Premedical - biology

Mitosis and Cell cycle
Physiological modes of somatic cell

Proliferation in:
- ontogenesis
- physiological renewal of cells
- reparation and wound healing
- immune response
Resting (Quiescent) Cells: G0

G0 phase relates to terminal stages of differentiation

e.g. hepatocytes divide 1x a year;
neurons, myocytes do not divide;
epithelial cells divide 1-2x a day
Cell cycle

G ~ Gap/Growth
S ~ DNA synthesis
The cell cycle

- M phase and interphase
- M phase: Mitosis and cytokinesis
- Interphase: G1, S, G2 phase
- 46 chromosomes, 23 chromosomes from each parent
- Mitosis – distribution of identical sets of 46 chromosomes to daughter cells
Cell Cycle

- **G1 phase** – the longest and the most variable part of the cell cycle
  - growth of the cell
  - completion of organelles (ribosomes, mitochondria, endoplasmic reticulum etc.)
  - RNA and protein synthesis
  - synthesis of nucleotides, preparation for replication
- **S phase** – replication of nuclear DNA (extranuclear DNA replicates during the whole interphase)

- **G2 phase** – cell growth, protein and RNA synthesis, origin of cell structures

- **M phase:**

  - **Mitosis** - division of the nucleus
  - **Cytokinesis** – division of the cell
Schematic view of chromosome pair – homologous chromosomes - during cell cycle.

- in G1 - 1 chromatid
- in G2 - 2 chromatids
Mitosis – animal cells

**Interphase:** one or more nucleoli. Centrosome replicates to pair of centriolas. Chromosomes have been already duplicated.

**Prophase:** Chromatin fibers are getting coiled, spiralized. Nucleoli disappear and microtubuli begin to form mitotic spindle

**Prometaphase:** Nuclear envelope fragments. Mitotic spindle interacts with chromosomes. Chromosomes are getting more condensed.
Nucleosome:
DNA double helix + histone core
Histone core = octamere of two copies of H2A, H2B, H3, H4 histons
Spacer segment between two nucleosomes is free or associated with H1 histone
String of nucleosomes is coiled into **solenoid** (6 nucleosomes in each turn)
Solenoid is packed into loops, attached to **nonhistone protein scaffold** (Laemli loops). Nonhistone protein scaffold with loops is coiled into spiral structure of chromatides
**Metaphase:** Spindle poles are at opposite positions. Chromosome are located on the metaphase plate (in equatorial plane). Each chromosome is attached by kinetochore to the mitotic spindle.

**Anaphase:** Chromatids move to opposite poles of the cell. Kinetochore microtubules are getting shorter, the poles move further apart. There are at the end two collection of chromosomes.

**Telophase:** Non-kinetochore microtubules elongate. Nuclear envelope generates. Cytokinesis start to run.
Cytokinesis

Cleavage

- contractile ring of actin microfilaments
- cell plate in plant cells
Mitotic spindle

- Fibers made of microtubules, spindle starts from **centrosome** – centrioles - 9 sets of triplets of microtubules from subunits tubulin α, β

- **Microtubule organizing center**

- Mitotic spindle elongates by incorporating subunits of protein tubulin

- Microtubule polarity
• Kinetochore microtubules
• Non-kinetochores
• Astral microtubules

**Kinetochore** – proteins and chromosomal DNA at the centromere
Cell cycle

- External signals and internal network of interactions – signalling transduction pathways regulate the cell cycle
- **Cancer cells have escaped from cells cycle controls**
- somatic cell in proliferation states
Control system of cell cycle

- **Cyclin** – cyclic accumulation and degradation of proteins during the cell cycle

- **Cdk** – cyclin dependent kinases (CDK)
  
  = enzymes that phosphorylate other proteins
  
  active states = *activation by cyclin*

complex cyclin / kinase => protein

phosphorylation => triggers cell cycle phases
Check points

trigger and coordination of key events

**Checkpoints** are critical points, where signals can stop or go-ahead to the next phase of cell cycle:

- **G1 checkpoint**
- **G2 checkpoint**
- **M checkpoint**
http://cs.wikipedia.org/wiki/Soubor:Bun%C4%9B%C4%8Dn%C3%BD_cyklus_CDK.svg
Genes regulating cell cycle:

Protooncogenes

- products **stimulate** cell division
- Genes for **growth factors, receptors, regulatory proteins, Ras proteins**
- mutated forms = **oncogenes** => permanent or increased mitotic activity
  (effect of one allele mutated)
Tumor suppressor genes (TSG) „antioncogenes“

- products **inhibit** mitotic division
- effect of **both** alleles mutated

- **Rb1** gene, product RB protein
  - Mutations in retinoblastoma and other tumors

- **TP 53** gene, **p53** product – induction of DNA repair or apoptosis = programmed cell death
- mutations in many tumors
Carcinogenesis

**Mutator genes** – genes for reparation enzymes

Proteins encoded by proto-oncogenes and tumor-suppressor genes are components of cell-signalling pathways.

**Multistep model of cancer development**
Aging (senescence)

- limited number of cell division (maximum 50) → Hayflick’s limit
  - both in vivo and in vitro

- accumulation of mutations
- decreased cytokines response, increased synthesis of inhibitory proteins
- shortening of telomere sequences at the ends of chromosomes
Apoptosis = programmed cell death

- final stage of aging process in the cell
- elimination of cells, which can not be repaired
- during embryogenesis - reduction of redundant parts
- some diseases
- Purpose: elimination of cells, that accomplished their fate and could become destructive for the organism
Apoptosis:
- without disintegration of both plasma membrane and organelles
- chromatin condensation, surface blebbing, cell fragmentation → apoptotic bodies
- phagocytosis without inflammation

Necrosis:
disruption of plasma membrane and organelles, release of the cell content into extracellular space → inflammation
Caspases are a family of cysteine proteases that play essential roles in apoptosis (programmed cell death), necrosis, and inflammation.
Thank you for your attention

Repetition
6. From gene to protein

1. What are the differences between DNA and RNA?
2. Describe transcription in eukaryotic cell.
3. What is the product of transcription?
4. How is transcription regulated?
5. What is RNA processing?
7. What types of RNA do you know?
8. How is the genetic information encoded?
9. What is the product of translation?
10. How is the complete protein formed?