Research
Based
Curricula

Mitochondrial Dysfunction and Disease

Key Stage 4

Biology

2020

BROUGHT TO YOU BY RBC ACCESS ED

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Each resource is a chapter with activities to complete to demonstrate learning

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For Students
Getting started

RBC means Research-Based Curriculum,. Each RBC coursebook is written by a PhD student at a university about their cutting edge research.

Why complete an independent 'RBC' study pack?

RBC courses are challenge courses to sharpen your skills and resilience: finishing a RBC course is a major accomplishment to add to your academic CV. To get into the university, you must demonstrate that you are intellectually curious, and will make the most of the academic opportunities available to you. Completing a pack will allow you to gain invaluable experience to write about in your university application..

It allows you to:

- ✓ Build your subject experience to mention in your UCAS Personal Statement
- ✓ Sharpen your academic skills
- ✓ Experience what it's like to study beyond school and at university
- ✓ Better understand what you enjoy and don't
- ✓ Improve your overall subject understanding ahead of final exams

For Students
Getting Started

What's in this booklet?

Your RBC booklet is a pack of resources containing:

- ✓ More about how and why study this subject
- ✓ Six 'resources' each as a lesson with activities
- ✓ A final assignment to gauge learning
- ✓ Extra guidance throughout about the university skills you are building
- ✓ End notes on extra resources and where to find more information

Who should complete this pack?

Anyone interested in improving their academic skills or understanding what they should do at university. *This pack is especially great for anyone interested in studying* ***Sciences,*** *particularly* **Biology,** *and want to learn more about an interesting an interdisciplinary topic.*

Even if you are unsure of where your interest in these subjects can take you, by completing this pack you will have a clearer idea of the variety of subjects that link to one another.

If you have any questions while you are using the resources in this pack, you can contact your teacher or email us directly at schools@access-ed.ngo.

Good luck with your journey to higher education!

For Students
University Skills

To complete this resource, you will have to demonstrate impressive academic skills. When universities are looking for new students, they will want young people who can study independently and go above and beyond the curriculum. All of these skills that you will see here will demonstrate your abilities as a university student – while you're still at school!

Every time you have to look something up, or write up a reference you are showing that you can work independently.

Every time that you complete a challenging problem or write an answer to a difficult question, you might demonstrate your ability to think logically or build an argument.

Every time that you evaluate the sources or data that you are presented with, you are showing that you can "dive deep" into an unfamiliar topic and learn from it!

Skills you will build for university:

independent research	your ability to work on your own and find answers online or in other books
creativity	your ability to create something original and express your ideas
problem solving	your ability to apply what you know to new problems
building an argument	your ability to logically express yourself
providing evidence	your ability to refer to sources that back up your opinions/ ideas
academic referencing	your ability to refer to what others have said in your answer, and credit them for their ideas
deep dive	your ability to go above and beyond the school curriculum to new areas of knowledge
source analysis	your ability to evaluate sources (e.g. for bias, origin, purpose)
data interpretation	your ability to discuss the implications of what the numbers show
active reading	your ability to engage with what you are reading by highlighting and annotating

Where can this subject take me?

Pathways

Studying Biology or Psychology can open the doors to many degrees and careers. It intersects with microbiology, chemistry, physiology, and sociology. Whatever interests you is likely to relate to biology in some way. See a snapshot of where studying Biology and Psychology can take you.

'Transferrable skills' from Biology to a career:

- research and data analysis
- problem-solving and creative thinking
- delivering successful projects
- communication, through report writing and presentations
- teamworking and collaboration
- the ability to work independently
- numeracy and maths
- IT and computer literacy

What are some are the 'interdisciplinary' subjects in this course?

Interdisciplinary is a term you will hear used by higher education institutions. It's also how many professionals and academics in the real-world operate: they use multiple subjects, or disciplines, to achieve their work.

By thinking about which subjects you like, alongside maths, it can help you choose a career pathway later.

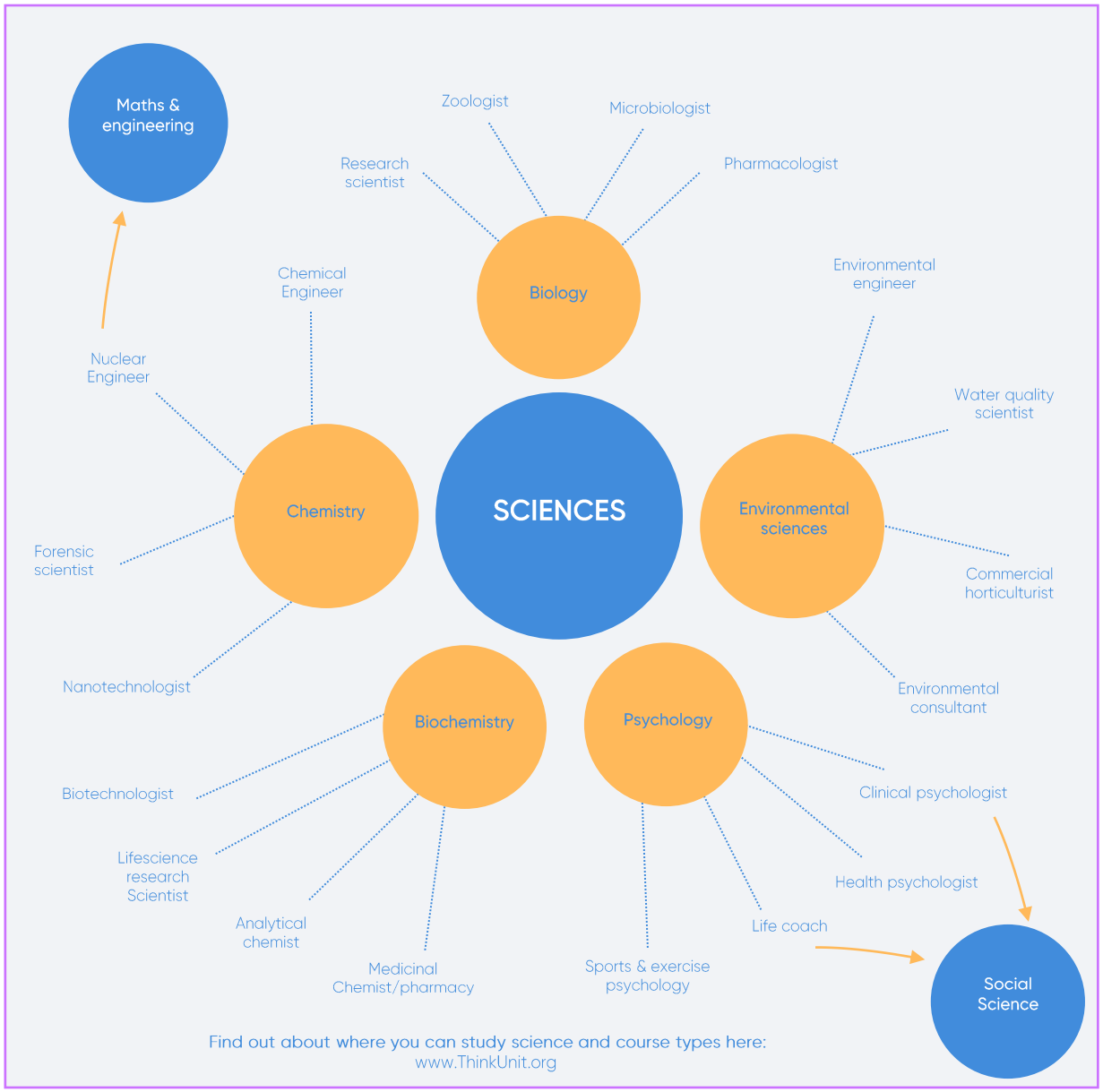
Read more about subject selection and careers pathways:

https://targetjobs.co.uk
https://www.prospects.ac.uk
https://thinkuni.org/

Subject map: Sciences

A degree in Sciences gives Students access to a large number of career choices. Many students who study sciences go on to pursue their Master's degree in Science. However, a significant portion of them also start looking out for jobs in the field of Cancer research, Stem Cell technology and other positions in this space.

Did you know? Being a scientist of any kind can open up may doors within any industries, from managing projects to labs to health policy teams with governments!



Find our about Science-related careers here:
PROSPECTS: https://www.prospects.ac.uk
TARGET JOBS: https://targetjobs.co.uk

For Teachers
RBC Guide

Learner aims

The Research-Based Curriculum aims to support student attainment and university progression by providing classroom resources about cutting-edge research at local universities. The resources are designed to:

- ✓ promote intellectual curiosity through exposure to academic research
- ✓ stretch and challenge students to think deeply about content that may be beyond the confines of the curriculum
- ✓ develop core academic skills, including critical thinking, metacognition, and written and verbal communication
- ✓ inform students about how subjects are studied at university, and provide information, advice and guidance on pursuing subjects at undergraduate level

Content

The programme represents a unique collaboration between universities and schools. Trained by AccessEd, PhD Researchers use their subject expertise to create rich resources that help bring new discoveries and debates to students.

The Research-Based Curriculum offers ten modules suitable for either KS4 or KS5 study. The modules span a range of disciplines, including EBacc and A-level subjects, as well as degree subjects like biochemistry. Each module includes six hours of teaching content, supported by student packs, teacher notes and slides. All modules are available online and free of charge for teachers at select schools.

Using the RBC pack

These resources are designed to be used flexibly by teachers. The resources can be completed by students individually or in groups, in or out of the classroom.

For Teachers
Using the RBC packs

Here are five examples of delivery options:

Extra-Curricular Subject Enrichment Clubs

The resources can be completed in small groups (4-8 pupils) across a series of weekly lunch clubs or after-school clubs. Groups can reflect on their learning by presenting a talk or poster on the subject matter at the end of the course.

University Access Workshops

The resources can be used by students to explore subjects that they are interested in studying at university. This can inform their decision making with regards to university degree courses, and allow students to write more effective personal statements by including reflections on the Research-Based Curriculum.

Research Challenge

The resources can be used to ignite curiosity in new topics and encourage independent research. Schools could hold a research challenge across a class or year group to submit a piece of work based on the resources. Pupils could submit individually or in small groups, with a final celebration event.

Summer Project

Resource packs can function as 'transition' projects over the summer, serving as an introduction to the next level of study between KS3 and KS4, or KS4 and KS5. Students could present their reflections on the experience in a journal.

Why offer these?

The Research-Based Curricula programme builds on the University Learning in Schools programme (ULiS), which was successfully delivered and evaluated through the London Schools Excellence Fund in 2015. The project was designed in a collaboration between Achievement for All and The Brilliant Club, the latter of which is the sister organisation of AccessEd. ULiS resulted in the design and dissemination of 15 schemes of work based on PhD research for teachers and pupils at Key Stage 3. The project was evaluated by LKMCo. Overall, pupils made higher than expected progress and felt more engaged with the subject content. The full evaluation can be found here: ULiS Evaluation.

Questions

For more information contact hello@access-ed.ngo

Introduction to Research Mitochondrial Dysfunction and Parkinson's disease

Parkinson's disease is the second most common age-related neurodegenerative disorder in developed societies, affecting 1% of those over the age of 60. The world wide economic cost of Parkinson's disease is estimated to be nearly $51.9 billion annually. With a continuously aging population, this figure is bound to rise. The development of Parkinson's disease is thought to be due to the destruction of cells in the brain and depletion of dopamine. Our understanding of Parkinson's disease has advanced in the last few decades, due to evidence of oxidative stress and mitochondrial involvement. This is beginning to shed light on the mechanism of pathogenesis and is starting to provide new approaches to treatment and prevention of disease.

The topics within this pack will include:

- The Importance of Cell Biology
- The Link Between Structure and Function
- Mitochondria, not just the Powerhouse of the Cell
- Disease, when things start to go wrong
- Mitochondria and Disease
- Discovering New, Better, Medicines

Parkinson's disease is characterised by damage to the nervous system, cognitive decline and alterations to brain function and behaviour. Some features of the disease include oxidative damage and mitochondrial dysfunction, which leads to death of neurons. It is thought that by the time of diagnosis, a Parkinson's disease patient has already lost 30-70% of the dopamine neurons in the substantia nigra region of their brain. The current therapies for neurodegenerative diseases are focused on the management of symptoms and are not capable of slowing, stopping or reversing the continued loss of neurons. To date, no therapy exits to restore mitochondrial function.

The investigation of mitochondrial dysfunction, will increase our understanding of the essential requirements for neuronal survival that can inform future neuroprotective therapies. With mitochondrial dysfunction acting as underlying features in most diseases, it stands as a potential target for many different fields of therapy research.

Introduction to Studying Biological Sciences at University

I have always been interested pursuing a career in Biology, but when it came to University, I didn't even know how many different types of Biology courses there were!

Choosing a degree subject isn't the same as choosing a degree course. The content delivered in a Biology degree can vary greatly. So I looked for a Biology course that covered a large range of topics and allowed me to really try everything before getting a bit more tailored to my interests in the later years! Luckily the University of Reading had exactly that. I studied my bachelors in Biological Sciences, which is a three year course, with the potential for a sandwich placement year in between the second and third year.

In my first year I learnt all about human physiology, the basis of disease, ecology, conservation biology and humankind's impact on biodiversity. This course has a strong practical element, and this was what I enjoyed most. In my second and final year modules were mainly from the "Biomolecular" stream and covered subjects such as mammalian reproduction, viral pathogens and neurobiology. My third year involved an independent research project, in which I joined a research lab for a term. Not everyone does a lab-based project though, some of my friends did survey-based projects or teaching-based projects.

My course put a large emphasis on transferable skills such as computer literacy, information retrieval, data handling and communication skills. So it can lead to employment in a wide range of roles across sectors including healthcare, agriculture, commercial manufacturing, environmental management and publishing. Some of my friends have ended up in vastly different roles. Some staying in research, others training to become a physician's associates or teachers, or venturing into medical sales or medical writing after completing this course!

Meet the PhD Researcher Charlie Collingham

I studied Maths, Biology and Chemistry at A level, because I thought this would set me up nicely for University. But as long as you have a Biology A level, you only need to do one other science and this includes psychology, geography and chemistry (double check the course requirements). Something from every other science A level comes up at some point during a Biological Sciences degree, so they don't assume any prior knowledge. There are even modules you can choose to take like "Fundamental Concepts in Chemistry" that are a really good catch up if you didn't do it at A level. I studied Art & Design for AS Level but kept it up as a hobby ever since, and this has really helped me keep an artistic outlet throughout my science heavy academic life.

After having a very wide-ranging first year, in my second year I started to specialise into human biology. I found that human health and disease, and the mechanism behind it, was extremely interesting. I really wanted to learn more about how we come up with treatments and cures for all sorts of different diseases. This lead me to complete a summer internship in a microbiology lab, doing some research on a protein involved in the development of Chlamydia. I would definitely say that this 6-week placement helped start my love for working independently in a lab. It was on a subject that I never thought I'd be interested in, but suddenly I really, really was! This placement really helped to set me up for any practical experience I did later, so I can't recommend finding some lab experience enough!

Following this, I began my 11-week third year research project. This time my research was focussed on platelets, the small cells in your blood that help you clot and prevent you from bleeding to death. I was interested in what happens when platelets aren't doing their job properly, leading to blood clots in places where they aren't supposed to be, leading to blockages in blood vessels in the brain or heart.

Meet the PhD Researcher Charlie Collingham

Following my undergraduate degree I decided I really wasn't done with being a student just yet, and was enjoying learning too much. So I applied and did my Masters in Molecular Medicine. This course had a huge emphasis on human disease including cancer, synthetic biology, cardiovascular disease, stem cells and regenerative medicine. I got to spend a few months working on adipose tissue and researching how maternal obesity can have negative effects on the offspring. This project gave me my most valuable lesson yet; not all science works the way you want it to. Half of the project was spent tackling a contamination and watching my cells die. The other half was spent desperately trying to turn the small amount of results I got into a decent Masters thesis. But I managed it and ended up with a much better work ethic and understanding of molecular research as a result.

I then spent a year working independently as a research technician in a lab, carrying out a variety of techniques every day and also getting an opportunity to supervise undergraduate students during their final year research project. I really enjoyed helping these students and think that this is something I would like to continue to do in my career.

I was really lucky that my PhD project was advertised around the time my research technician job was coming to an end, because I really feel like it was made for me. My project is interdisciplinary, and I get to perform a huge range of techniques. I use computational biology to study the effects the drug might be having on a protein by modelling it. I use crystallisation techniques to express and purify pure protein with drug bound to get a real-life image of how they interact in a vacuum. Then finally I use cell biology to study the effects that drugs actually have on cells *in vitro* (outside the organism).

Meet the PhD Researcher Charlie Collingham

I work with collaborators at a different university who run animal and human trials to understand the overall effect of the drug *in vivo* (within the organism). I get to combine all of the knowledge I have learnt from my previous projects, and I love that I get to be in the lab most of the time. My project has allowed me to experience many new and different styles of research, and I get to work with lots of different people across all disciplines, from chemists, Doctors, computational scientists, and more!

My supervisor was one of my lecturers from my undergraduate degree, and her greatest quality is how enthusiastic she is about science, it's infectious! My tip for anyone wanting to get some lab experience, find lecturers like this and speak to them! Ask them if you can get some experience in their lab or even just ask them about their research, showing some interest will go a long way! My PhD is based on discovering a new therapy for Parkinson's disease. This is a disease extremely close to my heart because I have several family members who have been diagnosed with the disease. I am now in the final year of my PhD, I do not know what will come next, but I am excited for the next chapter!

