TOPIC 3: VOICE OF THE GENOME

For the Edexcel Biology A Level (SNAB)

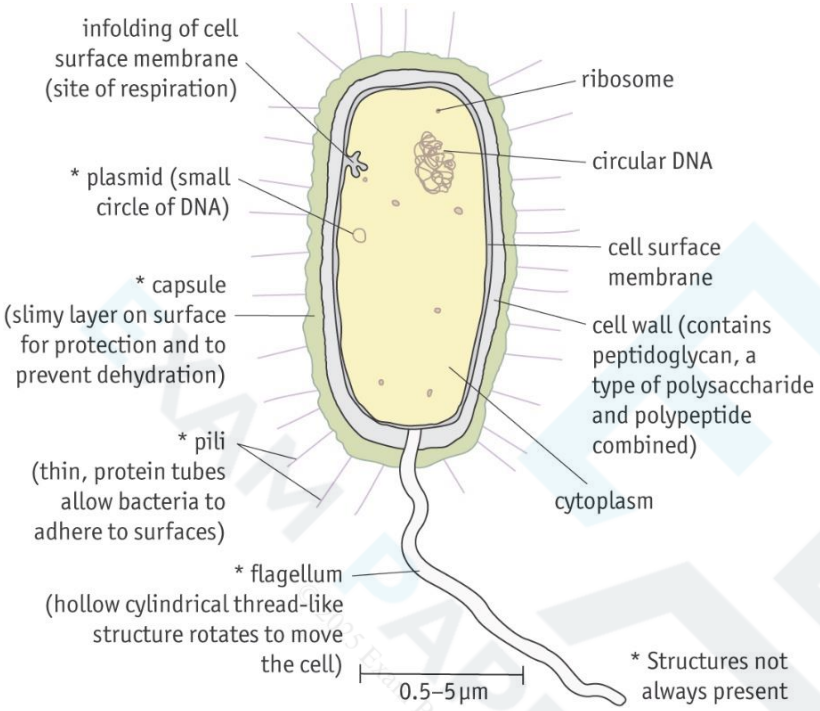
TOPICS COVERED

- Bacterial Structure
- Eukaryotic Cell Ultrastructure
- Protein Trafficking
- Reproduction
- Producing Gametes: Meiosis, Crossing Over and Independent Assortment
- Gene Linkage: Autosomal and Sex-Linked
- Cell Cycle including Mitosis
- Stem Cells
- Controlling Development: Regulating Gene Expression by Inhibition in Prokaryotes and by Transcription Factors in Eukaryotes
- Epigenetics
- Cell Organisation
- Cancer
- Variation

Cell Ultrastructure

Key Terminology

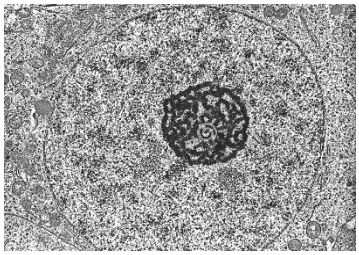
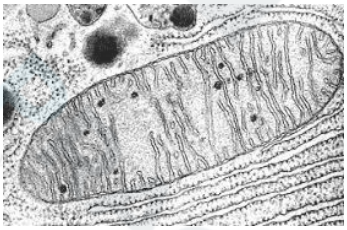
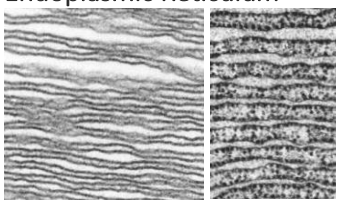
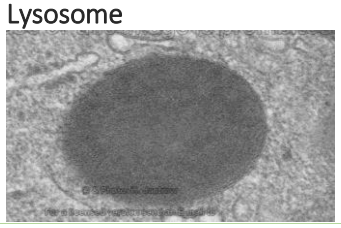
Term	Definition
Prokaryote	Unicellular organism lacking a nucleus, including bacteria
Eukaryote	Multicellular organisms with DNA contained within a distinct nucleus
Endosymbiosis	Theory explaining the evolution of eukaryotic cells with chloroplasts and mitochondria by a host cell taking in photosynthetic and aerobic prokaryotes

