Adv H Biology Learning Outcome checklist
Unit 1.1 Laboratory Techniques for Biologists

1.1a Health and Safety

	I can state or explain the following
	substances, organisms, and equipment in a laboratory can present a hazard
	Hazards in the lab include toxic or corrosive chemicals, heat or flammable substances, pathogenic organisms, and mechanical equipment.
	Risk is the likelihood of harm arising from exposure to a hazard.
	Risk assessment involves identifying control measures to minimise the risk.
	Control measures include using appropriate handling techniques, protective clothing and equipment, and aseptic technique.

1.1b Liquids and solutions

	I can state or explain the following
	dilutions in a linear dilution series differ by an equal interval, for example 0·1, 0·2, 0·3 and so on.
	Dilutions in a log dilution series differ by a constant proportion, for example 10^{-1} , 10^{-2} , 10^{-3} and so on.
	a standard curve is used to determine an unknown: plotting measured values for known concentrations to produce a line or curve allows the concentration of an unknown to be determined from the standard curve.
	buffers are used to control pH
	addition of acid or alkali has very small effects on the pH of a buffer, allowing the pH of a reaction mixture to be kept constant.
	colorimeters are used to quantify concentration and turbidity:
	calibration of colorimeter with appropriate blank as a baseline
	use of absorbance to determine concentration of a coloured solution using suitable wavelength filters
	use of percentage transmission to determine turbidity, such as cells in suspension.

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1.1c Separation techniques

	I can state or explain the following
	a **centrifuge** is used to separate substances of differing density:
	In a centrifuge more dense components settle in the pellet; less dense components remain in the supernatant.
	paper and thin layer **chromatography** can be used for separating different substances such as amino acids and sugars
	the speed that each solute travels along the chromatogram depends on its differing solubility in the solvent used.
	affinity chromatography is used in separating proteins
	In affinity chromatography a solid matrix or gel column is created with specific molecules bound to the matrix or gel. Soluble, target proteins in a mixture, with a high affinity for these molecules, become attached to them as the mixture passes down the column. Other non-target molecules with a weaker affinity are washed out.
	gel electrophoresis is used in separating proteins and nucleic acids: charged macromolecules move through an electric field applied to a gel matrix.
	In gel electrophoresis charged macromolecules move through an electric field applied to a gel matrix.
	native gels do not denature the molecule so that separation is by shape, size and charge.
	SDS-PAGE separates proteins by size alone
	SDS–PAGE gives all the molecules an equally negative charge and denatures them, separating proteins by size alone.
	proteins can be separated from a mixture using **their isoelectric points** (IEPs):
	IEP is the pH at which a soluble protein has no net charge and will precipitate out of solution.
	A solution is buffered to a specific pH, only the protein(s) that have an IEP of that pH will precipitate.
	proteins can also be separated using their IEPs in electrophoresis
	Soluble proteins can be separated using an electric field and a pH gradient
	A protein stops migrating through the gel at its IEP in the pH gradient because it has no net charge.

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1.1d Detecting proteins using antibodies

	I can state or explain the following
	immunoassay techniques are used to detect and identify specific proteins
	immunoassay techniques use stocks of antibodies with the same specificity, known as monoclonal antibodies.
	an antibody specific to the protein antigen is linked to a chemical 'label': the 'label' is often a reporter enzyme producing a colour change, but chemiluminescence, fluorescence and other reporters can be used
	in some cases the immunoassay uses a specific antigen to detect the presence of antibodies.
	Western blotting is a technique, used after SDS–PAGE electrophoresis, in which the separated proteins from the gel are transferred (blotted) onto a solid medium so that the proteins can be identified using specific antibodies that have reporter enzymes attached.

1.1e Microscopy

	I can state or explain the following
	bright-field microscopy is commonly used to observe whole organisms, parts of organisms, thin sections of dissected tissue or individual cells.
	fluorescence microscopy uses specific fluorescent labels to bind to and visualise certain molecules or structures within cells or tissues.

