1 # ANAT3231 - Cell Biology Lecture 09

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2 ## UNSW Copyright Notice

3 ## Cell Division References

- Textbooks
  - Essential Cell Biology: Ch17
  - Molecular Biology of the Cell: Ch17,18
  - Molecular Cell Biology: Ch13
  - The Cell: Ch14,15
  - Dev Biology: Ch12
- Slides
  - UNSW Cell Biology
    - ANAT3231 Lecture 10 Cell Division
  - http://cellbiology.med.unsw.edu.au/units/science/lecture0510.htm

4 ## Cell Division Milestones

5 ## Embryo Mitosis

6 ## Mitosis Animation

7 ## Cell Cycle- Mitosis

8 ## Cell Lifespan

- Body Cell Types
  - About 210 types
- Lifespan
  - Born
  - Differentiate
  - Function
  - Die

9 ## Cell Lifespan

- Neutrophil
  - 6-7 hours circulating
  - 4 days in tissue
- Red blood cell
  - 120 days
- Brain neuron
  - 50 - 100 years

10 ## Lifespan Processes

- Birth
  - Mitosis

    - Except germ cells
        - meiosis
- Death
    - Covered in next Lecture
  - Apoptosis
    - Programmed cell death
  - Necrosis

11 Cell Cycle Overview

12 Cell Cycle

- Mitosis (M phase)
  - Cell birth(division)
  - small time of cell cycle
- Interphase
  - Most cell life
  - Cell growth, function
  - DNA synthesis
  - organelle development

13 Cell Cycle

- Time cell comes into existence until that cell divides again
  - Rapidly growing human cells 20-24 hr
  - Liver cells 1-2 year
  - Neurons 1 only
    - Quiescent G_0

14 Cell Cycle- Stages

- Rapidly dividing cell
  - 20-24hr
- Mitosis
    - M 1 hr
- Interphase
  - G_1 Phase
    - cellular growth 9hr
      - Most variable time
      - Can exit to G_0
  - S Phase
    - DNA duplication 9hr
  - G_2 Phase
    - prepare for mitosis 4 hr

15 Xenopus

16 Cell Cycle Differences

- Early embryonic cycle
  - no growth occurs
  - two daughter cells are half size of parent cell
  - cycle time is very short
  - S phases and M phases alternate without intervening G1 or G2 phases

17 Mitosis Phases Movie

18 Cell Cycle Regulation

- Cell proliferation

  - strictly regulated
- Cancer
  - Unregulated/abnormal proliferation

19 DNA Organisation

20 Cyclin/MPF

- MPF
  - M-phase promoting factor
- Protein kinase
- Chromosomes condense
- Nuclear envelope breakdown
  - By disassembly of nuclear lamina
- Microtubule reorganisation
  - Early spindle formation
- Complex
  - Cyclin+ Kinase

21 CDC2 MPF

22 Cell Cycle- Regulators

- Cyclins
  - Cyclically synthesized and degraded each cell cycle
- Cyclin-dependent Kinases
  - Inactive until bound to a specific cyclin

23 Cyclin-Dependent Kinases

- Drive M to S Phase
  - cdk1 and cdk2
  - Cdk1 activated at G2 to M
  - Cdk2 activated at G1 to S

24 Cell Cyclins

25 Cell Cycle- Mitosis

26 Mitosis Progeny

- 2 Daughter cells identical to parent (diploid)
  - Cdk1 activation

27 Meiosis Progeny

- Germ cell division (haploid)
  - Reductive division
  - Generates haploid gametes (egg, sperm)
  - Each genetically distinct from parent
    - Genetic recombination (prophase 1)
      - Exchanges portions of chromosomes maternal/paternal homologous pairs
    - Independent assortment of paternal chromosomes (meiosis 1)

28 Cell Birth - Mitosis and Meiosis

29 Cell Cycle- External Regulators

- External factors
  - can also regulate progression through cycle

- Cell replacement in different tissues
  - regulated by polypeptide growth factors
    - factor can be specific for specific cell types

30 Growth Factor Model

- Fibroblasts in culture
- Serum- Proliferation
  - Prepared by clotting
- Plasma- no proliferation
  - Prepared by centrifugation (no clotting)
- Clotting
  - Allows platelets to release secretory granules
  - Platelet-derived growth factor (PDGF)
    - Connective tissue cells express PDGF receptors which bind the small PDGF glycoprotein

31 Other Growth Factors

- Interleukin-2 (IL-2)
  - Stimulates T lymphocytes
- Nerve Growth Factor (NGF)
  - Promotes neuronal survival and growth
- Epidermal Growth Factor (EGF)
- Vascular Endothelial Growth Factor (VEGF)
- Insulin-like growth factors (IFG-1, IGF-2)

32 Cell Division Features

- 2 mechanical processes
- Mitosis
  - segregation of chromosomes and formation of 2 nuclei
- Cytokinesis
  - splitting of the cell as a whole into 2

33 Cell Changes

- Nucleus
  - Chromosome condensation
  - Nuclear envelope breakdown
- Cytoplasm
  - Cytoskeleton reorganization
    - Spindle formation (MT)
    - Contractile ring (MF)
  - Organelle redistribution