A-Level Subjects	Biology, Chemistry, Maths
Undergraduate	BSc Biological Sciences
Postgraduate	MSc Molecular Medicine

Glossary

Term	Definition
Aetiology	The cause, set of causes, or manner of causation of a disease or condition
Chromosome	A threadlike structure of nucleic acids and protein found in the nucleus, carrying genetic information in the form of genes
Congenital	(A disease or physical abnormality) present from birth
DNA	Deoxyribonucleic acid. The main constituent of chromosomes. The carrier of genetic information.
Enzyme	A substance produced by a living organism which acts as a catalyst to bring about a specific biochemical reaction
Free radicals	An uncharged molecule (typically highly reactive and short-lived) having an unpaired valency electron
Gene	The basic physical unit of heredity; a linear sequence of nucleotides along a segment of DNA that provides the coded instructions for synthesis of a protein
Genome	The complete set of genes or genetic material present within an organism
In vitro	Outside a living organism
In vitro	Within an entire, living organism
Metabolism	The chemical processes that occur within a living organism in order to maintain life

Glossary

Term	Definition
Redox	Oxidation and reduction considered together as complementary processes
Skeletal muscle	A muscle that is connected to the skeleton
Symbiosis	Interaction between two different organisms living in close physical association, typically to the advantage of both

Resource One Overview

Topic	The Importance of Cell Biology
A-level Modules	Foundations in Biology Structure of Eukaryotic Cells
Objectives	By the end of this resource, you will be able to: ✓ Distinguish between different organelles and define their functions within the cell ✓ Explain how different cell types are important for their different functions within the human body ✓ Understand how individual cells work together to create a functioning, healthy individual.
Instructions	1. Read the data source 2. Complete the activities 3. Explore the further reading

Image: Cell Illustration. Source: Dave Asprey

Resource One
Data Source

Section A

What is a cell?

Data interpretation

The activities of all organisms are based on the activities of **cells**. For instance, the movement of your eyes as you read this text is based on activities of muscle and nerve cells. Understanding how cells work is a major focus of all biological research.

Robert Hook first discovered cells in 1665. he gave them their name because they resembled the *cella* (Latin for "small rooms") where Monks lived in monasteries. Cells are tiny packages that contain factories, warehouses, border control, transport systems and power plants. They function on their own, creating their own energy and self-replicating, but work together to keep the whole organism alive. Animal cells come in all shapes and sizes. Their size can range from micrometres (neurons) to centimetres (female egg cell). The largest known animal cell is the ostrich egg, which has a 5 inch diameter.

All cells share certain characteristics. For example, every cell is enclosed by a membrane that regulates the passage of materials between the cell and its surroundings, called the **plasma membrane**. And every cell uses **DNA** as its genetic information. A eukaryotic cell is further subdivided into various membrane enclosed **organelles** (Figure 1). The term organelle is derived from the word 'organ' and refers to compartments within the cell that form a specific function. The organelles are usually isolated from the rest of the cell by an internal membrane, similar to the plasma membrane.

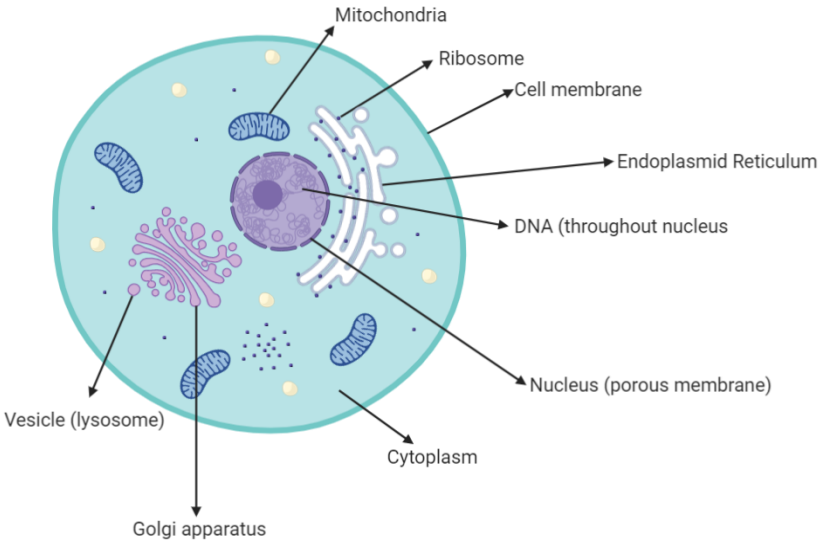
Resource One
Data Source

Figure 1

Labelled Animal Cell Diagram.

Created with BioRender.com

Source: Campell, Biology, Ninth Edition.



Resource One
Data Source

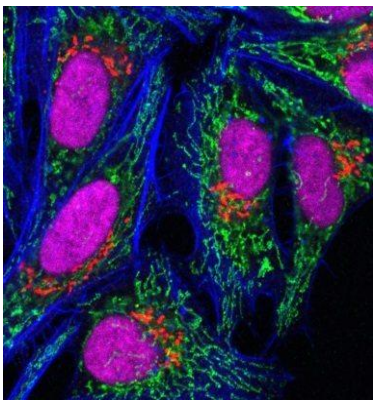
The **plasma membrane** is a thin membrane made up of proteins and lipids that covers the cell. It separates the cell's components from the surrounding medium. It also functions to control the passage of substances in and out of the cell.

The **nucleus** is often the most prominent organelle in the cell, you can often see it clearly under a microscope (Figure 2). It is usually a spherical shape and is located in the middle of the cell. It is surrounded by a double membrane, called the **nuclear envelope**. This membrane separates the components of the nucleus from the cytoplasm, but its pores allows substances to pass between the nucleus and the cytoplasm.

Figure 2

Fixed cell staining of HeLA cells using nuclear dye (magenta), mitochondria dye (green) and cytoskeleton (blue).

Image from Sigma Aldrich.



The **cytoplasm** is a fluid-like substance present between the cell membrane and the nucleus. It is mainly composed of water, microtubules, actin filaments and intermediate filaments. These structures give the cell its shape and help organise its components.

The **endoplasmic reticulum** (ER) is a network of membranous canaliculi that extends in the cytoplasm. It forms an internal transport system that transfers substances from one part of the cell to another.

Ribosomes are round organelles that synthesize protein within the cell. Some of them are present in the cytoplasm, but most are attached to the outer surface of the ER.

Resource One
Data Source

The **Golgi apparatus** is a series of flat membrane-bound sacs. It is designed to receive molecules secreted by the ER. It then classifies and modifies the molecules and distributes them across the cell.

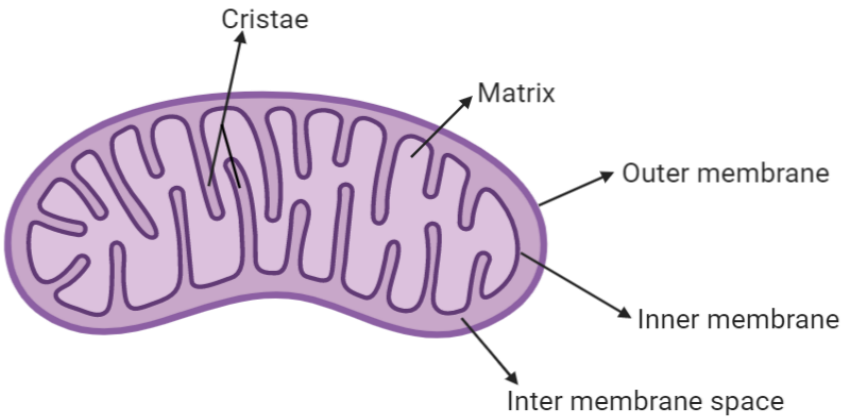
Lysosomes are small, round, membranous vesicles form by the Golgi apparatus. They contain digestive enzymes. The function of lysosomes is to get rid of cells and organelles that are no longer performing their jobs properly. They are also used to defend the cell. For example, white blood cells use lysosomes to engulf and destroy pathogens that invade the cell. The cell is not affected by the enzymes because they are isolated from them by the lysosome membrane.

Mitochondria are membranous organelles that produce energy within the cell (Figure 3). They have two membranes, the inner and outer membranes, which is separated by the inner membrane space. A group of folds, known as cristae, extends from the inner membrane. The function of the cristae is to increase the membrane's surface area, as this is where the chemical reactions that produce energy take place. The space within the inner membrane of the mitochondrion is known as the matrix, which contains enzymes and mitochondrial DNA.

Figure 3

Labelled Mitochondria Diagram.

Created with BioRender.com



Resource One
Data Source

Section C

Functions of Different Cells

Cells communicate with one another and connect to create a solid, functioning organism. Cells build tissues, which form organs, and organs work together to keep the organism alive.

When you consider the complexity of the human body, it is no surprise that there are hundreds of diverse cell types. Below is a small selection of human cell types and their functions:

Active reading

Blood cells are made up of three major types; red blood cells (RBC), white blood cells (WBC) and platelets. RBC are responsible for carrying oxygen around the body, WBC are part of the immune system and platelets help blood clot to prevent blood loss after injury. RBC do not contain any organelles, this frees up room for haemoglobin molecules, and prevents the cell from using the oxygen that it is carrying. Platelets do not contain a nucleus either, they are often considered cell fragments, rather than true cells. However, platelets do contain mitochondria and endoplasmic reticulum fragments. Platelets also contain adhesive proteins that allow them to adhere to other cells during activation and clot formation. There are different types of WBCs (granulocytes, monocytes and lymphocytes) and they are all used to help the body fight infection and other diseases. They have a nucleus, are capable of motility and defend the body by ingesting foreign materials and cellular debris.

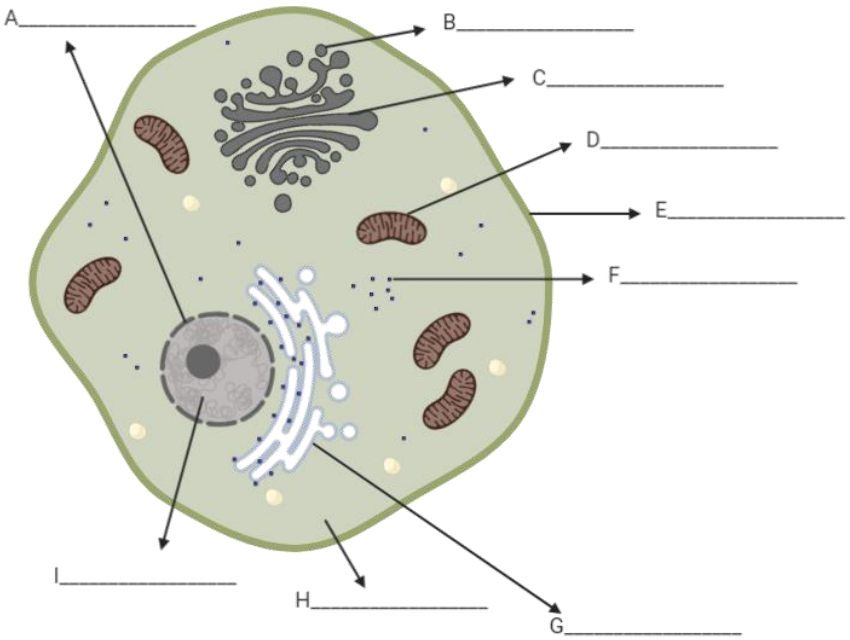
Muscle cells are long, tubular cells. They are important for a huge range of functions, including movement, support and internal functions. Thousands of muscle cells make up an individual skeletal muscle. The best known function of skeletal muscle is its ability to contract and cause movement. But they also function to maintain posture, ensure balance and stability, protect internal organs and even generate heat to maintain homeostasis of the body.

Fat cells are the main constituent in adipose tissue. They contain stored fats called triglycerides that can be used up as energy when needed. They also function to provide thermal insulation, cushioning for organs and production of hormones.

Resource One Activities

Activities

1. Fill in the blanks on the image below:
Created using BioRender.com



2. Consider the cell as a city. Which organelle would be associated with which role? Justify your answers.

    a) Transport system

    b) Power Plant

    c) Border control

    d) Waste disposal

    e) Army

Problem solving

3. Summarise the function of a membrane (cell or organelle)

Resource One Activities

Activities

4. Muscle cells will have increased amounts of which organelles? Discuss why in your answer.
    a) Ribosomes
    b) Chloroplasts
    c) Nuclei
    d) Mitochondria

5. Explain how individual organelles present within a cell contribute to the cell's overall function within a whole organism.

6. Tay Sachs is a **congenital** disorder in which waste molecules are not properly digested and instead accumulate in cells, causing toxicity. Dysfunction in which organelle can lead to Tay Sachs? Justify your answer. (Use your knowledge of the function of different organelles to decide)
    a) Nucleus
    b) Endoplasmic reticulum
    c) Golgi apparatus
    d) Lysosome

Problem solving

Resource One
Further Reading

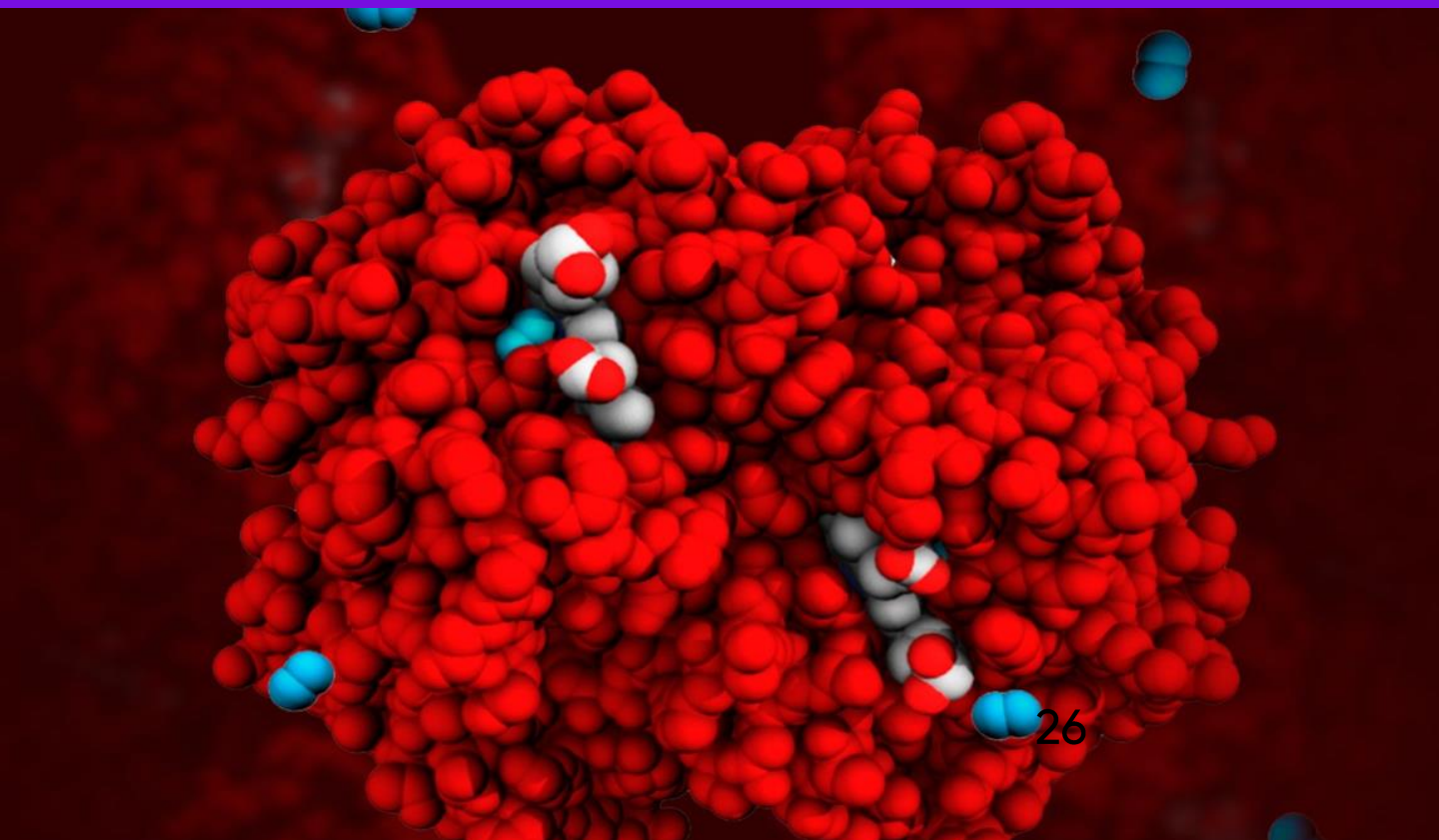
Explore

- Biology: Cell Structure | Nucleus Medical Media
  https://www.youtube.com/watch?v=URUJD5NEXC8
- Khan Academy – Cellular Organelles and Structure.
  https://www.khanacademy.org/test-prep/mcat/cells/eukaryotic-cells/a/organelles-article

Resource Two Overview

Topic	The Link Between Structure and Function
A-level Modules	Amino acids and proteins
Objectives	By the end of this resource, you will be able to: ✓ Draw the structure of a peptide formed up to three amino acids ✓ Identify primary, secondary and tertiary structures of a protein ✓ Explain how protein structure is maintained ✓ Relate the structure of proteins to their function
Instructions	1. Read the data source 2. Complete the activities 3. Explore the further reading

Image: Haemoglobin PDB structure 4hhb. Source: rscb.org



Resource Two
Data Source

Section A

The Basics of Life

The knowledge that form fits function is everywhere. For example, a screwdriver is suited to tighten or loosen screws, a hammer to hit nails. How a device works is correlated to its structure. Applied to biology, this theme is a guide to the anatomy of all life at all structural levels. An example is seen in the leaf; the thin, flat shape maximises the amount of sunlight that can be captured by its chloroplasts. Analysing a biological structure can give us clues as to what it does and how it does it.

Amino acids are organic compounds that combine to form **polymers**, which in turn form **proteins**. Amino acids and proteins are considered the building blocks of life. When proteins are digested or broken down, amino acids are left. The human body uses amino acids to make more proteins, help to body to break down food, grow, repair body tissues and many other functions. Some amino acids can be produced by the human body, while others need to be taken in by the diet.

There are 20 amino acids required for human life, and they are classified into two groups; **essential amino acids** and **nonessential amino acids**. Essential amino acids cannot be made by the body and include histidine, lysine, methionine. As a result, they must come from food. Nonessential amino acids are produced by the body and include asparagine and serine.

Source: Campell, Biology, Ninth Edition.

