

Lectures 9 and 10

1. products of meiosis in animals vs. plants, fungi and algae

- Meiosis in animals: zygotes divide by mitosis, gametes produced by meiosis
- In plants: Spores and zygotes divide by mitosis in haploid and diploid phases
- In fungi and algae: Spores divide by mitosis, formed by meiosis
- The only gametes on the planet made by meiosis are in animals

2. timing of meiosis in vertebrate life cycles

- The life cycle of nearly all eukaryotes alternates between a haploid and diploid phase but there is a wide variety in the relative timing of mitosis, meiosis, and fertilization among different species
- In plants, the haploid products of meiosis are spores, not gametes
- These spores divide by mitosis to form multicellular bodies that then make gametes by mitosis. Many organisms make gametes by mitosis
- Animals are haploids only as sperm and egg and fertilization restores the diploid phase of the life cycle. Meiosis is followed directly by gamete formation
- Plants and fungi alternate between haploid and diploid generations in which either generation may dominate the life cycle and mitotic divisions occur in both phases
- Fertilization produces the diploid generation (sporophytes)

- After the sporophytes grow to maturity, some of their cells undergo meiosis, producing haploid, genetically different reproductive cells called spores. These spores are not gametes, they germinate and grow directly by mitosis into a generation of haploid individuals called gametophytes
- At maturity, the nuclei of some cells in the gametophytes develop into egg or sperm nuclei which arise from mitosis, not meiosis
- Fusion of a haploid egg and sperm nucleus produces a diploid zygote that divides by mitosis to produce the diploid sporophyte generation again
- The life cycle of most fungi and algae follow the third life cycle pattern: in these organisms, the diploid phase is limited to a single cell, the zygote, produced by fertilization. Immediately after fertilization, the diploid zygote undergoes meiosis to produce the haploid phase. Mitotic divisions occur only in the haploid phase

3. main differences between meiosis and mitosis

- The essence of mitosis is sameness, but meiosis changes both chromosome number and DNA sequence. The essence of meiosis is difference
- Meiosis produces a halved chromosome number and recombined DNA sequence
- Two representatives of each chromosome in a diploid cell represent a homologous pair which have the same genes, arranged in the same order in the DNA of the chromosome
- One chromosome of each pair is the paternal chromosome and the other is the maternal chromosome
- Although the two homologous chromosomes carry the same genes in the same order, different versions of these genes (alleles) may be present on either chromosome
- Meiosis reduced the number of chromosomes from diploid ($2n$) to haploid (n). Each cell produced by meiosis therefore carries only one member of the homologous pair

- When an egg and sperm cell join in fertilization, the diploid number is restored. Mitosis then works to make sure the diploid number is maintained in body cells
- Meiotic cell division also produces genetic recombination of the actual DNA sequence on the chromosomes. As a result, each chromosome passed onto an offspring is a novel mixture of both maternal and paternal DNA sequence

4. characteristics of homologous chromosomes

- Homologous chromosomes have the same genes in the same order, but with different version of the genes (alleles) being present. Same size and shape

5. characteristics of STR loci that make them useful for forensic DNA analysis (DNA fingerprinting)

- DNA fingerprinting is a technique used to distinguish between individuals of the same species using DNA samples. Done by analyzing DNA variations at various loci in the genome. Each locus is an example of an STR
- Short tandem repeat (STR) sequences has a different repeated sequence and the number of repeats varies among individuals in a population
- One STR locus could have a sequence repeated between 8 and 20 times
- As well, an individual could be homozygous or heterozygous for an STR allele
- Because each individual has an essentially unique combination of alleles, analysis of multiple STR loci can discriminate between DNA of different individuals

6. mechanism of DNA recombination

- Genetic recombination requires two DNA molecules that differ from one another, a mechanism for bringing the DNA molecules in close proximity, and a collection of enzymes to “cut”, “exchange”, and “paste” the DNA back together
- Most recombination occurs between two DNA molecules that are similar but not identical in the sequence of bases

