Researchers in Schools

# How to uncover the secret code for cancer

## Key Stage 4 Programme

Pupil Name

Coursebook Designed by **Dr Malik**

# Timetable and Assignment Submission

## Timetable – Tutorials

| Tutorial | Date | Time | Location |
|---|---|---|---|
| 1 | 9/12/19 | 12:00-15.45 | Royal West of England Academy, Bristol |
| 2 | 13/01/20 | 15:00-16:00 | Hans Price |
| 3 | 20/01/20 | 15:00-16:00 | Hans Price |
| 4 | 27/01/20 | 15:00-16:00 | Hans Price |
| 5 | 03/02/20 | 15:00-16:00 | Hans Price |
| 6 (Feedback) | 24/02/20 | 15:00-16:00 | Hans Price |
| 7 (Feedback) | 09/03/20 | 15:00-16:00 | Hans Price |

## Timetable – Homework Assignments

| Homework Assignment | Description | Due Date |
|---|---|---|
| Tutorial 1 | BASELINE ASSIGNMENT: How are chromosomes, DNA, genes and proteins related to each other and how do DNA mutations effect the protein that a gene codes for? | 13/12/19 |
| Tutorial 2 | Discuss why some cancers are caused by DNA mutations. | 20/01/20 |
| Tutorial 3 | Poster presentation about cancers caused by DNA methylation. | 27/01/20 |
| Tutorial 4 | Complete the COBRA flowchart. | 03/02/20 |
| Tutorial 5 | FINAL ASSIGNMENT: Describe how changes to the genome can contribute to the development of cancers. | DRAFT: 24/02/20<br>FINAL: 02/03/20 |

## Assignment Submission – Lateness and Plagiarism

| Lateness | |
|---|---|
| Submission after midnight on **Friday 6th March 2019** | 10 marks deducted |
| **Plagiarism** | |
| Some plagiarism | 10 marks deducted |
| Moderate plagiarism | 20 marks deducted |
| Extreme plagiarism | Automatic fail |