Resource Two
Data Source

All amino acids follow a general structure (Figure 4). According to this formula, each amino acid consists of:

- A carboxyl group (-COOH)
- An amino group ($-NH_3$)
- An alpha carbon
- A hydrogen atom
- A side chain (-R)

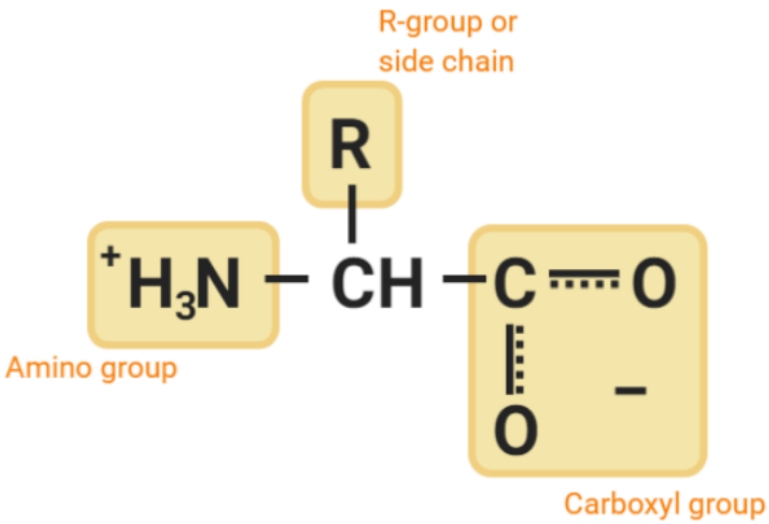


Figure 4

General structure of amino acids.

Created using BioRender.com

Resource Two
Data Source

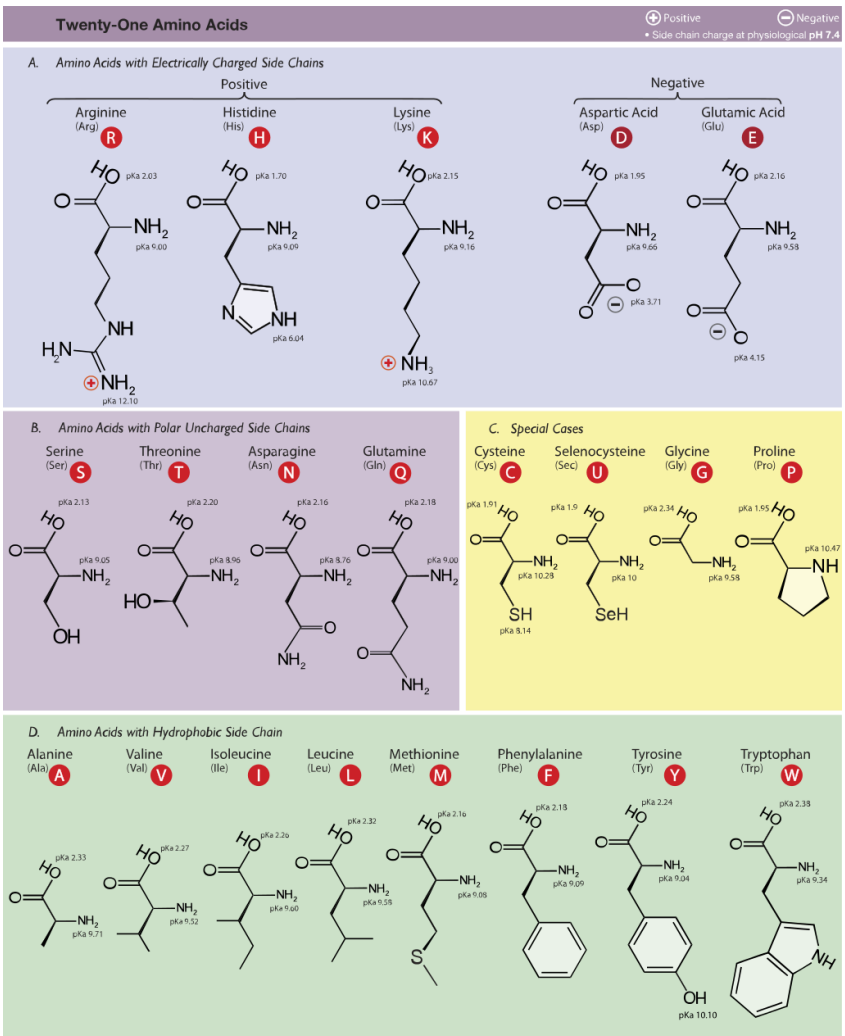
Figure 5

Structure of amino acids, containing their three letter and one letter codes.

Source: OpenStax

Data interpretation

The properties of amino acids are highly dependent on the **side chain** (-R) and are highly variable (Figure 5). These amino acids can be classified into groups depending on their properties (e.g. polarity, charge).



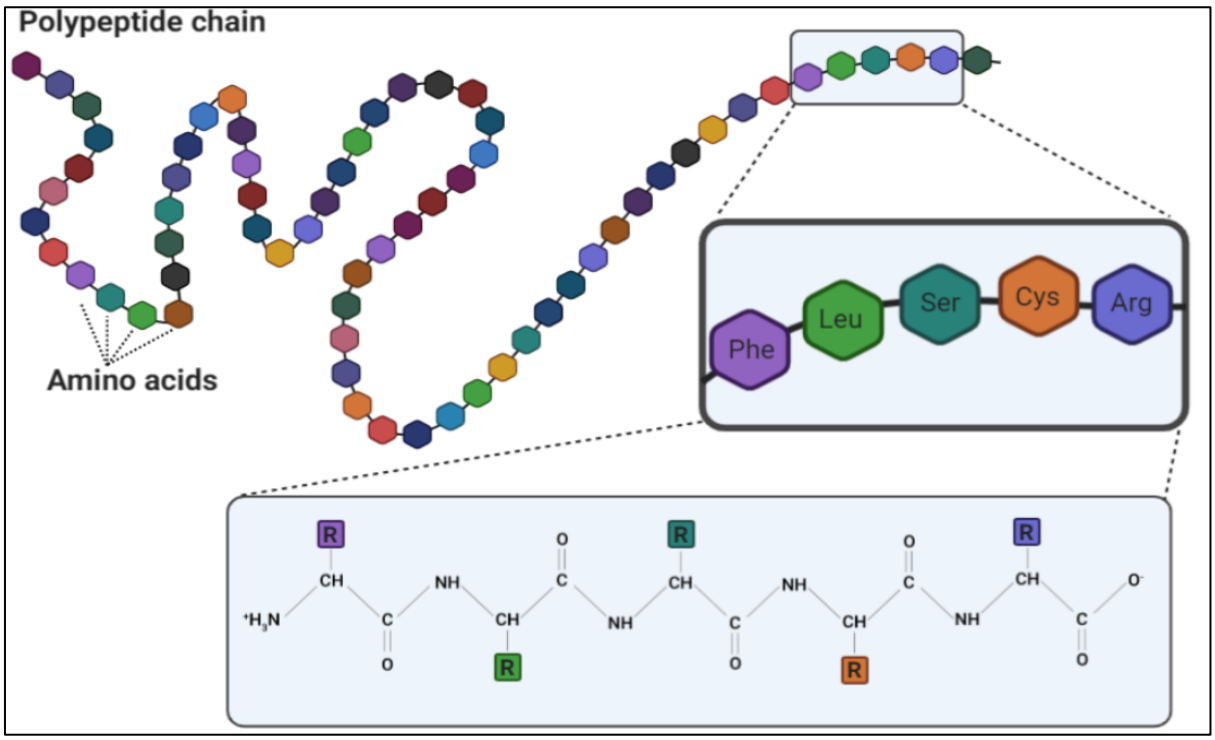
Resource Two
Data Source

Figure 6

Structure of amino acids making up a polypeptide chain.

Created using BioRender.com
Source: OpenStax

A peptide bond is formed when the amino group of one amino acid reacts with the carboxylic group of another amino acid and a water molecule is released. The resultant compound is called a **dipeptide**. The dipeptide that forms has a free amino group at one end and a free carboxylic group at the other. It can form additional peptide bonds at both these ends resulting in elongation of the **polypeptide chain** (Figure 6). The order of the amino acids determines the primary structure of the protein. Proteins can be many thousands of amino acids long.



Resource Two
Data Source

Section B

Protein Structure

Amino acid chains are arranged in a series of structures to create the finished 3D protein. There are up to four levels of structural arrangements in a protein (Figure 7), primary, secondary, tertiary and quaternary.

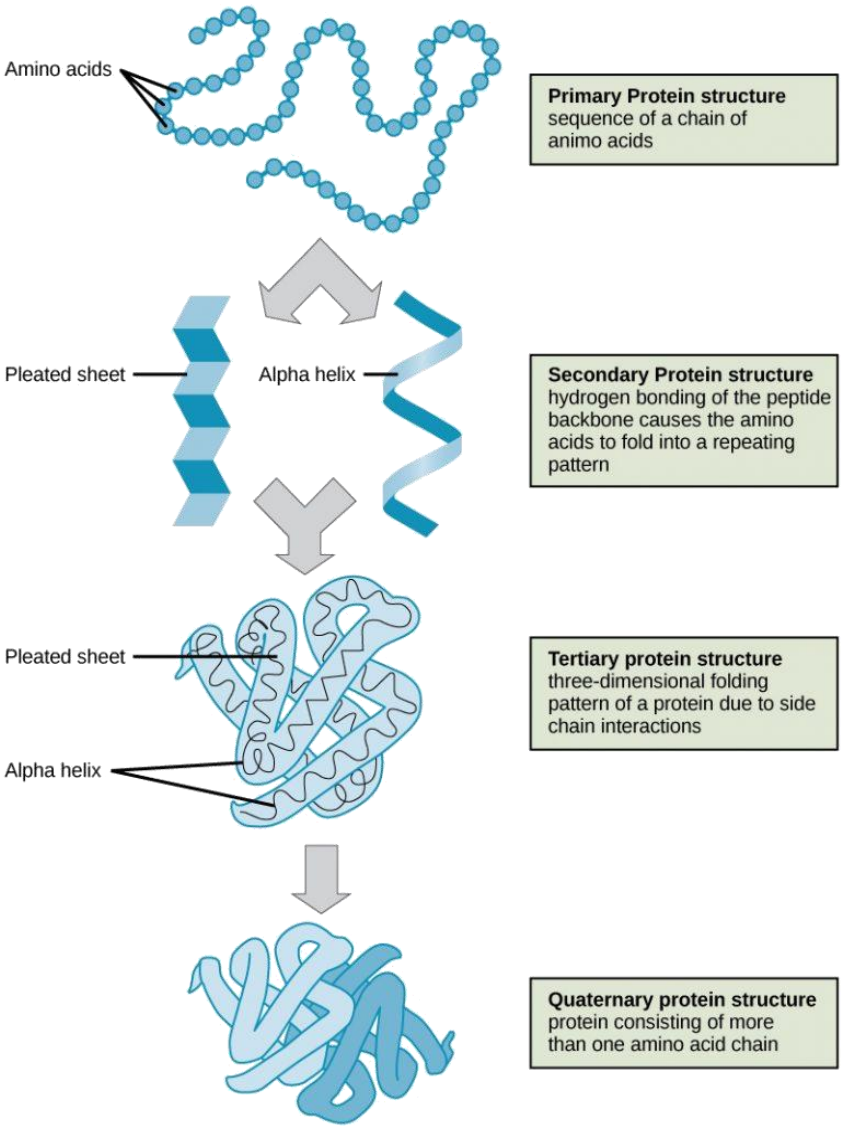


Figure 7

The four levels of protein structure.

Source: OpenStax

Resource Two
Data Source

Primary Structure

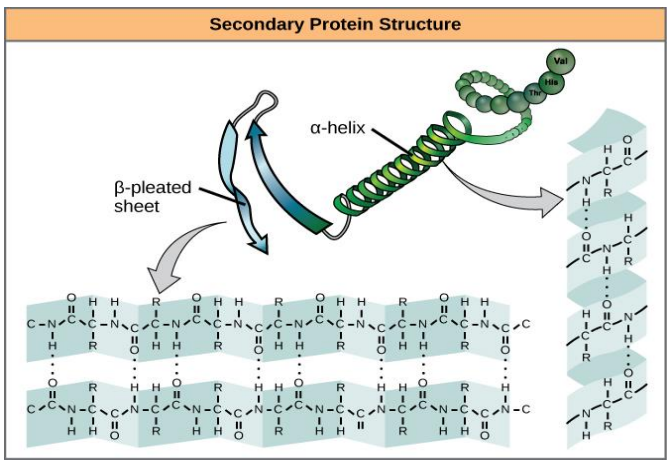
The simplest level of protein structure, primary structure, is simply **the sequence of amino acids in a polypeptide chain**. The sequence of amino acids is determined by the **DNA** of the **gene** that encodes the protein. The specific order of amino acids will alter how the protein further folds and is bonded enabling unique functions.

Secondary Structure

Active reading

The sequence of amino acids causes parts of a protein molecules to bend into **alpha helices** or fold into **beta pleated sheets** (Figure 8). **Hydrogen bonds** between the carboxyl groups of one amino acid and the amino group of another are what hold the secondary structure in place. Hydrogen bonds are individually weak bonds, but when there are large numbers of them they provide collective strength.

A common alpha helix has 3.6 amino acid residues in every helical turn. The R groups of the polypeptide protrude out from the alpha-helix chain. In the beta pleated sheet, the "pleats" are formed by hydrogen bonding between atoms on the backbone of the polypeptide chain. The pleated segments align parallel or antiparallel to each other, and hydrogen bonds form between the partially positive nitrogen atom in the amino group and the partially negative oxygen atom in the carboxyl group of the peptide backbone.



Resource Two
Data Source

Tertiary structure

The **unique 3D structure** of a polypeptide is its tertiary structure. This structure is in part due to **chemical interactions** within the polypeptide chain. Primarily, the interactions among R groups creates the complex 3D tertiary structure of a protein. The nature of the R groups found in the amino acids involved can counteract the formation of the hydrogen bonds described in the standard secondary structures. For example, R groups with similar charges are repelled by each other and those with unlike charges are attracted to each other (**ionic bonds**). When protein folding takes place, the hydrophobic R groups of nonpolar amino acids lay in the interior of the protein because they are repelled by the water present in the environment, whereas the hydrophilic R groups lay on the outside. The former types of interactions are also known as **hydrophobic interactions**. Interaction between cysteine side chains forms disulphide linkages in the presence of oxygen, forming a **covalent bond**.

Quaternary Structure

In nature, some proteins are formed from several polypeptides, also known as subunits, and the **interaction of these subunits** forms the quaternary structure. Weak interactions between the subunits help to stabilise the overall structure. For example, haemoglobin (a globular protein) has a combination of hydrogen bonds and disulphide bonds that cause it to be mostly clumped into a ball shape (Figure 9).

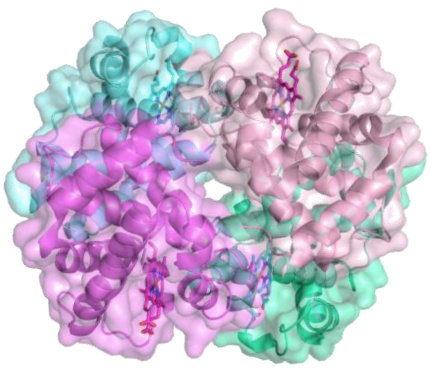


Figure 9

Structure of haemoglobin (PDB 1buw). Chains coloured and shown as ribbon. Haem group shown as sticks.

Created using PyMOL

Resource Two
Data Source

Section C

How alterations to the protein structure can cause disease.

Sickle cell anaemia is a genetic disease with severe symptoms, including pain and anaemia. The disease is caused by a mutated version of the gene that helps make haemoglobin – a protein that carries oxygen in red blood cells. People with two copies of the sickle cell gene have the disease. People who carry only one copy of the sickle cell gene do not have the disease, but may pass the gene on to their children. This disease demonstrates how the effects of mutations can be traced from the DNA level up to the level of the whole organism (Figure 10).

Haemoglobin normally functions by carrying oxygen from the lungs to the rest of the body. Sickle cell anaemia is caused by the substitution of a single amino acid chain (Glu to Val). This amino acid is normally found on the surface of the protein. Val is hydrophobic and it causes haemoglobin proteins to aggregate together, so each RBC carries less oxygen than normal.

Interestingly, 80% of cases of Sickle cell anaemia occur in Sub-Saharan Africa. In areas such as this, it is actually a evolutionary advantage to have Sickle cell anaemia, because protects the individual from developing Malaria, which is a serious and sometimes fatal disease.

Resource Two
Data Source

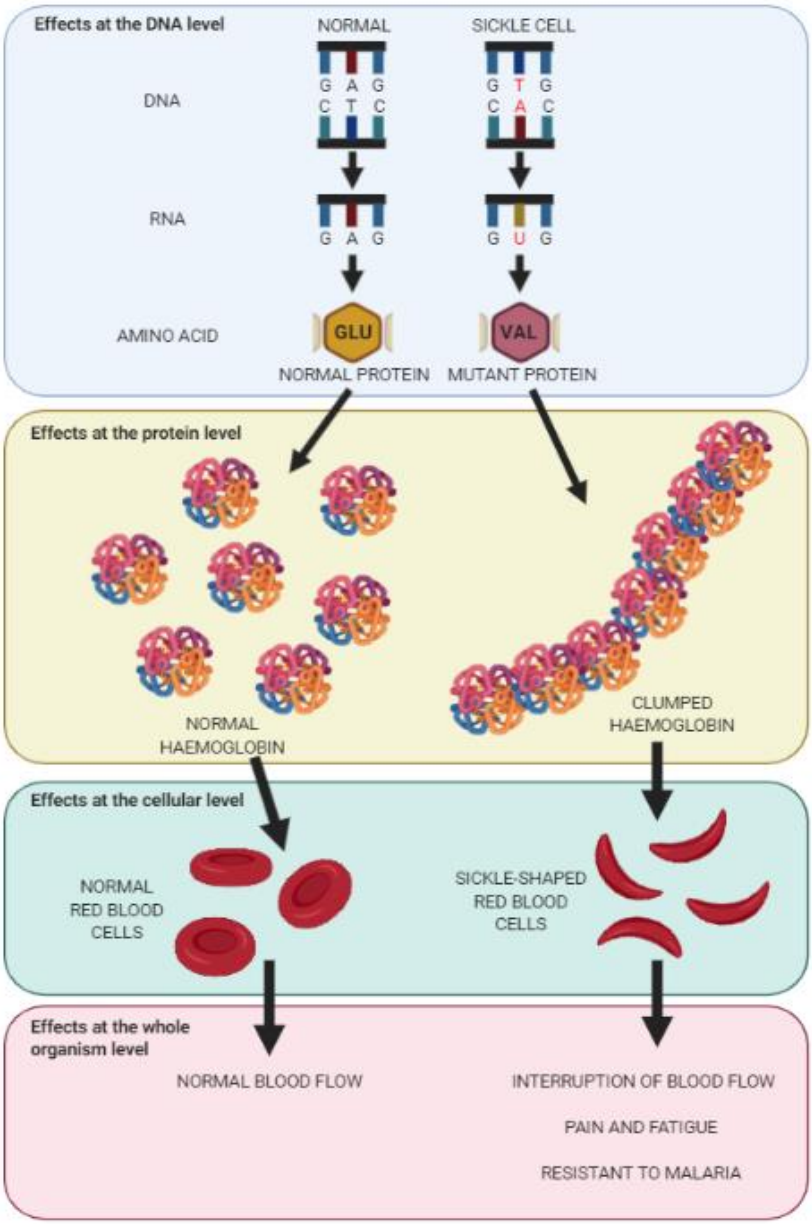
Figure 10

The mechanism behind Sickle Cell Anaemia from DNA level to whole organism.

