --> S

5. changes in amount of DNA throughout the cell cycle.
   - Meiosis:
     - Before replication: 2n 2C (in a diploid cell, there are 2 copies of DNA)
     - After replication: 2n 4C (in a diploid cell, DNA replicates and there are 4 copies of DNA)
     - After the first division: 1n 2C (in a haploid cell, homologous chromosomes have split leaving 1 replicated chromosome, or 2 copies of DNA)
     - After the second division: 1n 1C (in a haploid cell, chromosomes divide there is 1 copy of DNA)
   - Mitosis:
     - Before replication: 2n 2C (in a diploid cell, there are 2 copies of DNA)
     - After replication: 2n 4C (in a diploid cell, DNA replicates and there are 4 copies of DNA)
     - After division: 2n 2C (in a diploid cell, chromosomes divide and there are 2 copies of DNA)

Spindle fibre anatomy
Centromere- point where the sister chromatids are closest
- Microtubules are apart of the cytoskeleton, a long polymer of proteins called tubulin
- The microtubules have many proteins attached to them during mitosis
  - One class is motor proteins: can generate force and transport cellular components, in mitosis they move

proteins

If not all chromosomes have properly connected microtubules

Lecture

Homologous chromosomes contain the same genes, but they may have different DNA sequences for each gene.

The gene occurs at the same location for each homologous chromosome, but each has a different version of this gene. These different versions are called alleles.

Ex. A gene would be eye colour, an allele would be blue eye colour

Independent assortment: each daughter cell randomly and independently receives one of the two homologous chromosomes from each pair

List of Mechanisms to Ensure Inheritance of "Sameness"

1. Complementary base pairing
2. DNA polymerase proofreading and repair
3. Enzyme proofreading and repair

List of Mechanisms that Promote Inheritance of "Differences"

1. Transportable elements (Transposons, retrotransposons)
2. Recombination of chromatids during prophase of the first meiotic division
3. Random segregation of homologous chromosomes in meiotic division
4. Random segregation of the chromatids of replicated chromosomes
5. Random joining of male and female gametes in fertilization
6. Tautomeric instability causing mutations
7. Replication slippage (CNV)

Where would cells in a tree divide

- Outside
- Meristematic cells
- Would repair
- Root tips

Why might cells be programmed to die? (apoptosis)

- Surplus cells
- They are too old
- Cell walls are dead (plants, act as a skeleton)

They are too old- they know how old they are by noticing how long their telomeres are, once shortened to a critical length apoptosis is triggered
Over expression of telomerase in a mouse would cause an increase in cancer
Since we need telomeres to shorten the expression of genes telomerase is highly regulated, essentially turned off
Majority of cancers express telomerase inappropriately

Origins of Variation

October-03-12
10:54 AM

Pre Lecture

1. mechanism of proofreading and likely result of proofreading defects
   - Polymerization activity of DNA polymerase adds DNA nucleotides to the new chain in the 5' --> 3' direction using complementary base pairing rules
   - Rarely, DNA polymerase adds a mispaired nucleotide
   - DNA polymerase recognizes the mismatched base pair. The enzyme reverses, using 3' --> 5' exonuclease to remove the mispaired nucleotide from the strand
   - DNA polymerase resumes its polymerization activity in the forward direction, extending the new chain in the 3' --> 5' direction

   - In bacteria the likely hood of an error is about 1 in 1million nucleotides

2. mechanism of mismatch repair
   - DNA polymerase reversal

   - Enzyme recognition and repair, if errors escape DNA polymerase:
     - Repair enzymes move along the DNA scanning for distortions in the double helix due to a mispaired base. The enzymes break the backbone of the new strand on each side of the mismatch
     - The enzymes remove several to many bases, including the mismatched base, leaving a gap
     - DNA polymerase fills in the gap with its 5' --> 3' polymerizing activity, using the template strand as a guide
     - DNA ligase seals the nicks left after gap filling to complete the repair