# Contents


**Course Rationale** **P4**

**Mark Scheme** **P5**

**Baseline Assignment (Essay Based): Pupil Feedback Report** **P8**

**Final Assignment (Essay Based): Pupil Feedback Report** **P9**

**Subject Vocabulary** **P10**

**Tutorial 1 – The Recipe for Life** **P11**

Activity 1 – It's Good to Be in Control **P12**

Activity 2 – Make A Sweet DNA Model **P12**

Activity 3 – Spot the Mutation **P14**

Activity 4 – Mutate It! **P16**

Activity 5 – DNA Makes RNA Makes Protein **P16**

Tutorial Glossary **P18**

Notes **P18**

Homework – Baseline Assignment **P19**

**Tutorial 2 – The C-Word** **P20**

Activity 1 – What is Cancer? **P21**

Activity 2 – Genes Not Jeans! **P22**

Activity 3 – It Takes Two Hits **P24**

Activity 4 – Fact or Fiction **P24**

Tutorial Glossary **P25**

Notes **P26**

Homework **P27**

**Tutorial 3 – The Secret Cancer Code** **P28**

Activity 1 – Uncovering the Secret Code **P29**

Activity 2 – Switching off Genes **P30**

Activity 3 – Research It! **P31**

Tutorial Glossary **P32**

Notes **P32**

Homework **P34**

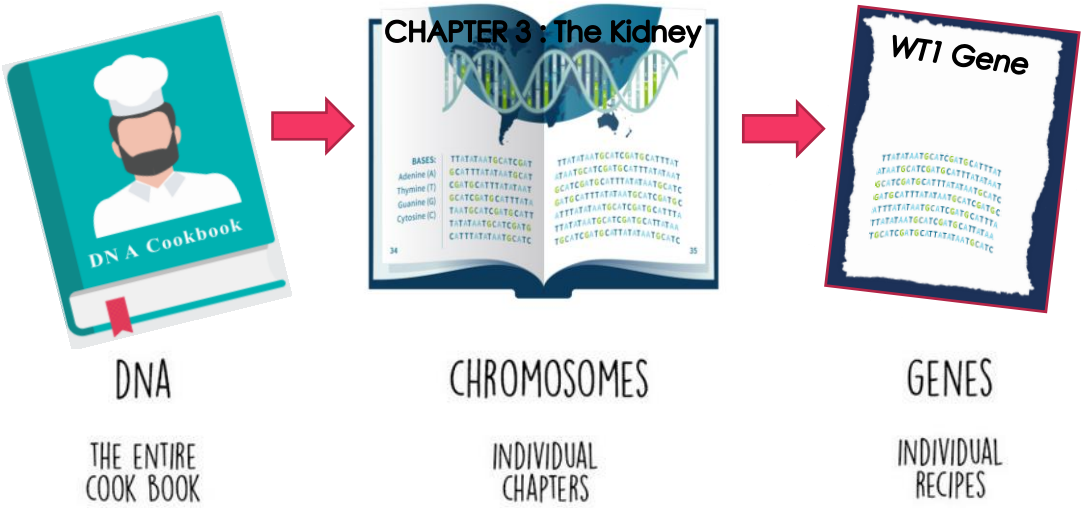
**Tutorial 4 – Detecting DNA Methylation** **P35**
Activity 1 – How to Extract Genomic DNA **P35**
Activity 2 – It's All in the Sequence **P37**
Activity 3 – Predict the Pattern **P39**
Activity 4 – Separating and Viewing DNA **P40**
Tutorial Glossary **P41**
Notes **P41**
Homework **P43**
**Tutorial 5 – How to Write a Great Essay** **P45**
Activity 1 – Plan It! **P45**
Activity 2 – Structure It! **P47**
Activity 3 – Good Versus Bad **P47**
Activity 4 – Reference It! **P48**
Notes **P49**
Homework – Final Assignment **P51**
**Tutorial 6 – Feedback Tutorial** **P52**
Reflection on Feedback **P52**
**Tutorial 7 – Final Tutorial** **P54**
Reflecting on the Course **P54**
**Appendices** **P57**
Appendix 1 – Referencing Correctly **P57**
Appendix 2 – Cancers Caused by DNA Methylation **P59**
**Notes** **P61**

# Course Rationale

Cancer is a disease that occurs when the cells in our body don't know how to stop dividing and growing. This is because some of the genes in those cells become faulty.

A gene is like a recipe as it contains all the instructions to tell the cell what proteins to make, or code for.

Think about when you bake a cake, if the recipe has mistakes in it then your lovely cake might not cook properly and will look very different to the picture in the recipe book. So, if the gene has mistakes in its information then the proteins won't work properly or aren't made at all, then a normal cell can become a cancer cell.




Scientists are like detectives who look for these mistakes in genes by comparing the recipes contained within normal and cancer cells. Any differences could point to the reason why a cell turned cancerous.

During these Uni pathways tutorials, you will:

- Become a DNA detective and use your investigative skills to uncover possible mistakes in a gene.
- Develop real skills that scientists use to research cancer in the laboratory.
- Understand how to analyse data and draw your own conclusions.
- Learn how to write a scientific essay with references, a very important skill needed for University.