Created using BioRender.com

Source: OpenStax

Data interpretation



Resource Two Activities

Activities

1. Fill in the blanks. An amino acid is made up of:
    - An _____ carbon
    - Carboyxl group
    - _____ group
    - Hydrogen group
    - Side chain (___)

2. Fill in the blanks:

Amino Acid	Three Letter Abbreviation	Single Letter Abbreviation
Alanine	Ala	
	Arg	R
	Asn	N
Aspartic Acid		D
Cysteine		C
	Gln	
	Glu	E
	Gly	
Histidine		H
Isoleucine	Ile	I
Leucine		L
Lysine		K
Methionine	Met	
	Phe	F
	Pro	P
Serine	Ser	S
Threonine		T
Tryptophan		W
Tryosine	Tyr	
	Val	V

Problem solving

3. Define the following terms:
    - Amino acid
    - Polypeptide chain
    - Primary Structure

Resource Two Activities

Activities

4. How many amino acids make up one turn in a common alpha helix?

5. Where are hydrophobic amino acids typically found in the 3D protein structure? Justify your answer.

6. Discuss how changes to a protein structure can lead to human disease. In your answer, consider all levels of protein structure, and the role of proteins in the body.

Resource Two
Further Reading

Explore

- OpenStax, Biology. Chapter 3: Biological Macromolecules. OpenStax CNX. 9th Nov 2020 https://cnx.org/contents/GFy_h8cu@14.1:7mHTlb7m@6/Introduction
- "DNA and Mutations." Understanding Evolution. University of California Museum of Paleontology. 24 October 2020. https://evolution.berkeley.edu/evolibrary/article/0_0_0/mutations_06.
- Proteins: Primary and Secondary Structure | A-level Biology | OCR, AQA, Edexcel https://www.youtube.com/watch?v=a56ChCHTa3w

Resource Three Overview

Topic	Mitochondria, not just the Powerhouse of the Cell
A-level Modules	Homeostasis and energy
Objectives	By the end of this resource, you will be able to: ✓ Understand and explain what the roles of the Mitochondria are within the cell ✓ Elaborate on the reason mitochondria are found in higher amounts in certain cells
Instructions	1. Read the data source 2. Complete the activities 3. Explore the further reading

Image: Mitochondria. Source: Dave Asprey

Resource Three
Data Source

Section A

Structure of Mitochondria

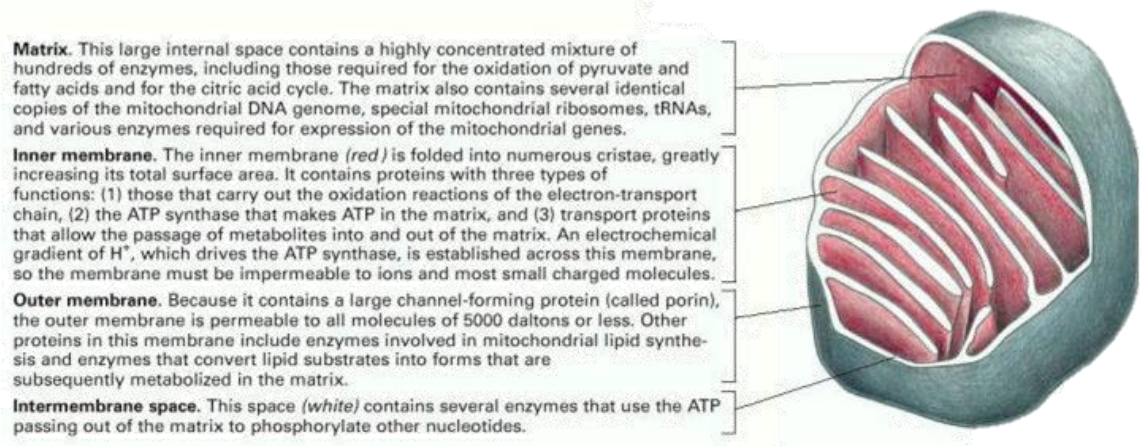
Mitochondria are dynamic organelles that are vital for the regulation of cell life and death. They produce most of the cellular **adenosine triphosphate** (ATP) and are essential in several signalling pathways. Mitochondria are ~ 1x2µm in size, and are found in large numbers in almost all eukaryotic cells. Typically, there are about 2,000 mitochondria per cell in the human body. Mitochondria are thought to have developed during an early phase of evolution from aerobic bacteria that entered into **symbiosis** with primeval anaerobic eukaryotes.

The structure of mitochondria has been covered previously (Resource 1 – Section B). A more detailed description can be found in Figure 11, below.

Figure 11

The general organisation of a mitochondrion.

Source: Molecular Biology of the Cell. 4th Edition.



Source: Campell, Biology, Ninth Edition.

Resource Three
Data Source

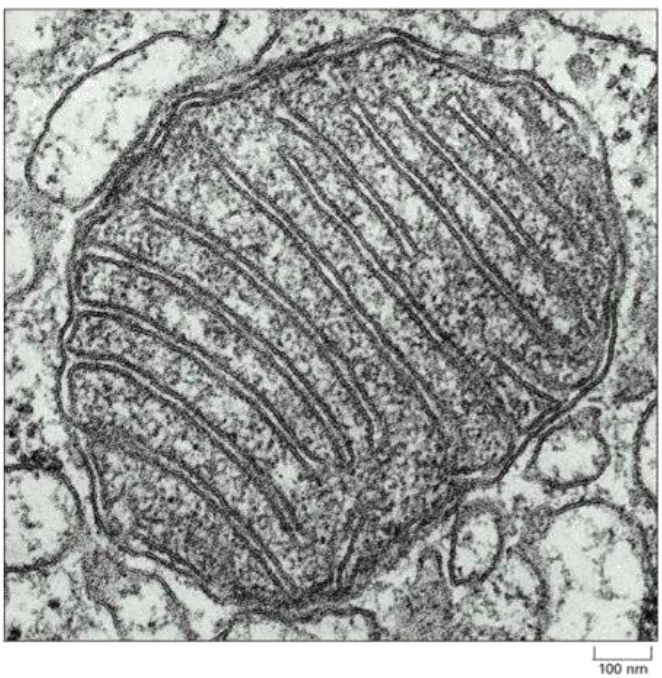
Figure 12

Mitochondrion through an electron microscope.

Source: Molecular Biology of the Cell. 4th Edition.

The number and shape of the mitochondria, as well as the number of cristae they have, can differ widely between cell types. Tissues with intensive oxidative metabolism, e.g. heart muscle, have mitochondria with particularly large numbers of cristae. Mitochondria are mobile, plastic organelles, that are often depicted as stiff, elongated cylinders. However, within one type of tissue, the shape of mitochondria can vary depending on their functional status (Figure 12). They are mobile, plastic organelles.

The amount of mitochondria in an individual cell depends on how much energy that cell needs to produce. Muscle cells, for example, have lots of mitochondria because they need to produce energy to move the body. Whereas, RBCs, which carry oxygen to other cells, have none, because they do not need to produce energy.



Resource Three
Data Source

Section B

Mitochondria, energy production

A dominant role for the mitochondria is the **production of ATP**, as reflected by the large number of proteins present in the inner membrane for this task. Using oxygen within the cell, mitochondria convert chemical energy from food to energy in a form that is usable to the host cell. The process is called **oxidative phosphorylation** and it happens inside mitochondria (Figure 13). In the matrix of mitochondria the citric acid cycle produces a chemical called NADH. NADH is then used by enzymes within the inner membrane to generate ATP in the **electron transport chain** (ETC).

During the ETC, a proton gradient is created when the protons are pumped from the mitochondrial matrix into the intermembrane space, which also helps drive ATP production. The ETC involves a series of reactions that rely on protein complexes to transfer electrons from a **donor** molecule to an **acceptor** molecule. As a result of these reactions, the proton gradient is produced, enabling mechanical work to be converted into chemical energy, allowing ATP synthesis. The complexes are embedded in the cristae of the mitochondria.

Active reading

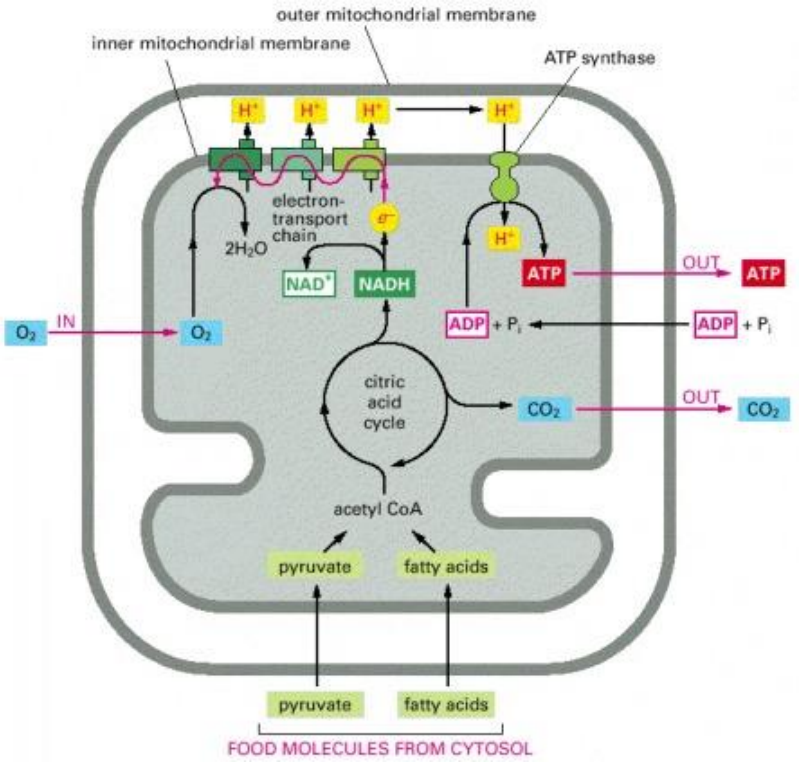
Pyruvate and fatty acids enter the mitochondrion and are broken down to acetyl CoA. Acetyl CoA is then metabolised by the citric acid cycle, which reduces NAD+ to NADH. In the process of oxidative phosphorylation, high-energy electrons from NADH are passed along the ETC in the inner membrane to oxygen (O2). This transport of electrons generates a proton gradient across the inner membrane, which is used to drive the production of ATP by ATP synthase.

Resource Three Data Source

Figure 13

A summary of energy-generating metabolism in mitochondria.

Source: Molecular Biology of the Cell. 4th Edition.



Resource Three
Data Source

Section C

Other functions of Mitochondria

Mitochondria divide using their **own circular strand of DNA**. Mitochondrial DNA is only inherited through the maternal line. Any mitochondrial DNA contributed by the father is actively destroyed by programmed cell death after a sperm fuses with an egg.

Mitochondria assist in **safeguarding cell survival** and assist the progress of **apoptosis** when essential. They control the intrinsic apoptosis pathway, and release **cytochrome *c*** in response to cell stresses such as heat, infection or reduced nutrient levels. Cytochrome *c* activates **caspase**, which is a major enzyme involved in apoptosis.

Mitochondria have an antiviral signaling protein (MAVS) which plays a key role in the **innate immune response** to viral infections, helping to induce antiviral and anti-inflammatory pathways.

Mitochondria are also responsible for maintaining **calcium homeostasis** within the cell. Mitochondria control the flow of calcium in and out, and this is an important process in metabolic regulation and cell death.

During the process of energy production mitochondria produce waste products are called **reactive oxygen species** (ROS). ROS can damage DNA, causing mutations, which can lead to apoptosis. These mutations affect mitochondria affect areas of high energy demand, such as the brain, muscles, central nervous system and eyes. People suffering from diseases such as Parkinson's disease have a much higher mitochondrial DNA mutation rate than healthy people do, so the functioning of mitochondria is implicated in diseases such as this.

Resource Three
Data Source

Section E

Fission and Fusion

Mitochondria rely on **fission and fusion** to maintain function during metabolic or environmental stress (Figure 14). Fusion helps control cell stress by mixing the contents of partially damaged mitochondria as a form of complementation. Fission is needed to create new mitochondria, but also contributes to quality control by enabling the removal of damaged mitochondria. Impairment of fission or fusion can affect normal development, and are implicated in many neurodegenerative diseases. Loss of mitochondrial fusion not only decreases the efficiency of ATP production, it also triggers mitochondrial genome mutation and loss, resulting in lethal mitochondrial myopathy.

Fusion rescues stress by allowing functional mitochondria (green) to complement dysfunctional mitochondria (yellow) by diffusion and sharing of components between organelles (Figure 14). During fission multiple **heterogeneous** mitochondria are produced leading to an increase in healthy mitochondria, mitophagy and apoptosis (turnover).

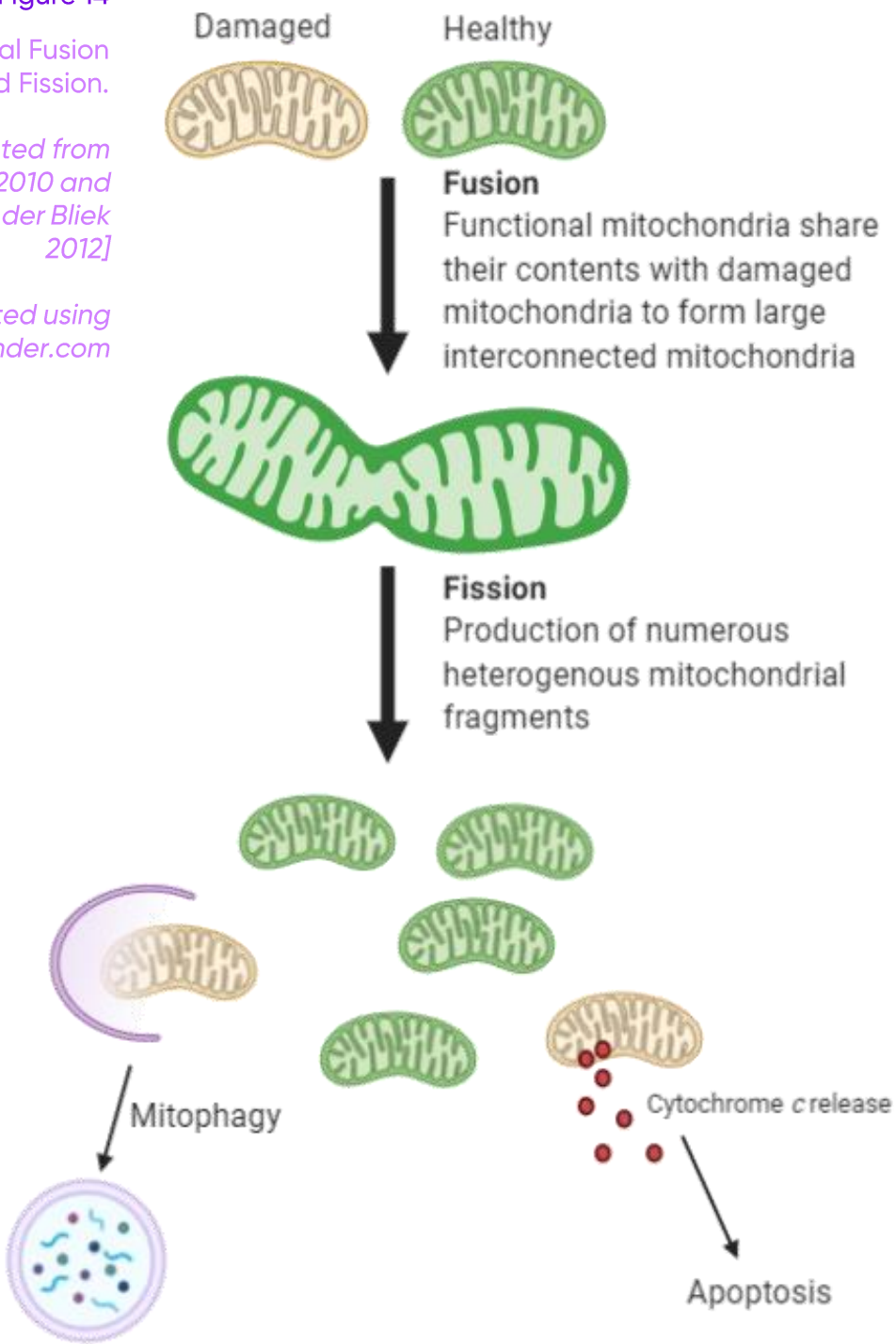
Resource Three
Data Source

Figure 14

Mitochondrial Fusion and Fission.