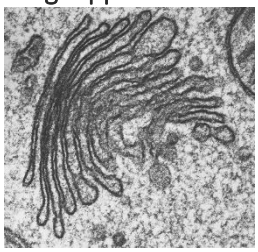
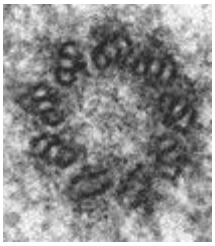


Bacteria and cyanobacteria form the Prokaryotae Kingdom, and are extremely small at around 0.5-5µm. DNA lies freely within the cytoplasm. Prokaryotes always have a cell wall containing peptidoglycan.

All other organisms contain discrete membrane-bound organelles like nuclei, chloroplasts and mitochondria. These eukaryotes are around 20µm or more in size.

Microscopy can be used to identify cell structures. The table below lists these structures and their functions

Name and Image	Structure and Function	Name and Image	Structure and Function
Nucleus and Nucleolus 	Contains chromatin and DNA for protein synthesis. Enclosed by an envelope of two membranes with pores for mRNA movement. Outer membrane connects to rER. Contains *nucleolus*, dense site of ribosome production	Mitochondrion 	Site of aerobic respiration. Inner of its two membranes folds to form projections called cristae, spanned by proteins. The matrix contains 70S ribosomes, DNA and enzymes
Endoplasmic Reticulum  sER rER	System of interconnected membrane-bound, flattened sacs transporting proteins around a cell. Rough ER has ribosomes attached to the surface. sER has no ribosomes and produces lipids and steroid. Ribosomes, made of RNA and protein, are the site of protein synthesis and can be found free in the cytoplasm	Cell Surface Membrane 	Plasma membrane; phospholipid bilayer with proteins and other molecules controlling movement of substances through the cell
		Lysosome 	Vesicle containing digestive enzymes, involved in the breakdown of unwanted substances in the cell and in destruction of whole cells before replacement

Golgi Apparatus 	Stacks of flattened, membrane-bond sacs formed by fusion of vesicles from the ER. Modifies proteins and packages them in vesicles for transport	**Centrioles** 	Every animal cell contains one pair of centrioles, made of a ring of nine protein microtubules to form hollow cylinders. They are involved in spindle formation during nuclear division and transport in the cytoplasm

The Theory of Endosymbiosis describes how eukaryotic cells evolved from prokaryotic cells, as a host cell took in an aerobic bacterium or a photosynthetic bacterium, allowing the host itself to respire and photosynthesise. The evidence for this theory comes from mitochondria and chloroplasts dividing by binary fission, these organelles having their own DNA and ribosomes, and both structures having two membrane layers, one similar to ancestral prokaryotes and another similar to the host's cell membrane.

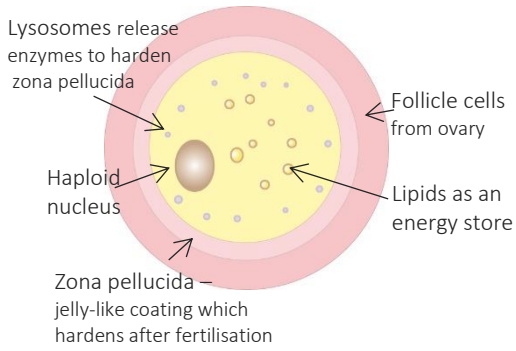
Cells are dynamic, with organelles working closely together. An example of this is protein trafficking.

