Biomolecules

Hydrolysis by protease

- Hydrolysis reaction occurs, where peptide bond between amino acids are broken with the addition of a water molecule

Structure of protein

- Primary structure is the unique sequence of amino acids.
- Folding of polypeptide to form tertiary structure held by R group interactions eg… to bring together catalytic and contact residues in the active site, gives enzyme active site a specific 3D conformation that is complementary in shape and charge to substrate

Cellulose

- Each cellulose molecule is made up of a large number of B glucose monomers, giving a large molecule that is insoluble in water. Alternate glucose monomers are inverted 180 deg relative to one another to allow the formation of B(1,4) glycosidic bonds, resulting in a straight cellulose chain. Straight parallel chains with OH groups projecting in all directions from each chain, allowing large number of hydrogen bonds to cross link neighbouring chains, allowing bundling of cellulose chains into microfibrils, macrofibrils and fibres, resulting in high ensile strength. In plant cell wall, this prevents plant cells from bursting when placed in solutions of high water potential, maintains the shape of the cell, protects cells from physical and mechanical injury, cellulose has large intermolecular spaces between macrofibrils, allows the passage of water and olute molecules through the plant cell wall.

Collagen

- Collagen is a fibrous protein made up of a chain of amino acids joined by peptide bonds. The sequence is usually a repeating unit: glycine-X-Y, where X is usually proline and Y is usually hydroxyproline. Three loose helical chains coil and are held together by hydrogen bonds, forming the triple helix of tropocollagen. Covalent bonds exist between staggered tropocollagen molecules to form a collagen fibril and bundles of collagen fibril form a collagen fibre

Glucagon vs Glycogen

Point of comparison	Glucagon	Glycogen
Type of macromolecule	Globular protein	Extensively branched polysaccharide made of helical chains
Type of monomer	Amino acid residues with different R groups	Alpha glucose only
Types of bonds between monomers	Amino acid residues joined by peptide bonds	Alpha glucose joined by alpha 1-4 glycosidic linkages with branched alpha 1-6 glycosidic linkages
Number of monomer per molecule	Fixed number of amino acid per molecule	Variable number of glucose per molecule
Solubility in water	Soluble in watr as it is globular in structure	Insoluble in water as it has a large molecular weight
synthesis	Produced by alpha cells in the pancreas in the islets of Langerhans	Glycogen is synthesised in liver and muscle cells when blood glucose is high
Function	Hormone/signal protein that regulates blood glucose	glyco

Lipids store more energy than carbohydrates

- Lipids contain more energy per unit mass compared to carbohyrates. Since animals are more active than plants, more energy is required. Eg migrating birds will have less load and more energy storing lipids compared to carbohydrates. Lipids stored in fat cells allow buoyancy, thermal insulation and protection of vital organs. Lipids provide more metabolic water compared to carbohydrates and hence useful for storage in desert animals eg camel. Lipids in the form of energy reserves are required in animals to hibernate through winter.
- Triglycerides release twice as much energy on oxidation during respiration per unit mass compared to carbohydrate due to greater hydrogen to oxygen ratio

Structure of haemoglobin helps maintain solubility and stability of hb

- Hydrophilic R groups of amino acid residues point outwards and their hydrophobic R groups point into the centre of the molecule. Outward-pointing hydrophilic R groups on the surface of the Hb molecule interact with the polar water molecules. Hydrophobic R groups inside the Hb molecule interact in a non-polar environment, holding the molecule in its correct 3D conformation.

Enzymes

Mode of action

Interaction/binding

- Enzymes have a specific active site which is complementary in shape and charge to the substrate. Effective collisions between enzyme and substrate form a temporary enzyme-substrate complex. Based on the lock and key hypothesis, enzyme is the lock and substrate I the key. Based on the induced fit hypothesis, substrate induces a change in the shape of enzyme active site so that active site has a more precise fit for substrate for effective catalysis. Enzyme-substrate complex held together by weak interactions e.g. hydrogen, ionic bonds hydrophobic interactions.

Catalysis

- Enzyme lowers the activation energy barrier by
    - Aligning substrates next to each other in active site for reaction to occur
    - Strain on bonds to be broken/distorts the substrate and reduces activation energy to achieve transition state
    - Orientates substrate such that its bonds are exposed to attack
    - Provide a favourable microenvironment
    - R groups of amino acid residues in active site participate in direct catalysis e.g. acid-base catalysis

Release

- Products no longer fit active site and are released → enzyme is unchanged and can be used again

Effect of pH

- Each enzyme has an optimum pH at which it is most active. The rate of reaction is max at this optimal pH. Rate decreases as pH deviates from optimum pH. Excess H+ or OH- ions may affect the ionisation of R groups of amino acids, where excess H+ results in –COO- groups becoming COOH and excess OH- results in NH3+ becoming NH2.
- Hence disrupt ionic bonds and hydrogen bonds that stabilises the specific conformation of active site → denaturation of enzyme.
- pH may also change the specific charge the R groups of the catalytic residues in the active sit, so catalytic activity of enzyme may be lost
- the changes to the specific charge of the contact residues in the active site may affect the temporary binding between the enzyme and substrate → no enzyme-substrate complex formed thus may affect the catalytic process itself.

pH

- low pH alters the ionic charge of the acidic and basic R groups of amino acids at the active site of ezyme, thus ionic bonds and hydrogen bonds that help to maintain the specific shape of the active site are disrupted, leading to loss of 3D conformation of active site, hence enzyme is denatured. Substrate can no longer bind to active site of enzyme to form enzyme-substrate complex, decresain the rate of formation of E-S complexes and hence decreasing the rate of reaction.

Induced fit hypothesis

- In the induced fit hypothesis, catalytic R groups of the active site come into correct orientation and bind to the protein. The bind causes conformational change that fits the enzyme more closely to the substrate and in so doing causes a strain in the structural bond lowering the activation energy.

Km the same for both non-competitive inhibitor and without inhibitor

- Km is derived by measuring half Vmax of each respective graph. Since binding of the inhibitor is at a site other than the active site/allosteric site, there is no change in affinity of the active site of the enzyme to its substrate and Km value remains the same. The 3D conformation of the active site is changed with the binding of the inhibitor

Non-competitive inhibitor

- Non-competitive inhibitor has no structural similarity to the substrate and binds to the enzyme at site other than the active site. Binding of the non-competitive inhibitor causes 3D conformation to change such that its active site's conformation is altered and substrate an no longer bind to the active site. Increase in substrate conc will not reverse the inhibition even at very high substrate concentration, the max rate of reaction in the presence of non-competitive inhibitor is lower than that of reaction in the absence of non-competitive inhibitor.

Cell Structure and Membrane

Fluid mosaic

- It is referred to as 'fluid' because the cell membrane comprises of phospholipids and proteins which are free to move laterally within a layer, the phospholipids can flip flop from one layer to the other but this is a rare occurrence. It is referred to as mosaic because the random arrangement of the proteins embedded amongst the phospholipid molecules resemble a mosaic pattern
- Fluid: phospholipids free to move within the membrane. Allow synaptic vesicles containing neurotransmitters to fuse with plasma membrane of pre-synaptic neurone to be released into the synaptic cleft/allow membrane proteins to change conformation even when embedded in membrane.
- Mosaic: presence of a variety of proteins scattered in the membrane. V.g. Ca2_ ion channels which allow Ca2+ influx across pre-synaptic membrane upon membrane depolarisation/chemically gated Na+ ion channels which allow Na+ influx across post-synaptic membrane upon binding of neurotransmitters to their specific receptors

Membrane fluidity

- Fluidity: phospholipids and proteins are free to move laterally within membrane. Unsaturated hydrocarbon tails have kinks which keep the phospholipid molecules in the membrane from packing close together, enhancing memb fluidity. Cholesterol found in between phospholipids disrupts close packing of phospholipids in the memb at low temp. ydrophobic interactions between cholesterol and phospholipid tails rstrict phospholipid movement at high temp. hence cholesterol prevents memb from freezing at lower temp and membrane prevented from becoming overly fluid, integrity of membrane is maintained at high temp. membs have higher fluidity if it has a higher proportion of phospholipids with unsaturated hydrocarbon tails and cholesterol.
- Importance of fluidity
    - Need for invagination/pinching in of cell surface membrane during cytokinesis and endocytosis
    - Need for formation of pseudopodia in cell surface memb to engulf substances during phagocytosis