- Such regions are called homologues. Homology allows different DNA molecules to line up and recombine precisely
 - Once homologous region of DNA are paired, enzymes break a covalent bond in each of the four sugar-phosphate backbones. The free ends of each backbone are then exchanged and reattached to those of the other DNA molecule
 - The result is two recombined molecules
 - Cutting and pasting *four* DNA backbones results in *one* recombination event
7. stage of meiosis when recombination occurs
- During mitosis, homologous chromosomes are paired in prophase I. They may undergo recombination by exchanging segments during this time

Lectures

Lecture 9

1. Reason why incorrect tautomers of bases are not recognized as mismatches and removed by excision repair
 - ATGC bases are usually stable but can shift to a tautomeric form
 - Tautomericly unstable bases give rise to SNP after two rounds of replication
 - The tautomeric form is not recognized and repaired because this pairing doesn't distort the helix so the enzymes don't detect it
2. Mutagenic mechanism of action of base analogues such as 5 Bromouracil
 - Some mutagens are tautomericly unstable base analogues
 - Ex. 5 Bromouracil looks very much like thymine, DNA polymerase has a hard time telling the difference which makes 5-Bromouracil a base analogue
 - It gets incorporated into DNA by mistake

- The problem with these compounds is that they are very tautomericly unstable so mispairing could easily result from 5-Bromouracil undergoing a tautomeric shift
- But chemicals are not necessary, tautomeric shifts happen perfectly naturally

3. Mutagenic mechanism of action of UV radiation

- UV radiation causes thymine dimers that distort the helix
- Photons of UV light have just the right amount of energy to be absorbed by the rings of pyrimidine bases and that can reorganize the bonding to hook the two bases together
- It is very difficult for DNA or RNA polymerase to transcribe or replicate through a dimer

4. Mechanisms of repair of UV photodamage

- In some organisms, DNA polymerase relaxes its pairing rules to get through the dimer
- The two bonded thymine bases do not present hydrogen bonds in the right places so DNA polymerase just puts in anything across from the damage
- But that creates all kind of damage and mutations. Of course, if DNA polymerase could not get through the damage at all, the cell would not be able to replicate and would die
- It's a last ditch method but it saves the cell
- Other organisms deal with UV damage with an enzyme called photolyase
- Photolyase breaks the dimer bonds and puts the bases back as they were
- Photolyase is powered by white light
- It's brilliant because whenever you're exposed to UV light, you're exposed to white light
- But humans don't have photolyase
- Humans and mammals deal with UV damage by excision repair
- The backbone has to be cut, the dimer has to be taken out, and the DNA replaced
- The ability to repair damage or not affect the diversity of your genome

5. Mutagenic mechanism of in/del damage during replication

- The error arises during replication
- Slippage during replication can result in adding or deleting base pairs
- Whenever there's a strand of repetitive sequences, it's possible for some to loop out but the rest are still stably bound enough so DNA polymerase doesn't notice and replicates a base pair an extra time. The strand ends up with too many of a base
- But if the other strand loops, you lose a base
- This is an *in/del* (insertion/deletion) *mutation*

6. Mutagenic mechanism of ionizing radiation

- Radioactive atoms are simply unstable isotopes which decay
- Decay of radioactive iodine and cesium creates "ionizing radiation"
- Radioactive iodine is dangerous because it is bio accumulated in the thyroid
- High energy ionizing radiation, when it passes through your body's cells, rips electrons from molecules, particularly oxygen. This creates reactive oxygen species (ROS) which damage DNA
- Reactive oxygen can break DNA backbones and if you break both backbones then the chromosome is broken
- Repairing double stranded breaks can cause rearrangements like deletions, duplications, inversions, or translocations. These are CNVs and can cause cancer

7. Types of chromosomal rearrangement resulting from attempts to repair double strand breaks

- Deletions: an enzyme can remove a base pair from the sequence
- Duplications: an enzyme can replicate the same base pairs twice
- Inversions: an enzyme can switch the base pairs around, copying them backwards
- Translocations: an enzyme can replicate part of one chromosome on the end of another chromosome if both are broken

8. Possible consequences of relocation of DNA sequences within or between chromosomes

- Relocation can cause deregulation of a gene (Burkitt lymphoma)
- Repairing double stranded breaks is one of the ways CNVs arise in a genome

9. Possible advantages of gene duplication

- If one gets damaged, you have a back-up
- Twice as much protein
- The second gene can diverge now and take on a new function

