BACKGROUND TO ACTIVITY

Function Finders is a paper-based activity that demonstrates the concept of genes encoding proteins. Students translate DNA sequences into amino acid chains and use this information to search their booklet for a protein that contains that sequence.

The activity can be used as a basis to discuss the role of proteins in the human body and other organisms, and the different functions they serve.

Estimated duration: 20 – 35 minutes depending on level of discussion

MATERIALS TO RUN THE ACTIVITY

- Student worksheets
- Protein Profile booklet
- Codon Wheel sheets
- Function Finders presentation files

Optional animations (recommended for AS Level)
DNA to protein animation: www.yourgenome.org/video/from-dna-to-protein

Optional activity: View the proteins in 3D
Rasmol (available from www.rasmol.org) is a molecular modelling software that can be used to view the protein structures in 3D. This can be used either as a demonstration by the teacher as part of the discussion or by the students to view the proteins they have identified. It can lead to discussion about the tertiary structure of proteins, however it is not essential for completing the activity.

ACTIVITY PREPARATION

The following components need to be prepared before the activity commences.

1. Protein Profile booklet

Print out the protein sheets. It is recommended that the sheets are laminated to prevent damage, however this is not essential. Ring bind the sheets to create a booklet or attach them together using treasury tags.

Working in pairs, students require:
- One Function Finders worksheet
- One Protein Profile booklet
- One Codon Wheel sheet

We recommend working in pairs, however the activity can be run in small groups if preferred.

OPTIONAL ACTIVITY PREPARATION

1. Download Rasmol program (optional)

If you wish to use the Rasmol program to view the protein structures, download the program from www.rasmol.org and select "Latest windows installer" at the top of the page.

2. Save protein files

If you plan to use the Rasmol program, ensure you have the protein files saved in an accessible folder or on the desktop. The protein files are downloadable from the Function Finders activity page on www.yourgenome.org/activities/function-finders.

POWERPOINT PRESENTATION

In this powerpoint, you'll find two ways to access the answers: one short version that summarises the exercise answers in tabular form or a longer version which deals which each protein in turn. The longer version allows for class discussion about the role of these proteins and their relevance to our lives.

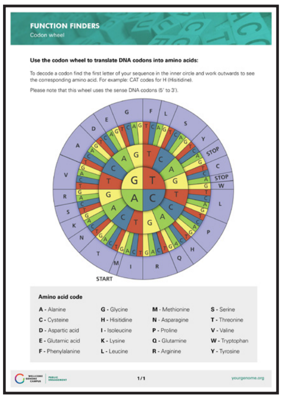
INSTRUCTIONS FOR RUNNING THE ACTIVITY

Introducing the Codon Wheel

Slide 2 of the Function Finders presentation demonstrates how to use the Codon Wheel (shown right).

The Codon Wheel is central to the activity as it enables students to translate the DNA sequence into amino acids.

To use the wheel students should work from the inside circle out to the outer circle. For example, if the first triplet of the sequence is CAT, the amino acid it codes for is Histidine (H).

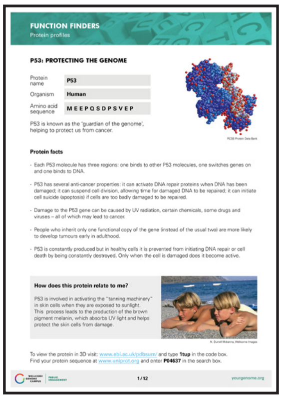


The Codon Wheel.

Completing the worksheet

The worksheet has 10 different DNA sequences that the students translate into sequences of 12 amino acid letters. This is the amino acid sequence featured on each protein profile in the booklet.

Once the students have completed their translations they find the corresponding proteins by cross referencing their amino acid sequence with those on the protein profiles. It is important to stress that this is not the entire amino acid sequence, but a subset that we can use to search online databases.



Example of a protein profile.

Before the students start the activity it is recommended that you use the following examples:

- Translate the following sequence:
  atg gag gag ccg cag tca gat cct agc gtc gag ccg

  Amino acid sequence: MEEPQSDPSVEP

- Translate the following sequence:
  atg gag ttt act ttg agg caa gag gct tta gtt aat

  Amino acid sequence: MEFTLRQEALVN

Look through the Protein Profile booklet to fnd a matching amino acid sequence.

When the students find the matching sequence, they should complete the additional sections on the sheet - that is the protein name and a description of its function.

DISCUSSING THE ANSWERS

Depending on which part of the presentation you have chosen, you can discuss the results and individual proteins with the group.