- Budding/pinching off vesicles for transport of proteins from RER to GA, from trans face of GA during protein sorting to outside of cell
- Fusion of vesicles membrane from ER to GA for protein modification, with cell surf memb to release secretory molecules from cell/exocytosis/fusion of endocytotic vesicles with lysosomes for digestion
- Fluidity allows movement of proteins embedded on cell surface memb for dimerization of receptors
- Diffusion of small or non-polar molecules through transient pores between phospholipids in memb
- Impt for transmemb transport proteins changing conformation eg sodium-potassium pump/ligand gated Na+ ion cahnnel
- Fluidity required for embedment of protein molecules such as ETC in thylakoid memb/channel proteins

Transmembrane proteins

- Glucose is polar while ions are charged, both are hydrophilic. Cell membranes have a hydrophobic core making them impermeable to these solutes. Transmembrane transport proteins can be a channel or carrier that provides a hydrophilic channel through the membrane for passage of the solutes, because a transport protein is specific to its own solute, different transport proteins are needed for different solutes

No channels for insulin

- Insulin is a peptide hormone that s too large to cross the membrane via a channel. A channel with a big enough hydrophilic channel for insulin will allow many other molecules to pass through as well, so insulin is packaged in membrane-bound Golgi vesicles and released through process of exocytosis instead

Exocytosis

- Secretory vesicles containing insulin will be transported towards the cell membrane along the microtubules. Secretory vesicles will fuse with the cell membrane, releasing insulin to the exterior of the cell by exocytosis

Cells with chloroplasts also contain mitochondria

- Mitochondria are the sites for aerobic cellular respiration, producing ATP. ATP produced by mitochondria released for use in cytosol. ATP from mitochondria is used for active transport/macromolecule synthesis, formation of cytoskeleton in cell division, vesicle movement etc. However ,ATP produced in chloroplasts during the light dependent stage is subsequently used in the light independent stage of photosynthesis and is not available for use for active processes in the cytosol

Comparison between chloroplasts and mitochondria

- Similarities
    - Both are bound by a double membrane, inner membrane encloses a fluid-filled cavity containing 70S ribosomes, circular DNA strands and enzymes. Electron transport chain found in the internal membranes of both organelles. Stalked particles ATP synthase are found in both organelles
- Differences

Point of comparison	Chloroplast	Mitochondria
Size	Larger	Smaller
shape	Lens shaped	Generally spherical or rod shaped
Inner membrane	Not folded, not arranged into folds and do not contain stalked particles	Extensively folded as inner portion of membrane contains stalked particles. Arranged into folds known as cristae
Granules/grains present	Starch grains present	Numerous phosphate granules are present, no starch grains
Internal membrane system	Present *iyn* the form of stacks of thylakoids and intergranal lamella	An internal membrane system is absent
Location of stalked particles	Found on thylakoid membranes	Found on inner membrane

Coloured pigments	Presence of photosynthetic pigments on thylakoid membranes eg chlorophyll	Absence of coloured pigments

Function of transmembrane protein

- Allows the transport of large polypeptides into the cisternal lumen as these cannot traverse the hydrophobic core of the phospholipid bilayer of the RER. Channel protein functions as a receptor to bind to the signal peptide sequence of the polypeptide. Channel protein also holds the bound ribosomes in position on the RER

Route of proteins synthesised at RER

- Protein enter the lumen of the cisterna of the RER. Transport vesicles bud off from the RER and carry the proteins to the Golgi apparatus. They fuse with the cis face of the GA. A secretory vesicle containing the modified protein will then bud off from the trans face of the GA, and fuse with the cell surface membrane, releasing the protein content of the vesicle by exocytosis. Microtubules direct the movement of the transport vesicle to the GA and the secretory vesicle to the cell surface membrane

Nucleoli

- Nucleoli are the sites of rRNA synthesis through transcription/sites of assembly of ribosomal subunits, hence appear denser in cancer cells. Cancer cells undergo higher rates of protein synthesis in preparation for faster rate of cell division. Higher rates of translation is facilitated by a greater number of ribosomes hence the higher rRNA content in cancer cells. Different cancer cells have different mutations resulting in / dysregulation of gene expression in cancer cells lead to different cells having different rates of protein synthesis and greater variation in rRNA content.

Post translational modification of ribosomal proteins is needed

- Plays a role in the regulation of rate of translation/rate of protein synthesis/translation accuracy. Affects the 3D conformation of ribosomal proteins, which affects their binding with rRNA and assembly of ribosomal subunits. Contributes to the stability of ribosomal proteins, making them more resistant to degradation by proteases. Provides for diversity in protein structure beyond that allowed by the 20 encoded amino acids.

RER remains close to nucleus

- The nuclear envelope is continuous with the membrane system of the RER

Mitosis/Meiosis

Anaphase

- centromeres divide, kinetochore microtubules attached to the centromeres shorten and pull the sister chromatids which are now daughter chromosomes to poles of the cell

Early Metaphase

- Kinetochore microtubule shorten and the centromeres do not divide. This pulls the poles closer causing the initial decrease in distance between poles.
- After 25 min, distance between poles increases they move apart. This is because the non-kinetochore microtubules elongate and slide past each other causing the cell to elongate to prepare for cytokinesis

Role of centromeres

- They are non-coding tandem repeat sequences at one location along the length of a chromosome where sister chromatids to adhere to each other and allow proteins called kinetochores and subsequently kinetochore microtubules to attach. Thus allowing the alignment of chromosomes at the equator during

metaphase and subsequent separation of sister chromatids. The chromosomes formed can be pulled to opposite poles.

Meiosis vs mitosis

Pt of comparison	mitosis	Meiosis
Pairing of homologous chr	Homologous chr do not pair up via synapsis and there is no formation of bivalent	Homologous chr pair up by a process called synapsis to form bivalents at prophase I
Crossing over	There is no chiasma formation and crossing over and hence no exchange of equivalent portion of genetic material or alleles occurring between homologous chr	Chiasma formation and crossing over occurs such that exchange of equivalent portion of genetic material or alleles occur between non-sister chromatids of homologous chromosomes during prophase I
Arrangement of chr at metaphase	Chr arranged singly at the metaphase plate during metaphase	Homologous chr arranged as pairs at metaphase plate during metaphase I
Behaviour of chr at anaphase	It involves division of centromeres and separation of sister chromatids at anaphase	It involves the separation of homol chr at anaphase I. centromeres do not divide at anaphase I and division of centromeres and separation of non-identical sister chromatids at anaphase II.

Why chromosome has double arm structure

- In the S phase of interphase, each chr has undergone semiconservative DNA replication to form 2 identical sister chromatids that are held together at the centromere

G1 checkpoint

- Checks that sufficient nutrients are present, environment is favourable/need for new cells for replacement, sufficient growth of the cell, sufficient organelles, DNA not damaged and can be replicated, and growth factors are present.

M checkpoint

- Checks for attachment of spindle fibres to kinetochores of chromosomes, ensures correct alignment of chr at metaphase plate, allows separation of sister chromatids equally at anaphase

G2 phase

- Synthesis of proteins/RNA/enzymes, formation of new organelles, ATP production

Quiescence vs senescence

- quiescence occurs when cells are neither dividing nor preparing to divide (exit from cell cycle) while senescence occurs in response to DNA damage or degradation that would make a cell's progeny nonviable/when cells reach the Hayflick limit.

Second meiotic division

- The number of chromosomes at the end of the division remained the same as that during prophase, of 6 chromosomes per cell. During anaphase II, chromatids were separated to opposite poles and each chromatid is considered as an individual chromosome (hence number of chromosomes remain unchanged). The number of chromosomes at the end of meiosis 1 would have been half that of the parent cell.

Tubulin inhibitors

- Tubulin inhibitors prevent polymerisation of tubulin dimers to form microtubules/spindle fibres that makeup the mitotic spindle. Without spindle fibres, chromosomes cannot divide/mitosis stops at prophase/mitosis cannot take place. Hence affected cells exit the cell cycle, and uncontrolled cell division is prevented

Significance of meiosis in genetic variation

- Crossing over between non-sister chromatids of homologous chromosomes takes place during prophase I, gives rise to new combinations of alleles from both parental chromosomes which creates genetic variation in gametes
- Independent assortment of homologous chromosomes in pairs at the metaphase plate during metaphase I and their subsequent separation during anaphase I, results in 2^n possible types of gametes where n is the number of homologous pairs.