10. General use of gene families to create phylogenetic trees

- Gene duplication causes gene families. CNVs among different organisms
- Gene duplication occurs over evolutionary time so we can trace genes to common ancestors and see when the gene duplication took place
- Gene families reflect evolutionary history of relatedness
- It seems CNVs have enable groups to differentiate and diverge

Lecture 10

1. Reason why meiosis I is "reductional" and meiosis II is "equational"

- In meiosis I, chromosome number is reduced from diploid to haploid. Homologous pair, go to different cells, and the resulting cells have half the number of chromosomes (reductional division)
- In meiosis II, the amount of DNA in a cell is reduced ($1x2C$) but the chromosome number is not (equational division)

2. Changes in C and n during meiosis

- In meiosis I, the number of chromosomes ($2n$) is reduced by half to make a haploid cell (n) but the amount of DNA stays the same ($2C$)

- In meiosis II, the number of chromosomes remains haploid, but the amount of DNA is reduced to half (C)
- The products of meiosis go from a cell with $2n$ and $2C$, to a cell with n and $2C$, to the final product, a haploid cell with half as much DNA as its parent ($1n$, $1C$)
- Daughter cells are haploid not because they are unreplicated, but because there's only one of each homologue

3. Mechanism of recombination during prophase

- In prophase of meiosis I, homologous pair and recombine (sexual recombination not reproduction)
- Homologues with very similar DNA sequences and recombination enzymes make cuts in the backbone and then they paste the two non-sister chromatids from homologous chromosomes. Each homologue can cross over multiple times
- Recombination is mutagenic but the switch is very precise (so usually no problems)
- Meiosis is a powerful generation of variation (CNV's, new combination of alleles, etc.)

4. Role of cohesin and synaptonemal complex

- Cohesin hold sister chromatids together
- Synaptonemal complex holds the two homologues together during recombination

5. How homologues pair in order for all non-sister chromatids to participate in recombination

- Homologues pair front to back (not side by side) in order for all non-sister chromatids to be close enough to each other to participate in recombination

6. Mechanism by which recombination creates new combinations of alleles

- When a homologous pair crosses over, alleles switch between the two non-sister chromatids. When that happens, new combinations of alleles are created

7. Mechanism by which recombination creates copy number variation (CNV)

- Unequal crossing over creates CNVs
 - If there's a region of repetitive sequencing, the pairing can slip and become unequal after recombination. There can be more repeats on one chromosome and less on the other (this is a CNV from an error in recombination, not replication)
8. Randomness of alignment of homologous pairs at metaphase I
- Each non-homologous chromosome could go randomly to either cell
 - Independent assortment happens in different cells. Alignment of one homologous pair is independent of others
 - One of the powers of meiosis is the ability to put random alleles in each gamete
9. Relationship between distance separating genes and the likelihood of recombination between them
- The space between two genes can be narrow so the likelihood of them crossing over is rare. Genes that are close together on the chromosome have relatively little DNA between them that can be recombined
 - The recombination frequency is relatively low between genes that are close linked and relatively high between distant genes
10. Way in which meiosis can be thought of as a kind of DNA "repair". That is, how can you inherit mutations on both homologues of chromosome 6 but give a chromosome 6 with no mutations to your offspring?
- If you get one bad allele from you mom and another from your dad, you're stuck. But you can recombine them and give your kids a perfectly fine homologue
 - Chromosomes formed by recombination can have more good genes than their originals
11. Mechanism by which errors in MI or MII give rise to aneuploid products of meiosis
- Non-disjunction happens when homologues fail to separate in MI

- Too many chromosomes can separate into one cell and too few in another
- Being in mitotic arrest for 35 years (in women) is believed to cause a problem with the spindle. This causes more non-disjunction events
- Meiosis II would proceed normally after a non-disjunction but the gametes would be unbalanced (aneuploid)
- Non-disjunction is the name of the failure in meiosis I spindles to separate the chromosomes properly
- Misdivision results when chromatids fail to separate in meiosis II. Also results in aneuploid gametes
- Must be able to predict the outcome of these problems, must be able to look at an aneuploid gamete and predict where the problem went wrong