1 Cell biology

Introduction

- eukaryotes have a much more complex cell structure than prokaryotes; evolution allowed cell specialization and cell replacement
- cell division is essential but is carried out differently in pro- and eukaryotes
- biological world is very diverse; cells have universal features

1.1 Introduction to cells

The cell theory

- internal structure is built up from very small individual parts
- large organs are made up from number of different tissues: microscope allows examination
- with microscope certain features were seen again and again: cell theory was developed to explain the basic features of structure: cells are fundamental building blocks of living organisms
- smallest organism is unicellular, larger organisms are multicellular
- cells vary in size but share following features: surrounded by membrane, contain genetic material, many activities are chemical reactions catalyzed by enzymes, own energy release system: cells thought to be smallest living structures, nothing smaller can survive

Unicellular organisms

- functions of life: things an organism has to do to survive
- in unicellular organisms a cell has to carry out all functions of life: structure of unicellular organisms is more complex than most cells in multicellular organisms
- 7 functions: nutrition, metabolism, growth, response, excretion, homeostasis, reproduction
- many unicellular organisms have a method of movement (some remain fixed)

Limitations on cell size

- metabolic rate of the cell is proportional to the volume of the cell
- substances must be absorbed and waste products removed for metabolism to continue
- substances move through plasma membrane: rate at which they cross the membrane depends on surface area
- surface area to volume ratio is important: if it is too small substances will not enter as quickly as needed and waste products won't leave fast enough
- if the ratio is too small then cells may overheat because the metabolism produces heat faster than it is lost over the cell's surface

Multicellular organisms

- some unicellular organisms live together in colonies: they cooperate but are not fused together to form a single cell mass and so are not a single organism
- organisms consisting of a single mass of cells fused together are multicellular
- intensively researched multicellular organisms is worm *Caenorhabditis elegans*
- *C. elegans* cells called neurons (most located in front: like brain): though the brain coordinates responses to worm's environment to does not control how individual cells develop: cells in this and other multicellular organism can be regarded as cooperative groups without leader
- characteristics of whole organism, including that it is alive, are known as emergent properties
- emergent properties arise from interaction of the component parts of a complex structure

Cell differentiation in multicellular organisms

- different cells perform different functions: division of labour
- group of cells specialize in the same way to perform the same function: called a tissue
- becoming specialized they can carry out their function more efficiently: develop ideal structure
- development of cells in different ways to carry out specific functions is called differentiation

Gene expression and cell differentiation

- multicellular organisms have different cell types but all have the same set of genes

- cells have the genes needed to specialize in every possible way; in most cell types less than half of the genes will ever be used (expressed)
- development of cell involves switching on particular genes, expressing them, but not others
- cell differentiation happens because different sequence of genes is expressed in different cell types

Stem cells

- new animal life starts when a sperm fertilizes an egg cell to produce a zygote; embryo is formed when zygote divides repeatedly; at early stages cells are capable of dividing many times
- embryo cells are extremely versatile and can differentiate along different pathways into any of the cell types found in that particular animal: all adult tissues stem from them: stem cells
- stem cells have two key properties: can divide again and again, not fully differentiated
- embryonic stem cells could be used to produce regenerated tissue, might even grow whole organs: types of use are therapeutic (provide therapies for diseases, other health issues)
- non-therapeutic uses: produce large quantities of meat for human consumption
- stem cells are most versatile in early embryonic stage; during embryo development cells commit themselves to a pattern of differentiation, once committed the cell can still divide but all of these will differentiate in same way: no longer stem cells
- small number of stem cells remain present in adult body (found in bone marrow, skin, liver): considerable powers of regeneration and repair; stem cells in other tissues only allow limited repair (e.g. brain, kidney, heart)

1.2 Ultrastructure of cells

The resolution of electron microscopes

- unaided eye can see things with size of 0.1 mm as separate objects, but no smaller
- light microscope allows to see cells, size 0.2 µm (limited by wavelength of light)
- resolution: making separate parts of an object distinguishable by eye
- electron beams have shorter wavelength: electron microscopes have higher resolution (1 nm)
- light microscopes reveal structure of cells, electron microscopes reveal ultrastructure
- Millimetres x 1’000 = Micrometers (µm); Micrometers x 1’000 = Nanometers (nm)