Fertilisation

- Random fusion of gametes leads to greater variation with different genotypes and phenotypes in offspring, and restores the diploid number of chromosomes

Mendelian Genetics

Importance of chi-square test

- To determine if the difference between observed phenotypic ratios and expected 9:3:3:1 dihybrid ratio was significant or due to chance

Epistasis

- rr is epistatic over E and e locus (recessive epistasis). rr prevents the formation of any pigment hence rrEE, rrEe or rree will give only white phenotypes. R produces enzyme R which converts a colourless precursor to red and with presence of E, the red pignment is converted to a purple pigment

How to determine homozygous recessive

- cross this plant with unknown genotype with a pure breeding red plant (RRee)
- Resultant offspring would have either all red or red and purple grains. If purple grains seen, then the original plant must have at least one E allele at the E/e locus.

Genetic mapping

- Examine the percentage of recombinants where the percentage of recombinants reflect distance between the pair of traits. The greater the percentage of recombinants, the greater the distance between genes. The distance between linked genes is expressed in map units where 1% recombinant frequency=1 map unit. If the expected phenotypic ratio is obtained such as 1:1:1:1 when a double heterozygote is test crossed, then there is no linkage.

Null hypothesis

- There is no significant difference between observed and expected data ie the observed data follows a 2:1:1 distribution. Any difference is due to chance.

Phenotype affected by environment

- Fur colour/synthesis of black pigment in Himalayan rabbit. Exposure to heat leads to white fur formed instead of black fur, no synthesis of black pigment.

Double cross over

- A double cross-over restores the grouping of the linked alleles to the parental combination

Difference between observed and expected numbers in monohybrid cross

- Sample size too small, chance of variation is statistically insignificant, difference in survival rate of sperm/ova with particular genotypes, difference in survival rates of zygotes with particular genotypes

Significance of p value

- P value is the probability that the difference between observed and expected ratio is due to chance alone. Since p is more than 0.05, there is no sig difference between O and E ratio of 1:1

Variation in phenotype

- Environmental factors eg nutrition affected the expression of allele coding for normal wings

Mutation rate is low

- Mutant alleles may confer selective disadvantage, resulting in alleles being removed by natural selection/unable to survive, reproduce and pass on the alleles. Mutant alleles are recessive and their effect on the phenotype can be masked by the normal dominant allele

Epistasis

- Interaction between two genes coding for gene products controlling the same characteristic/in the same metabolic pathway. Epistatic gene overrides expression of hypostatic gene to express its own phenotype.

Reciprocal cross

- A reciprocal cross is done to determine whether the 2 gene loci are sex-linked. The same F1 results are observed suggesting that the two genes are autosomal/not sex-linked.

Photosynthesis & Respiration

Role of oxygen in oxidative phosphorylation and photophosphorylation

- In oxidative phosphorylation, oxygen is the final electron acceptor as it combines with electrons and H+ to form water. In photophosphorylation, oxygen is formed as a by-product from photolysis

Anaerobic respiration

- Partial oxidation of glucose during glycolysis in the absence of oxygen. 1 molecule of glucose is broken down to 2 molecules of pyruvate with net yield of 2 ATP by substrate level phosphorylation and 2 NADH. Alcoholic fermentation occurs to regenerate NAD+ for glycolysis to continue. Pyruvate is decarboxylated to form acetaldehyde with the removal of carbon dioxide. Acetaldehyde is then reduced to ethanol by accepting H atoms from NADH to regenerate NAD+, resulting in an increase in concentration of alcohol from 0 to 16% from 24 to 96 hr.

Why no further alcohol produced

- Yeast is killed at 16% ethanol. Ethanol is organic and thus dissolves and disrupts phospholipid bilayer of the cell membranes in yeast. Enzymes in yeast are also denatured by the high ethanol concentration

Calvin cycle vs krebs cycle

Pt of comparison	Krebs cycle	Calvin cycle
site	Occurs in matrix in the mitochondrion	Occurs in the stroma in the chloroplast
Electron carriers	NAD+ and FAD accepts the electrons and protons to become NADH and FADH2	Reduced NADPH is oxidised to become NADP+
Carbon dioxide	produced	Incorporated into sugars
ATP	Produced during substrate level phosphorylation	Used up

Nature of process	Catabolic process, releasing energy stored in acetyl coA to ATP and reduced NADH and FADH2	Anabolic process, converting energy in the form of ATP and NADPH to producing starch

Small yield of ATP under anaerobic conditions

- In absence of oxygen, the final electron acceptor, members of the ETC that have previously picked up electrons and protons from NADH/FADH2 cannot be re-oxidised. Oxidative phosphorylation eventually stops as no further electrons are passed down the chain, hence no ATP will be produced via chemiosmosis. NAD and FAD cannot be regenerated hence Krebs cycle and link reaction cannot proceed. No ATP produced via Krebs cycle via substrate level phosphorylation. The regeneration of NAD+ in cytoplasm allowed glycolysis to proceed, produced 2 net ATP per glucose molecule via substrate level phosphorylation. In yeast cytoplasm, pyruvate is first decarboxylated to ethanal, then reduced to ethanol by NADH via alcoholic fermentation. In mammals, cytoplasm, pyruvate was reduced by NADH to lactate via lactate fermentation.

Similarity in ATP production in mitochondria and chloroplasts

- ATP synthesis in both organelles occur through chemiosmosis where in both, electrons are passed down a series of e carriers that are increasingly electronegative. Energy is released and is coupled to the pumping of H+ from the mitochondrial matrix into the intermembrane space in mitochondria, and from stroma into thylakoid in chloroplasts. Results in build-up of a proton gradient across the inner mitochondrial membrane and thylakoid membrane. H+ flows down its conc gradient through ATP synthase, energy from proton motive force sued to phosphorylate ADP to form ATP.

Respiration quotient

- RQ is the ratio of carbon dioxide given out to oxygen taken in during respiration
- RQ is high at early stages of germination → the seed coat still covers eh seed, and the seed is embedded deep in the soil, making it difficult for oxygen to penetrate inside. Respiration in seed is partly anaerobic.

CO2 assimilation rate levels off at high light intensity

- at higher light intensity when CO2 assimilation rate levs off, the the chloroplasts are light saturated and photosynthesis is occurring at max rate. Light is no longer a limiting factor and other factors such as temp is the limiting factor

Light compensation point

- Where the rate f respiration equals the rate of photosynthesis
- Amount of CO2given out during respiration is equivalent to the amount of CO2 fixed during the light independent stage of photosynthesis. Thus, there is no net gain in dry mass and no growth as the products of photosynthesis are used up in respiration

Anaerobic respiration vs calvin cycle

Pt of comparison	Anaerobic respiration	Light independent reaction (Calvin cycle)
Reduced co-enzyme	Uses NADH in the reduction of pyruvate to ethanol	Use of NADPH in the conversion of glycerate-3-phosphate to glyceraldehyde-3-phosphate
ATP	ATP synthesised via substrate-level phosphorylation	ATP used in the conversion of glycerate-3-phsphate to glyceraldehyde-3-phosphate
CO2	CO2 produced in the conversion of pyruvate to ethanol	CO2 incorporated with RuBP to form citric acid
location	cytoplasm	stroma
Molecule regenerated	NAD+	RuBP and NADP+

Significance of photosynthetic membranes

- Hold the photosynthetic pigments in a suitable position for absorbing the max amount of light energy. Provides a large surface area which holds the photosynthetic pigments.

