nucleus: DNA & chromosomes

chapter 5

nuclear envelope
- nuclear membrane
  - actually two membranes
  - continuous with RER
  - nuclear lamina
    - intermediate filaments
    - lamins

nuclear membrane
- nuclear pore complex
  - gateway for proteins and RNAs
  - composed of nucleoporins
  - 15-30x as big as ribosome
  - 8 copies of each element
  - constantly changing

nuclear organization
- nuclear structure
  - nuclear envelope
  - nucleoplasm
  - nuclear matrix
  - nucleolus

nuclear envelope
- nuclear membrane
  - actually two membranes
  - continuous with RER
  - nuclear lamina
    - intermediate filaments
    - lamins

nuclear pore complex
- gateway for proteins and RNAs
- composed of nucleoporins
- 15-30x as big as ribosome
- 8 copies of each element
- constantly changing
**nuclear membrane**

- nuclear pore complex
  - central scaffold
  - central channel
  - nucleoporin lining
    - FG-repeat domains
  - proteins destined for the nucleus contain specific sequence of amino acids (NLS)

- transport of proteins
  1. protein with NLS binds to importin
  2. complex associates with cytoplasmic filament
  3. complex moves through pore
  4. interacts with Ran-GTP, dissociates
  5. importin β transported back to cytoplasm

**nuclear matrix**

- nuclear matrix
  - insoluble fibrillar network
  - may serve to organize chromatin
  - may be involved in maintenance of nuclear shape
  - probably not a static structure

**nuclear organization**

- chromosome territories
  - chromatin fibers not randomly dispersed
  - transcription factories
    - different loci on different chromosomes may interact during transcription
  - speckles
    - mRNA processing machinery
    - 20-50 irregular domains
    - dynamic
nuclear organization

- **nucleolus**
  - may be 1 or more (disassemble during mitosis)
  - not membrane bound
  - rRNA transcription (result from rRNA processing)
  - ribosome assembly
    - 4 types of RNA
      - 5S, 5.8S, 18S, 28S (svedberg units)
    - used to form large and small ribosomal subunits
- 3 regions
  - fibrillar center
  - dense fibrillar component
  - granular component

DNA structure

- **nucleotides**
  - two types of nitrogenous bases
    - pyrimidines
      - thymine
      - cytosine
    - purines
      - guanine
      - adenine
  - Base composition rules
    - pyrimidines = purines
    - A=T, G=C
    - A+T ≠ G+C
**DNA structure**

- Watson and Crick proposal
  - 2 strands
  - strands spiral dextrally
  - strands are antiparallel
  - sugar-phosphate chain
  - bases make up rungs
    - bases held together by hydrogen bonds
  - distance from phosphorus to phosphorus atom = 1nm

- pyrimidines pair with purines
  - C-G, A-T
- minor and major groove
  - allow place for proteins to sit
  - makes on complete turn every 10 residues
- strands are complementary

**Genetic material**

- three functions required of genetic material
  - must contain info that codes for heritable traits
  - must contain info that directs assembly of proteins
  - must contain info that directs duplication

**History**

- chromosomes
  - 1880s
    - Walther Flemming
      - noted thread-like material in nucleus
    - Theodore Boveri
      - noted that chromosomes have qualitative differences
    - Edouard van Beneden
      - half the chromosomes in each gamete
    - Oscar Hertvig
    - August Weismann
      - described meiosis and reduction division
  - 1903 - Walter Sutton
**chromosome structure**

- mitotic chromosomes
  - centromere
    - site of obvious constriction
  - satellite DNA
    - binds to centromeric proteins
    - CENP-A
    - helps assemble the kinetochore
    - sequence probably not important in function
    - spindle fibers attach to kinetochore

- mitotic chromosomes
  - distinct and predictable shape
    - length and centromere position
    - karyotype
    - telomeres
    - repeated sequences at the ends of each DNA molecule + DNA binding proteins
    - sequence conserved for vertebrates
    - TTAGGG -- about 500-5000x repeated
    - telomeres normally shrink
    - telomerase

**supercoiling**

- DNA can exist in supercoiled state
  - negatively supercoiled (plectonemic)
    - occurs when underwound
  - positively supercoiled (solenoidal)
    - occurs when overwound

- topoisomerases
  - topoisomerase I
  - topoisomerase II

**chromatin**

- organization of chromatin
  - nucleosomes
    - organized by histones
    - 5 classes
    - highly conserved
  - histone octamer
    - 2 copies of H2A, H2B, H3 and H4
  - H1 - linker histone
  - nucleosomes arranged like beads on a string
chromatin

- higher-level chromatin structure
  - 30nm fibers
    - nucleosomes bundled into larger fibers
    - not clear how 30nm fibers form
  - looped domains
    - 30nm filaments looped
    - connected to matrix
    - topoisomerase II

- chromatin-remodeling complexes
- euchromatin
  - disperses after mitotic division
- heterochromatin
  - remains compacted
  - little transcription
  - two classes
    - constitutive heterochromatin
      - permanently compacted
    - facultative heterochromatin
      - inactivated

reannealing

- denaturation
- renaturation
  - nucleic acid hybridization
    - rate of renaturation
      - for bacteria and viruses
        - related to complexity of genome
        - all sequences present at roughly same concentration
      - for eukaryotes
        - more complex renaturation curves

- highly repeated DNA sequences (1-10% of DNA)
  - satellite DNAs
  - minisatellite DNAs
  - microsatellite DNAs

genome structure
**genome structure**

- highly repeated DNA sequences (1-10% of DNA)
  - satellite DNAs
  - minisatellite DNAs
  - microsatellite DNAs
- moderately repeated DNA sequences (20-80% of DNA)
  - repeated coding DNAs
  - repeated non-coding DNAs
- non-repeated sequences

**genomic stability**

- polyploidy
  - in plants - hybridization event
  - in animals - duplication in zygote or diploid gametes
    - sympatric speciation
    - can result in many copies of chromosomes