Prokaryotic cell structure

- all organisms are divided into two groups according to cell structure: eukaryotes have a compartment within cell (nucleus with chromosomes), prokaryotes don’t have a nucleus
- prokaryotes were first organisms to evolve as they have the simplest cell structure
- all cells have a cell membrane, but some have cell wall (including prokaryotes)
- prokaryote’s cytoplasm is not divided into compartments: one uninterrupted chamber
- prokaryotes don’t have cytoplasmic organelles apart from ribosomes; these are smaller than in eukaryotes: 70S (Svedberg units)
- part of cytoplasm appears lighter: region contains DNA, usually in form of one circular DNA molecule; not associated with proteins; region is called nucleoid

Cell division in prokaryotes

- all living organisms need to produce new cell: only possible by division of pre-existing cells
- cell division in prokaryotes is called binary fission (asexual reproduction): circular chromosome is replicated, copies move to opposite cell ends, cytoplasm divides
- daughter cells are genetically identical

Eukaryotic cells structure

- much more complicated internal structure: eukaryotic cells are compartmentalized
- divided into partitions: partitions are single or double membranes
- most important compartment is nucleus (contains chromosomes)
- compartments in cytoplasm are organelles: each organelle has a distinctive structure and function
- advantages of compartmentalization: enzymes and substrates can be more concentrated, substances causing damage can be kept inside membrane of organelle, pH can be maintained at ideal level, organelles and contents can be moved around in cell

1.3 Membrane structure

Phospholipid bilayer

- hydrophilic: substances attracted to water; hydrophobic: not attracted to water
- phospholipids have both properties: amphipathic (phospholipid molecule is hydrophilic, two hydrocarbon tails are hydrophobic)
- when mixed with water phospholipids arrange in double layers (hydrocarbon tails facing inwards, phosphate heads facing outwards): phospholipid bilayer
- stable structure and forms basis of all cell membranes

Membrane proteins

- cell membranes have wide range of functions; primary function is forming a barrier through which ions and hydrophilic molecules cannot easily pass: carried out by phospholipid bilayer
- almost all other functions are carried out by proteins: hormone binding sites (hormone receptors), immobilized enzyme with active site on outside (e.g. intestine), cell adhesion (form tight junctions), cell-to-cell communication (receptors for neurotransmitters in synapses), channels for passive transport (for hydrophilic particles, facilitated diffusion), pumps for active transport (use ATP)
- varied functions lead to very diverse structure and position in membrane of membrane proteins
- integral proteins: hydrophobic on at least one part, embedded, many are transmembrane
- peripheral proteins: hydrophilic on surface, not embedded, most are attached on surface of integral proteins (attachment often reversible), some have single hydrocarbon chain holding them to membrane surface
- proteins are orientated to fulfill functions correctly
- protein content of membranes is very variable: depending on function

Cholesterol in membranes

- in addition to phospholipids and proteins animal cell membranes contain cholesterol
- type of lipid but not fat or oil, is a steroid
- most of it is hydrophobic, attracted to hydrocarbon tails in centre of membrane; on end it has a hydroxyl group (-OH) which is hydrophilic: cholesterol is positioned between phospholipids
- amount of cholesterol varies

1.4 Membrane transport

Endocytosis

- vesicle: small sac of membrane with fluid inside; spherical, dynamic
- easily constructed and destructed due to fluidity of membrane
- to form a vesicle small region of membrane is pinched off, done by proteins using ATP
- vesicle formed inside of cell, containing fluid from outside of cell: method of taking materials into the cell: endocytosis
- vesicles from endocytosis contain water and solutes, but also larger molecules that cannot pass across plasma membrane