Role of accessory pigments

- Strongly absorb wavelengths of light which cannot be captured by chlorophyll. Transfer the energy from these wavelengths of light to special chlorophyll a

Low light

- Light is a limiting factor as it is needed during the light dependent reactions to excite and boost electrons in the reaction centre of the photosystems to higher energy level. With less light, fewer electrons would be excited and less photophosphorylation can occur leading to less ATP and NADPH formed. Therefore light independent stage would be less active/calvin cycle will not occur, thus no formation of GP and thus no formation of TP, hence no glucose and hence cellular

Role of NADP

- Acts as a coenzyme, hydrogen and electron carrier. NADP is reduced to NADPH and NADPH carries electrons and protons from light dependent reactions to light independent reactions, providing reducing power for the light independent reactions for the reduction of glycerate-3-phosphate to glyceraldehyde-3-phosphate, leading to regeneration of NADP for subsequent light dependent reactions

Products of photolysis

- Oxygen used by cells for aerobic respiration, excess oxygen is released out of plant through stomata. Protons diffuse through ATP synthase from thylakoid space to stroma to generate ATP, and protons combine with electrons from PSI and NADP to form NADPH. Electrons are used to replace electrons lost form PSII, electrons are transported along ETC by electron carriers of progressively lower energy levels. In cyclic photophosphorylation, electron from PSI goes back to PSI, in non-cyclic photophosphorylation, electrons from PSI combine with protons and NADP to form NADPH

DNA

Semi-conservative replication

- DNA unzips and strands separate as hydrogen bonds between bases break. Both strands serve as templates for the synthesis of new strand by complementary base pairing. New molecule of DNA has one new strand and one original strand

Replication only occurs in 5' to 3' direction

- The active site of DNA polymerase is complementary to and binds to the free 3'OH group of the growing DNA strand. DNA polymerase adds DNA nucleotides to this 3' end as the free 3' OH group is needed for DNA polymerase to start polymerisation

Diff between human and bacterial chromosomes

- Human chromosome is linear while bacteria chr is circular. Human DNA is arranged in nucleosomes wrapped around histones while bacteria DNA is naked. Human DNA has introns/telomeres/centromeres not present in bacteria but bacteria DNA has operons. Human chr occur in pairs while bacteria chr occur singly

Replication of human chr takes a long time

- DNA in human chr are very long containing many non-coding DNA. DNA in humans are packaged into nucleosomes and can be very condensed requiring time to uncoil
- Sped up by: replication of DNA in humans involve multiple origins of replication where many DNA pol can replicate DNA simultaneously

RNA synthesis in bacteria

- RNA polymerase binds to cellulose gene promoter, causing DNA double helix to unzip and separate. One of the two DNA strands serves as template strand. Free ribonucleotides form complementary base pairing with bases on the template DNA strand. RNA pol catalyses formation of phosphodiester bonds between ribonucleotides via condensation reactions. Template DNA strand is read from 3' to 5' direction, and mRNA is synthesised from 5' to 3' direction. Transcription ends when RNA pol transcribes a terminator sequence.

Role of rRNA in protein synthesis

- rRNA along with ribosomal proteins forms the structural component of ribosome (large and small subunit). rRNA is responsible for catalytic function of ribosome in the formation of peptide bond between amino acids (found at the large subunit). rRNA in the small ribosomal subunit binds to 5' end of mRNA sequence during protein translation. rRNA at the A site binds to the amino-acyl tRNA while the rRNA at the P site binds to the peptidyl-tRNA

Transcription vs Replication

- both occur in the nucleus, both require DNA as template strand, formation of phosphodiester bonds between nucleotides in DNA replication and transcription, reading of DNA template strand is from 3' to 5' direction for both DNA replication and transcription, elongation of the newly synthesised strand occurs from 5' to 3' direction

Transcription	Translation
Synthesis of RNA strand	Synthesis of DNA molecule
Uses 1 DNA strand as template to synthesise mRNA	Uses 2 DNA strands as template to synthesise DNA
RNA uses nucleotides as monomers to form polynucleotide chain	DNA nucleotides are used in DNA replication
Phosphodiester bond formation catalysed by RNA polymerase	Phosphodiester bond formation catalysed by DNA polymerase
Transcription can be initiated without primer	DNA rep requires a pre-existing strand known as a primer to provide a 3'OH group for polymerase to add nucleotides to
Only certain region/gene is being transcribed in a single process	Whole DNA molecule is replicated in a single process

Gene mutation vs chromosomal mutation

Gene mutation	**Chromosomal mutation**
Change in structure of DNA or nucleotide sequence of a gene/single locus on a chromosome	Change in chr structure, DNA nucleotide sequence of gene mostly unchanged
Caused by deletion, insertion, substitution or inversion of one/several nucleotides	Deletion, inversion, translocation or duplication of chromosomal fragments
Gives rise to new alleles	Rearrangement of loci of genes/alleles/reshuffling/recombination of alleles
More frequent than chromosomal mutations because genes outnumber chromosomes by several thousand to one	Less frequent
Play more impt role in evolution than chr mutations because new alleles increases gene pool for natural selection to operate	Play a less impt role in evolution than gene mutations because chromosomal mutations involve onlty reshuffling of alleles that already exist in gene pool

Replication vs Translation

- both processes require enzymes, involve complementary base pairing, regulate by regulatory factors, compartmentalised int eh cell, errors can occur, only occur when required by the cell

Semi-conservative DNA rep

- at the first gen, there is only 1 14N/15N hybrid band, which suggests the parental strands that contain 15N separate to serve as a template for the synthesis of newly synthesised strand, which contains 14N.
- At the second gen, there is 1 14N/15N hybrid band and 1 light band which align with the semi-conservative model of replication as the former contains DNA with 1 strand containing 15N and another containing 14N whereas the latter contains DNA with both strands containing 14N
- For the third gen, there is still one 14N/15N hybrid band and 1 14N/14N band and the intermediate band becomes thinner whereas the light band becomes thicker due to more DNA molecules containing 14Non both strands.
- Alternative: conservative/dispersive

TIC

- General transcription factors must assemble at the promoter to position RNA polymerase correctly at the promoter. Binding to transcriptional activator proteins to enhancer results in bending of spacer DNA to bring bound activators in contact with other proteins of the TIC, stabilizing RNA polymerase for high rate of transcription.

Translation

- tRNA with anticodon UA carrying the aa asn binds to mRNA codon AAU via formation of H bonds between complementary base pairs at A site of large ribosomal subunit. Formation of peptide bond between asn and val catalysed by peptibdyl transferase. Ribosome translocates in 5' to 3' direction, tRNA with growing polypeptide chain is now at P site. tRNA carrying val is now at the E site and is released.

tRNA structure and function

- contains amino acid attachment arm for attachment of specific amino acid via ester bond. Contains anticodon that binds to mRNA codon via H bonds between complementary base pairs. Clover leaf shape contributes to specific 3D configuration, allows binding to amino acyl tRNA synthetase and ribosome peptidyl transferase.

Packing of chromosomes

- DN molecule wrapped around histone proteins, forming a nucleosome. Nucleosome linked by DNA linkers forming 10nm beads on a string structure, further coiled into a solenoid with 6 nucleosomes per turn, forming 30nm fibre. 30nm fibre associates with scaffold proteins to form 300nm fibre, further coiling to form 700nm chromatid

Termination of translation

- Ribosome reads a sequence on mRNA coding for a stop codon (UAA, UAG, UGA), ribosome stops translocating. Protein release factor recognises and binds to the stop codon on mRNA. Addition of water molecule causes hydrolysis/cleavage of the ester linkage of the fully translated polypeptide from the tRNA, releases polypeptide from ribosome.

Importance of complementary base pairing

- Complementary base pairing between bases of the two template strands is important as it stabilises the double stranded helix structure of DNA for storage of genetic information
- Complementary base pairing enables the formation of daughter strands during DNA replication before mitosis in order to transmit genetic information to daughter cells, the proofreading function of DNA polymerase to find and repair mutations to maintain genetic fidelity, the formation of mRNA during transcription in order to transmit information for the synthesis of the primary sequence of polypeptides in protein synthesis. Complementary base pairing between mRNA codons and tRNA anticodons during translation transmits information for the primary sequence of polypeptides in protein synthesis.

Amino acid activation

- The process that joins the correct amino acid to the tRNA is known as amino acid activation. Attachment of amino acid to a specific tRNA is catalysed by an enzyme called aminoacyl tRNA synthetase. These enzymes have active sites which will recognise a specific combination of amino acid and anticodon of a tRNA that are complementary to the active sites. As there are 20 different amino acids, there will be at least 20 different aminoacyl tRNA synthetases. The synthetase enzyme catalyses the covalent attachment of amino acid to tRNA in an energy releasing process driven by hydrolysis of ATP. The resulting aminoacyl tRNA complex is released from the enzyme and will deliver its amino acid to the growing polypeptide chain on a ribosome. Ensures that correct amino acid as specified by genetic code is matched to the correct tRNAs.