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1.1f Aseptic techniques and cell culture

	I can state or explain the following
	aseptic technique eliminates unwanted microbial contaminants when culturing microorganisms or cells: aseptic technique involves the sterilisation of equipment and culture media by heat or chemical means and subsequent exclusion of microbial contaminants.
	aseptic technique involves the sterilisation of equipment and culture media by heat or chemical means and subsequent exclusion of microbial contaminants.
	a microbial culture can be started using an inoculum of microbial cells on an agar medium, or in a broth with suitable nutrients.
	Many culture media exist that promote the growth of specific types of cells and microbes.
	animal cells are grown in medium containing growth factors from serum.
	Growth factors are proteins that promote cell growth and proliferation.
	Growth factors are essential for the culture of most animal cells.
	plating out of a liquid microbial culture on solid media allows the number of colony forming units to be counted and the density of cells in the culture estimated.
	serial dilution is often needed to achieve a suitable colony count.
	A haemocytometer is used to estimate cell numbers in a liquid culture.
	vital staining is required to identify and count viable cells.

Adv H Biology Learning Outcome checklist <u>1.2a The Proteome</u>

Sub section	I can state or explain the following
a) the proteome	the proteome is the entire set of proteins expressed by a genome.
	the proteome is larger than the number of genes, particularly in eukaryotes, because more than one protein can be produced from a single gene as a result of alternative RNA splicing.
	not all genes are expressed as proteins in a particular cell type.
	Genes that do not code for proteins are called non-coding RNA genes and include those that are transcribed to produce tRNA, rRNA, and RNA molecules that control the expression of other genes.
	the set of proteins expressed by a given cell type can vary over time and under different conditions.
	Some factors affecting the set of proteins expressed by a given cell type are the metabolic activity of the cell, cellular stress, the response to signalling molecules, and diseased versus healthy cells.

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1.2b The synthesis and transport of proteins

Sub section	I can state or explain the following
bi) Intracellular membranes	eukaryotic cells have a system of internal membranes, which increases the total area of membrane.
	because of their size, eukaryotes have a relatively small surface area to volume ratio. The plasma membrane of eukaryotic cells is therefore too small an area to carry out all the vital functions carried out by membranes.
	the endoplasmic reticulum (ER) forms a network of membrane tubules continuous with the nuclear membrane.
	the golgi apparatus is a series of flattened membrane discs
	lysosomes are membrane-bound organelles containing a variety of hydrolases that digest proteins, lipids, nucleic acids and carbohydrates.
	vesicles transport materials between membrane compartments.
b ii) synthesis of membrane components	lipids and proteins are synthesised in the ER.
	Rough ER (RER) has ribosomes on its cytosolic face while smooth ER (SER) lacks ribosomes.
	Lipids are synthesised in the smooth endoplasmic reticulum (SER) and inserted into its membrane
	synthesis of all proteins begins in cytosolic ribosomes.
	The synthesis of cytosolic proteins is completed there, and these proteins remain in the cytosol.
	Transmembrane proteins carry a signal sequence, which halts translation and directs the ribosome synthesising the protein to dock with the ER, forming RER.
	Translation continues after docking, and the protein is inserted into the membrane of the ER.
	A signal sequence is a short stretch of amino acids at one end of the polypeptide that determines the eventual location of a protein in a cell.