[Adapted from Westermann 2010 and Youle and van der Bliek 2012]

Created using BioRender.com



Resource Three Activities

Activities

1. Why does the inner membrane fold up into cristae? Explain why this is important for the function of mitochondria.

2. Describe the difference between mitochondrial fission and fusion, and the importance of both.

3. Kearns-Sayre syndrome is a disease caused by deletions in circular DNA that codes for proteins of the electron transport chain. What is the inheritance pattern of this disease? Justify your answer.

    a) Through the maternal line

    b) Autosomal recessive

    c) Through the paternal line

    d) X-linked

4. Explain the role that mitochondria play in the following mechanisms:

    - Protection against viruses
    - Homeostasis
    - Apoptosis

5. Define the role of the proton gradient within the electron transport chain.

Resource Three
Further Reading

Explore

- Campello, S. and Scorrano, L. (2010), Mitochondrial shape changes: orchestrating cell pathophysiology. EMBO reports, 11: 678-684. https://doi.org/10.1038/embor.2010.115
- Alberts B, Johnson A, Lewis J, et al. Molecular Biology of the Cell. 4th edition. New York: Garland Science; 2002. The Mitochondrion. Available from: https://www.ncbi.nlm.nih.gov/books/NBK26894/
- Roger, AJ., Muñoz-Gómez, SA., Kamikawa, R. The Origin and Diversification of Mitochondria. 2017. Current Biology. 27(21). https://doi.org/10.1016/j.club.2017.09.015
- Powering the Cell: Mitochondria https://www.youtube.com/watch?v=RrS2uROUjK4

Resource Four Overview

Topic	Disease, when things start to go wrong
A-level Modules	Evolution and disease

Objectives

By the end of this resource, you will be able to:

- ✓ Understand the different ways to classify disease
- ✓ Appreciate the difference between risk factors and cause
- ✓ Recognize the origin of different types of disease

Instructions

1. Read the data source
2. Complete the activities
3. Explore the further reading

Image: Human Health and Disease. Source: Massachusetts Institute of Technology.

Resource Four
Data Source

Section A

Different types of Disease

Disease can be grouped into two different types:

- **Communicable**, which are caused by **pathogens** and can be transferred from one person to another, or from one organism to another. E.g. measles, food poisoning or malaria (transmitted via mosquito, as seen in Figure 15).
- **Non-communicable**, which are not transferred between people or other organisms. E.g. cancer, diabetes, heart disease or neurological disorders.

There are several other ways to classify disease. Some commonly used are; topographic, anatomic, physiological, pathological, etiologic and juristic.

With **topographic** classification, diseases are subdivided into categories relating to the body region or system, such as gastrointestinal, vascular, abdominal etc.

In the **anatomic** classification, disease is categorised by the specific organ or tissue affected. For example, heart disease, liver disease, lung disease.

The **physiological** classification of disease considers the underlying functional imbalance caused by a specific disorder. This includes respiratory and metabolic diseases. For example, a metabolic disease includes those in which there is a disturbance of the body's chemical processes are a feature, such as diabetes.

Figure 15

Aedes aegypti mosquito.

Source: James Gathany, Centres for Disease Control and Prevention.

Resource Four
Data Source

Pathological classification is based on the nature of the disease process. Neoplastic (tumour growth) or inflammatory diseases are examples of this.

With **etiologic** classification of disease, diseases are subdivided by cause, if it is known. An example of this is when the disease results from a living organism, such as staphylococcal or fungal.

The **juristic** classification is determined by the legal circumstances in which death occurs. It is predominantly involved with sudden death.

Resource Four
Data Source

Section B

Risk Factors of Disease

Data interpretation

Something that increases the likelihood of an individual developing a certain disease is called a **risk factor**. These risk factors are all around us. A nearby sneeze may raise your chances for catching the flu. Obesity increases your odds you'll get diabetes and smoking increases your risk for many cancers. Risk doesn't mean that something bad will definitely happen. Smoking does not guarantee that you'll get lung cancer, nor does it mean if you develop lung cancer, you must've once smoked.

Someone's personal health risk factors include their age, family history, lifestyle and more. Some risk factors can't be changed, such as genes or ethnicity. Others are within an individual's control, like diet, physical activity and whether they wear a seatbelt in the car. Some risk factors can be found in Table 1.

Table 1

Table source: Skin Cancer Foundation, Cancer Research UK, British Heart Foundation, BBC Bitesize.

Risk Factor	Disease	Effects
Obesity	Type 2 diabetes	The body's cells no longer respond to insulin; blood glucose cannot be regulated properly
Alcohol	Cirrhosis	Scar tissue is formed in the liver; the liver is unable to remove toxins
Smoking	Lung cancer	Carcinogens in cigarette smoke cause cells to become cancerous
Being female	Breast cancer	The female hormones oestrogen and progesterone are growth promoting, and can stimulate cancerous cells within the breast
Family history	Heart disease	You can inherit conditions such as high blood pressure and high cholesterol from your parents, which are risk factors for heart disease
Sunburn	Skin cancer	Sunburn accelerates skin aging and is a leading cause in the majority of cases of skin cancer

Table 1: Risk factors for disease.

Resource Four
Data Source

The leading global risks for mortality in the world include high blood pressure, smoking, high blood glucose, physical inactivity and obesity. Many risks factors are preventable.

However, an individual's socio-economic status can increase or decrease their risk of developing a disease. Poverty can increase the risk of developing a disease that is preventable or treatable in developed countries. This is due to circumstances such as a lack of: adequate shelter, safe drinking water, nutritious food, sanitation or access to health services. People living in developing countries have less access to education. Therefore they miss out on important lessons such as sex-education, which help prevent the spread of sexually transmitted disease such as HIV.

Individuals living in developed countries are more likely to have time to exercise and have access to more nutritious food. Reducing their risk for many diseases including malnutrition and obesity.

Figure 16

No smoking sign.

Source: WHO

Resource Four
Data Source

Section C

Origins of Disease

The search for the **cause**, or **aetiology**, of a disease goes back to the 4th Century BCE, when Hippocrates first adopted the concept that disease is not a punishment of the gods, but rather is caused by earthly influences. Since then, scientists have persistently searched for the causes of disease, and have discovered the causes of many.

Many diseases are still of unknown (**idiopathic**) origin, and in other diseases, the cause may be suspected, but not yet definitively proved. In a few instances, discovery of a disease cause is the result of the achievement of one individual. However, it is more likely that the final breakthrough was made possible by hundreds of earlier scientists who provided bits and pieces of knowledge, all vital to the final accepted cause.

Active reading

Diseases of genetic origin

Some human diseases result from **mutations** in the sequence of amino acids contained in the **DNA** of **chromosomes**. A gene is a discrete linear sequence of amino acids of DNA that codes for a protein. There are approximately 25,000 different genes in the human genome. Any alteration of the DNA may result in the defective synthesis and subsequent malfunctioning of one or more proteins. If the mutated protein is key in normal metabolism, the error may have serious or even fatal consequences.

Large mutations, affecting chromosome structure and number, are quite rare as they would typically cause such major disruptions to development that the fetus is naturally aborted by the mother's body. However, certain alterations are not immediately lethal, and the fetus goes on to survive with a characteristic disorder. An example of this is Down syndrome.

Source: Britannica.com

Resource Four
Data Source

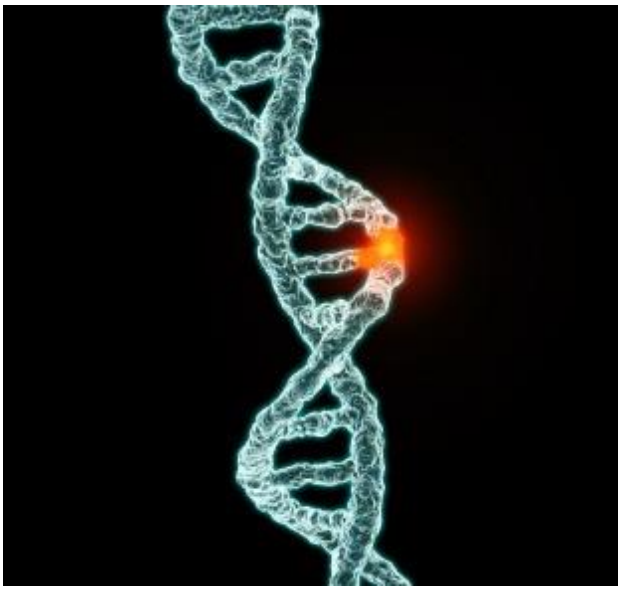
Small mutations are more common and include point mutations, deletions or insertions. This may cause an abnormal protein to be synthesized (e.g. sickle cell anemia) or may prevent the protein from being made at all. Mutations that occur in the DNA of cells cannot be inherited, but they can cause congenital malformations and cancers. However, mutations that occur in germ cells (i.e. the gametes) are transmitted to offspring and are responsible for inherited diseases.

The causes of mutations are poorly understood. Certain factors, such as maternal age, are thought to be important. The frequency of Down syndrome and of congenital malformations increases with the age of the mother. This is thought to be for a variety of reasons. Women are born with all the eggs they will ever have, unlike men who produce new sperm continuously. Therefore, her eggs are unprotected from the same internal and external agents that the woman experiences, and the longer she is exposed to such factors, the higher chance of injury to the eggs. Other factors that can cause mutations include radiation, viruses and certain drugs.

Figure 17

Mutated DNA molecule.

Source: Bio News Texas



Resource Four
Data Source

Chemical and Physical Injury

Chemical injury includes **poisoning**, where a small quantity of a poison is ingested and causes illness or death. Examples of poisonous substances include alcohol, carbon monoxide, cyanide or lead.

Physical injuries are those caused by mechanical trauma, extreme temperatures, electrical currents, changes in pressure or radiation.

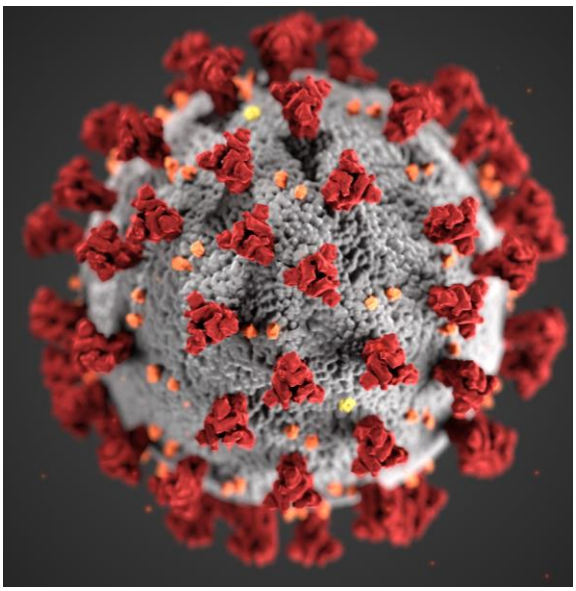
Diseases of Biotic Origin

Biotic agents relate to living organisms, and include viruses (Figure 18), bacteria, fungi and parasites. Some of these organisms rely on the host for survival. All animals are infected with biotic agents at a given time, but they are often **non-pathogenic** or **commensal**, and therefore do not cause disease. Those that invade and cause disease are characterised as **pathogenic**.

Figure 18

Ultrastructural morphology of coronaviruses.

Source: Centres for Disease Control and Prevention.



Source: Britannica.com

Resource Four
Data Source

Source: Britannica.com

Abnormal Growth of Cells

The growth of cells within the body is typically closely controlled. Areas of increased cell growth, due to injured tissue or organs, is called **hyperplasias**. Hyperplasias come about to meet special requirements of the body, and subside once the needs are met. The mechanism of cell growth is controlled by increased stimulatory influences and decreased responses to growth-inhibitory factors. Cells can lose their ability to respond to these growth-inhibitory factors, this causes their growth to become incontrollable, and may result in **cancer**.

Diseases caused by the Immune System

The role of the immune system is to protect against infectious disease, but at times it is responsible for causing disease. Disorders of the immune system are subdivided into two categories; those that arise when part of the host's immune system fails to prevent infection (**immune deficiencies**) and those that occur when the immune response is directed at an inappropriate **antigen**, such as a non-infectious agent in an allergic reaction, or towards the cells in a transplanted organ.

Diseases of Metabolic-Endocrine Origin

The term **metabolism** covers all the chemical reactions vital to the **development** and **maintenance** of the body. Defects in metabolism are found in almost every disease condition. All endocrine disease stems from either an overproduction or underproduction of some hormone-secreting endocrine gland.

Resource Four
Data Source

Nutritional Diseases

Undernutrition and **nutritional excess** encompass diseases of nutrition. Examples of undernutrition include shortages of total caloric intake (malnutrition). The most common disease caused by nutritional excess is Obesity, and generally results from excessive caloric intake, but can also be influenced by emotional, genetic and endocrine factors.

Neuropsychiatric Diseases

The key function of the **nervous system** is to gather information about the body and its external environment, process this information and organise the body's response. This is extremely complex and requires each nerve cell (**neuron**) to receive and transmit signals in a long signalling pathway.

Active reading

Psychiatric diseases are mental illnesses that cover a spectrum of diseases from obsessive-compulsive personality disorder to dementia. Many of these diseases are thought to be associated with decreased brain levels of certain neurotransmitters, such as serotonin in depression, or dopamine in schizophrenia. There is also often a heredity factor with these diseases.

Neurological diseases include Alzheimer's disease and Parkinson's disease. They are age-related, and to often manifest as decline of mental function such as the loss of memory and of motor skills. Hyperactive apoptosis can lead to neurodegenerative diseases. For example, Parkinson's disease is characterised by the loss of dopaminergic neurons within the certain areas of the brain.

Source: Britannica.com

Resource Four
Data Source

Section D

Treating Disease

Different types of medicines are currently available to treat many different communicable and non-communicable diseases. Some medicines only treat the symptoms and others cure the disease. Some examples are discussed below.

Painkillers are drugs that relieve symptoms but do not kill pathogens. Examples include paracetamol and aspirin, which can relive a headache or sore throat.

Antibiotics are substances that slow down or stop the growth of bacteria. They include penicillin and amoxicillin. Antibiotics are effective at killing bacterial pathogens. Penicillin was the first antibiotic to be discovered. It was discovered after **Alexander Fleming** left some bacteria in a petri dish in 1928, which was later killed by the naturally occurring *Penicillium* mould. Antibiotics damage bacterial cells but do not harm the host cells. However, **antibiotic resistance** has become a serious problem. All populations have variation, and resistance of bacteria to an antibiotic can be brought about by just one mutation in a single gene. As bacteria reproduce quickly, the number of bacteria with this mutation can increase very rapidly. The non-resistant bacteria are destroyed by the antibiotics, which removes competition. With no competition for space and food, the resistant genetic variant can spread quickly.

Resource Four
Data Source

Figure 19

Antibiotics.

Source: solarseven/ Shutterstock.

Viral diseases cannot be cured by antibiotics, as they reproduce within the host cells. It is very difficult to develop **antiviral** drugs, as they might damage the host cell whilst killing the virus. Antiviral drugs only slow down viral development, and viruses change their antigens quickly, which means new drugs (e.g. flu vaccinations) have to be generated regularly.

Because cancer often results from the dysregulation of cell cycle and inhibition of apoptosis, most **chemotherapy** drugs target cells at different phases of the cell cycle. However, some chemotherapy drugs cannot tell the difference between healthy cells and cancer cells. Resulting in destruction of normal cells.

Steroids, such as corticosteroids, are **anti-inflammatory medicines.** They are a man-made version of hormones normally produced by the body, and work by reducing inflammation and dampen the immune system.

Resource Four Activities

Activities

1. Define the following terms:
    - Communicable disease
    - Risk factor
    - Immune deficiency
    - Biotic agent
    - Hyperplasia
    - Etiological classification

2. Link the following diseases to the most appropriate origin:

Problem solving

Schizophrenia	Biotic agent
Malnutrition	Immune
Hyperthyroidism (excess of thyroid hormone)	Genetic
Cancer	Endocrine
Coronavirus	Nutritional
Hay fever	Psychiatric
Frostbite	Physical injury
Sickle cell anaemia	Growth of abnormal cells

Resource Four Activities

Activities

4. Many diseases have a huge impact globally, some examples include HIV, malaria and cholera. Malaria affects over 200 million people worldwide, particularly in developing countries.
    a) Is malaria an example of a communicable or non-communicable disease?
    b) What parasite causes malaria?
    c) Suggest why diseases such as malaria is more prevalent in developing countries?

5. Describe the process of evolution of antibiotic resistance in bacteria.

6. Discuss the difference between risk and cause. In your answer give examples of both.

Resource Four
Further Reading

Explore

- Britannica, Science, Human Disease, https://www.britannica.com/science/human-disease
- Drexler M; Institute of Medicine (US). What You Need to Know About Infectious Disease. Washington (DC): National Academies Press (US); 2010. I, How Infection Works. Available from: https://www.ncbi.nlm.nih.gov/books/NBK209710/
- World Health Organization. Noncommunicable diseases. https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases

Resource Five Overview

Topic	Mitochondria and Disease
A-level Modules	Evolution and Disease Homeostasis and Energy
Objectives	By the end of this resource, you will be able to: ✓ Appreciate the importance of mitophagy and understand how it works ✓ Understand how mitochondrial dysfunction can result in different diseases with different symptoms ✓ Recognise the process that leads to mitochondrial dysfunction, and eventually disease ✓ Comprehend how mitochondrial DNA is more susceptible to damage than regular DNA
Instructions	1. Read the data source 2. Complete the activities 3. Explore the further reading

Image: Mitochondria. Source: Dave Asprey

Resource Five
Data Source

Section A

Mitochondria and Disease

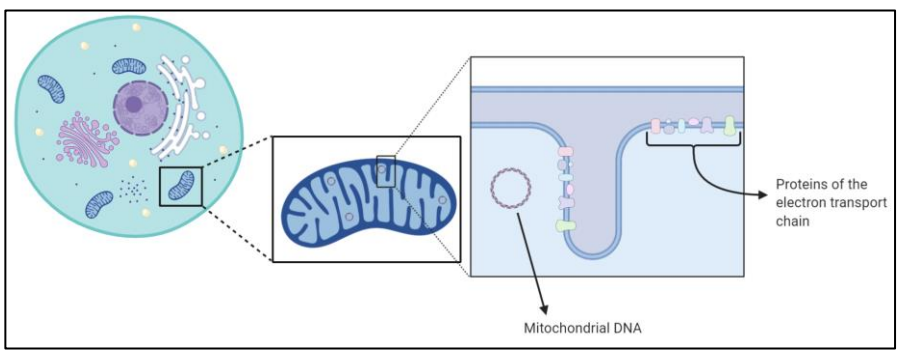
Mitochondria provide 95% of the body's energy requirements through the turnover of ATP via a series of redox reactions. However, as previously discussed (Resource 3), their function is not limited to ATP production. Mitochondria are essential regulators of cell survival and death and play a central role in aging. Mitochondrial diseases are chronic, genetic and often inherited disorders. They can be present from birth but can also occur at any age.

Mitochondrial DNA (mtDNA) is more susceptible to damage than nuclear DNA. This is due to the proximity of the mitochondrial DNA to the toxic free radicals that are produced by the **electron transport chain** (ETC) (Figure 20). In addition, mitochondrial lack the same protective mechanisms found in the nucleus of the cell, such as the nuclear envelope. Persistent mtDNA damage leads to loss of mitochondrial function, arrested growth, increased and morphological changes.