COPEG + cancer

Gene mutation

- Alteration in the DNA nucleotide sequence. Can be a deletion or insertion mutation, where one or several nucleotides are removed or added into a DNA nucleotide sequence. Can be a substitution mutation where one nucleotide is replaced by another. Can be an inversion mutation, where a segment of nucleotide sequence separates from the allele and rejoins at the original position, but is inverted.

Mutation affect structure of product

- Substitution mutation
    - One nucleotide is replaced with a different one. Change in codon in mRNA and an amino acid with a R group of different chemical property is coded for, results in changes in interactions involved in maintaining tertiary structure e.g. ionic, disulphide, hydrogen and hydrophobic interactions, lead to alteration of 3D conformation of protein.
- Frameshift mutation
    - Due to deletion/insertion of nucleotides not in multiples of 3. Result in ribosomes reading mRNA template as incorrect triplets during translation/alteration of reading frame. All codons downstream of point mutation will be read incorrectly, produce a different sequence and number of amino acids, results in non-functional protein/pre-mature termination of polypeptide should a stop codon by generated.

Loss of function mutation → recessive

- Loss of function mutation gives rise to a non-functional/absence of p53 protein. Effect can be masked by presence of a normal dominant allele that will result in sufficient copies of the normal protein beings synthesised to exert effect.

Mutations have no effect

- Genetic code is degenerate, where more than one type of codon can code for the same amino acid. Mutations at 3rd nucleotide of codon can still result in a codon coding for the same amino acid.
- Mutation results in a codon coding for an amino acid with an R group having similar chemical properties to original amino acid.
- Mutation in the introns which is spliced out and not translated, hence no change in amino acid sequence
- Mutation affect regions that are away from DNA binding site, no change in conformation of DNA binding site of p53, hence p53able to bind to the same specific regions on the DNA

Change in amino acid effect on haemoglobin

- Hydrophilic and charged glutamic acid is replaced by hydrophobic and non-polar valine. At low O2 conc, loss of O2 from HbS results in an abnormal conformational change that causes a hydrophobic region to stick out. This hydrophobic region attaches to hydrophobic regions on other HbS causing them to polymerise into insoluble fibres
- Long insoluble HbS fibres within RBC causes its shape to be distorted from a normal biconcave shape to a sickle cell shape. Sickle RBCs are more fragile resulting in them having a shorter life span→ results in shortage of RBCs and poor O2 transport resulting in anaemia. Sickle-shaped RBCs being pointed and

elongated, may also get lodged in small capillaries and therefore interfere with blood circulation. This may result in organ damage.

How HbF reduce symptoms of SCA

- Elevated levels of HbF will result in a relatively lower proportion of HbS in RBC. Less polymerisation of haemoglobin occurs. This leads to fewer sickled cells and less cell lysis, resulting in a longer life span of RBC and hence improved oxygen carrying capacity of the blood. Compared to HbS, HbF has a greater affinity for oxygen.

Factors increasing chances of cancer

- Exposure to UV light, carcinogens eg tar in cigarette smoke, benzene, formaldehyde, ethidium bromide. Viruses like avian sarcoma virus, HPV
- Increases chances of DNA damage and mutations leading to loss of function mutation of tumour suppressor genes and/or gain of function mutation of proto-oncogenes to form oncogene. Disruption of these regulatory genes will lead to excessive cell proliferation and inability to repair damaged DNA, resulting in formation of a malignant tumour capable of metastasizing to other parts of the body to form secondary tumours

Proto-oncogene

- Found in normal cells, gene that codes for a protein involved in cell proliferation/division

Oncogene

- Mutated form of proto-oncogene. There is excessive production of the protein or it codes for a protein with increased activity/more resistant to degradation, leading to greater than normal/uncontrolled cell proliferation/division resulting in cancer

How proto-oncogene becomes oncogene

- Myc gene in chromosome 8 is regulated by a normal promoter, expressing normal amount of Myc protein. Translocation is a chromosomal mutation when Myc gene being transferred from chr 8 to chr 14 to be under the influence of an enhancer of IgH gene, resulting in high level of expression and transcription of yc gene to produce excessive amount of Myc protein or growth factors. Thus this is a gain in function mutation, excessive amount of myc protein stimulates cells to undergo greater cell division, leading to tumour formation.

Amplification lead to multi-drug resistance

- Gene amplification resulting in more copies of MdrI gene, therefore more membrane-bound transporters transcribed and translated to ensure greater pumping of drugs out of cels so that drugs cannot accumulate and reach toxic levels for cells→ greater resistance

Overcome drug resistance

- Anti-sense RNA that will bind to mRNA transcripts of Mdr1 gene to prevent translation of membrane-bound transporter so that number of transporters will decrease. Molecular inhibitors that bind directly to membrane-bound transporters to prevent their pumping activities so that there will be no efflux of the anticancer drugs

Role of telomeres

- Telomeres are non-coding tandem repeat sequences found at both ends of linear chr
- Each round of DNA replication will result in the shortening of daughter molecules at the telomeres because DNA polymerase is unable to replace the RNA primers with DNA (end rep problem)
- Since telomeres are non-coding, this ensures that vital genetic information are not lost with each round of replication.

- By forming a loop with 3' overhang, they protect and stabilise terminal ends of chr, hence preventing fusion of the ends with those of other chr, prevent triggering of pathways that lead to cell arrest or cell death, because exposed 3' overhang will be perceived as DNA damage/DNA double stranded break
- The 3' overhang of the telomeres allow their own extension, by providing an attachment point for the correct positioning of the enzyme telomerase in certain cells e.g. germ cells

Function of telomerase reverse transcriptase

- Telomerase has an active site that is complementary in conformation and charge to a specific telomeric DNA sequence. Using telomerase RNA as a template, telomerase reverse transcriptase forms a complementary DNA sequence through complementary base pairing where by adenine base pairs with uracil, thymine with adenine, cytosine with guanine, guanine with cytosine.
- Catalyses the formation of phosphodiester bonds between deoxyribonucleotides.
- It then translocates 6 base pairs in the 5' to 3' direction of the DNA overhang to repeat the above processes.
- After many rounds, a series of tandem repeats of GGTTAG elongates the overhang which can then form a complementary DNA sequence, thus elongating the telomere DNA

Role of telomerase RNA

- 5 nucleotides of the telomerase RNA anneals and forms complementary base pairs with the single-stranded overhang at 3' end of the telomere which aligns the telomerase reverse transcriptase wrt the DNA. It serves as the template for formation of a complementary DNA sequence whereby A pairs with U…, resulting in tandem repeat sequences

Parts of telomerase are double stranded

- Double stranded nature of parts of telomerase RNA would stabilise the molecule and this was achieved by complementary base paring. It folds into a precise 3D conformation complementary to the active site of the enzyme.

Resolve end-rep problem

- An enzyme, telomerase adds telomere repeat sequences to the 3' end of DNA strands to act as a buffer for the end-replication problem. Telomerase has a short molecule of RNA that serves as a template which is complementary to the non-coding telomere repeat

Chromosomal mutation

- Translocation mutation is a form of chromosomal mutation where a portion of chromosome 9 is transferred to chromosome 22. Mutation involving ras gene is a form of gene mutation where guaninge is substituted for by thymine

Tumour cells exhibit diff levels of resistance to drugs

- Different tumour cells exhibit variation due to random mutation of certain genes/differential gene expression, leading to formation of new alleles coding for transporter proteins that pump out drugs, tubulin with a non-complementary binding site where the drug usually binds to, enzymes that hydrolyses the drug, inhibitors that bind to the drugs and render them ineffective.

Viruses & Bacteria

Viruses

Synthesis of glycoproteins

- Viral glycoproteins are translated at the RER from the mRNA of the provirus transcribed in the host. Glycoproteins are then transported and inserted into the host cell membrane via vesicles. The nucleocapsid

will then be assembled near the cell surface and it will bud off from the host cell membrane that is studded with viral glycoproteins to form a new virus

Inhibition

- HIV protease inhibitors bind to the active site of HIV protease and blocks the substrate from binding, so that the viral polyprotein cannot be cut into the necessary structural proteins and enzymes. Newly formed virus not infective/functional and unable to infect further cells
- Inhibitor has similar shape and charge to viral polyprotein or complementary in shape and charge to active site of enzyme, does not break down easily/stable so can remain in active site.

