Human Genome and Genome Structure

Take home points

- Complexity isn't defined by its genome size or the number of genes
- Much complexity is added by mechanisms at other levels (transcription, RNA processing, translation)
- Our genome= many diff. genetic elements, only a small part codes for protein sequences
- Extrachromosomal elements can affect human cellular functions: mitochrondria, viruses, bacteria (plasmids)

Objectives

1) Basic features of DNA
2) Genome complexity
3) Nuclear and organelle genomes
4) Med relevance

1)

- DNA-> RNA-> polypeptide-> mature protein
- Sugar-phosphate backbone w/nitrogenous base, bases face each other
- 5' to 3' orientation
- Double helix, anti-parallel
- A=T, CIIIG (triple bond), more stable
- B form, right-handed most common. Other forms, Z and L-handed (Supercoiling).
- DNA supercoils, to unwind/relax it, we have topoisomerases to cut and reanneal
  - Two main types: I cuts 1 strand and II cuts 2 strands
  - Tops= drug targets (antibiotics and chemo)

2)

- DNA-> nucleosome-> beads on a string-> 30nm fiber->active chromosome-> metaphase chromosome
- Human genome: 22 autosome pairs+ 2 sex chromosomes = 46 overall chromosomes
- Tendency for complexity to increase and genome size increases, but this isn't true all the time, and the size of the genome doesn't determine complexity (ex. lily genome > human genome)
- Number of genes varies a lot among/in species
- Reason we are so complex, but have fewer genes than some less complex? We do so much processing/regulation! One gene can lead to many different gene products due to
  - Transcriptional regulation: how much/at all a certain gene is transcribed
  - RNA processing: does it get translated? does it reg. effeciency? introns getting cut out...
  - Translational regulation
  - Post-translational regulation: what we put on proteins (ex. phosphorylate them)
  - AKA one gene can lead to many different gene products!
- Our genome is about 20,000 genes
- Only 1% of our genome encodes proteins
- 45% was/is a mobile genetic element
  - Sines= short interspersed nuclear elements
  - Lines= long interspersed nulcear elements
  - Retroviral like elements
  - Above 3 can make copy of selves (derived from retrotransposons) and put in genes
  - DNA transposon fossils cut and paste
  - = TRANSPOSONS
- 12% tandem repeats (aka satellite DNA)
  - Simple seq. DNA
  - TTAGGG 100s of times

Often at centromeres and telomeres, mostly junk DNA

3)

- Mitochrondria
  - Inherited maternally
  - 17,000 bp, 37 genes (protein, tRNA, mitoch. ribosome)
  - Pretty much all systems can be affected in mitochrondrial disorders
- Viruses
  - DNA or RNA, huge range in size (3000-1.2 billion bp)
  - Can replicate only in host, so most don't kill it!
  - Source of some jumping genes (transposons)
- Plasmids
  - Mostly proks, some lower euks
  - Non-essential genes
  - R factors, antibiotic resistance (via conjugation= when an R factor is transferred from one bacteria cell to another)= HORIZONTAL GENE TRANSFER
  - 2 other HGTs
    - Transformation- take up DNA from envi
    - Transduction- virus med. exchange of genetic material between bacterial cells

4)

- Genome -> genetic diseases
- Differential susceptibility