	Translation continues after docking, and the protein is inserted into the membrane of the ER
b iii) movement of proteins between membranes	once the proteins are in the ER, they are transported by vesicles that bud off from the ER and fuse with the Golgi apparatus.
	as proteins move through the Golgi apparatus they undergo post-translational modification.
	molecules move through the Golgi discs in vesicles that bud off from one disc and fuse to the next one in the stack.
	In the golgi, enzymes catalyse the addition of various sugars in multiple steps to form the carbohydrates.
	the addition of carbohydrate groups is the major modification.
	vesicles that leave the Golgi apparatus take proteins to the plasma membrane and lysosomes.
	vesicles move along microtubules to other membranes and fuse with them within the cell.
b iv) the secretory pathway	secreted proteins are translated in ribosomes on the RER and enter its lumen.
	peptide hormones and digestive enzymes are examples of secreted proteins.
	the proteins move through the Golgi apparatus and are then packaged into secretory vesicles.
	The secretory vesicles move to and fuse with the plasma membrane, releasing the proteins out of the cell.
	many secreted proteins are synthesised as inactive precursors and require proteolytic cleavage to produce active proteins.
	proteolytic cleavage is another type of post-translational modification.

	Digestive enzymes are one example of secreted proteins that require proteolytic cleavage to become active. (you don't need to learn specific examples of digestive enzymes)

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1.2c Protein Structure, Ligand Binding and conformational change

Sub section	I can state or explain the following
C i) amino acids and protein structure	Proteins are polymers of amino acid monomers.
	amino acid sequence determines protein structure.
	amino acids are linked by peptide bonds to form polypeptides.
	You should be able to recognise the chemical structure of a peptide bond from a diagram.
	amino acids have the same basic structure, differing only in the R group present.
	R groups of amino acids vary in size, shape, charge, hydrogen bonding capacity and chemical reactivity.
	amino acids are classified according to their R groups: basic (positively charged); acidic (negatively charged); polar; hydrophobic. [no need to know individual named examples of amino acids' structures]
	the wide range of functions carried out by proteins results from the diversity of R groups.
	the primary structure is the sequence in which the amino acids are synthesised into the polypeptide.
	hydrogen bonding along the backbone of the protein strand results in regions of secondary structure — alpha helices, parallel or antiparallel beta-pleated sheets, or turns.
	the polypeptide folds into a tertiary structure.
	The conformation of the tertiary structure is stabilised by interactions between R groups: hydrophobic interactions; ionic bonds; London dispersion forces; hydrogen bonds; disulfide bridges.
	disulfide bridges are covalent bonds between R groups containing sulfur.
	quaternary structure exists in proteins with two or more connected polypeptide subunits.
	quaternary structure describes the spatial arrangement of the subunits.
	a prosthetic group is a non-protein unit tightly bound to a protein and necessary for its function.
	An example of a prosthetic group is the ability of haemoglobin to bind oxygen is dependent upon the non-protein haem group.
	the interactions of the R groups can be influenced by temperature and pH.

	increasing temperature disrupts the interactions that hold the protein in shape; the protein begins to unfold, eventually becoming denatured.
	the charges on acidic and basic R groups are affected by pH.
	As pH increases or decreases from the optimum, the normal ionic interactions between charged groups are lost, which gradually changes the conformation of the protein until it becomes denatured.
c ii) Ligand Binding	a ligand is a substance that can bind to a protein.
	R groups not involved in protein folding can allow binding to ligands.
	binding sites will have complementary shape and chemistry to the ligand.
	as a ligand binds to a protein-binding site the conformation of the protein changes
	The change in conformation caused by ligand binding causes a functional change in the protein.
	allosteric interactions occur between spatially distinct sites.
	for example, the binding of a substrate molecule to one active site of an allosteric enzyme increases the affinity of the other active sites for binding of subsequent substrate molecules.
	this allosteric effect is of biological importance because the activity of allosteric enzymes can vary greatly with small changes in substrate concentration.
	many allosteric proteins consist of multiple subunits (have quaternary structure).
	allosteric proteins with multiple subunits show co-operativity in binding, in which changes in binding at one subunit alter the affinity of the remaining subunits.
	allosteric enzymes contain a second type of site, called an allosteric site.
	Modulators regulate the activity of the enzyme when they bind to the allosteric site.
	following binding of a modulator, the conformation of the enzyme changes and this alters the affinity of the active site for the substrate.
	positive modulators increase the enzyme's affinity for the substrate, whereas negative modulators reduce the enzyme's affinity.
	the binding and release of oxygen in haemoglobin shows co-operativity
	changes in binding of oxygen at one subunit alter the affinity of the remaining subunits for oxygen.
	temperature and pH influence the binding of oxygen