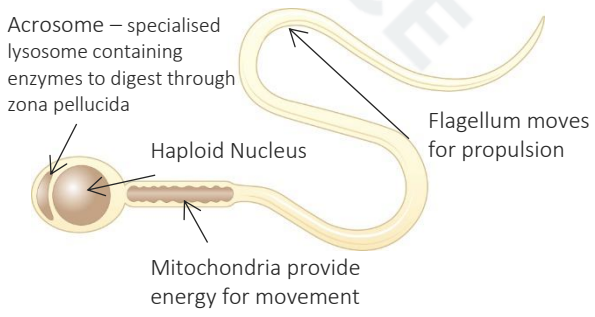
1. Gene is transcribed and mRNA is produced
2. mRNA moves to the ribosome through nuclear pores and is translated on a ribosome
3. The protein which has been produced enters the rER
4. The protein moves along the ER, folding into its tertiary structure along the way
5. Vesicles pinch off the rER, containing the protein
6. Vesicles from the rER fuse to form the flattened sacs of the Golgi apparatus
7. Proteins are modified within the Golgi, with potential addition of carbohydrate, lipid and target sequence to determine location, and vesicles pinched off the Golgi containing modified protein
8. Vesicles either fuse with the cell surface membrane to release the protein by exocytosis or move elsewhere within the cell

Reproduction

Key Terminology

Term	Definition
Acrosome	Specialised lysosome containing enzymes to digest through zona pellucida
Zona pellucida	Jelly-like coating which hardens after fertilisation
Chemotaxis	The chemical attraction created by a cell triggering movement
Meiosis	Division used in the production of gametes
Independent Assortment	Random arrangement of chromosomes from a homologous pair leading to genetically varied gametes
Crossing Over	Exchange of alleles between non-sister chromatids
Linkage	Tendency for two or more non-allelic genes to be inherited together
Locus	Location of genes on a chromosome
Centromere	Point at which two chromatids attach



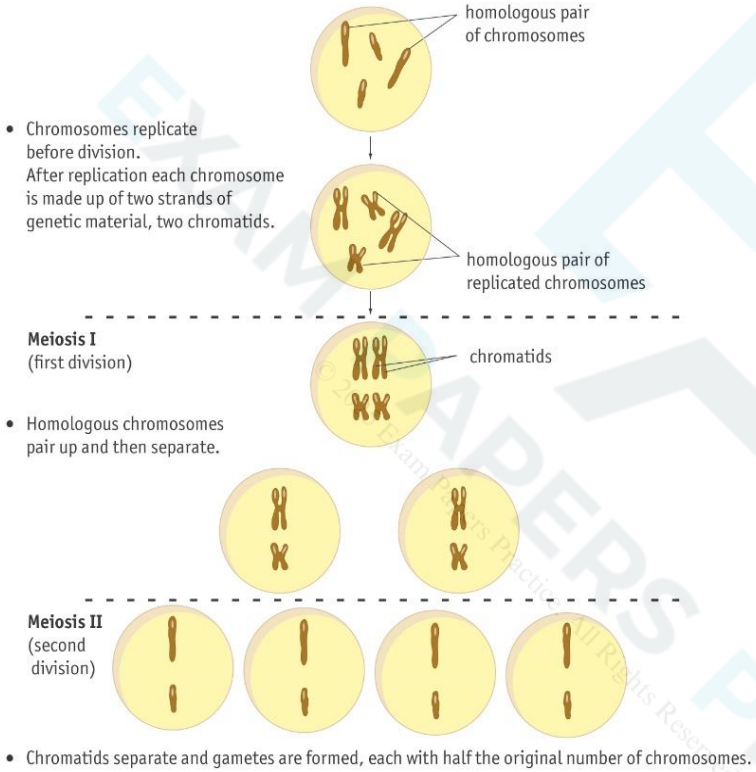


Sperm cells are small to increase efficiency of motility and so many can be released per ejaculate. Ova must be large enough to contain nutrients and be detected by the sperm

The steps preceding fertilisation in involves the sperm travelling through the open cervix, into the womb and through the Fallopian tube, where, propelled by chemotaxis, it approaches the ovum.