3. differences among insertion sequences, transposons and retrotransposons
   - Insertion sequences- the simplest TE (transposable elements), small and contain only genes for transposition, notable the gene for transposase: an enzyme that catalyzes some of the recombination reactions for inserting or removing the TE from the DNA
     - On either side of an IS there are inverted repeat sequences, a DNA sequence that runs opposite in either direction. These allow transposase to identify the ends of TE.
     - 2 Types:
   1. Transposons- have inverted repeat sequences on either side of the central region which contains one or more genes. In many bacterial transposons, the inverted sequences are insertion sequences which provide the transposase for movement of the element.
      - Simply, when there are 2 insertion sequences side by side they offer an insertion of genes between the
   2. Retrotransposons- similar to transposons however they transpose by a copy-and-paste mechanism, occurs by an immediate RNA copy of the TE. The copy is made into DNA by the enzyme reverse transcriptase, which is encoded by one of the genes of the retrotransposon. The DNA is then inserted

4. implications of insertion of mobile elements into DNA
   - Many antibiotics were once successful in curing bacterial infections, however they have become much less effective due to resistance genes in transposons. Movement of these transposons increases the spread of genes, providing antibiotic resistance to infecting cells

5. why transposons are not actually "jumping" genes
   - TE transposition starts with contact between the TE and the target site. This also means that

TEs do not exist free of the DNS in which they are integrated, therefor the term "jumping" genes is inaccurate

6. basic structure of retrovirus genome
   - Made up of RNA which is transcribed into DNA
   - DNA is then transposed into the host DNA

Lecture

Which of the following enzymes is involved in repairing mismatched bases during DNA replication?
A: DNA polymerase

DNA replication in the replisome and during mismatch repair involves extending a 3'OH on a properly paired base.
A: True
   - DNA transcription must always follow the 5' --> 3' direction

What is one characteristic that all mobile DNA elements seem to have in common?
A: Repeated DNA at the ends

When mutations are thought of they think of a single base pair change

CNV- copy number variation

SNP- single nucleotide polymorphisms

People are different due to CNV

As well as variants in insertion of retro elements

Comparison of SNPs in 10 person genomes

Some have a significant amount of unique SNPs

Where do SNPs come from?

base pairing normally:

hydrogen bonds have one atom to donate and the other to accept

between G and C there are 3 H bonds, A and T there are 2 H bonds

H- donor O, N- acceptor

base paring does not work due to H bonds (normally)

tautonerism occurs when- a double bond in a molecule moves so that the molecular formula stays the same but a different molecule forms

when tautonerism occurs in guanine it is then possible to H bond to thymine

during replication if tautonerism occurs and A-C base pairs this is called damage

The change in the double stranded pair replicates into a mutation

happens naturally

requires DNA replication

Origins of Variation 2

October-10-12
11:50 PM

Pre Lecture

1. characteristics of STR loci that make them useful for forensic DNA analysis (DNA fingerprinting).
   - Each locus is an example of a *short tandem repeat* (STR) sequence, meaning that it has a short sequence of DNA repeated in a series , with each repeat about 3-5 bp
   - Each locus has a different repeat sequence and the number of repeats varies among individuals in a population
   - Each individual has an essentially unique combination of alleles coding for this combination (as well as homozygous and heterozygous combinations) creating a unique DNA fingerprint for a locus
   - Analysis of STR loci can discriminate between DNA of different individuals

2. mechanism of DNA recombination
   - breaking the covalent bonds of the DNA backbones, matching complementary sequences and non-sister chromatids, exchanging the ends and restoring the bonds

3. stage of meiosis when recombination occurs
   - During prophase 1 of the first meiotic division the replicated chromosomes condense and come together and pair as the spindle forms in the cytoplasm
   - While they are paired the chromatids of homologous chromosomes undergo recombination

Lecture

In a tautomeric T-G why does the Thymine not get removed?
Hydrogen bonds are not very stable and are broken all the time
DNA polymerase does not detect a mismatch repair
    - involved in proofreading
Thymine can switch back but the guanine will still be there
The pair doesn't distort the double helix!

