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Genetic
Disorders
UK

TEACHER'S NOTES

TOXIC TANGLES

OVERVIEW

Aimed at **key stage 4** pupils. This is a hands-on activity to help pupils understand how a change in a protein causes Huntington's disease (HD).

LEARNING OBJECTIVES

- To understand that proteins are made from a linear string of building blocks called amino acids
- To understand that the shape of a protein is crucial to how it works
- To understand that in HD the shape of the HTT protein is altered, which leads to cell death and the symptoms of HD

CURRICULUM LINKS

- KS4:** The ways in which organisms function are related to the genes in their cells
- KS4:** Human health is affected by a range of environmental and inherited factors, by the use and misuse of drugs and by medical treatments

Activity

- Introduce the genetic condition - Huntington's disease
- Show the film Luke's story on www.genesareus.org
- Ask the pupils to read the worksheet and answer Q1-5
- Lead the class through building models of proteins with beads and elastic. This is a simple model to mimic the HTT protein in Huntington's disease.
- Provide pupils with one piece of elastic (just long enough to hold 25 coloured beads) and 30 beads
- Instruct pupils to tie the first bead on to the bottom of the elastic to secure it and then add the other 24 beads in any order
- Tie off the elastic at the other end and place it in a 'U' shape – the elastic should be relaxed enough to allow it to stay in this shape on the desk. This is the desired curved shape they are trying to achieve.
- Ask them to draw the shape of this protein model; explain that this shape is essential for the protein to function properly
- Instruct the pupils to untie the knot and try to add some additional beads; they should stretch the elastic and try to add as many beads as possible (while still being able to tie the beads off at the end)
- Finally, they need to see whether the 'protein' will stay in its 'correct' curved shape; the elastic will not be very flexible once it is stretched and it is unlikely to stay in the desired 'U' shape
- Ask them to draw the shape of the longer protein

you will NEED

- 30 beads per pupil(or pair of pupils)
 - 1 piece of elastic per pupil(or per pair of pupils)
- Each piece of elastic should be the same length (approximately 25cm) and just long enough to accommodate 25 beads, including a little extra for tying off

PREPARATION

- Ensure that it is possible to comfortably fit 25 beads on the length of elastic and tie a knot at either end. If not, use a longer piece of elastic.

ANSWERS

1. Fill in the table below

Name	Is it a protein?	What does it do?
Insulin	Yes	Helps to regulate blood sugar levels
Glucose	No	Gives us energy
Keratin	Yes	It's an important part of our nails and hair
Collagen	Yes	It helps connect tissues together inside the body
Amylase	Yes	It's an enzyme that breaks down complex sugars (like starch) into simple sugars (like glucose)
DNA	No	Carries the information to help organisms grow, develop and work
Melanin	Yes	Protects our skin against harmful UV rays from the sun
Antibodies	Yes	Part of our immune system and helps fight disease

2. Explain why changes in the shape of the HTT protein can cause problems?

The shape of proteins is crucial to their working properly – misshapen (or 'misfolded') proteins often don't work as they usually would, which is problematic. In HD, misshapen HTT protein clumps together to form inclusions, further reducing its ability to do its usual job. These inclusions cause problems for the neurons and ultimately many of these neurons die, which causes the symptoms of HD.

3. What is the name for different versions of the same gene?

c) alleles

4. The allele that causes HD is...

a) dominant

5. What is the risk of someone affected by HD passing this condition onto their children?

a) 50%

FURTHER information

The website created by The Huntington's Disease Youth Organization is fantastic and provides extensive information on the condition in a style suitable for teenagers <http://en.hdyo.org/you>

There are various websites that cover genes and protein synthesis, but they tend to do so at a slightly higher level, including transcription and mRNA. However, the University of Utah has particularly good online learning tools for genetics: <http://learn.genetics.utah.edu/>

FOR MORE RESOURCES GO TO WWW.GENESAREUS.ORG

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TOXIC TANGLES

Huntington's disease (HD) is caused by a change in a single gene. But what is the change and why does it have such a dramatic and serious effect?

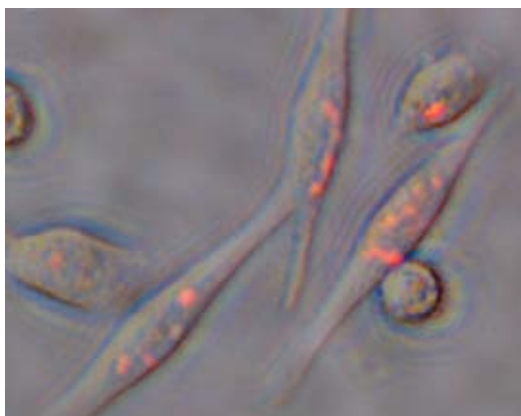
Genes are short sections of DNA. Usually, they are an instruction set for how to make a special type of chemical called a protein. Proteins are the chemicals in your body that 'do things' – your muscles are full of proteins called actin and myosin; the colour of your skin is determined by how much melanin you have; your hair and nails are made of keratin, and how much sugar is in your blood is partly regulated by insulin.