	A decrease in pH or an increase in temperature lowers the affinity of haemoglobin for oxygen, so the binding of oxygen is reduced.
	Reduced pH and increased temperature in actively respiring tissue will reduce the binding of oxygen to haemoglobin promoting increased oxygen delivery to tissue
ciii) reversible binding of phosphate	the addition or removal of phosphate can cause reversible conformational change in proteins.
	The addition or removal of phosphate is a common form of post-translational modification
	protein kinases catalyse the transfer of a phosphate group to other proteins
	The terminal phosphate of ATP is transferred to specific R groups.
	protein phosphatases catalyse the reverse reaction.
	phosphorylation brings about conformational changes, which can affect a protein's activity.
	the activity of many cellular proteins, such as enzymes and receptors, is regulated in this way.
	some proteins are activated by phosphorylation while others are inhibited.
	adding a phosphate group adds negative charges. Ionic interactions in the unphosphorylated protein can be disrupted and new ones created.

Adv H Biology Learning Outcome checklist 1.3 Membrane Proteins

Subsection	I can state, describe or explain the following
1.3 a movement of molecules across membranes	the fluid mosaic model of cell membranes.
	regions of hydrophobic R groups allow strong hydrophobic interactions that hold integral membrane proteins within the phospholipid bilayer.
	Integral membrane proteins interact extensively with the hydrophobic region of membrane phospholipids.
	some integral membrane proteins are transmembrane proteins.
	peripheral membrane proteins have hydrophilic R groups on their surface and are bound to the surface of membranes, mainly by ionic and hydrogen bond interactions.
	many peripheral membrane proteins interact with the surfaces of integral membrane proteins.
	the phospholipid bilayer is a barrier to ions and most uncharged polar molecules.
	some small molecules, such as oxygen and carbon dioxide, pass through the bilayer by simple diffusion.
	facilitated diffusion is the passive transport of substances across the membrane through specific transmembrane proteins.
	to perform specialised functions, different cell types have different channel and transporter proteins.
	most channel proteins in animal and plant cells are highly selective.
	channels are multi-subunit proteins with the subunits arranged to form water-filled pores that extend across the membrane.
	some channel proteins are gated and change conformation to allow or prevent diffusion.
	ligand-gated channels are controlled by the binding of signal molecules, and voltage- gated channels are controlled by changes in ion concentration.
	transporter proteins bind to the specific substance to be transported and undergo a conformational change to transfer the solute across the membrane.
	transporters alternate between two conformations so that the binding site for a solute is sequentially exposed on one side of the bilayer, then the other.
	active transport uses pump proteins that transfer substances across the membrane against their concentration gradient
	a source of metabolic energy is required for active transport.
	some active transport proteins hydrolyse ATP directly to provide the energy for the conformational change required to move substances across the membrane.
	I can state that ATPases hydrolyse ATP.