i. Chemicals released from the ovum trigger the acrosome reaction as the sperm reaches the oocyte. The acrosome then swells and fuses with the sperm cell surface membrane
ii. Digestive enzymes from the acrosome are released and allow the sperm to digest through follicle cells and the zona pellucida
iii. The sperm fuses with the ovum membrane and its nucleus enters the ovum
iv. Enzymes released from lysosomes in the ovum thicken the zona pellucida, preventing entry of other sperm
v. Nuclei of the ovum and the sperm fuse to produce a diploid zygote

Producing Gametes: Meiosis, Crossing Over and Independent Assortment



Meiosis occurs in germline tissues to produce genetically distinct haploid gametes. Meiosis allows sexual reproduction and facilitates evolution. During meiosis, existing genetic material is essentially shuffled to create genetically varied gametes

Crossing Over occurs during meiosis I. Homologous chromosomes pair, and at the points where they come into contact, called chiasma, the chromatids break. The non-sister chromatids exchange corresponding sections of DNA, swapping alleles for the same genes.

Independent Assortment occurs when chromosomes from homologous pairs arrange randomly during meiosis I. The many pairs line up in different ways to produce genetically varied gametes. The number of possible combinations is 2^n where n = number of chromosome pairs.

Linkage

Linkage is the tendency for two or more non-allelic genes to be inherited together. This can be autosomal or sex-linked

Sex-linkage applies to genes that are located on the sex chromosomes. These genes are considered sex-linked because their expression and inheritance patterns differ between males and females.

X-linked disorders are conditions where the causative allele has a locus on the X chromosome, and are much more likely in males, as past the centromere, chromosomes are non-homologous and even if only one allele is present, this allele will always be expressed. Since males only have once X chromosome, there is a higher likelihood of a faulty allele being expressed

Autosomal linkage occurs in two ways:

- Genes that are located together on the same chromosome show linkage as they do not assort independently and are likely to be inherited together
- Genes that have loci closer together on a chromosome show stronger linkage as the further away genes are from each other, the more likely they are to be separated during crossing over

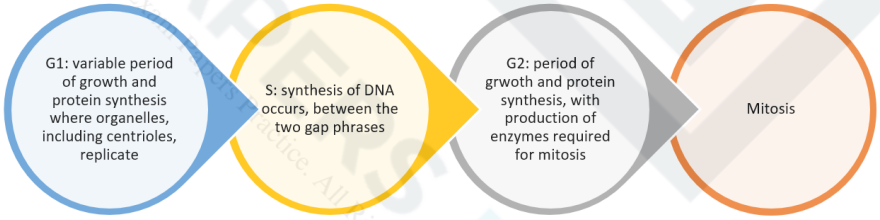
The Cell Cycle

Key Terminology

Term	Definition
Cell Cycle	Pattern of events in which a cell that has just resulted from a cell division eventually itself divides to form new cells
Chromatin	DNA double helix in the nucleus is packaged by histones, forming the complex chromatin, which is loose enough for transcription to occur
Stem Cell	A cell that can continue to divide (i.e. shows self-renewal) and has the potential to give rise to specialised cells
Differentiation	Process by which a cell becomes specialised in order to perform a specific function. Cellular differentiation is the generation of specialised cells
Totipotency	Stem cells have the potential to give rise to any and all cells, with the ability to form an entire organism
Pluripotency	Stem cells can give rise to all tissue types. However, these cells are incapable of giving rise to an entire organism as the genes required are deactivated
Multipotency	Stem cells are less plastic and more differentiated, only able to give rise to a limited range of cells within a tissue type

The Cell Cycle is the sequence of events which a cell goes through. This consists of a long period of interphase, before entering mitosis.**Interphase** is the part of the Cell Cycle between mitotic division where new organelles are produced and DNA replicated.

DNA exists in a double helix. DNA winds around histone proteins, and these coil to form chromatin; this is how DNA exists during interphase, as it is accessible for transcription. In preparation for mitosis, the chromatin attaches to a protein scaffold, forming loops. This scaffold folds to produce a condensed chromosome, which is seen during divisions.