5-Bromouracil and Thymine cannot be differentiated by DNA polymerases
    - gets replicated into DNA during replication
    - does not always behave like Thymine, very tautomerically unstable
    - changes tautomers very often
    - a mutogen, increases the mutation frequency

The ring structure of thymine is very susceptible to absorbing the photons of UV light
    - reorganizes the structure to adjacent thymines and bonds them together
    - base-base: distorts the helix
    - very difficult for polymerases to deal
    - very difficult to replicate at a **dimer**
    - causes stalling of cell division and possibly death of cell
    - severe damage
    - sometimes some cells relax their polymerase such that they can put any base in across from a dimer
        - saves the life of the cell but creates mutations and problems for the cell

Life would not have developed on earth if there was no way to deal with dimers
Photolyase- breaks the dimer bonds and restores thymines to the way they were
    - driven by a photon of visible light (blue)
    - whenever light was exposed to UV light it was also exposed to visible light

Mammals do not have photolyase
- lost over evolution

Stuck with the excision repair mechanism
- dimers are cut out and replaced

Dimer:
The addition or deletion of a base pair, causes a looping out of a base
- occurs in repeating bases, slipping out and is stabilized
- creates a mutation when replicated

Huntingtons- triplet repeat disease
- slippage causes the disease to get worse

Living near highly radioactive areas

Radioactivity- the decay of unstable elements
- each element has a characteristic number of protons
- the decay releases dangerous radioactivity
- a characteristic of unstable isotopes

Ionizing Radiation creates ROS that damages DNA
- ROS: reactive oxygen species
- Decay of radioactive iodine and cesium creates "ionizing radiation".
- Iodine has a relatively short half-life (1 wk); cesium relatively long (30 yrs).
- Iodine is concentrated in thyroid glands.

I and Cl release beta and gamma radiation
Pass through body and rip e- from Oxygen creating ROS- reactive oxygen species
- look for e- that has been lost
- strip from anywhere they can be found
- results in breaking chromosomes
- if both backbones of the chromosome break than the chromosome breaks

Broken chromosome repair systems
- not perfect, can lose pieces of chromosome, duplications, many problems
- can create more mutations
- insertion or deletion

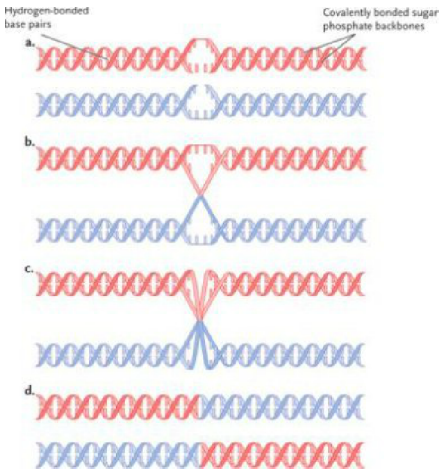
Inversions could take place on the chromosomes
Translocations- piece of one chromosome can end up on another chromosome
- can be very severe in their consequences
- can deregulate a gene
- where a gene is on a chromosome effects how and when it is expressed

Gene duplication creates gene families
Gene families- CNV between species
Betaglobin- gene for
Sudoglobin- X: no longer there
Can construct genetic trees from genes

Amphibians, fruit fly and mice all have very similar gene order
- expressed in the same order

We can go backwards to find the common ancestor
- CNV over evolutionary time

Mutations are double-stranded changes
- Crossing over during meiosis is a double stranded change and therefor fits our definition of a mutation


Hydrogen-bonded base pairs
Covalently bonded sugar phosphate backbones
a.
b.
c.
d.