Vesicle movement in cells

- vesicles can be used to move materials in the cell
- example: protein synthesized by ribosomes on rough endoplasmic reticulum, vesicles bud off and move to Golgi apparatus (fuse with it) which processes it into its final form, vesicle buds off again and moves to place where protein is secreted
- example: growing cell: area has to increase: ribosomes synthesize membrane proteins, vesicles bud off the rough endoplasmic reticulum, move to plasma membrane and fuse with it
- this method can also be used for increase of organelles (lysosomes, mitochondria) in cell

Exocytosis

- release of material from cells using vesicles: process of getting the contents out of the cell
- example: digestive enzymes released by gland cells by exocytosis; synthesized, moved to Golgi apparatus, then to membrane; this case called secretion (useful substance released)

- exocytosis used to expel waste products and unwanted material: removal of excess water from unicellular organisms (e.g. Paramecium)

Simple diffusion
- one of the four methods of moving particles across membrane
- diffusion: spreading of particles due to continuous random motion
- particles move from area of high concentration to low conc.: down the concentration gradient
- diffusion is a passive process (no need of energy)
- simple diffusion across membranes: particles passing between phospholipids in membrane
- inner part of membrane hydrophobic: non-polar particles move easily through (e.g. Oxygen) but positively or negatively charged (polar) can only diffuse at low rates (smaller ones faster)

Facilitated diffusion
- ions and other particles that cannot diffuse between phospholipids can pass through channels
- channels are holes with very narrow diameter, consist of protein, chemical properties ensure that only one type of particle can pass: cell decides which channels to synthesize and place
- channels help particles move from a high to a low concentration

Osmosis
- water can mostly move freely in and out of cells; if more water moves into one direction than the other it is called osmosis
- occurs due to differences in solutes (substances dissolved in water); intermolecular bonds between substance and water, restrict water to move freely
- regions with a higher solute concentration have lower free water molecules: movement of water from regions with lower solute concentration to region of higher solute concentration
- despite water molecules being hydrophilic they can move through phospholipid bilayer because they are small enough; some cells have channels called aquaporins (e.g. kidney)

Active transport
- cells take in substances, though the concentration in the cell is higher: against the concentration gradient, is not diffusion
- ATP is used as energy source
- carried out by globular proteins: pump proteins
- once the ion or molecule enters the middle chamber ATP is used for conformational change of protein: opens up into the cell

1.5 The origin of cells
Cell division and the origin of cells
- since 1880s: theory that cells can only be produced by division of a pre-existing cell
- there is a continuity of life from its origins on Earth to the cells in our body today

Origin of the first cells
- tracing back should eventually lead to the earliest cell to have existed
- cells must have arisen from non-living material (unless they arrived from outer space)
- hardest question for biology: how could a structure as complex as the cell have arisen by natural means from non-living material?
- complex structures cannot arise by evolution; evidence that it could have formed over millions of years in a series of small steps; hypotheses how main steps could have occurred
- 1. Production of carbon compounds such as sugars and amino acids: Miller and Urey create atmosphere of early Earth (methane, hydrogen, ammonia), electrical discharges simulate lightning, amino acids and other carbon compounds needed for life were produced
- 2. Assembly of carbon compounds into polymers: origin of first carbon compounds around deep-sea vents, hot water carrying reduced inorganic chemicals (e.g. iron sulphide), chemicals represent readily accessible supplies of energy
- 3. Formation of membranes: if phospholipids or other amphipathic carbon compounds were among first, they would have naturally assembled into bilayers, allows different internal chemistry from that of the surrounding to develop

- 4. Development of a mechanism for inheritance: genes are made of DNA, to pass them on enzymes are needed, but to produce enzymes genes are needed; solution is that an earlier phase of evolution had RNA as genetic material, it is self replicating