# Uni Pathways Mark Scheme 2019 – Essay-based assignments

| | Skills | 1st (70-100) | 2:1 (60-69) | 2:2 (50-59) | 3rd (40-49) | Mark /100 |
|---|---|---|---|---|---|---|
| Subject knowledge | Knowledge and understanding | ○ All content included and materials used are relevant to the general topic and to the specific question/title<br>○ Good understanding of all the relevant topics.<br>○ Technical terms are defined and used accurately throughout<br>○ Clear justification of how the material and content included is related to the specific issues that are the focus of the assignment | ○ Most of the materials used and content included are relevant to the general topic and to the specific question/title<br>○ Good understanding of most the relevant topics<br>○ Technical terms are mostly defined and used accurately<br>○ Adequate justification of how the material used and content included are related to the specific issues that are the focus of the essay | ○ Some of the materials used and content included are relevant to the general topic and to the specific question/title<br>○ Good understanding on some of the relevant topics but occasional confusion on others<br>○ Technical terms are sometimes used and defined accurately<br>○ Some justification of how the material used and content included are related to the specific issues that are the focus of the essay | ○ The content included and materials used are not applied to the question/title in a relevant manner<br>○ There is confusion in how understanding of the topics is expressed | |
| Critical thinking | Research and evidence | ○ Includes rich sources of research findings, data, quotations or other sourced material as evidence for the claims/ideas<br>○ Uses evidence/calculations to support claims/assertions/ideas, consistently clearly and convincingly<br>○ Evidence of further reading beyond materials provided which were used in an appropriate context<br>○ Data is effectively analysed and appropriate assumptions/ conclusions are reached | ○ Includes adequate sources of research findings, data, quotations or other sourced material as evidence for the claims/ideas<br>○ Uses evidence/calculations to support claims/assertions/ideas, mostly clearly and convincingly<br>○ Evidence of further reading beyond materials provided<br>○ Data is analysed and the assumptions/conclusions that are reached are mostly appropriate | ○ Includes some sources of research findings, data, quotations or other sourced material as evidence for the claims/ ideas<br>○ Uses evidence/calculations to support claims/assertions/ideas, at times clearly and convincingly<br>○ Limited evidence of further reading beyond materials provided<br>○ There is an attempt to analyse data and draw assumptions/conclusions | ○ Inclusion sources and materials is very limited and mostly not attributed<br>○ Applicable sources are rarely used to support ideas.<br>○ Data is used but there are limited appropriate conclusions drawn from it. | |
| | Developing an argument | ○ A point of view or position in relation to the title or question is consistently clear. The position is developed effectively and consistently throughout the essay<br>○ Argument is exceptionally well-developed and well-justified<br>○ Makes links effectively between subjects that have not previously been associated<br>○ Uses concepts from the tutorials in an unfamiliar context and does so accurately and confidently.<br>○ Content is analysed effectively to support the argument | ○ A point of view or position in relation to the title or question is adequately clear. The position is well-developed in most of the essay<br>○ Argument is clear and well-developed, and position is justified<br>○ Some evidence of linking subjects that have not previously been associated<br>○ Uses some concepts from the tutorials in an unfamiliar context, but not always accurately<br>○ Analyses content to support the argument | ○ A point of view or position in relation to the title or question is somewhat clear. The position is well-developed in parts of the essay<br>○ Argument is clear but not well-developed<br>○ Limited evidence of linking subjects that have not previously been associated<br>○ Limited use of concepts from the tutorials in other contexts<br>○ Uses some analysis of content to support the argument | ○ There is not a clear point of view or position taken and sometimes the argument is not clearly established | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Critical evaluation | ○ Moves beyond description to an assessment of the value or significance of what is described<br>○ Evaluative points are consistently explicit/systematic/reasoned/justified<br>○ Effectively critiques the reliability of sources provided | ○ Mostly description but some assessment of the value or significance of what is described<br>○ Evaluative points are mostly explicit/systematic/reasoned/justified<br>○ Some evidence of critiques on the reliability of sources provided | ○ Describes with minimal assessment of the value or significance of what is described<br>○ Evaluative points are at times explicit/systematic/reasoned/justified<br>○ Limited evidence of critiques on the reliability of sources provided | ○ The work is descriptive in nature and there is a lack of critical engagement in the value of sources | |
| Written communication | Structure and presentation | ○ Ideas are presented in paragraphs and arranged in a logical structure that is appropriate for the assignment<br>○ The introduction clearly outlines how the essay/report will deal with the issues<br>○ The conclusion summarises all the main points clearly and concisely<br>○ All sources are referenced correctly in an agreed format | ○ Ideas are presented in paragraphs and arranged in a structure that is mostly appropriate for the assignment<br>○ The introduction adequately describes how the essay/report will deal with the issues<br>○ The conclusion summarises most of the main points clearly<br>○ Most sources are referenced correctly in an agreed format | ○ Ideas are presented in paragraphs and arranged in a structure<br>○ The introduction mentions how the essay/report will deal with the issues<br>○ The conclusion summarises some of the main points clearly<br>○ Some sources are referenced correctly in the agreed format with occasional errors | ○ Ideas are presented in paragraphs but there is a lack of structure in how the work is presented<br>○ The work lacks an introduction that establishes the scope of the question<br>○ The work lacks a conclusion that summarise the main points raised<br>○ Work is not referenced accurately | |
| | Language and style | ○ No spelling, grammar or punctuation errors<br>○ Writing style consistently clear, tone appropriate and easy to follow<br>○ Accurate and consistent use of technical language and vocabulary | ○ Minimal spelling, grammar or punctuation errors<br>○ Writing style mostly clear, tone appropriate and easy to follow<br>○ Some attempts of using technical language and vocab alary, but not always accurate | ○ Some spelling, grammar or punctuation errors<br>○ Writing style moderately clear, tone appropriate and easy to follow<br>○ Use of simple language and vocabulary effectively but struggles to use technical language | ○ There are a significant number of spelling, grammar and punctuation errors<br>○ Use of simple language and vocabulary effectively but a lack of technical language | |
| Overall Mark (average of the 6 marks from the criteria above) | | | | | | |