Meiosis

October-15-12
10:00 PM

Pre Lecture

1. products of meiosis in animals vs. plants, fungi and algae
   - Animals: haploid gametes
   - Plants: haploid spores
   - Fungi and Algae: spores

2. timing of meiosis in vertebrate life cycles
   - In human females oogenesis begins before birth, when cells being meiosis I. The immature ova arrest in meiosis I and do not resume oogenesis until adulthood as a part of ovulation
   - In males, the production of sperm through sexual recombination in meiosis occurs after puberty

3. main differences between meiosis and mitosis
   - Meiosis II only occurs in reproductive tissue, is not preceded by an S phase, and results in genetically different daughter cells

4. characteristics of homologous chromosomes
   - Homologues are same size, shape and banding patters
     - same genes in the same places
     - the alleles may be different

Lecture

Before the meiosis lecture, most students in Biology 1001A would likely agree with the general statement; "The products of meiosis are haploid gametes that do not divide."
However, the following statements contradict these ideas.
Which of the following statements is true?
A: Plants, algae and fungi make their haploid gametes by mitosis, not meiosis.

Baby rattlesnakes hatching from a clutch of eggs are brothers and sisters; yet they all have a different combination of alleles as a result of genetic recombination.
When did this recombination occur?
A: When the parent snakes made gametes.
   - Genetic recombination occurs during meiosis by crossing over

When the parent snakes made gametes.
A: Homologous chromosomes are different in being inherited from different parents.
A: Homologous chromosomes are different in carrying different alleles for many genes.
A: Homologous chromosomes are different in having different distributions of retro-transposon insertions.

Meiosis I- Reduction division of meiosis
Meiosis II- Equational

WRONG- Gametes are made by meiosis
In animals gametes are made by meiosis
In plants meiosis does not make gametes
    - meiosis makes spores, they reproduce through mitosis
In fungi and algae meiosis makes spores
    - mitosis makes gametes

- reverse of animals

WRONG- sexual reproduction
Many organisms reproduce without sexual interactions
Sexual recombination*
- involves the DNA of two different parents coming together in the same cell

Recombination meets our definition of a mutation
- a change in the sequence

Homologous chromosomes do not recombine side by side
Males experience prophase of meiosis after sexual maturity
men are engaging in sexual recombination all the time
Females experience prophase of meiosis as a fetus (meiotic arrest)
females have already engaged in sexual recombination
fertilization is what triggers the continuation of meiosis
Regardless of the time the process of meiosis is the same

Recombination can go wrong and generate CNV
- the pairing can slip and create unequal homologous chromosomes
- unusual mechanism of CNV
Meiosis is a very powerful generator of genetic variation

Mutations are double-stranded changes
Genes that are close together have little DNA between them that can be recombined
- lower frequency
Likely hood of recombination of genes close together is low as opposed to genes that are farther apart
Independent assortment
- among different cells the chromosomes are lined up in different order and split differently

Non-disjunction, can suffer a mistake
Problem with spindle as years progress
Aneuploid --> zygote
Failure of meiosis I spindle to segregate spindle properly
Misdivision --> aneuploid gametes

Aneuploid- having a chromosome number that is not a multiple of the haploid number

Inheritance of Variation

October-17-12
10:59 PM

Pre Lecture

1. arrangement of genes and alleles on homologous chromosomes in a dihybrid organism
   - The alleles of genes that govern the two characteristics segregate during formation of gametes
     - In monohybrid a Pp separates to 1/2 gametes P and 1/2 gametes p
     - In dihybrid Aa Bb X Aa Bb can be treated as: Aa X Ax and Bb X Bb

2. how independent assortment creates 4 different products of meiosis from a dihybrid parent
   - Principle of Independent Assortment: during the segregation of alleles into gametes, the alleles of different pairs assort differently (R/r and Y/y alleles give four combinations in gametes in equal proportion)