How enveloped H5N1 virus enters host cell

- Haemagglutinin binds to sialic acid receptor on host cell membrane. Virus then enters host cell by endocytosis, where host cell membrane invaginates and pinches off, placing virus in an endocytotic vesicle. Vesicle then fuses with a lysosome and the resulting drop in pH stimulates fusion of viral envelope with vesicle membrane, releasing nucleocapsid into cytosol

RNA dependent RNA polymerase required

- Such RNA segments code for RNA-dependent RNA polymerases which are not present in the host cell. The RNA dependent RNA polymerases are required for the replication of viral RNA and synthesis of viral mRNA used for translation into viral proteins.

Inhibiting neuraminidase prevent influenza

- When neuraminidase is inhibited, it cannot cleave the sialic acid to release the viruses from the infected cells to infect other cells

Replication of influenza virus

- Viral RNA genome is transcribed to mRNA by viral RNA-dependent RNA polymerase inside nucleus. The mRNA is transported to the cytoplasm and translated to viral structural proteins and viral enzymes by host cell ribosomes. The mRNA in the nucleus is also used as a template to replicate new RNA genomes for new influenza viruses. Capsid proteins are transported back to the nucleus to bind with viral RNA to form ribonucleoproteins. Neuraminidase and Haemagglutinin are transported through the Golgi apparatus and incorporated onto the cell surface.

Limitation of neuraminidase inhibiting drug

- Concentration of inhibitors may not be high enough to target all neuraminidase/large number of host cells, difficult to ensure inhibitors reach all the host cells. Antigenic drift/shift/mutation in neuraminidase gene will result in a different 3D conformation of neuraminidase, so drug needs to be continually updated.

Lysogenic life cycle	Influenza life cycle
Use tail tip to bind to specific receptors on bacterial cells	Use haemagglutinin to bind to sialic acid receptors on epithelial cells
Only DNA is injected into host cell, capsid left outside	Capsid and viral RNA enters host cell
Viral DNA integrated into host cell genome directly	Viral RNA transcribed into mRNA by RNA dependent RNA polymerase directly
Do not result in death of host cell	Release of influenza virus by budding may result in death of host cell

Obligate parasites

- Lack organelles and enzymes to survive eg lacks ribosomes for protein synthesis, contains only 1 type of nucleic acid either DNA or RNA but not both, hence need to take over host cell metabolic machinery for the production/replication of progeny viruses

HIV fusion vs budding

Pt of comparison	Fusion	Budding
Virus entry/exit	Virus is entering the host cell during fusion	Virus is leaving the cell via budding
Membrane interaction	During fusion, viral envelope fuses with cell surface membrane	During budding, virus acquires host cell surface membrane as viral envelope
Cytoskeleton involvement	Both processes involve rearrangement of the cytoskeleton at the cell surface membrane	
Requirement of energy	Both processes require ATP	
Rearrangement of phospholipid	Both processes involve the rearrangement of phospholipid	

HIV vs T4 phage release

- Release of HIV via budding will not directly kill the host cell but release of T4 phages via osmotic lysis will kill the host cell
- For t release of T4phages, a phage-encoded enzyme, lysozyme, will break down the bacterial peptidoglycan cell wall, causing osmotic lysis and release of the intact new bacteriophages, whereas for the release of HIV no enzymes are involved.

Viral inhibitors

- Tenofovir has similar conformation to adenosine triphosphate, it competes with adenosine triphosphate for the active site of reverse transcriptase, which lacks a 3'OH group, hence incoming nucleotide cannot form phosphodiester bond with the DNA molecule. Reverse transcription cannot be completed resulting in a truncated viral DNA molecule

How HIV infection result in cell death

- HIV infected cells may undergo apoptosis, multiple bound cells may fuse, forming a giant multinucleated cell or syncytium. The syncytium may rupture, or is destroyed by the body's immune system.

Cleavage of polyproteins

- Polyprotein cleaved by viral protease to produce enzymes eg Reverse transcriptase, integrase, HIV protease, structural proteins eg capsid proteins, glycoproteins gp 120 and gp41

Need more than one inhibitor

- Point mutations in genes coding for reverse transcriptase alters its tertiary structure, resulting in inhibitors being unable to bind to these sites
- As two mutations of the same gene are unlikely to occur at the same time, taking a mixture of two drugs prevents/reduces the chance of drug-resistant HIV strain from developing

How HIV causes diseases

- HIV infects and kills T helper cells. B lymphocytes cannot produce antibodies without the help of

Bacteria

Lac operon

- Made up of DNA and within it are 3 structural genes. Lac Z codes for beta galactosidase, lac Y codes for lactose permease, Lac A codes for lactose transacetylase, structural genes have a common promoter sequence upstream which has a RNA polymerase binding site. Situated within the promoter is also a catabolic activator protein binding site. The operator has a site which allows for an activated repressor to bind. There is a terminator sequence downstream at the end of the lac operon. Further upstream of the operon is the regulator gene Lac I which codes for the repressor protein

Presence of lactose

- In the absence of lactose, a basal level of B galactosidase and permease is present within the cell because repression of the lac operon by the repressor is 'leaky'. (weak interactions between repressor and operator hence repressor may dissociate from the operator occasionally to allow the RNA polymerase access to the lac operon). A small number of permease is therefore present to transport lactose from the surrounding medium into the cell. Some lactose will be converted to allolactose by B galactosidase in the cell. Allolactose acts as an inducer molecule which binds to the repressor protein at its allosteric site. This alters the conformation of the DNA binding site of the repressor such that the repressor is inactivated and is no longer complementary in shape and charge to the operator and thus cannot bind to the operator. RNA polymerase is now able to bind to the promoter and can move downstream to transcribe the structural genes to form a polycistronic mRNA. Glucose is absent thus high level of cAMP will activate the Cap which binds to the promoter of the lac operon at the CAP binding site to increase the frequency of transcription. Operon is now turned on with increased synthesis of B galac, permease and transacetylase for metabolism of lactose

Operons are necessary in bacteria

- Clustering gene of related functions together under the control of a promoter allows for regulation of gene expression. This allows bacteria to only produce enzymes when required and allow quick responses to changes in the external environment. This allows efficient use of energy and conservation of resources. This ability to adapt to changes in the environment confers a selective advantage to the bacteria. This also allows bacteria to be able to use a variety of sugars/substrates

F plasmid vs bacterial chr

- F plasmid has significantly fewer base pairs than bacterial chr. F plasmid contains non-essential genes/genes which confer advantages such as antibiotic resistance unlike bacterial chr which codes for essential genes such as enzymes for cell metabolism

Conjugation

- Sex pilus of F+ bacterial cell makes contact with a F- cell and retracts to bring the F- cell closer soa mating bridge is formed between the 2 cells. One of the 2 strands of the plasmid DNA in F+ cell is nicked and transferred from the F+ cell to the F- cell through mating bridge via rolling circle mechanism as the other DNA strand is used as a template for elongation. The single strand F plasmid DNA circularises in F- cell and is used as a template to synthesise a complementary strand for a double-stranded F plasmid DNA resulting in F+ cell

Adv of recipient

- Gains new alleles that when expressed, allow it to survive in a different environment e.g. antibiotic resistance. Use of a new metabolite/resources e.g. new carbon source by producing relevant enzymes, can receive relatively large amount of DNA at once.

Transformation

- Fragments of foreign naked DNA in the surrounding medium are taken up by a bacterial cell via surface proteins. The foreign DNA is incorporated into the bacterial chromosome/DNA via crossing over/homologous recombination. If the foreign DNA contains a diff allele that is now expressed in the bacterial cell, the bacterial cell has transformed.