34 Cell Cycle- Cytoskeleton

35 Cell Cycle- Cytoskeleton

- Cytoskeleton in M phase
  - mitotic spindle
    - assembles first and segregates the chromosomes
  - contractile ring
    - assembles later and divides the cell in two

36 Microtubule Organisation

37 Mitosis Phases

- Based on
  - light microscopy of living cells
  - light and electron microscopy of fixed and stained cells
- 5 Phases
  - prophase, prometaphase, metaphase, anaphase, and telophase
- Cytokinesis
  - 6th stage overlaps the end of mitosis

38 Mitosis- Interphase

- Not a mitotic phase
  - Discussed in earlier slides
- Chromosomes dispersed in nucleus
  - Gene expression
- Cytoskeleton and cell organelles
  - Distributed and functioning as described in earlier lectures
  - Mitochondria
    - undergo independent proliferation/division

39 Chromosome Changes

40 Mitosis- Prophase

- Chromosome DNA has been earlier duplicated (S Phase)
- Chromosomes begin condensing
  - Chromosome pairs (chromatids) held together at centromere
- Microtubules disassemble
- Mitotic spindle begins to form
- At end of prophase nuclear envelope breaks down

41 Mitosis- Prometaphase

- Microtubules now enter nuclear region
  - Nuclear envelope forms vesicles around mitotic spindle
- Kinetochores
  - form on centromere
  - attach to some MTs of spindle
- At end of prometaphase chromosomes move to metaphase plate

42 Sea Urchin Mitotic Spindle Movie

43 Mitotic Spindle Movie

44 Mitotic Spindle

45 Kinetochore

46 Kinetochore Movement

47 Mitosis- Metaphase

- Kinetochore MTs align chromosomes in one midpoint plane
- Metaphase ends when sister kinetochores separate

48 Mitosis- Anaphase

- Separation of sister Kinetochores and shortening of Kinetochore MTs pulls chromosome to spindle pole

- Anaphase ends as nuclear envelope (membrane) begins to reform

49 **Two telophase HeLa cells expressing GFP–tagged human Aurora B**

- Microtubules - red
- inner-centromere protein - blue
- Aurora B–GFP - green
- DNA - white

50 Mitosis- Telophase

- Chromosomes arrive at spindle poles
- Kinetochore MTs lost
- Condensed chromosomes begin expanding
- Continues through cytokinesis

51 Mitosis- Cytokinesis

- Division of cytoplasmic contents
- Contractile ring
  - forms at midpoint under membrane
  - Microfilament ring
  - Contracts forming cleavage furrow
  - Eventually fully divides cytoplasm

52 Cell Birth - Mitosis and Meiosis

53 Abnormal Growth - Cancer

- "Transformed cells"
  - Cells escape normal cell cycle regulation
    - continue to grow under conditions where "normal" cells will not (confluent monolayer)
  - Study of these cells identified genes and proteins that regulate cell cycle
    - Oncogenes and Protooncogenes

54 Cancer Proteins

- Oncogenes
  - Mutated genes that are responsible for developing cancer
- Protooncogene
  - Non-mutated normal cellular gene
    - Note cancers appear to develop as a series of independent gene mutations
- Block- tumour suppressor genes

55 Oncogenes/Protooncogenes

- Treat cells with mutagen (UV light)
  - Damages DNA
  - Grow and identify transformed cells
    - Analyse DNA
    - Transfer DNA fragments to normal cells and see whether they transform recipients
- Analyse tumour viruses
  - Many viruses stimulate tumourgenic growth
  - RNA tumour viruses "retroviruses"

56 Genome Modifications

- chromosomal translocations
- Philadelphia chromosome
  - Chronic myelogenous leukemia
  - Piece of Chr9 exchanged with Chr22
    - Generates truncated abl
    - Overstimulates cell production

57 Tumour Suppressor Genes

- "anti-oncogenes"
- Repress cell growth and division
- Mutation loss of these genes leads to transformation
- Retinoblastoma gene (Rb)
  - Regulates gene transcription
- P53
  - Senses DNA damage

58 Cell Cycle Arrest Points

59 Tumour Suppressor Genes- P53

60 Retinoblastoma Protein (Rb)

61 Meiosis- First Division

- Homologous chromosomes pairing unique to meiosis
  - Each chromosome duplicated
    - then as attached sister chromatids before pairing occurs
- Genetic Recombination
    - shown by chromosomes part red and part black
  - chromosome pairing involves crossing-over between homologous chromosomes
      - For clarity only one pair of homologous chromosomes shown
        - » Text modified from MBoC

62 Comparison of Meiosis/Mitosis

- After DNA replication
  - two nuclear (and cell) divisions required to produce haploid gametes
  - Each diploid cell in meiosis
    - produces four haploid cells
  - Each diploid cell mitosis
    - produces two diploid cells
      - Note only one pair of homologous chromosomes shown
        - » text modified from MBoC

63 Meiotic Nondisjunction

- Occurs when homologues fail to separate
  - during meiotic division I or II
- Down Syndrome
  - Caused by an extra copy of chromosome 21

64 Online References

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- The Cell- A molecular approach
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65 Mitosis GIT Movie