3. application of the sum and product rule of probability
   - Product rule- the probability of A and B occurring at the same time = the probability of each multiplied
     - (1/6 x 1/6 = 1/36) the probability of rolling 2 4's in dice
       - Applications: the chance of having 4 children the same sex in a row = (1/2 x 1/2 x 1/2 x 1/2 = 1/12)

         In a F1 generation Pp x Pp where 1/2 contain P and 1/2 contain p a zygote with PP = 1/2 x 1/2 = 1/4
   - Sum rule- the probability of A or B occurring = the probability of each added together
     - (1/6 + 1/6 = 1/3) the probability of rolling a 3 or a 4
       - Applications: In a F1 generation Pp x Pp where 1/2 contain P and 1/2 contain p a zygote with Pp = (1/2 x 1/2) + (1/2 x 1/2) = 1/2
         - Since there are two different ways for gametes to combine and produce Pp zygotes

Lecture

Imagine that you are heterozygous for the CCR5-32 allele that makes you more resistant to HIV infection. (The CCR5 gene is on the short arm chromosome 3.)
Imagine your cells in G2 of the cell cycle. If there is one CCR5-32 allele on one chromatid of the chromosome 3 inherited from your mother, then where is there another CCR5-32 allele?
A: On the sister chromatid.

Consider an organism that is heterozygous for 3 different genes (Aa Bb Cc) carried on three different chromosomes. (Maybe make a quick sketch.)
How many different combinations of alleles are possible in the resulting products of meiosis as a result of independent assortment? (If this was you, how many different types of gametes would you make?)
A: 8
- # of allele combinations ^ # of alleles x # of genes
- 2^3

Where are genes for making a uterus?
- On X chromosomes from her mother
- On X chromosomes from her father
- On autosomes

Mendal: changed the idea that inheritance was blending
- mixing paint (red + blue = purple)

Polygenic traits show continuous variation in a population
Polygenic traits: inheritance of a phenotypic characteristic (trait) that is attributable to two or more genes and can be measured Quantitatively.

Inheritance is particulate
2 parents that are intermediate can produce zygotes of extreme alleles
- cinnamon parents can produce mayonnaise and coal babies

Mendal created the model that stated:
- Variation in traits due to different alleles
- Alleles segregate randomly into gametes
- Organisms inherit two alleles for each trait

Had the correct idea
Mendal's first law: alleles are put randomly into gametes
Organisms have two copies of these factors
When there are two factors the allele that determines the phenotype of a heterozygote is the dominant one

Chance of getting pp from Pp x Pp = ½ x ½ = ¼ pp

Reciprocal crosses demonstrate sex linkage
- the distributions are different when genes are sex linked
- the Y chromosome doesn't carry the allele for the white eyes at all

If a recessive deadly gene on a female fruit fly is crossed with a normal male fruit fly, what fraction of the offspring would die?
A: ¼
X+X- x X+Y

Blood type has 3 alleles, mendal's traits had 2 alleles
Possible from mother: A, B, i
Possible from father: A, B, I

Inheritance in Populations

October-22-12
8:59 PM

Pre-Lecture

1. strategy to distinguish between a phenotype that results from codominance relative to incomplete dominance
    Incomplete dominance: the effects of recessive alleles can be detected to some extent in heterozygotes
        White and Red phonotypes in flowers create Pink flowers
    Codominance: alleles have approximately equal effects in individuals, making the two alleles equally detectable in heterozygotes
        White and Red phenotypes in flowers create spotted flowers with both phenotypes expressed

2. characteristics that identify a pleiotropic allele
    Pleiotropy: when a single gene effects more than one characteristic
        Example: Sickle cell disease is caused by a recessive allele of a single gene that affects hemoglobin structure and function. However, the altered hemoglobin protein, the primary phenotypic change of the sickle cell mutation leads to blood vessel blockage, which can damage many tissues and organs in the body and thus affect many body functions, producing wide-ranging symptoms. These are pleiotropic effects of sickle cell disease

3. conditions under which Hardy Weinberg Equilibrium is possible in a population.
- The point at which neither allele frequencies nor genotype frequencies change in succeeding generations
    a. No mutations are occurring
    b. The population is closed to migration from other populations
    c. The population is infinite in size
    d. All genotypes in the population survive and reproduce equally well
    e. Individuals in the population mate randomly with respect to genotypes

Lecture

Which of the following characteristic of dominant alleles?