In the short version the correct answers are presented in a table on slides 3 and 4. Each answer is animated so can be revealed by clicking the mouse or pressing the cursor keys. The answer table can be used to encourage participation by asking students to feed back their results to the rest of the class.

As you reveal the answers you can encourage the students to discuss the role and relevance of the proteins. Overleaf are a few discussion points for each protein to assist you. Weblinks are provided that offer additional sources of information for your reference.

In the longer presentation each protein has its own slide with picture, description and discussion questions.

DISCUSSION POINTS

The section below provides some additional information on the proteins to encourage a group discussion on the role and relevance of the different proteins.

1. Antifreeze Protein type III

The Antifreeze protein (AFP) is essential to prevent organisms like the wolf fish from freezing in extremely cold conditions.

Q. Is this just exclusive to this one species / what other species may use AFPs?

AFPs are also found in some species of plants, bacteria and invertebrates, such as the Snow flea.

Q. How can this protein be relevant to us?

Understanding the structure and function of AFPs can help improve the preservation of donor organs. Currently it is not possible to freeze organs harvested for transplant operations as the freezing process irreversibly damages the tissue. However scientists are studying AFPs to see if they can be used to successfully freeze, thaw and transplant organs such as hearts and kidneys.
www.the-scientist.com/?articles.view/articleNo/34190/title/Icing-Organs/

Antifreeze proteins also have applications in food science, for example preventing ice crystallisation in ice cream, creating smoother creamier ice cream.
www.phys.org/news/2008-01-edible-antifreeze-unwanted-ice-crystals.html

2. Green Fluorescent Protein (GFP)

Green fluorescent proteins are used to communicate by organisms such as jellyfish (*Aequorea victoria*). It can also be used as a reporter gene to identify if genetic modification has been successful or to see where in an organism a particular protein is being produced. Other fluorescent proteins exist and are used as reporter genes.
www.newscientist.com/article/dn17003-fluorescent-puppy-is-worlds-first-transgenic-dog/

Q. Why is this protein relevant to us?

Reporter genes such as GFP are important for development studies. GFPs can be used to track proteins in developing embryos to get a better understanding of the location and function of the protein products of specific genes.

The image in the PowerPoint shows one day old zebrafish embryos that express green fluorescent protein in the muscle precursor cells (myotomes).

3. Luciferase

Luciferase is a protein used by fireflies to attract a mate. Luciferase catalyses a chemical reaction where chemical energy is converted to light energy. This process of light production by a living organism is called bioluminescence.

Q. What organisms use bioluminescence

A range of organisms use bioluminescence including plankton, fungi, bacteria and insects, such as fireflies and glow worms.

Q. Why is this protein relevant to us?

Like GFPs, luciferase systems are widely used as reporter genes in molecular biology techniques used in the lab.

4. Odorant receptor protein 1 (OR1)

Odorant receptor protein 1 enables *Anopheles* mosquitoes to identify human sweat and find a source of a blood meal.

Odorant receptor proteins allow organisms to detect chemical compounds in their local environment, which can help them locate and identify food or a potential mate. There are a wide range of different odorant receptors, with as many as 1,000 odorant receptor genes in the human genome. Not all of these genes are expressed or produce a functional protein.

Q. Why is this protein relevant?

Malaria is a major global disease killing around one million people every year, mostly children under the age of 5 years old. Understanding this protein and the odour compound it recognises could be used to develop solutions to help with the battle against the disease.

For example, creating a mosquito repellent that blocks the odorant receptors, preventing the mosquito from smelling and biting humans.
www.cell.com/current-biology/abstract/S0960-9822%2807%2901780-0

5. HER2

HER2 is a cell membrane surface-bound receptor normally involved in the signal transduction pathways leading to cell growth and differentiation. It acts as a molecular switch, which can turn pathways influencing cell division and growth on and off.

Q. Why is it relevant to us?

HER2 is associated with breast cancers in which the *HER2* gene is over-expressed, giving the cell more HER2 protein receptors and leading to increased and uncontrolled cell growth.

Understanding the role of the gene and the protein in uncontrolled cell growth aids diagnosis and treatment of cancers involving the altered gene. Herceptin is an anti-cancer drug that specifically targets HER2 receptors and can be highly effective where mutations in *HER2* are present. Research programmes such as the Cancer Genome Project at the Wellcome Trust Sanger Institute are identifying and cataloguing mutations such as those found in *HER2*. This type of data can be used to inform the design of clinical trials of new cancer drugs.
www.sanger.ac.uk/news/view/2008-12-23-a-new-search-for-cancer-treatments

6. Alpha-bungarotoxin

Alpha-bungarotoxin is a component in the venom of a type of snake called the Taiwanese banded krait (*Bungarus multicinctus*). Alpha-bungarotoxin binds irreversibly to the receptor of the neurotransmitter acetylcholine in the victim, causing paralysis, respiratory failure and death.