Figure 20

Location of mitochondrial DNA in relation to the electron transport chain.

Created with BioRender.com



Resource Five
Data Source

When mitochondria stop functioning, the cell they are in is starved of energy. So, depending on the location in the body and type of cell this is occurring, symptoms can vary widely. As a rule, cells that need the largest amounts of energy, such as heart muscles and nerves, are most affected by faulty mitochondria.

The following passage comes from the United Mitochondrial Disease Foundation:

"Because mitochondria perform so many different functions in different tissues, there are literally hundreds of different mitochondrial diseases. [...] Because of the complex interplay between the hundreds of genes and cells that must cooperate to keep our metabolic machinery running smoothly, it is a hallmark of mitochondrial diseases that identical mtDNA mutations may not produce identical diseases."

Symptoms of mitochondrial diseases vary greatly, but some common ones include: loss of muscle coordination and weakness, muscle pain, problems with vision or hearing, learning disabilities, gastrointestinal problems, neurological problems and increased risk of infection.

Conditions that are thought to involve mitochondrial dysfunction include: Parkinson's disease, Alzheimer's disease, bipolar disorder, schizophrenia, chronic fatigue syndrome, diabetes and autism.

Sources:

Medical News Today

Yakes and Van Houten, 1997. https://doi.org/10.1073/pnas.94.2.514

Resource Five
Data Source

Section B

Mitochondria and Mitophagy

Data interpretation

Mitophagy is the main route for metabolising old or damaged mitochondria, and acts as **a quality control system**. As shown in Figure 21, stimuli like ROS, oxidative stress, UV rays, or a lack of nutrition, causes the mitochondria to signal to autophagosomes about their damage by sending proteins to their surface that aren't present on healthy mitochondria. The autophagosome engulfs the mitochondria and fuses with a lysosome, which leads to the **degradation** of the mitochondria.

Under stimuli like ROS, mitochondria undergo depolarisation of their membrane and present proteins on their surface. This attracts an auto-phagophore which engulfs the damaged mitochondria. This autophagosome is then fused with a lysosome which leads to degradation of the mitochondria.

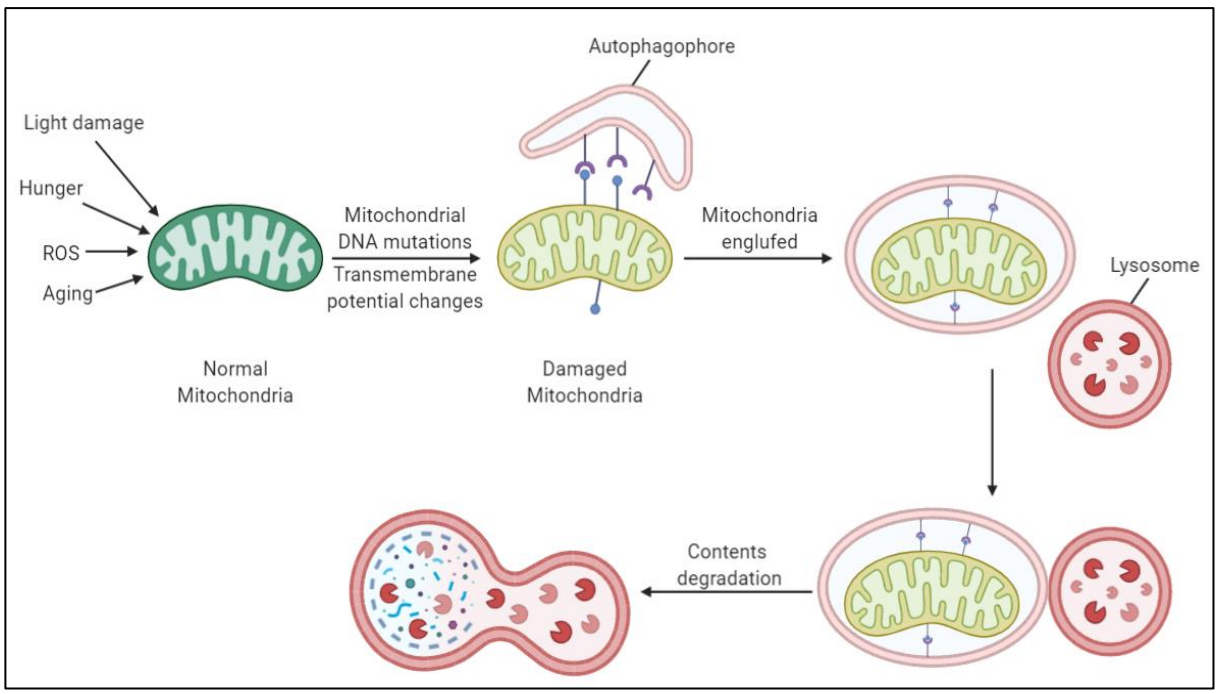
After mitophagy, abnormal mitochondria are cleared, the stability of the cell is maintained, and necrosis is prevented. Therefore, mitophagy is important for preventing some diseases, such as neurodegenerative diseases, cancer and diseases of the immune system. A deficiency of mitophagy disables cells to clear the damaged mitochondria, leading to an accumulation in the cell, causing the cell to undergo apoptosis.

Resource Five
Data Source

Figure 21

Mitophagy.

Source: adapted from Song, et al. 2015. Created using BioRender.com



Resource Five
Data Source

Mitochondria and the Aging Brain

Mitochondria and Aging

Aging induces many flaws and is a common risk factor for adult human diseases. Mitochondrial activity was found to be reduced by 40% in the elderly. It has also been shown that the maximal ATP production rate of mitochondria decreases 8% every decade that an individual is alive for. During aging, oxidative stress increases, and this causes dysfunctional mitochondria to accumulate.

Active reading

Reactive oxygen species (ROS) are produced in mitochondria, as a by product of the production of ATP. ROS are highly charged particles that can damage DNA, fats and proteins. The production of ROS damages the mitochondria, and damaged mitochondria produce even more ROS, **exacerbating the problem**. In addition to ROS, **replication errors** and **failure of repair mechanisms** also lead to the accumulation of mutations in mtDNA. Because mtDNA replication is independent of cellular division, the replication rate is higher than that of normal DNA. Furthermore, there is a lower rate of DNA repair enzymes in aged tissue. The level of both autophagy and mitophagy decline with aging. All these factors lead to the accumulation of dysfunctional mitochondria, increased oxidative stress, and ultimately apoptosis.

Sources:

Wang, et al. 2019. https://doi.org/10.1111/cns.13116

Resource Five
Data Source

Mitochondria and Parkinson's Disease

Mitochondrial dysfunction is an underlying feature of most neurodegenerative diseases. In Parkinson's disease, several important genes including PARK7, alpha-synuclein, parkin, PINK1, or LRRK2 have pathogenic mutations which cause defects in mitochondrial dynamics and function. Deletions in the PINK1 gene results in amplified oxidative stress.

The most compelling piece of evidence of the involvement of mitochondrial dysfunction in Parkinson's disease is when a group of Californian drug users suddenly displayed symptoms of Parkinson's disease. Researchers discovered that they had ingested the toxin 1-methyl-4-phenyl-1,2,3, 6-tetrahydropyridine (MPTP) after a new batch of synthetic heroin went badly. MPTP acts via inhibition of complex 1, an important protein in the mitochondrial transport chain, and leads to the death of midbrain dopaminergic neurons with significant specificity. MPTP has since been used in disease models for Parkinson's disease as it replicates the disease so well.

Sources:

Wang, et al. 2019. https://doi.org/10.1111/cns.13116

Resource Five
Data Source

Section C

Targeting Mitochondria

The maintenance of a healthy mitochondrial population is crucial for homeostasis of the cell, and the entire organism. Drugs that can recover mitochondrial function, remove excess ROS, or enhance mitophagy may have the potential to treat neurodegenerative diseases. However, pharmacological agents enhancing mitochondrial function to treat neurodegenerative diseases are not yet on the market. Even though the mechanisms of mitophagy has been extensively studied, several questions remain to be answered about neuronal mitophagy.

Sources:

Wang, et al. 2019. https://doi.org/10.1111/cns.13116

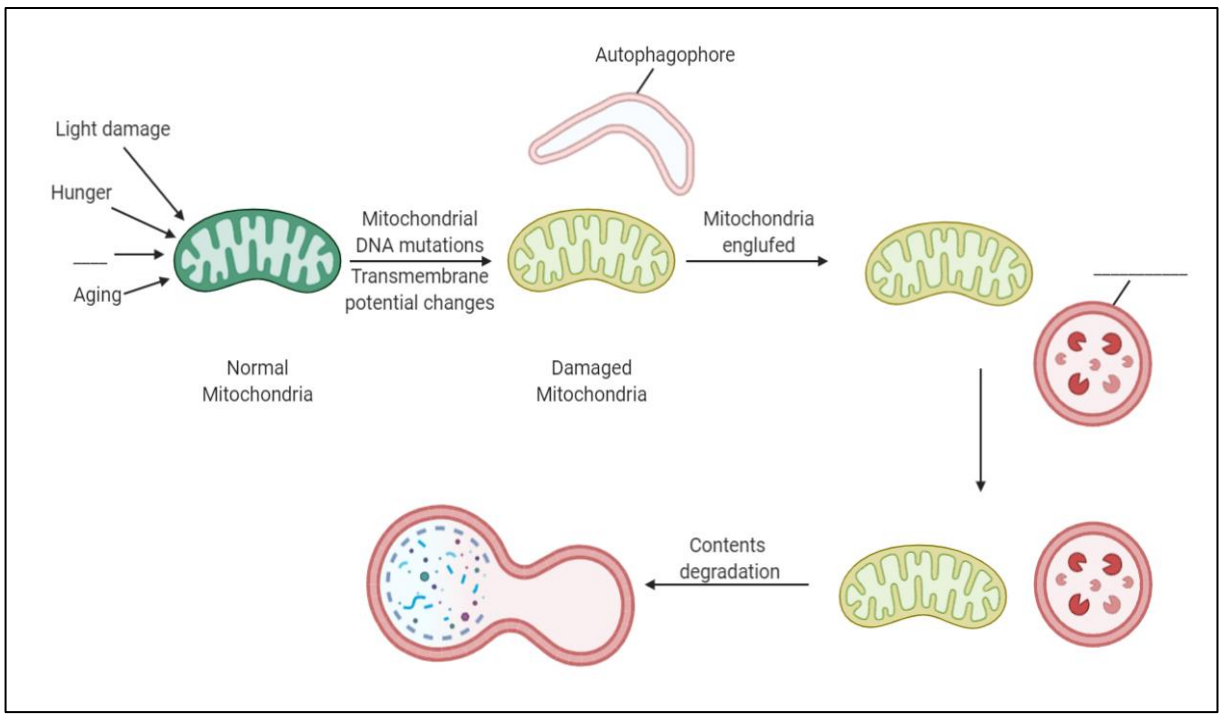
In addition, since mitochondria are so vital to all life, it is difficult to successfully target processes related to them. As it could result in causing downstream effects to mitochondria in other places in the body.

Resource Five Activities

Activities

1. Why is mitochondrial DNA more susceptible to DNA damage than nuclear DNA?

2. Draw in the missing features and labels of the process of mitophagy below:



Problem solving

3. If mitochondria are the problem in so many diseases, why can't we just destroy all cells with faulty mitochondria?

4. How many mitochondria are found in a cell?

Resource Five Activities

Activities

5. Discuss how mutations to mitochondrial DNA can present as diseases with such varying symptoms.
    - Consider the different roles that mitochondria have within the cell
    - Reflect on the different roles that mitochondria have within an individual
    - Discuss how dysfunction of these roles might cause the different symptoms and an overall disease

Resource Five
Further Reading

Explore

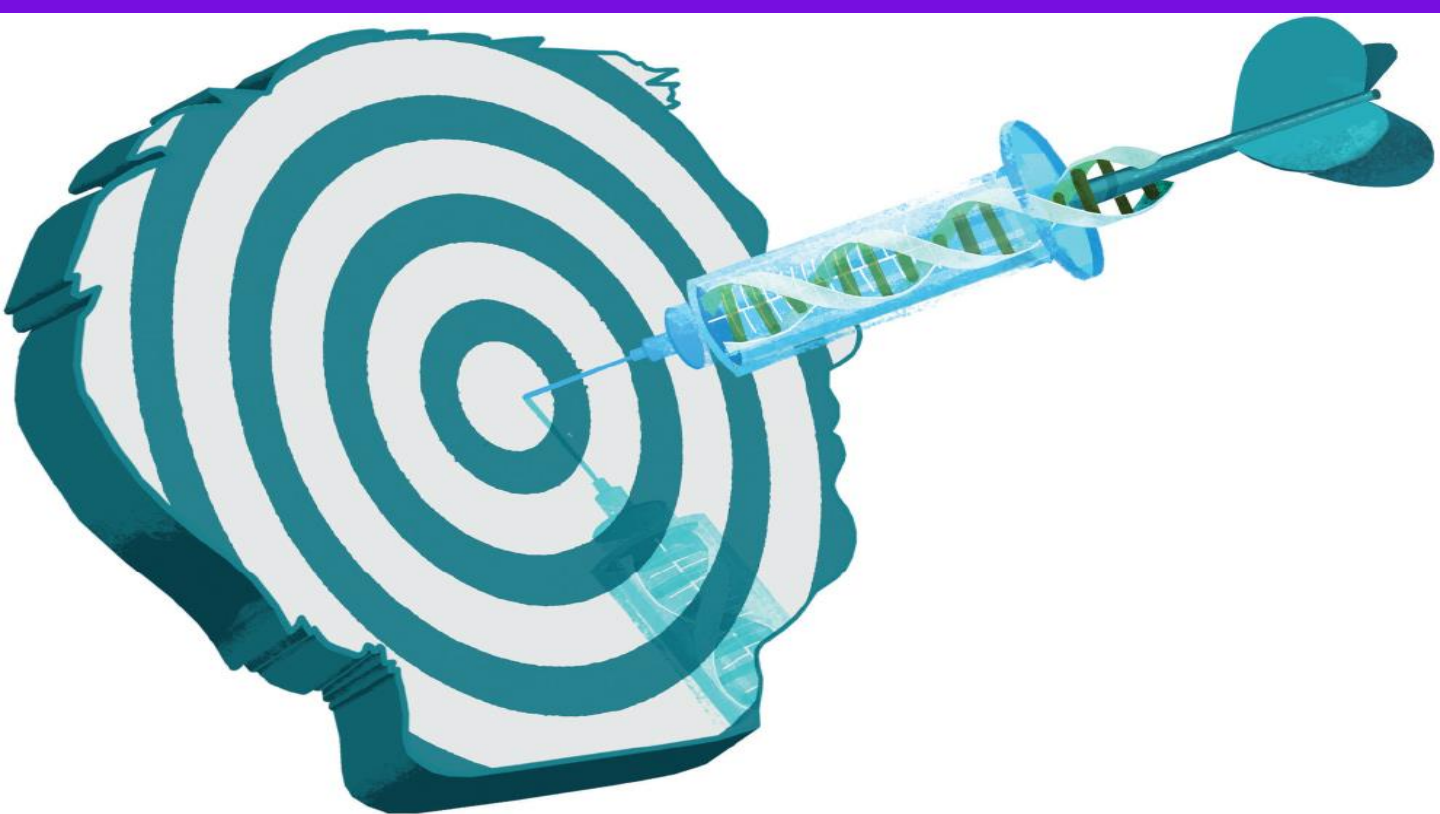
- Lionaki, E., Markaki, M., Palikaras, K., & Tavernarakis, N. (2015). Mitochondria, autophagy and age-associated neurodegenerative diseases: New insights into a complex interplay. *Biochimica et biophysica acta*, *1847*(11), 1412–1423. https://doi.org/10.1016/j.bbabio.2015.04.010

- Langston J. W. (2017). The MPTP Story. *Journal of Parkinson's disease*, *7*(s1), S11–S19. https://doi.org/10.3233/JPD-179006

Resource Six Overview

Topic	Discovering New and Better Medicines
A-level Modules	Disease Genetics
Objectives	By the end of this resource, you will be able to: ✓ Understand how new medicines are discovered ✓ Recognise that old drugs can be altered and re-purposed for new therapies ✓ Appreciate the route a new drug must take to get to market and why it can take so long and cost so much money
Instructions	1. Read the data source 2. Complete the activities 3. Explore the further reading

Image: Precision Medicine. Source: Eva Vázquez



Resource Six
Data Source

Section A

The Discovery of New Medicines

New medicines are being developed constantly. Historically, medicines came from nature, extracted from plants and microorganisms. However, a more recent advance is the development of synthetic medicines.

Certain medicines can be extracted from **natural sources**, and have been known about for a long time. For example, willow bark was used by the ancient Greeks to help cure fevers and pains. It was later discovered that the active ingredient was salicylic acid. This was modified into a substance we know as aspirin, which is less irritating to the stomach than salicylic acid. In ancient Chinese medicine, bile acids taken from the gallbladders of bears were used for the treatment of heart, ocular and gynaecological conditions. These days, bile acids are used for the treatment of liver diseases, but are being considered for the treatment of many other diseases, including neurodegenerative, inflammation and cancer.

Figure 22

Asian Black Bear used in bear bile farm.

Source: World Animal News.

Resource Six
Data Source

Section A

The Discovery of New Medicines

Gene technology is changing the face of medicine. Studying the genome of a pathogen or the mechanism of a disease can suggest a **target** for a new medicine. The target could be an antigen or a protein involved in an apoptosis pathway. Having found a target, **screening** takes place to try to find a **pre-existing substance** which will react with the target. The pre-existing substance can then be altered in order to make a more targeted therapy for the disease, or to remove side effects.

The more we discover about a human disease, and the mechanism that causes it, the more we can specifically target our therapy to treat the disease. This is easiest to see in cancer therapy, as there is a whole category of treatment called **targeted therapy.** For example, 20-25% of breast cancer have an upregulation of a protein called human epidermal growth factor receptor 2 (HER2). This protein makes tumour cells grow. If the tumour is HER2 positive, a patient can be prescribed Herceptin, which is a monoclonal antibody that attaches itself to HER2 receptors on tumour cells and blocks them from receiving any growth signals. By blocking these signals, Herceptin can slow or stop the growth of breast cancer. In addition, Herceptin also flags these cells for destruction by the immune system.