If you mated a pure-breeding black pig with a pure-breeding brown pig what do you think the piglets will look like?
A: all black

If you cross two of the piglets together what will the resulting offspring look like?
A: both black and brown pigs in a 3:1 ratio
- Therefor the black allele is dominant

If we start with a dominant allele that is common and a recessive allele that is rare, what will eventually happen?
A: Allele frequencies will not change much

Would this change if there was a large number of rare recessive allele and a very small number of dominant common allele?
A: Allele frequencies will not change much

In a large population, in the absence of selection, what influences future allele frequencies?
A: The starting allele frequencies

What if a population contains many alleles?
    B (p=0.3) W (q=0.3) and R (r=0.4)
    How many possible genotypes are there?
A: 6

Selection and Fitness

October-24-12
6:55 PM

Pre-lecture

Genotype: a combination of genes
Allele: a version of a gene

1. Meaning of deme, population, allele frequency, genotype frequency
   Deme: a local population of a species; in sexual forms, a local interbreeding group
   a.k.a.- a local population of organisms of one species that interbreed with one another and share a distinct gene pool
   - Structural features of an environment- a river that individuals cannot cross, or a landslip- reduce effective deme size

   Allele frequencies: the proportion of different alleles in a population
   Ex. (p=0.7 q=0.3)
   Genotype frequency: the frequency of a genotype — homozygous recessive, homozygous dominant, or heterozygous — in a population
   Ex. (CrCr= 0.45 CrCw= 0.50 CwCw=0.05)
   - Finding the q and p
     - p = 2CrCr + CrCw / 2CrCr + 2CrCw + 2CwCw
       (0.9 + 0.5) / 2.0 = 0.7
     - q = CrCw + 2CwCw / 2CrCr + 2CrCw + 2CwCw
       (0.5 + 0.1) / 2.0 = 0.3

2. Allele frequencies in a population, given the genotype frequencies
   - Allele frequencies do not depend upon dominance or recessiveness (genotype frequency)
   - Remain essentially unchanged from one generation to the next, *provided* that mating is random and all genotypes are equally viable

3. Genotype frequencies in the next generation, given the allele frequencies and assuming Hardy-Weinberg equilibrium
   - By confining our attention to alleles rather than genotypes, we can predict allele and genotype frequencies in future generations
     - Once Hardy-Weinberg equilibrium is reached the genotype frequencies will remain the same

4. Assumptions of Hardy-Weinberg equilibrium
   1. Parents represent a random sample of the gene frequencies in the population
   2. Genes segregate normally into gametes (heterozygotes for any gene pair produce their two kinds of gametes in equal frequencies)
   3. Parents are equally fertile (gametes are produced according to the frequency of the parents)
   4. The gametes are equally fertile (all have an equal chance of becoming a zygote)
   5. The population is very large (all the possible kinds of zygotes will be formed in frequencies determined by the genetic frequencies)
   6. Mating between parents is random (not determined by any preferences associated with specific genotypes)
   7. Gene frequencies are the same in both male and female parents
   8. All genotypes have equal reproductive ability

Simply put:
1. Random mating in large populations
2. Equilibrium allele frequencies
3. Absence of gene flow into the population

Lecture

A populatio of pigs contains 3 MC1R alleles: B (p=0.3) W (q=0.3) R (r=0.4)
If this population is in Hardy-Weinberg equilirui at MC1R what proportion of pigs are genotype WR
A: (0.3 x 0.4) x 2 = 0.24

- Multiply by 2 due to the ability to have WR or RW