Transduction

- Generalised: A phage infects a bacterium, injecting its viral genome into the host cell. Hydrolytic enzymes degrade the host bacteria chromosome into fragments. A small fragment of the host cell's degraded DNA is improperly packaged within a capsid rather than phage genome due to an error during the viral particle assembly process. Upon cell lysis, the defective phage will infect another bacterium and inject bacterial DNA from the previous host cell to the new bacterium. The foreign bacterial DNA can replace the homologous

region in the recipient cell's chromosome if crossing over/homologous recombination takes place, possibly allowing the expression of a different allele from the previous host

- Specialised: a temperate phage infects a bacterium, injecting its viral genome into the host cell. The viral DNA is integrated into bacterial chr forming a prophage, which may be improperly excised to include adjacent segment of bacterial DNA during an induction event. Bacterial DNA may be packaged into a capsid head during the spontaneous assembly of new viruses. Upon cell lysis, the defective phage will infect another bacterium and inject bacterial DNA from the previous host cell into the new bacterium. The foreign bacterial DNA can replace the homologous region in the recipient cell's chr if homologous recombination takes place, possibly allowing the expression of a diff allele from the prev host
- **Advantageous to bacteria**
    - A small piece of a bacteria DNA can be incorporated into the phage capsid due to mistakes during viral assembly/a small region of bacterial DNA may be excised together with the prophage and packaged into progeny virus. The resulting phages infect other bacteria and newly infected bacteria acquires DNA from the previous bacterial host. Allows genetic recombination, increases genetic variation, increases adaptability of the bacteria to changes in the environment

Binary fission vs mitosis

Pt of comparison	Binary fission	Mitosis
Type of cells it occurs in	prokaryotes	Eukaryotes
Location	Occurs in the nucleoid/cytoplasmic region of prokaryotic cell	Occurs in the nucleus of eukaryotic cells
Type of DNA involved	Occurs on circular double-stranded DNA	Occurs on linear double-stranded DNA
Number of chromosomes involved	Only 1 chromosome	More than 1 chromosome
Separation of daughter cells	There is division of parental cell to give rise to 2 daughter cells	No division of parental cell to give rise to 2 daughter cells during mitosis. This occurs during cytokinesis
Type of division	Cell division	Nuclear division
Origin of replication	DNA replication occurs at 1 point of origin	DNA replication occurs at multiple points on the genome
Utilisation of spindle fibres	There is no spindle fibre formation	Spindle fibre formation occurs
Presence/absence of end rep-problem	No end rep-problem	End-rep problem occurs

Homeostasis & Cell Signalling

Stages

- Binding of A to receptor tyrosine kinase A receptor causes the two receptor subunits to dimerise. This is followed by cross-phosphorylation of X and Y by intrinsic kinase activity of receptor
- Activated X and Y will in turn phosphorylate tyrosine residues on intracellular domain of the A receptor. M and N proteins will bind to the activated tyrosine residues via SH2 domains and will I turn become phosphorylated. M and N then dissociatefrom A receptor and the two subunits dimerise

Ligand cannot act directly on DNA in nucleus

- Interferon is too large, cannot pass through any transient pore from within cell surface membrane. OR cannot pass through hydrophobic core of cell surface membrane because it is polar and will be repelled

Advantages of cell signalling pathway

- Facilitate signal amplification as only a small number of signal molecules is needed to solicit a large response from cell
- Provides multiple checkpoints for regulation so that the cellular response can be regulated and controlled at each step
- Multiple responses to 1 signal molecule because 1 signal molecule can trigger multiple signal transduction pathways to elicit different responses
- Ensures specificity because the specific signal molecule binds to a specific receptor to elicit specific reaction via specific pathway in each cell type
- Ability of signal molecule to activate genes in nucleus upon binding to cell surface receptor without the need to move into nucleus
- Ability of a signal molecule to activate many different cells simultaneously

Mutation in GTPase in Ras

- Mutation of intrinsic GTPase of Ras → GTP bound to Ras cannot be hydrolysed to GDP, Ras remains active. Kinase B is always activated by Ras, kinases L and K are always phosphorylated and active, resulting in continuous trigger of phosphorylation cascade. Specific transcription factor D is always phosphorylated and thus is able to bind to the proximal control element via complementary shape and charge, accelerating and stabilising formation of TIC and hence high rate of transcription of mdm2

High levels of mdm2 increases chances of cancer

- Ubiqutinated p53 is degraded by proteasome int short peptides. Absence of p53 to trigger transcription of genes that code for proteins involved in cell cycle arrest, DNA repair, apoptosis. Fail to inhibit cell cycle, no DNA repair, allow evasion of mutated cells from apoptosis, accumulation of mutations in other proto-oncogenes/tumour suppressor genes occur, uncontrolled cell division

Nervous System

Why no action potential generated

- Acetylcholine from P will cause depolarisation while GABA from Q will cause hyperpolarisation. Spatial summation of these potentials counteracts each other resulting in a weak stimulus in neurone B

Enhances neurotransmitter activity

- B binds to GABA receptor and causes more influx of Cl- and efflux of K+ ions
- Prevents enzyme from degrading GABA
- Prevents GABA from unbinding rom GABA receptor

Summation

- Summation of EPSPs produced by repeated stimulation of only ONE presynaptic neurone at high frequency. If more neurotransmitters are released into the cleft before the first EPSP is destroyed, additive effects of several EPSPs may exceed threshold potential to result in an action potential in the post synaptic neurone

Refractory period

- absolute RP: no stimulus can initiate another action potential
- Relative RP: stronger than normal stimulus required to initiate action potential

Interval between action potentials

- Time interval between action potentials is dependent on the refractory period and on the strength of the incoming signal. B has maximal stimulus compared to A which has sub maximal stimulus
- Adv: variation of signal frequency determines sensitivity of the neuron

Myelin sheath

- With the presence of the myelin sheath, signal conductance down the neuron is even faster due to saltatory conduction at the nodes of Ranvier.
- In myelinated neurone, myelin acts as electrical insulator, preventing movement of ions across the axon. Cause AP to be generated only at nodes of Ranvier, nerve impulse jumps from node to node via saltatory conduction. In non-myelinated axon, AP is generated along whole length of axon via continuous conduction

No uptake of dopamine

- Cocaine blocks dopamine transporters, no uptake of dopamine. Dopamine accumulates in the synaptic cleft, continued binding of dopamine to dopamine receptor→ temporal summation of graded potential resulting in increased depolarisation thus continued feelings of pleasure.

No longer to feel pleasure

- Decrease number of receptors, fewer dopamine can bind to dopamine receptors, insufficient Na+ influx to reach threshold potential thus fewer AP generated

Roles of synapses

- Ensur one-way transmission
- Filter out infrequent impulses/temporal summation, alow spatial summation/convergence of impulse/interconnection of many nerve cells
- Allow transmission of info between neuron
- Prevent overstimulation

Evolution

How phenotypic differences arose

- There was geographical isolation that prevented interbreeding and thus disrupted gene flow because there were many isolated islands and the broadleaved woodlands were not continuous different regions had different environments, thus each sub-population was exposed to different selection pressures. With variation in phenotypes among birds, natural selection will select for those best adapted to their environment, who are more likely to survive, reproduce and pass on their alleles to the next generation. Allele frequencies change because of natural selection and genetic drift. As the different populations evolve independently from each other, they accumulate different genetic mutations and allele frequency changes over time and hence their distinct phenotypic differences

Same species

- A group of organisms of the same species are capable of interbreeding and producing fertile viable offspring, are reproductively isolated from other species, have a common gene pool and same chromosome number, usually have similar morphological, physiological and behavioural features.

Selection pressure

- Different types of food available in the environment. If seeds available in the habitat are hard or large, finches with low beak depth will not be able to crush these seeds and hence selected against. Limited availability of food results in competition which exerts a selection pressure to exploit varied food sources

Molecular evidence supports natural selection

- X gene is a homologous gene present in the common ancestor and all its descendants. There was modification in terms of different levels of gene expression in the two genes resulting in variations in beak shape in the population. Selection pressure is the type and availability of food. Finches with beaks suited to

feed on a particular type of food available in the env are selected for and will survive and reproduce fertile viable offspring to pass on their favourable alleles to their next generations.