Sources:

BBC Bitesize

Breastcancer.org

Wang and Carey, 2014. WJG.

Resource Six
Data Source

Section B

Testing Medicines

New medicines need to be tested and trailed before doctors can prescribe them for patients to take. This allows them to be checked for:

- Safety: important as some drugs can be toxic and have harmful side effects
- Effectiveness: also known as efficacy, this checks how well the medicine cures the disease, or how well it improves symptoms
- Dosage: how much of the drug an individual needs to take. This can vary and has to be closely controlled. Too high a concentration can be toxic and too low may not be effective.

Source: BBC Bitesize

Resource Six
Data Source

Active reading

There are three main stages of **testing** for new drugs:

1. Pre-clinical testing

The medicines are tested using **computer models** and **disease models**. A **disease model** is an animal or cells displaying all or some of the pathological processes that are observed in an actual human. Studying disease models aids understanding of how the disease develops and helps test potential treatment approaches.

First, the medicine is tested with live **cells** (*in vitro*) that are grown in a laboratory. This allows the **efficacy** and any potential **downstream effects** to be investigated. **Cell culture** models of disease have provided not only adaptability, but also huge reductions in experimental cost and time, compared with whole animal and tissue model systems. Cell culture is the only reproducible, ethical human model system there is. Therefore, it is of unprecedented importance in the study of human disease. Many substances fail this test because they damage cells or do not seem to work. Some commonly used cell lines include HeLa (cancerous), HEK293 (kidney) and Chinese Hamster Ovary Cells.

Glossary

In vivo – within an entire, living organism

In vitro – outside a living organism

Medicines that pass this first stage are then tested on **live animals** *(in vivo)*. A typical tests involves giving a known amount of the substance to the animals, then monitoring them carefully for any side effects. Many drugs fail here too, as the drug may not work the same way as it did *in vivo,* or the animal systems may just be too different.

Sources:

BBC Bitesize

Nebiolab.com

Resource Six
Data Source

2. Clinical Testing – healthy volunteers

Medicines that have passed pre-clinical testing are moved on to **clinical trials**. The first stage of human trials is using healthy volunteers. This determines if the drugs are safe.

3. Clinical Testing – volunteers with the illness

The second stage of clinical testing is where the medicine is tested on individuals with the illness to confirm that they are safe **and** that they are effective. Low doses of the drug are used initially, and after this is found to be safe, the dosage is increased until the optimal dosage is determined.

Finally, there are **long-term** human trials to determine if the medicine is effective over a long period of time, and that there are not more side effects.

Why are medicines so expensive?

Pharmaceutical or research companies must pay for staff and equipment while developing new medicines, which often result in no useful outcome. Even if the medicine does complete clinical trials, every new medicine must go through rigorous testing by the MHRA (Medicines and Healthcare products Regulatory Agency) to prove that the medicine is safe and effective. Only a very small percentage of potential new medicines complete these tests. Often the cost of a new medicine does not only reflect the cost of developing the final drug, but also the many drugs that failed before it. It can sometimes take 12-15 years for a new drug to get to market and can cost upwards of $1 billion.

Sources:

BBC Bitesize

Nebiolab.com

Resource Six
Data Source

Section C

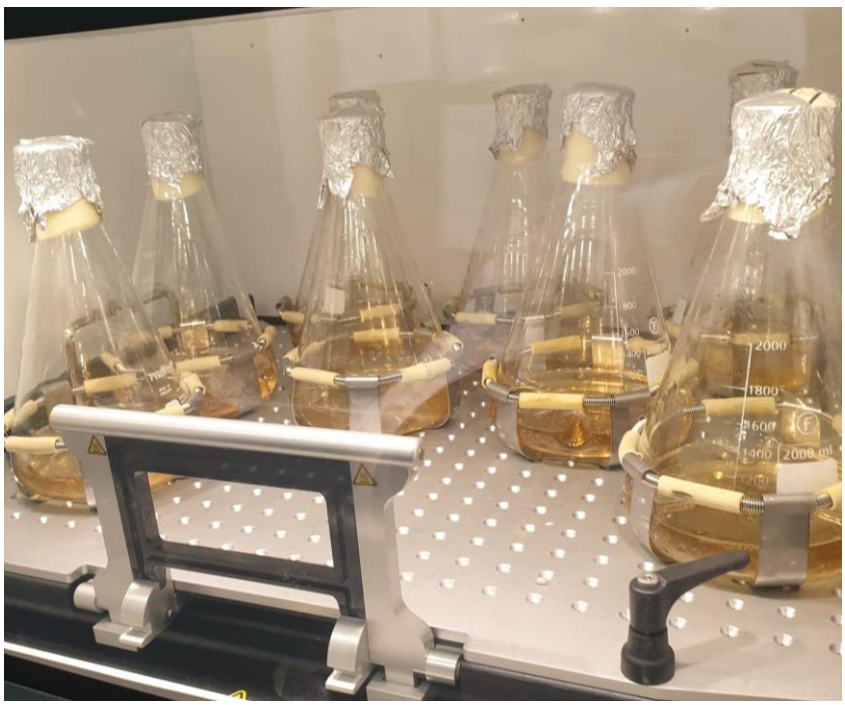
Modelling Disease

Until a medicine has been proved safe enough to trial in humans, they instead use various cell, plant, bacterial, fungal and animal species as model organisms for their research (Table 2). The use of models allows the researcher to closely control the conditions of the experiment, manipulating one **variable** while keeping others constant, then observing the consequences of that change. Model organisms can be manipulated to represent disease by altering the genome to over-express, under-express or completely knock out certain genes.

Figure 23

Flasks of *E. coli* used for protein production.

Source: Charlie Collingham



Resource Six
Data Source

Section C

Modelling Disease

Model Organism	Common Name	Research Applications
Immortal cell lines from Homo sapiens	HeLa	Used for research into cancer, AIDs, Polio, effects of radiation and toxic substances, gene mapping, etc
Escherichia coli	E. coli	Widely used for DNA manipulation and protein production
Saccharomyces cerevisiae	Yeast	Used for biological studies of cell processes (e.g. mitosis) and diseases (e.g. cancer)
Pisum sativum	Pea plant	Used to describe patterns of inheritance
Drosophila melanogaster	Fruit fly	Employed in a wide variety of studies including large scale mutant screens to identify genes related to specific biological functions
Caenorhabditis elgans	Roundworm (nematode)	Valuable for studying the development of simple nervous systems and the aging process
Danio rerio	Zebra fish	Used for mapping and identifying genes involved in organ development
Mus musculus	House mouse	Commonly used to study genetic principles in human disease
Rattus norvegicus	Brown rat	Commonly used to study genetic principles in human disease

Table source: Nature, (2008). The Use of Animal Models in Studying Genetic Disease. ...

Table 1: Models used to study genetic principles and human diseases.

Resource Six
Data Source

Section D

Eliminating Bias

It is important to eliminate **bias** from clinical trials, and there are different ways to do this. A **placebo** is used in most trials. Placebos look exactly like the trial medicine, but has no active ingredient in it. Alternatively, a '**control group**' is used if there is already medicine available. At the end of the trial, the placebo/control group and the treatment group are compared in order to determine if the trial treatment is an improvement.

When it comes to administering the medicine and documenting results and side effects, the doctors/researchers can be prevented from knowing who is being given what drug. Knowledge of which patient is in which group could affect the way symptoms are reported. In a **blind trial**, the person administrating the treatment knows which group the volunteer is in, but the patient does not. This is important when the medicine has potentially harmful side effects that need to be closely monitored. In a **double-blind trial** neither the patient or the medical staff know what group the patient is in. an **open-label trial** may be used if there is no way to hide which group is which. It may also be used if the patients are so unwell, they are likely to die without treatment.

Placebos are used to ensure that the drug is having an effect and that any changes are not due to the experimental trial process. For example, with major surgeries, the surgery itself could cause side effects. This can lead to the **placebo effect;** in which a patient believes they have had the real medicine and their body begins to display positive or negative effects.

Source: BBC Bitesize

Resource Six
Data Source

Section E

Why are drug trials so important?

Why we have such Rigorous Testing

It is extremely important for a drug to undergo laborious testing before it can be administered to the general public. The rules we have in place today have been shaped by cases in history where the procedures were not as stringent, and the outcomes were tragic.

Thalidomide Case Study

Thalidomide is a medical drug that entered the market in 1957 as an over the counter sleeping pill. It was advertised as "completely safe" for everyone, as its developers "could not find a dose high enough to kill a rat". It was also thought to be useful for easing morning sickness in pregnant women, so doctors began to prescribe it to their patients. However, it had never been tested in this way.

This resulted in **unexpected and serious damage** to unborn babies, as it was found to impair the development of unborn babies, especially if it had been taken in the first four to eight weeks of pregnancy. More than 10,000 babies were affected and were born with phocomelia, where their limbs were very short or incompletely formed.

As a consequence of this disaster, thalidomide was banned, and drug testing was made more demanding than before.

Source: BBC Bitesize

Resource Six Activities

Activities

1. In terms of disease therapy, explain why it is important to keep biodiversity in plants?

2. Sort the following stages of clinical testing into the correct order, and describe briefly why this stage is done:
    - Administering the drug to a small number of people with the illness – low dose
    - Administering the drug to healthy volunteers
    - Testing the drugs on live animals
    - Administering the drug to a small number of people with the illness – optimum dose
    - Testing the drugs on human cells grown in the lab
    - Computer modelling of drug interaction

Problem solving

3. Discuss the advantages and disadvantages of studying a disease on a human cell line, such as HeLa cells?
4. Define the following terms:
    - Bias
    - Open-label trial
    - Dosage
    - Placebo
    - Placebo effect
5. Consider why it takes approximately 12-15 years to approve a new drug.

Resource Six Activities

Activities

6. Discuss why is it so important to ensure proper testing has been performed on a drug before it goes to market.

7. Would it be better to discover a whole new drug or re-purpose an already used drug for a different disease? Justify your answer.

8. Contemplate the considerations that a researcher must have before choosing a disease model to study the effects their potential drug has on a particular disease.

Resource Six
Further Reading

Explore

- How Herception Works: https://vimeo.com/12434125
- Pandey, Abhay. (2020). "Drug Discovery and Development Process." *North East BioLab.* https://www.nebiolab.com/drug-discovery-and-development-process/
- Rehman, W., Arfons, L. M., & Lazarus, H. M. (2011). The rise, fall and subsequent triumph of thalidomide: lessons learned in drug development. *Therapeutic advances in hematology*, *2*(5), 291–308. https://doi.org/10.1177/2040620711413165
- Simmons, D. (2008) The use of animal models in studying genetic disease: transgenesis and induced mutation. *Nature Education* 1(1):70. https://www.nature.com/scitable/topicpage/the-use-of-animal-models-in-studying-855/

Final Reflection Activity

Deep Dive

BROUGHT TO YOU BY RBC ACCESS ED

You are part of a research group who have just discovered an important protein (called X) in the process of mitochondrial dysfunction, which you think would be a really good target for a new therapeutic drug for Parkinson's disease if you could find a drug that inhibits its action. So you screen Protein X and find a hit with a drug that is commonly used for liver disease (Drug Y). Use the information you have learnt to create a research proposal from initial tests, right up to clinical testing.

Structuring your proposal with the following sections:

- Title
- Introduction to the research
- Aim & Objectives of your research
- Study design and methods
- Issues that may arise

Consider the following:

- Roles of healthy mitochondria
- Mitochondrial dysfunction
- Mitochondria and disease
- Repurposing current drugs
- Appropriate cellular models
- Appropriate animal models
- Clinical trial design

Be as specific and detailed as possible using the help of the resources. Use further reading to explore the subject more. Explain the reasoning behind your choices.

Part 3 – Study Skills, Tips & Guidance

This section includes helpful tips to help you complete this pack, as well as improve your study skills for any courses you take next year.

It also includes a few fantastic easy-to-use resources to know what to do next if you are hoping to go to university in the next few years, like UCAS advice and web links to more academic opportunities.

In this section:

University Study Skills:

- ✓ Cornell Notes
- ✓ Key Instruction Words
- ✓ Academic Writing
- ✓ Referencing
- ✓ Evaluating Your Sources

University Guidance:

- ✓ What next?

Subject Guidance:

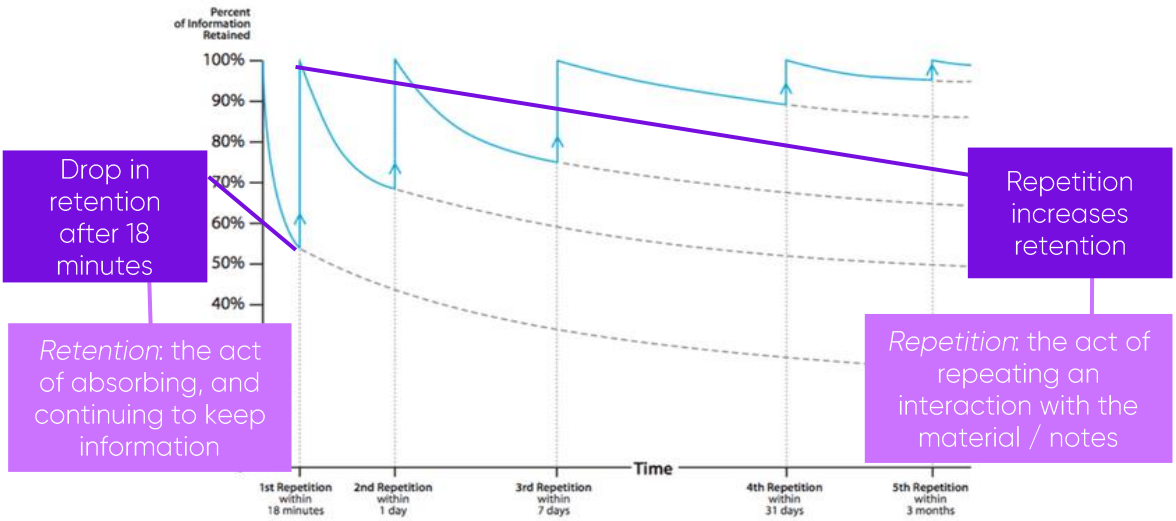
- ✓ More on studying your subject

University Study Skills
Cornell Notes

Why is good note taking important?

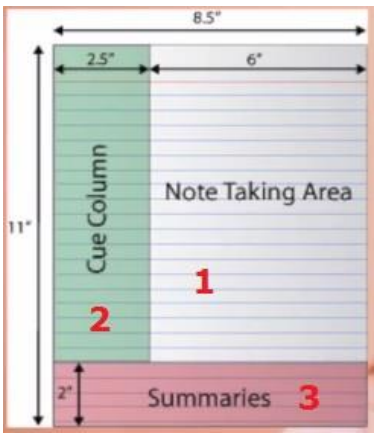
If it feels like you forget new information almost as quickly as you hear it, even if you write it down, that's because we tend to lose almost 40% of new information within the first 24 hours of first reading or hearing it.

If we take notes effectively, however, we can retain and retrieve almost 100% of the information we receive. Consider this graph on the rate of forgetting with study/repetition:



Learning a new system

The Cornell Note System was developed in the 1950s at the University of Cornell in the USA. The system includes interacting with your notes and is suitable for all subjects. There are three steps to the Cornell Note System.



Step 1: Note-Taking

1. Create Format: Notes are set up in the Cornell Way. This means creating 3 boxes like the ones on the left. You should put your name, date, and topic at the top of the page.

2. Write and Organise: You then take your notes in the 'note taking' area on the right side of the page. You should organise these notes by keeping a line or a space between 'chunks' /main ideas of information. You can also use bullet points for lists of information to help organise your notes.

University Study Skills
Cornell Notes

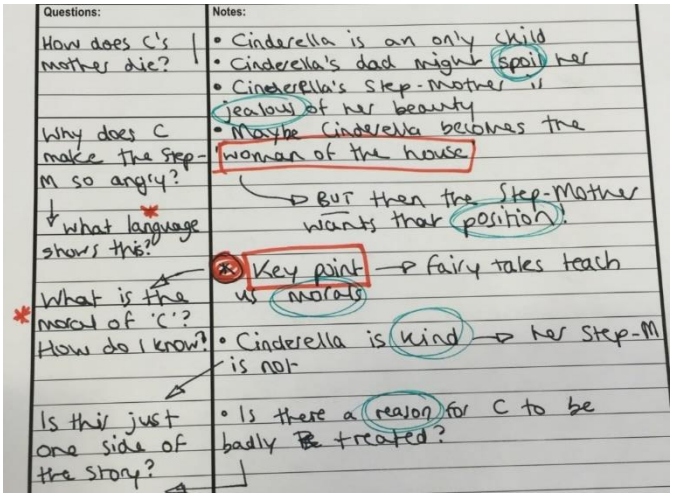
Step 2 Note-Making

1. Revise and Edit Notes: Go back to box 1, the note taking area and spend some time revising and editing. You can do this by: highlighting 'chunks' of information with a number or a colour; circling all key words in a different colour; highlighting main ideas; adding new information in another colour

2. Note Key Idea: Go to box 2 on the left hand side of the page and develop some questions about the main ideas in your notes. The questions should be 'high level'. This means they should encourage you to think deeper about the ideas. Example 'high level' questions would be:

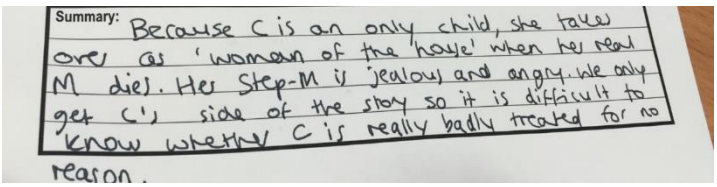
- Which is most important / significant reason for...
- To what extent...
- How does the (data / text / ideas) support the viewpoint?
- How do we know that...

Here is an example of step 1 and step 2 for notes on the story of Cinderella:



Step 3 Note-Interacting

1. Summary: Go to box 3 at the bottom of the page and summarise the main ideas in box 1 and answer the essential questions in box 2.



Give the Cornell Note Taking System a try and see if it works for you!

University Study Skills
Key Instruction Words

These words will often be used when university tutors set you essay questions- it is a good idea to carefully read instruction words before attempting to answer the question.