Mitosis is the process of cell division. This is required for growth, regeneration of lost cells for repair, and to ensure genetic consistency with cloned daughter cells from asexual reproduction

Prophase
Chromosome condense, forming two identical visible sister chromatids.
Microtubules from the cytoplasm form the spindle. Centrioles move to the opposite poles of the cell.
Nuclear membrane breaks down

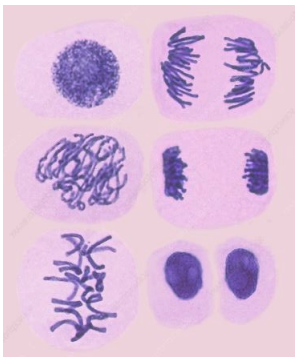
Metaphase
Chromosomes' centromeres attach to the spindle fibres at the equator

Anahase
Centromeres split. The spindles contract, drawing the chromatids to opposite poles
Anaphase ends when the separated chromatids reach the poles and the spindle breaks down

Telophase
Chromosomes unravel into chromatin and the endoplasmic reticulum extends to reform separate nuclear envelopes, enclosing the two sets of genetic code in separate nuclei. Nucleoli reappear

Cytokinesis
Cytoplasmic division splits cells. Plasma membrane constricts around the centre of the cell. A ring of protein filaments, bound to the inside of the cells, contracts until the cells divide

The stages of the cell cycle



Stem Cells

Stem cells become less potent and more differentiated over development. After fertilisation, the zygote undergoes the cell cycle to form eight totipotent stem cells, able to generate an entire human body. After five days, a blastocyte is formed, composed of an outer cell layer, which eventually forms the placenta, and an inner cell mass, containing pluripotent embryonic stem cells which can give rise to different tissue types. As the embryo develops further, cells lose the capacity to develop into a wide range of cells. However, even adult stem cells, which are multipotent, can differentiate into specific cell types.

Meristem tissue contains stem cells which are responsible for plant growth. These cells are totipotent and are able to dedifferentiate and develop into a new plant. This property allows for cutting and tissue culture to produce clones; this process is needed in plant breeding and conservation.

Stem Cells in Treating Human Disorders

- Stem cells can be used in medicine in the following ways:
  - → stem cell transplants to provide cells, tissue and organs for treatment
  - → drugs testing and tissue typing
  - → therapeutic cloning: also known as somatic cell nuclear transfer, this is the strategy for creating a viable embryo from a somatic cell and an egg cell by taking an enucleated oocyte and implanting a donor nucleus from a somatic cell
- Induced pluripotent stem cells are derived from skin or blood cells that have been reprogrammed into an embryonic stem cell state, removing the need for egg cells, potentially increasing scope
- In the UK, regulatory bodies such as the HFEA (Human Fertilisation and Embryology Authority) set the laws regarding ESC use by considering ethical aspects, then judge what is acceptable and set a code of practice. The body then checks that source of stem cells is acceptable. Such bodies decide on maximum age of embryo allowed for research, which is currently 14 days, where the nervous system develops and the embryo can potentially feel pain. Human cloning is illegal
- The ethical debate surrounding ESC use focuses on the moral principles of the duty to alleviate suffering and the duty to respect the value of human life; whilst potentially removing the significance of human life, therapeutic cloning can treat many diseases

Controlling Development: Regulating Gene Expression

Dolly the Sheep was created by somatic cell nuclear transfer. Genes from a cell in a donor sheep were used to produce a totipotent stem cell which divided to produce an entire organism. This provided evidence that the nucleus of a differentiated cell has all the DNA needed for normal growth and development, with the same potential as a totipotent cell.

The subtractive hybridisation experiment demonstrates that different genes are expressed in different cells. mRNA was extracted from frog cells in early and late stages of development. Complementary DNA strands were produced for all the mRNA in the differentiated cells using the enzyme reverse transcriptase. These cDNA strands were mixed with mRNA from the undifferentiated cell. Complementary strands of cDNA and mRNA combined to produce double strand hybrids – the cells were expressing some of the same genes. When these hybrids were subtracted, the remaining free cDNA suggested that the differentiated cell expressed certain genes which were not in the less developed cell.