subsection	I can state, describe or explain the following
1.3 b ion transport pumps and generation of ion gradients	for a solute carrying a net charge, the concentration gradient and the electrical potential difference combine to form the electrochemical gradient that determines the transport of the solute.
	a membrane potential (an electrical potential difference) is created when there is a difference in electrical charge on the two sides of the membrane.
	ion pumps, such as the sodium-potassium pump, use energy from the hydrolysis of ATP to establish and maintain ion gradients.
	the sodium-potassium pump transports ions against a steep concentration gradient using energy directly from ATP hydrolysis.
	the sodium-potassium pump actively transports sodium ions out of the cell and potassium ions into the cell.
	the action of the sodium-potassium pump: the pump has high affinity for sodium ions inside the cell; binding occurs; phosphorylation by ATP; conformation changes; affinity for sodium ions decreases; sodium ions released outside of the cell; potassium ions bind outside the cell; dephosphorylation; conformation changes; potassium ions taken into cell; affinity returns to start.
	for each ATP hydrolysed, three sodium ions are transported out of the cell and two potassium ions are transported into the cell
	the sodium-potassium pump establishes both concentration gradients and an electrical gradient.
	the sodium-potassium pump is found in most animal cells, accounting for a high proportion of the basal metabolic rate in many organisms.
	in the small intestine, the sodium gradient created by the sodium-potassium pump drives the active transport of glucose.
	In intestinal epithelial cells the sodium-potassium pump generates a sodium ion gradient across the plasma membrane.
	In the small intestine the glucose transporter responsible for this glucose symport transports sodium ions and glucose at the same time and in the same direction. Sodium ions enter the cell down their concentration gradient; the simultaneous transport of glucose pumps glucose into the cell against its concentration gradient.

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1.4: Communication and Signaling

Subsection	I can state, describe or explain the following
a) Coordination	multicellular organisms signal between cells using extracellular signalling molecules.
	steroid hormones, peptide hormones, and neurotransmitters are examples of extracellular signalling molecules.
	receptor molecules of target cells are proteins with a binding site for a specific signal molecule.
	binding changes the conformation of the receptor, which initiates a response within the cell.
	different cell types produce specific signals that can only be detected and responded to by cells with the specific receptor.
	signalling molecules may have different effects on different target cell types due to differences in the intracellular signalling molecules and pathways that are involved.
	in a multicellular organism, different cell types may show a tissue-specific response to the same signal.
b) Hydrophobic signals and control of transcription	hydrophobic signalling molecules can diffuse directly through the phospholipid bilayers of membranes, and so bind to intracellular receptors.
	the receptors for hydrophobic signalling molecules are transcription factors.
	transcription factors are proteins that when bound to DNA can either stimulate or inhibit initiation of transcription.
	the steroid hormones oestrogen and testosterone are examples of hydrophobic signalling molecules.
	steroid hormones bind to specific receptors in the cytosol or the nucleus; from there the hormone-receptor complex moves to the nucleus where it binds to specific sites on DNA and affects gene expression.
	the hormone-receptor complex binds to specific DNA sequences called hormone response elements (HREs). Binding at these sites influences the rate of transcription, with each steroid hormone affecting the gene expression of many different genes.

c) Hydrophilic signals and transduction	hydrophilic signalling molecules bind to transmembrane receptors and do not enter the cytosol.
	I can state that peptide hormones and neurotransmitters are examples of hydrophilic extracellular signalling molecules.
	transmembrane receptors change conformation when the ligand binds to the extracellular face; the signal molecule does not enter the cell, but the signal is transduced across the plasma membrane.
	Transmembrane receptors act as signal transducers by converting the extracellular ligand-binding event into intracellular signals, which alters the behaviour of the cell.
	transduced hydrophilic signals often involve G-proteins or cascades of phosphorylation by kinase enzymes.
	G-proteins relay signals from activated receptors (receptors that have bound a signalling molecule) to target proteins such as enzymes and ion channels.
	phosphorylation cascades allow more than one intracellular signalling pathway to be activated.
	phosphorylation cascades involve a series of events with one kinase activating the next in the sequence and so on.
	phosphorylation cascades can result in the phosphorylation of many proteins as a result of the original signalling event.
	binding of the peptide hormone insulin to its receptor results in an intracellular signalling cascade that triggers recruitment of GLUT4 glucose transporter proteins to the cell membrane of fat and muscle cells.
	binding of insulin to its receptor causes a conformational change that triggers phosphorylation of the receptor. This starts a phosphorylation cascade inside the cell, which eventually leads to GLUT4-containing vesicles being transported to the cell membrane.
	diabetes mellitus can be caused by failure to produce insulin (type 1) or loss of receptor function (type 2).
	Type 2 is generally associated with obesity.
	exercise also triggers recruitment of GLUT4, so can improve uptake of glucose to fat and muscle cells in subjects with type.