Analyse – When you analyse something you consider it carefully and in detail in order to understand and explain it. To analyse, identify the main parts or ideas of a subject and examine or interpret the connections between them.

Comment on – When you comment on a subject or the ideas in a subject, you say something that gives your opinion about it or an explanation for it.

Compare – To compare things means to point out the differences or similarities between them. A comparison essay would involve examining qualities/characteristics of a subject and emphasising the similarities and differences.

Contrast – When you contrast two subjects you show how they differ when compared with each other. A contrast essay should emphasise striking differences between two elements.

Compare and contrast – To write a compare and contrast essay you would examine the similarities and differences of two subjects.

Criticise – When you criticise you make judgments about a subject after thinking about it carefully and deeply. Express your judgement with respect to the correctness or merit of the factors under consideration. Give the results of your own analysis and discuss the limitations and contributions of the factors in question. Support your judgement with evidence.

Define – When you define something you show, describe, or state clearly what it is and what it is like, you can also say what its limits are. Do not include details but do include what distinguishes it from the other related things, sometimes by giving examples.

Describe – To describe in an essay requires you to give a detailed account of characteristics, properties or qualities of a subject.

Discuss – To discuss in an essay consider your subject from different points of view. Examine, analyse and present considerations for and against the problem or statement.

University Study Skills
Key Instruction Words

Con't

Evaluate – When you evaluate in an essay, decide on your subject's significance, value, or quality after carefully studying its good and bad features. Use authoritative (e.g. from established authors or theorists in the field) and, to some extent, personal appraisal of both contributions and limitations of the subject. Similar to **assess**.

Illustrate – If asked to illustrate in an essay, explain the points that you are making clearly by using examples, diagrams, statistics etc.

Interpret – In an essay that requires you to interpret, you should translate, solve, give examples, or comment upon the subject and evaluate it in terms of your judgement or reaction. Basically, give an explanation of what your subject means. Similar to **explain**.

Justify – When asked to justify a statement in an essay you should provide the reasons and grounds for the conclusions you draw from the statement. Present your evidence in a form that will convince your reader.

Outline – Outlining requires that you explain ideas, plans, or theories in a general way, without giving all the details. Organise and systematically describe the main points or general principles. Use essential supplementary material, but omit minor details.

Prove – When proving a statement, experiment or theory in an essay, you must confirm or verify it. You are expected to evaluate the material and present experimental evidence and/or logical argument.

Relate – To relate two things, you should state or claim the connection or link between them. Show the relationship by emphasising these connections and associations.

Review – When you review, critically examine, analyse and comment on the major points of a subject in an organised manner

University Study Skills
Academic Writing

What is academic writing?
'Academic writing' is a specific way of writing when communicating research or discussing an argument/point of view. It has a logical structure, and it uses formal language. There is a particular tone, 'voice' and style to the language. Unlike creative or narrative writing, academic writing will also use different sources of information to support what is being said.

The language of academic writing: do's and don'ts

- Do use words you know the meaning of and are confident using, it doesn't have to be complicated to be clear!
- Do not use contractions; don't, can't, doesn't, it'd. Do write out fully; do not, cannot, does not, it would.
- Do not use colloquialisms- this is 'writing as you speak'. Examples include misuse of the words 'literally' or 'basically', common phrases, such 'like chalk and cheese'.
- Do not use slang or jargon. For example, 'awks', 'lit', 'woke'.

Expressing your opinion in academic writing
In academic writing, it is best practice to express an opinion without writing in the first person, which can often be challenging. Always bear in mind that your work should read like a voice that is guided by the evidence and not basic personal intuition.

Therefore, rather than saying 'In my opinion, this proves that', you can express the outcome of your reasoning in other ways:

- 'This indicates that…';
- 'The aforementioned problems in Smith's argument reveal that…';
- 'Such weaknesses ultimately mean that…', and so on.

Signposting
Signposting guides your reader through different sections of your writing. It lets those who read your writing know what is being discussed and why, and when your piece is shifting from one part to another. This is crucial to for clear communication with your audience.

Signposting stems for a paragraph which expands upon a previous idea	Signposting stems for a paragraph which offers a contrasting view
Building on from the idea that … (mention previous idea), this section illustrates that … (introduce your new idea).	However, another angle on this debate suggests that … (introduce your contrasting idea)
To further understand the role of …(your topic or your previous idea) this section explores the idea that … (introduce your new idea)	In contrast to evidence which presents the view that … (mention your previous idea) an alternative perspective illustrates that …
Another line of thought on … (your topic or your previous idea) demonstrates that …	However, not all research shows that … (mention your previous idea). Some evidence agrees that …

University Study Skills
Referencing

What is a reference or referencing?

A reference is just a note in your assignment that tells your reader where particular ideas, information or opinions that you have used from another source has come from. It can be done through 'citations' or a 'bibliography'.

When you get to university, you will need to include references in the assignments that you write. As well as being academic good practice, referencing is very important, because it will help you to avoid plagiarism.

Plagiarism is when you take someone else's work or ideas and pass them off as your own. **Whether plagiarism is deliberate or accidental, the consequences can be severe.** You must be careful to reference your sources correctly.

Why should I reference?

Referencing is important in your work for the following reasons:

- It gives credit to the authors of any sources you have referred to or been influenced by.
- It supports the arguments you make in your assignments.
- It demonstrates the variety of sources you have used.
- It helps to prevent you losing marks, or failing, due to plagiarism.

When should I use a reference?

You should use a reference when you:

- Quote directly from another source.
- Summarise or rephrase another piece of work.
- Include a specific statistic or fact from a source.

University Study Skills
Referencing

Is it a source worth citing?

Question your sources before referencing using these tips:

Currency: the timelines of the information

- When was it published or posted? Has it been revised or updated? Does your topic require current information, or will older sources work as well?

Relevancy: the importance of the information for your needs

- Does the information relate to your topic or answer your question? Who is the intended audience? Have you looked at a variety of sources?

Authority: the source of the information

- Who is the author/publisher/source/sponsor? What are the author's credentials? Is the author qualified to write on the topic?

Accuracy: the reliability and correctness of the source

- Is the information supported by evidence? Has the information been reviewed or refereed? Can you verify whether it is a personal or professional source? Are there errors?

Purpose: the reason the information exists

- Does the author make the intensions/ purpose clear? Is the information fact opinion or propaganda? Are there are biases? Does the viewpoint appear objective?

University Study Skills
Referencing

How do I reference?

- There are a number of different ways of referencing, but most universities use what is called the Harvard Referencing Style. Speak with your tutor about which style they want you to use, because the most important thing is you remain consistent!

- The two main aspects of referencing you need to be aware of are:

1. In-text citations

- These are used when directly quoting a source. They are located in the body of the work, after you have referred to your source in your writing. They contain the surname of the author of the source and the year it was published in brackets.
    - E.g. *Daisy describes her hopes for her infant daughter, stating "I hope she'll be a fool—that's the best thing a girl can be in this world, a beautiful little fool."* ***(Fitzgerald, 2004)***.

2. Bibliography

- This is a list of all the sources you have referenced in your assignment. In the bibliography, you list your references by the numbers you have used and include as much information as you have about the reference. The list below gives what should be included for different sources.

- Websites – Author (if possible), *title of the web page*, 'Available at:' website address, [Accessed: date you accessed it].
    - E.g. *'How did so many soldiers survive the trenches?'*, Available at: http://www.bbc.co.uk/guides/z3kgjxs#zg2dtfr [Accessed: 11 July 2019].

- Books – Author surname, author first initial, (year published), *title of book*, publisher
    - E.g. Dubner S. and Levitt, S., (2007) *Freakonomics: A Rogue Economist Explores the Hidden Side of Everything,* Penguin Books

- Articles – Author, *'title of the article'*, where the article comes from (newspaper, journal etc.), date of the article.
    - E.g. Maev Kennedy, *'The lights to go out across the UK to mark First World War's centenary'*, The Guardian Newspaper, 10 July 2014.

University Study Skills
Evaluating your sources

Knowing about the different types of sources and what makes them worth using is important for academic work.

When doing research you will come across a lot of information from different types of sources. How do you decide which source to use? From newspaper articles to books to tweets, this provides a brief description of each type of source, and breaks down the factors to consider when selecting a source.

A platform for millions of very short messages on a variety of topics.

Blogs (e.g. Tumbler) are an avenue for sharing both developed and unpublished ideas and interests with a niche community.

A collection of millions of educational, inspirational, eye-opening and entertaining videos.

A reporting and recording of cultural and political happenings that keeps the general public informed. Opinions and public commentaries can also be included.

A collection of analytics reports that outline the objectives, background, methods, results and limitations of new research written for and by scholars in a niche field.

The information presented is supported by clearly identified sources. Sometimes each chapter has a different author.

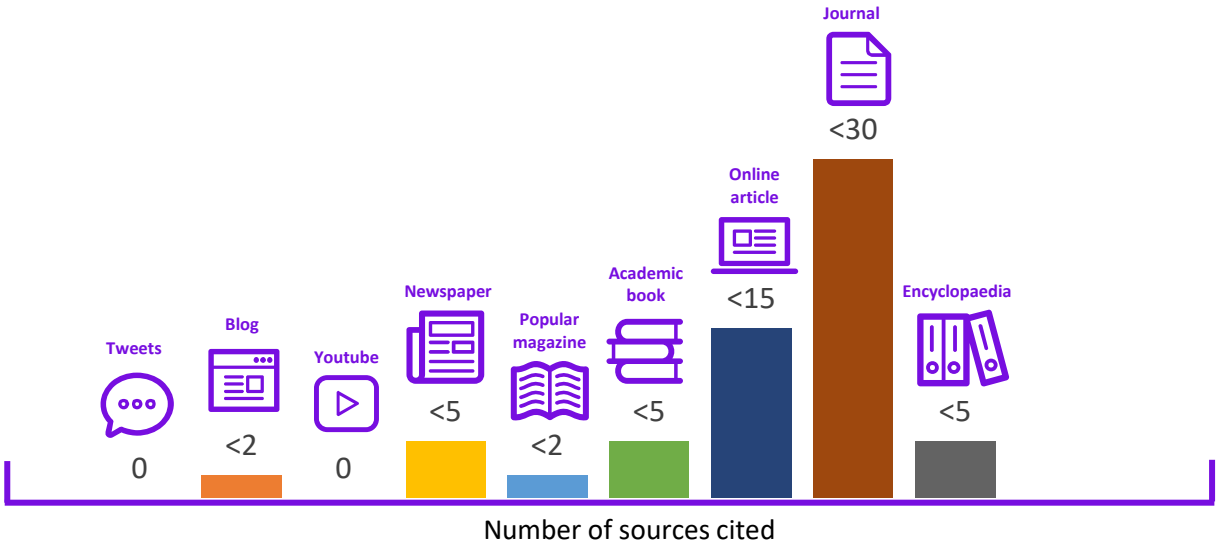
Books or online – giving information on many different subjects. Some are intended as an entry point into research, some provide detailed information and onwards references.

A glossy compilation of stories with unique themes intended for specific interests.

University Study Skills
Evaluating your sources

Number of outside sources

When an author used many outside sources into their writing, they demonstrate familiarity with ideas beyond their own. As more unique viewpoints are pulled into a source, it becomes more comprehensive and reliable. This shows the typical number of outside sources used in each publication.



Degree of review before a source is published

Two factors contribute to the amount of inspection that a source receives before it might be published: the number of reviewers fact-checking the written ideas, and the total time spent by reviewers as they fact-check. The more people involved in the review process and the longer the review process takes, the more credible the source is likely to be.

Number of reviewers	0 reviewers		
Time in review	seconds	minutes	minutes
	1-2 reviewers		
	hours	days	days
	3-4 reviewers		
	2-3 months	6-2 months	3-5 years

University Guidance
What next?

University Guidance

Different people go to university for different reasons. You might have a particular job in mind or just want to study a subject you are passionate about. Whatever your motivations, going to university can help improve your career prospects, as well as develop your confidence, independence and academic skills.

Choosing a course and university

Choosing the right course to study is an important decision so make sure you take time to research the different options available to you. Here are some top tips:

- ✓ You don't have to choose a course which you have already studied, there are lots of courses which don't require prior knowledge of the subject. You can apply skills gained from school studies to a new field.
- ✓ The same subject can be taught very differently depending on the course and university you choose. Take a look at university websites to find out more about the course content, teaching styles and assessment types.
- ✓ When choosing a university, think about what other factors are important to you. Do you want to study at a campus university or be based in a city centre? What accommodation options are there? Does the university have facilities for any extracurricular activities you're involved in?
- ✓ To research your options, have a look at university prospectuses and websites, as well as seeing if there are opportunities to speak to current students who can give you a real insight in to what life is like there.

Insight into: University of Reading

The author of this coursebook attends the University of Reading.

The University of Reading runs a large number of sessions to help find out more about the process of applying to university as well as taster sessions and Open Online Courses in a number of different subjects. To find out more, visit: www.reading.ac.uk/virtual-events.

Chat to current University of Reading students via Unibuddy and get their views on what university life is like!

University Guidance
What next?

Exploring Careers and Subject Options

- ✓ Find job descriptions, salaries and hours, routes into different careers, and more at https://www.startprofile.com/
- ✓ Research career and study choices, and see videos of those who have pursued various routes at http://www.careerpilot.org.uk/
- ✓ See videos about what it's like to work in different jobs and for different organisations at https://www.careersbox.co.uk/
- ✓ Find out what different degrees could lead to, how to choose the right course for you, and how to apply for courses and student finance at https://www.prospects.ac.uk/
- ✓ Explore job descriptions and career options, and contact careers advisers at https://nationalcareersservice.direct.gov.uk/
- ✓ Discover which subjects and qualifications (not just A levels) lead to different degrees, and what careers these degrees can lead to, at http://www.russellgroup.ac.uk/media/5457/informed-choices-2016.pdf

Comparing Universities

Use our platform ThinkUni.org to take a short quiz about your preferences and interests to find out which universities might be a great fit for you.

Other popular resources:

- ✓ https://www.ucas.com/
- ✓ https://www.whatuni.com/
- ✓ http://unistats.direct.gov.uk/
- ✓ https://www.thecompleteuniversityguide.co.uk/
- ✓ https://www.opendays.com/

University Guidance
What next?

UCAS and the university application process

All applications for UK degree programmes are made through UCAS. There is lots of information on the UCAS website to guide you through the process and what you need to do at each stage.

Apply

- Applications **open in September** the year before you plan to start university.
- You can apply for up to **five courses.**
- The deadline for most courses is **15 January**, though there is an earlier deadline of **15 October** for Oxford and Cambridge, medicine, veterinary medicine/science and dentistry.

Decisions

- Some courses may require an interview, portfolio or admissions test in addition to UCAS application. Check individual university websites details.
- Check UCAS Track which will be updated with decisions from the universities you have applied for and to see your deadline for replying to any offers.
- You should choose a firm (or first) choice university and an insurance choice. If you already have your exam results or a university thinks your application is particularly strong, you might receive an **unconditional offer**.

Results

- If you're holding a conditional offer then you will need to wait until you receive your exam results to have your place confirmed.
- Clearing & Adjustment allows you to apply to courses which still have vacancies if you didn't meet the conditions of your offer, have changed your mind about what or where you want to study, or have met and exceeded the conditions of your offer and would like to look at alternate options.

Personal statements

A really important part of your application is the personal statement. The personal statement gives you the opportunity to tell universities why they should offer you a place.

Here a few top tips for making your personal statement stand out:

- You can only submit one personal statement so it's important that you are consistent in your course choices. Make sure you have done your research to show your understanding of the subject area and passion for it.
- Start by brainstorming all your skills, experience and attributes. Once you have everything written down, you can begin to be selective – you only have 47 lines so won't be able to include everything.
- The ABC method: action, benefit and course can be a useful way to help demonstrate your relevant experience and how it applies to the course you're applying for.

University Guidance
What next?

Personal Statement do's and don'ts

Read the tips below from real life professors and admissions staff in university Biology and Psychology departments, on the 'do's' and 'don'ts' of what to include in your personal statement:

Biology

- Tell us why you want to study Biology
- What area of Biology fascinates you? I.e. ecosystems
- Demonstrate your interest by telling us what you have recently read, watched or listened to and how they helped your understanding of Biology
- What activities or practical work have you completed which helped to develop your lab-based skills?
- Describe how your school or individual work has equipped you with the necessary knowledge and ability to be a successful Biology student.

Further useful resources

Be sure you know what you'll need to do to apply to university in the UK:

- ✓ Key dates and deadlines: www.access-ed.ngo/timelines-for-applying-to-university
- ✓ Get tutor advice on writing a UCAS personal statement at www.access-ed.ngo/writing-your-ucas-personal-statement
- ✓ An easy template to start practising your personal statement: https://www.ucas.com/sites/default/files/ucas-personal-statement-worksheet.pdf
- ✓ Untangle UCAS terminology at https://www.ucas.com/corporate/about-us/who-we-are/ucas-terms-explained
- ✓ Discover more about the application process including when to apply and how to fill in your application on the UCAS website.
- ✓ Read more useful advice about what to include in your personal statement on UCAS, the Complete University Guide and The Student Room.
- ✓ Attend one of our virtual sessions to find out more about applying and personal statements.

More on studying this subject

A Deeper Look Into Biology

- ✓ **Read:** Science News for Students, an online publication bringing topical science news to students https://www.sciencenewsforstudents.org/
- ✓ **Read:** Books about science, such as "The Immortal Life of Henrietta Lacks" by Rebecca Skloot.
- ✓ **Read:** A science magazine such as "The New Scientist" https://www.newscientist.com/
- ✓ **Watch:** Scientific TED Talks, such as "A groundbreaking way to stop mitochondrial disease" https://www.youtube.com/watch?v=pc7MyUs_ORQ
- ✓ **Listen:** to the podcast "Tumble, A Science Podcast for Kids" available on most streaming services. A science podcast for the whole family about different science discoveries https://www.sciencepodcastforkids.com/
- ✓ **Listen:** to the podcast "The Infinite Monkey Cage" available on most streaming services. A comedy podcast about various scientific subjects hosted by Brian Cox and Robin Ince https://www.bbc.co.uk/programmes/b00snr0w/episodes/downloads
- ✓ **Do**: Experiments at home https://sciencebob.com/category/experiments/

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