Epigenetics

The epigenome influences which genes can be transcribed in a particular cell. During DNA replication, epigenetic markers are copied so that when a cell divides, the correct set of genes remain active.

- DNA methylation occurs when a CH_3 group attaches to a gene, usually on cytosine, preventing transcription of the gene – this is gene silencing. Demethylation stimulates gene expression
- Histone modification occurs when acetyl groups affect how tightly DNA winds around histone proteins. Acetylation of histones stimulates gene expression, whilst deacetylation reduces gene expression

Lac Operon

An operon is a group of genes that functions as a single transcription unit, compromised of an operator, a promoter, and one or more structural genes that are transcribed into one polycistronic mRNA. Polycistronic mRNA encodes several different polypeptide chains.

E coli produce the enzyme β-galactosidase to break down the disaccharide lactose into galactose and glucose. When lactose is not present, the lac i gene is transcribed and a lactose repressor molecule is produced. This protein binds to the promotor region for the enzyme, preventing RNA polymerase from being produced. This is energetically conservative and is therefore beneficial.

When lactose is present, it binds to the repressor and causes a conformational change in the repressor, preventing it from binding to the promotor, allowing for the enzyme to be produced and for the lactose to be broken down.

Eukaryotic Gene Regulation

Transcription factors are proteins that bind to promotors and enhancers. There are general transcription factors, present in every cell and part of the basal transcription machinery, and tissue-specific factors. These in turn are processed by genes that are themselves controlled by other transcription factors, allowing a cascade of regulatory effects. Regulator proteins are often needed for RNA polymerase to bind to genes.

Fibrodysplasia ossificans progressive is a rare inherited disease where extra-skeletal bone grows within muscle and connective tissue. Abnormal bone growth occurs because white blood cells produce a protein which turn on genes in the muscle cells, causing production of bone cells.

Cell Organisation

Cells → Tissues → Organ → Organ System

Cells have recognition proteins (adhesion molecules) on their surface membranes. They enable cells to identify each other, attach and influence each other's gene expression to change nearby cells' phenotypes. They are complementary to the same cell type, enabling tissues to develop and the extra-cellular matrix to form.

Master genes control the development of each segment of a body. Master genes transcribe mRNA, which cause production of signal proteins. These proteins switch on the gene responsible for producing the proteins needed for specialisation of cell in each segment, causing patterning.

Apoptosis is known as programmed cell death by suicide and this ability is built into every cell. A common intrinsic signal is the presence of high levels of oxidants such as peroxide ions. Apoptosis is needed for development, for example the formation of synapse and digits, in addition to disease management and defence against pathogens.

Genes and the Environment

Cancer

A cancer can occur when the rate of cancerous cell reproduction exceeds cell death. Such cells have regulated cell cycles and a tumour may be produced.

Cancers are caused by mutations, and are also influenced by epigenetic changes. Cancer risk increases with certain alleles, yet risk is heightened by UV, smoking, viruses and diet.

Cancer cells do not respond to control mechanisms that usually influence the cell cycle. Oncogenes code for proteins that stimulate the transition between stages of the cell cycle. Tumour suppressor genes produce proteins that inhibit cell cycle progression.

Variation

Continuous phenotypic variation can take any value in the data set, and is often the result of polygenic inheritance – controlled by many genes at different loci - and environmental interaction.

- Height is polygenic and is also influenced by growth conditions, in particular nutrients
- MAOA is an enzyme which breaks down neurotransmitters. Low MAOA levels have been linked to mental health problems. Production is monogenetic, but is influenced by certain drugs
- Animal hair colour is polygenic, but in some species is also environmental. Arctic foxes see seasonal changes in colour, turning lighter in winter.

Discontinuous variation has no range and shows discrete variation. It is usually qualitative and the result of a few genes alone, not the environment. An example is blood groups.