d) Nerve Impulse Transmission i) Generation of a nerve impulse	resting membrane potential is a state where there is no net flow of ions across the membrane.
	the transmission of a nerve impulse requires changes in the membrane potential of the neuron's plasma membrane.
	an action potential is a wave of electrical excitation along a neuron's plasma membrane.
	neurotransmitters initiate a response by binding to their receptors at a synapse.
	neurotransmitter receptors are ligand-gated ion channels.
	depolarisation of the plasma membrane happens as a result of the entry of positive ions which triggers the opening of voltage-gated sodium channels, and further depolarisation occurs.
	depolarisation is a change in the membrane potential to a less negative value inside.
	inactivation of the sodium channels and the opening of potassium channels restores the resting membrane potential.
	binding of a neurotransmitter triggers the opening of ligand-gated ion channels at a synapse. Ion movement occurs and there is depolarisation of the plasma membrane. If sufficient ion movement occurs, and the membrane is depolarised beyond a threshold value, the opening of voltage-gated sodium channels is triggered and sodium ions enter the cell down their electrochemical gradient. This leads to a rapid and large change in the membrane potential. A short time after opening, the sodium channels become inactivated. Voltage-gated potassium channels then open to allow potassium ions to move out of the cell to restore the resting membrane potential.
	depolarisation of a patch of membrane causes neighbouring regions of membrane to depolarise and go through the same cycle, as adjacent voltage-gated sodium channels are opened.
	when the action potential reaches the end of the neuron it causes vesicles containing neurotransmitter to fuse with the membrane — this releases neurotransmitter, which stimulates a response in a connecting cell.
	restoration of the resting membrane potential allows the inactive voltage-gated sodium channels to return to a conformation that allows them to open again in response to depolarisation of the membrane.
	ion concentration gradients are re-established by the sodium-potassium pump, which actively transports excess ions in and out of the cell.
	Following repolarisation the sodium and potassium ion concentration gradients are reduced. The sodium-potassium pump restores the sodium and potassium ions back to resting potential levels.

d) Nerve Impulse ii) Initiation of a nerve impulse in response to an environmental stimulus: the vertebrate eye	the retina is the area within the eye that detects light and contains two types of photoreceptor cells: rods and cones.
	rods function in dim light but do not allow colour perception. Cones are responsible for colour vision and only function in bright light.
	in animals the light-sensitive molecule retinal is combined with a membrane protein, opsin, to form the photoreceptors of the eye.
	in rod cells the retinal-opsin complex is called rhodopsin.
	retinal absorbs a photon of light and rhodopsin changes conformation to photoexcited rhodopsin.
	a cascade of proteins amplifies the signal.
	photoexcited rhodopsin activates a Gprotein, called transducin, which activates the enzyme phosphodiesterase (PDE).
	A single photoexcited rhodopsin activates hundreds of molecules of G-protein. Each activated G-protein activates one molecule of PDE.
	PDE catalyses the hydrolysis of a molecule called cyclic GMP (cGMP)
	Each active PDE molecule breaks down thousands of cGMP molecules per second. The reduction in cGMP concentration as a result of its hydrolysis affects the function of ion channels in the membrane of rod cells.
	this results in the closure of ion channels in the membrane of the rod cells, which triggers nerve impulses in neurons in the retina.
	A very high degree of amplification results in rod cells being able to respond to low intensities of light.
	in cone cells, different forms of opsin combine with retinal to give different photoreceptor proteins, each with a maximal sensitivity to specific wavelengths: red, green, blue or UV.