Q. Why is this protein relevant?

Understanding how the alpha-bungarotoxin protein works helps in the development of antivenoms that can save many lives. It can also have other uses in the medical field. The blocking effect of alpha-bungarotoxin on acetylcholine receptors in the brain is being investigated as a way of altering nervous activity in schizophrenia and epilepsy.

7. Histone H2B

Histone proteins play an important role in the packaging of DNA in chromosomes within cells. DNA wraps around histone proteins to form coils, which significantly reduces the space required in the nucleus to store DNA. If you imagine the DNA-histone complex as a reel of cotton, the histone protein is the reel around which the DNA 'cotton' is wrapped.

Q. Why is this protein relevant to us?

Histone proteins are essential to life. When histone proteins like H2B are removed from yeast cells they die. Not only do histone proteins give structure to our chromosomes but they have an important role in controlling the expression of genes. Modifications to histone proteins affect how tightly or loosely wrapped the DNA is and consequently whether genes are expressed or not. Heterochromatin is a tightly packed form of DNA which means the transcription machinery cannot get to the DNA and the genes cannot be expressed. They are silenced.

Modifications to histones are associated with the development of some cancers, including leukaemias, breast cancers and ovarian cancers.
www.ncbi.nlm.nih.gov/pmc/articles/PMC1949974/pdf/11055583.pdf

8. Mucin-1

Mucins are proteins that form protective films on the surfaces of cells. This protein is anchored to the apical surface (the outward facing or exposed surface) of the epithelial cells which line cavities throughout the body. It serves a protective function by providing a physical barrier to pathogens that could damage the cells.

Q. Why is this protein relevant?

Excessive levels of mucins can be associated with breast and ovarian cancers, because mucins can reduce the amount of P53 protein produced. P53 slows cell growth and division, so lower levels result in cells dividing more rapidly, which can lead to cancer.
www.nature.com/nrc/journal/v4/n1/execsumm/nrc1251.html

9. Caspase 1

Caspase 1 is an enzyme that destroys proteins in cells leading to programmed cell death (apoptosis).

Q. Why is this protein relevant?

For us to develop correctly some of our cells must die. One example is during the formation of our fingers and toes where the cells that make up the tissues between the digits die. The image on slide 23 of the PowerPoint presentation shows a light microscope image of the developing foot of a mouse embryo showing areas of dying cells between the digits. The limb starts off as a paddle shape, but programmed cell death (apoptosis) occurs in the areas between where the digits will form. The dead cells are removed by scavenging cells called macrophages (stained green).

10. Myosin 1

Myosin is a key protein found in muscle fibres and is essential for making muscles move.

Q. Why is this relevant to us?

Without myosin we couldn't move. It is attached to the end of the muscle fibres and makes them contract by binding to, and pulling on, another protein called actin. This pulling mechanism is powered by energy generated from the breakdown of a molecule called adenosine triphophate (ATP).

Myosin molecules generate force in skeletal muscle through a "power stroke" mechanism fuelled by the energy released from ATP hydrolysis. The "power stroke" occurs at the release of the products of ATP hydrolysis – ADP and phosphate – when myosin is tightly bound to actin. The effect of this release is a conformational change in the molecule that pulls against the actin. The combined effect of the "power strokes" throughout muscle fibres causes the muscle to contract. The "power stroke" can be likened to watching a rowing boat from above with the myosin molecules moving forward and back causing the muscle to move.

OPTIONAL EXTRA: MODEL THE PROTEIN USING RASMOL

Use of the Rasmol software provides another way of exploring the protein structure.

The file names for the proteins featured in the activity can be found on the Rasmol reference sheet.

If used as a demonstration tool only, it is recommended that all of these steps are completed prior to the session so you can click on your protein of choice:

1. Open Rasmol
2. Click 'File' 'Open…' and select the file you want

Rasmol controls

- **Zoom in and out:**
  Hold down 'Shift', 'Alt' & the left mouse button. Slide the mouse forwards and back.
- **To centre the structure in the window:**
  Hold down the right mouse button and move the mouse.
- **To rotate the structure:**
  Hold down the left mouse button and move the mouse.