Endosymbiosis and eukaryotic cells

- theory of endosymbiosis helps explaining evolution of eukaryotic cells: states that mitochondria were once free-living prokaryotic cells that had developed process of aerobic cell respiration
- larger prokaryotes that could only respire anaerobically took them in by endocytosis
- rather than killing and digesting them, they allowed them to continue to live in their cytoplasm
- as long as the smaller prokaryotes grew and divided as fast as the larger ones, they could persist indefinitely inside the larger cells: evolution made them the mitochondria of today
- the larger and smaller prokaryotes were in symbiotic relationship, both benefited (mutualistic relationship): smaller is supplied with food and carries out aerobic respiration to supply energy efficiently to the larger cell: natural selection favored cells with endosymbiotic relationship
- endosymbiotic theory also explains origin of chloroplasts: prokaryote that develops photosynthesis that was taken in by larger cell
- chloroplasts and mitochondria are no longer capable of living independently, but have features suggesting they evolved from independent prokaryotes: have own genes (circular DNA), own 70S ribosomes, transcribe their DNA and use mRNA to synthesize some own proteins, can only be produced by division of pre-existing mitochondria and chloroplasts

1.6 Cell division

The role of mitosis

- nucleus can divide to form two genetically identical nuclei by mitosis
- before mitosis, all of the DNA in the nucleus must be replicated (happens during interphase): each chromosome is converted into two identical DNA molecules (chromatids)
- mitosis is involved in embryonic development, growth, tissue repair, asexual reproduction
- mitosis is divided into four phases: prophase, metaphase, anaphase, telophase

Interphase

- cell cycle has two main phases: interphase and cell division
- interphase is a very active phase, many metabolic reactions occur
- DNA replication (in nucleus) and protein synthesis (in cytoplasm) only happen during interphase
- during interphase the number of mitochondria increases; in plants the same with chloroplasts
- interphase consists of three phases: G_1 phase, S phase, G_2 phase
- in S phase cell replicates all genetic material in its nucleus
- some do not progress beyond G_1 because they are never going to divide: enter G_0 which may be temporary or permanent

Supercoiling of chromosomes

- two chromatids making up each chromosome must be separated during mitosis
- DNA in chromosomes are immensely long: essential to package chromosomes into much shorter structures: condensation of chromosomes during first stage of mitosis
- condensation: repeatedly coiling DNA molecule (chromosome shorter and wider): supercoiling
- histone proteins associated with DNA help with supercoiling and enzymes are involved

Cytokinesis

- cells divide after mitosis when two genetically identical nuclei are present in cell
- process of division is cytokinesis: happens differently in plant and animal cells
- in animal cells plasma membrane is pulled inwards using contractile protein (actin, myosin)
- when cleavage furrow reaches centre, cell is pinched apart into two daughter cells
- in plant cells vesicles are moved to equator, they fuse to form tubular structures across equator
- then more vesicles fuse with tubular structures and form two layers of membrane, completing division of cytoplasm; next, pectins and other substances are deposited by exocytosis between two new membranes (forms middle lamella, links cell walls)
- cellulose is brought adjacent to lamella; each cell builds its own cell wall adjacent to equator

Cyclins and the control of the cell cycle

- each phase of cell cycle involves many important tasks: cyclins (proteins) ensure that tasks are performed at correct time and cell only moves to next stage when appropriate
- cyclins bind to cyclin-dependent kinases (enzymes): these become active and attach phosphate groups to other proteins: phosphorylation triggers proteins to carry out tasks
- four main types of cyclin in humans; unless cyclins reach threshold concentration, the cell does not progress: cyclins control cell cycle

Tumour formation and cancer

- tumours are abnormal groups of cells that develop at any stage of life in any part of body
- in some cases cells adhere, do not invade nearby tissues, unlikely to cause harm: benign
- other tumours become detached, move elsewhere and develop into secondary tumours: malignant and very likely to be life-threatening: cancers
- chemicals and agents causing cancer are known as carcinogens; all mutagens are carcinogenic
- mutagens are agents that cause gene mutations and mutations cause cancer
- mutations are random changes to base sequence of genes; the few genes that can become cancer-causing after mutating are oncogenes; in normal cell oncogenes are involved in control of cell cycle: this is why mutations can result in uncontrolled cell division
- several mutations must occur in same cell for it to become tumour cell: chance of happening is small but there are many cells in body so total chance in lifetime is significant
- when tumour cell has been formed it divides repeatedly: primary tumour; metastasis is movement of cells form primary tumour to set up secondary tumours in other part of body