Role of islands

- Islands provide means of geographical isolation by being surrounded by bodies of water such that gene flow is disrupted between islands that may cause speciation. Different islands have different env thus exposing the finches to diff selection pressures and the finches well adapted for that env will be selected for and survive to produce fertile, viable offspring

Advantages of using molecular methods in classifying orgs

- All known life is based on nucleic acids thus studies involving any taxa can use DNA sequence data.
- They can be used to compare species that are morphologically indistinguishable and to assess relationships between groups of organisms that are so phylogenetically distant that they share very few morphological similarities.
- They are objective and quantitative. Molecular character states are unambiguous (ACGT) whereas some morphological characters, such as those based on the shape of a structure, can be less easy to distinguish because of overlaps between different character states.
- Molecular data are easily converted to numerical form and hence are amenable to mathematical and statistical analysis. Amino acid sequences for many proteins and nucleotide sequences for a rapidly increasing number of genomes can be accessed from electronic databases and used for comparative study and classification.
- Offers a large and essentially limitless set of characters to be studied. Each nucleotide position can be considered a character and organism has millions to billions of nucleotide positions. A single experiment can provide information on many different characters: in a DNA sequence for eg every nucleotide position is a character with 4 character states ACGT. Large molecular data sets can therefore be generated relatively quickly
- The degree of relatedness can be inferred and quantified by calculating the number of nucleotide differences between species
- Molecular characteristics can clearly show if orgs are wrongly classified due to morphological characters that are similar between organisms due to convergent evolution

Classification vs phylogeny

- Classification is organisation of species according to particular characteristics, may not take into consideration evolutionary relationship between the species. Phylogeny is organisation of species according to particular characteristics which takes into consideration evolutionary relationship between the species

pt of comparison	Classification	Phylogeny
Basis of grouping orgs	Classification groups orgs based on overall/morphological similarities and does not take into account the evolutionary history of orgs	Phylogeny traces the evolutionary history of orgs based on ancestor-descendent relationships
System of organising organisms	System of naming. It involves grouping organisms into kingdom, phyium, class, order, family, genus species using a hierarchical classification system	Organisms are arranged based on their evolutionary relationship with each other, with each org assigned a position on a branching tree relative to other orgs
How species are presented	Using binomial nomenclature	Uses a phylogenetic tree where related orgs are grouped into the same branch on a phylogenetic tree
Nature of characteristics	Being based on morphological characters, does not discriminate between analogous or homologous characters	Makes use of homologous characters that are derived from a common ancestor to group orgs
Types of characters used	Uses only morphological characteristics	Uses morphological, anatomical, embryological as well as molecular

		characteristics such as DNA, RNA, amino acid sequences, also fossil records
Strengths and weaknesses	Easily places an org into its well defined group May wrongly classify orgs that are not related but look similar due to convergent evolution	Cannot immediately place an org into the phylogenetic tree as evolutionary history needs to be established from multiple sources Rarely classifies wrongly as convergent evolution will be placed in separate branches
Inference of speciation events	Does not allow inference of historical speciation events	phylogeny indicates speciation events as the node of the phylogenetic tree
Inference of relationships	Cannot infer how closely related 2 species are especially since they are grouped together in the same hierarchy 'species'	Allows accurate inference of how closely related 2 species are by looking at how recently they diverged from their common ancestor
Inference of common ancestors	Does not allow inference of common ancestors	Allows inference of common ancestors. Descendants of a common ancestor are presented in the same branch
Application of molecular clock	Not possible to apply molecular clock to date speciation events	If molecular evidence is used, can apply the molecular clock to infer time of speciation

Why cytochrome b gene is used

- The gene is a homologous gene meaning that it is conserved in all the species being compared and was found in their common ancestor. This forms the basis of comparison. Yet there are sufficient differences in the DNA of cytochrome b for scientists to distinguish the 3 closely related species. It is found in the mitochondria and hence do not undergo recombination and any mutation accumulates at a regular rate in the maternal line. Can be used for the molecular clock
- DNA sequence changes where there is a mutation such as base substitution. The DNA may be damaged by the reactive oxygen radicals generated in the mitochondrion/mitochondria DNA repair mechanisms may not be as robust.
- 19s rRNA gene will be present in all organisms which serves as a good basis of comparison between orgs, essential gene which changes very slowly, useful for estimating time of divergence that occurred long time ago. Accumulates mutations at a constant rate and therefore can be used to calibrate a molecular clock for the estimation of time of divergence between species

Neutral theory of molecular evolution

- graph shows that changes in DNA sequence occurs in a linear fashion, suggesting a constant rate of accumulation of mutations over time. This is possible only because the mutations would be selectively neutral and hence has no selective advantage or disadvantage on its phenotype. Examples of selectively neutral mutations are silent mutations where a change in nucleotide does not result in a change in amino acid sequence, or conservative mutations or mutations in non-regulatory, non-coding regions
- Linear graph shows mutation accumulates at a constant rate over time. Shows that most mutations/amino acid differences between organisms are neutral mutations. As the mutation does not come under selection pressure, frequency of the mutation in the population changes mainly due to genetic drift. Data can be used as a molecular clock to calculate number of years since divergence of a species from ancestral species.

Neutral mutation vs silent mutation

- Both do not affect the fitness of the organism, do not change the phenotype of an organism. Both involve a change in nucleotide sequence
- However silent mutation does not involve a change to the amino acid sequence of the polypeptide while neutral mutation includes changes to the amino acid sequence.

Adaptive radiation

- The large number of species suggests adaptive radiation had occurred
- There are different niches in different islands and they each have different selection pressures present. As a result of variation in populations, favourable traits are selected for via natural selection in the various niches. These favourable traits are passed on to the offspring. Speciation occurs when there is accumulation of mutations and changes in allele frequencies over time between the sub-populations due to disruption of gene flow

How to homologies support darwin's theory

- Presence of homologous structures in all the camelids shows that they inherited a common set of genes from common ancestor. Anatomical, embryological, molecular homologies→ modification arises due to natural selection selecting for better adapted traits in each population due to different selection pressure found in different geographical locations

Discontinuous distribution problematizes Darwin's theory

- Different species which are descendants of a common ancestor should be found close in geographical proximity as their range is limited by geographical barriers, the ocean between continents. Hence being found on different continents in present day suggest modern camelids may not descend from a common ancestor.

Analogy

- structures were analogous structures arising from convergent evolution. All are subjected to similar selection pressures eg same type of food. Similar structures were inherited from different ancestors but selected for.

Biogeography

- Numbats are more closely located to other Australian marsupial mammals than to giant anteaters. Supports the phylogenetic relationship that numbats are moer closely relatd to other Australianmarsupial mammals than to giant anteaters.

Not convergent evolution

- They share a recent common ancestor. Convergent evolution involves two phylogenetically different groups with no recent common ancestor. Homology of DNA sequence for cytochrome b shows high relation, they are subspecies.

Type of speciation

- Allopatric speciation due to presence of a physical barrier/sympatric speciation due to presence of overlapping geographical regions

If huge lake is reformed

- Numbers of each subpopulation increases initially due to increased space and food. Increased competition between subpops, reduction in numbers for some or all subpops. Some subpops outcompeted for food.habitat and therefore unable to survive and become extinct. Subpops may be abl to interbreed due to lack of reproductive barriers as tey only diverged from common ancestor recently. Interbreeding between subpops lead to hybrids, resulting in new subpops. Diff subpops occupy diff ecological niches, remain as diff subpops

Same species

- Both subpops able to interbreed to give viable fertile offspring. Absence of genetic isolation/reproductive barrier, gene flow between subpop still able to occur. Strong genetic compatibility few diff between DNA seqeuces, short time frame for accumulation of mutations indicates recent divergence from common ancestor, present in same geographical region overlapping habitat in C, indicates close relatedness according to biogeographical evidence as descendants from common ancestor tend to be located in the same region.

Mitochondrial DNA

- No recombination or crossing over takes place in mtDNA thus the differences reflect only mutations. If the coding region of mtDNA is used, it mutates very slowly as the genes in t coding region are very crucial for survival, but mutations are sufficient to allow for species differentiation. If non-coding mitochondrial control region of mtDNA is used, it has a more rapid mutation rate which allows for differences in DNA sequence to accumulate and allow better differentiation between closely related species for use in phylogenetic study. There are multiple mitochondria in a cell and hence multiple copies of mtDNA in each cell as compared to one copy of nuclear DNA in each cell, making it easier to obtain mtDNA. Mitochondrial chromosomes are circular and subjected to less degradation by exonucleases.

Different species

- Mole rats with diff number of chromosomes cannot interbreed to form fertile and viable offspring as not all chromosomes will be able to pair up in meiosis, producing offspring withodd number of chromosomes. Geographically isolated so unlikely to interbreed

Data analysis

Standard deviation bars

- To indicate the range of amount of myelin in samples of brain tissue to allow for statistical comparison