Adv H Biology Learning Outcome checklist

1.5: Protein Control of Cell Division

Subsection	I can state, describe or explain the following
(a) the cytoskeleton and cell division	the **cytoskeleton** gives mechanical support and shape to cells.
	the cytoskeleton consists of different protein structures including **microtubules**, which are found in all eukaryotic cells.
	microtubules are hollow cylinders composed of the protein **tubulin**.
	microtubules radiate from the microtubule organising centre (**MTOC**) or centrosome.
	microtubules control the movement of membrane-bound organelles and chromosomes.
	cell division requires remodelling of the cytoskeleton.
	formation and breakdown of microtubules involves **polymerisation** and **depolymerisation** of tubulin.
	microtubules form the **spindle fibres** that are active during cell division.
(b) the cell cycle	the cell cycle consists of **interphase** and **mitotic (M) phase**.
	interphase involves growth and DNA synthesis including **G1**, a growth phase; **S** phase, during which the DNA is replicated; and **G2**, a further growth phase.
	the mitotic phase involves **mitosis** and cytokinesis.
	in mitosis the chromosomal material is separated by the spindle microtubules. This is followed by cytokinesis, in which the cytoplasm is separated into two daughter cells.
	mitosis consists of prophase, metaphase, anaphase and telophase.
	prophase — DNA condenses into chromosomes each consisting of two sister chromatids. Nuclear membrane breaks down; spindle microtubules extend from the MTOC by polymerisation and attach to chromosomes via their kinetochores in the centromere region.
	metaphase — chromosomes are aligned at the metaphase plate (equator of the spindle).
	anaphase — as spindle microtubules shorten by depolymerisation, sister chromatids are separated, and the chromosomes are pulled to opposite poles.
	telophase — the chromosomes decondense and nuclear membranes are formed around them.

(c) Control of the cell cycle	progression through the cell cycle is controlled by **checkpoints**.
	checkpoints are mechanisms within the cell that assess the condition of the cell during the cell cycle and halt progression to the next phase until certain requirements are met.
	cyclin proteins that accumulate during cell growth are involved in regulating the cell cycle.
	cyclins combine with and activate **cyclindependent kinases** (CDKs).
	active cyclinCDK complexes phosphorylate proteins that regulate progression through the cycle. If sufficient phosphorylation is reached, progression occurs.
	at the G1 checkpoint, **retinoblastoma** protein (Rb) acts as a tumour suppressor by inhibiting the transcription of genes that code for proteins needed for DNA replication.
	phosphorylation by G1 cyclin-CDK inhibits the retinoblastoma protein (Rb). This allows transcription of the genes that code for proteins needed for DNA replication. Cells progress from G1 to S phase.
	at the G2 checkpoint, the success of DNA replication and any damage to DNA is assessed.
	DNA damage triggers the activation of several proteins including **p53** that can stimulate DNA repair, arrest the cell cycle or cause cell death.
	the metaphase checkpoint controls progression from metaphase to anaphase.
	at the metaphase checkpoint, progression is halted until the chromosomes are aligned correctly on the metaphase plate and attached to the spindle microtubules.
	an uncontrolled reduction in the rate of the cell cycle may result in **degenerative disease**.
	an uncontrolled increase in the rate of the cell cycle may result in **tumour formation**.
	a **proto-oncogene** is a normal gene, usually involved in the control of cell growth or division, which can mutate to form a tumour promoting oncogene.

(d) Control of programmed cell death	**apoptosis** is triggered by cell death signals that can be external or internal.
	the production of death signal molecules from lymphocytes is an example of an external death signal.
	DNA damage is an example of an internal death signal
	external death signal molecules bind to a surface receptor protein and trigger a protein cascade within the cytoplasm.
	an internal death signal resulting from DNA damage causes activation of p53 tumour suppressor protein.
	both types of death signal result in the activation of caspases (types of protease enzyme) that cause the destruction of the cell.
	apoptosis is essential during development of an organism to remove cells no longer required as development progresses or during metamorphosis.
	cells may initiate apoptosis in the absence of growth factors.