Proteins are made out of subunits called amino acids. Proteins are very complex molecules – initially the amino acids simply join up in a line, one after the other, but then they fold up to form a structured 3D shape. The final 3D shape of a protein is vital to how it works – if a protein is not folded correctly it won't work properly.

Even a very simple protein, such as insulin, still has 110 amino acids in it; haemoglobin, a more complex protein, has 574, and titin (a protein found in muscles and the largest human protein) has an incredible 34,350 amino acids!

1 Fill in the gaps in the table below

Name	Is it a protein?	What does it do?
Insulin	Yes	Helps to regulate blood sugar levels
Glucose		Gives us energy
	Yes	It's an important part of our nails and hair
Collagen		It helps connect tissues together inside the body
Amylase		
DNA		Carries the information to help organisms grow, develop and work
		Protects our skin against harmful UV rays from the sun
Antibodies		Part of our immune system and helps fight disease



Cells (not neurons) grown in a laboratory and containing clumps of a misfolded protein (glowing red.) In healthy cells, the red colour would be spread evenly throughout the cell.

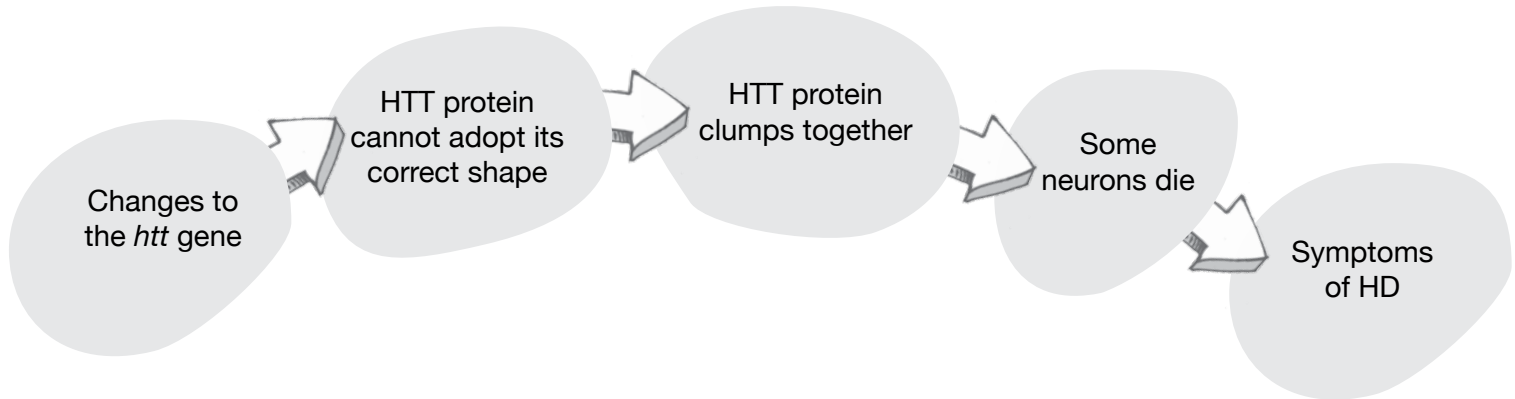
HD is caused by a change in the *huntingtin* gene, which is normally just written as *htt*. The *htt* gene makes the HTT protein. It is important to remember that we all have the *htt* gene – in fact, studies in mice have shown that if the *htt* gene is removed altogether, mice die before they are even born.

One part of the *htt* gene varies in length and when it is too long the HTT protein becomes misshapen.

Misshapen HTT proteins have a tendency to stick to other misshapen HTT proteins, forming large clumps called 'inclusions' inside a cell. These inclusions cause problems for nerve cells (neurons) and ultimately many neurons with inclusions made of the changed HTT protein die.

TOXIC TANGLES

The consequences of a longer *htt* gene



When neurons die, the brain is gradually affected and eventually it can no longer work properly. Specific areas of the brain are affected. This damage leads to the mental, physical and emotional changes associated with HD.

2 Explain why changes in the shape of the HTT protein can cause problems?

It's really important to remember that we get two copies of each of our genes – one from our mother and one from our father. People with HD nearly always have a 'healthy' version of the *htt* gene and a changed version that produces the changed HTT protein. People with HD will have a mixture of both the healthy HTT protein and the changed version, but just the presence of changed HTT is enough to cause HD.

3 What is the name for different versions of the same gene?

- a) proteins
- b) chromosomes
- c) alleles

5 What is the risk of someone affected by HD passing this condition onto their children?

- a) 50%
- b) 25%
- c) 4%

4 The allele that causes HD is...

- a) dominant
- b) recessive
- c) sex-linked

The importance of the protein's shape...

Draw the shape of the protein when there are 25 amino acids...

Draw the shape of the protein when there are 28+ amino acids...

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