# Baseline Assignment (essay based): Pupil Feedback Report

| | |
|---|---|
| Name of Pupil | |
| Name of School | Hans Price Academy |
| Name of RIS teacher | Dr Malik |
| Title of Assignment | How are chromosomes, DNA, genes and proteins related to each other and how do DNA mutations effect the protein that a gene codes for? |

How your assignment is graded:

| Grade | Marks | What this means |
|---|---|---|
| 1st | 70+ | Performing to an excellent standard at A-level |
| 2:1 | 60-69 | Performing to a good standard at A-level |
| 2:2 | 50-59 | Performing to an excellent standard at GCSE |
| 3rd | 40-49 | Performing to a good standard at GCSE |
| Working towards a pass | 0-39 | Performing below a good standard at GCSE |
| Did not submit | DNS | No assignment received by The Brilliant Club |

| Lateness | |
|---|---|
| Any lateness | 10 marks deducted |
| **Plagiarism** | |
| Some plagiarism | 10 marks deducted |
| Moderate plagiarism | 20 marks deducted |
| Extreme plagiarism | Automatic fail |

Marks

| | | | |
|---|---|---|---|
| OVERALL MARK / 100 | | FINAL MARK / 100 (including any deductions) | |
| DEDUCTED MARKS | | FINAL GRADE | |

If marks have been deducted (e.g. late submission, plagiarism) the teacher should give an explanation in this section:

Mark Breakdown and Feedback

| Knowledge and Understanding | | Research and Evidence | |
|---|---|---|---|
| | *mark* | | *mark* |
| **Developing an Argument** | | **Critical Evaluation** | |
| | *mark* | | *mark* |
| **Structure and Presentation** | | **Language and Style** | |
| | *mark* | | *mark* |

# Final Assignment (essay based): Pupil Feedback Report

| | |
|---|---|
| Name of Pupil | |
| Name of School | Hans Price Academy |
| Name of RIS teacher | Dr Malik |
| Title of Assignment | Describe how changes to the genome can contribute to the development of cancers. |

How your assignment is graded:

| Grade | Marks | What this means |
|---|---|---|
| 1st | 70+ | Performing to an excellent standard at A-level |
| 2:1 | 60-69 | Performing to a good standard at A-level |
| 2:2 | 50-59 | Performing to an excellent standard at GCSE |
| 3rd | 40-49 | Performing to a good standard at GCSE |
| Working towards a pass | 0-39 | Performing below a good standard at GCSE |
| Did not submit | DNS | No assignment received by The Brilliant Club |

| Lateness | |
|---|---|
| Any lateness | 10 marks deducted |
| **Plagiarism** | |
| Some plagiarism | 10 marks deducted |
| Moderate plagiarism | 20 marks deducted |
| Extreme plagiarism | Automatic fail |

Marks

| | | | |
|---|---|---|---|
| OVERALL MARK / 100 | | FINAL MARK / 100 (including any deductions) | |
| DEDUCTED MARKS | | FINAL GRADE | |

If marks have been deducted (e.g. late submission, plagiarism) the teacher should give an explanation in this section:

Mark Breakdown and Feedback

| Knowledge and Understanding | | Research and Evidence | |
|---|---|---|---|
| | *mark* | | *mark* |
| **Developing an Argument** | | **Critical Evaluation** | |
| | *mark* | | *mark* |
| **Structure and Presentation** | | **Language and Style** | |
| | *mark* | | *mark* |

# Subject Vocabulary

| Word | Definition | In a sentence |
|---|---|---|
| DNA | Inherited genetic material mainly found in the nucleus that contains all the instructions a cell needs to make proteins. DNA stands for **D**eoxyribo**n**ucleic **A**cid. | |
| Gene | A section of DNA sequence that contains the instructions (recipe) to make a particular protein. In the human cell, there are approximately 20, 000 genes. | |
| Chromosome | A long strand of DNA that contains genes and is coiled around proteins to help packaging into the nucleus. Most cells of the body contain 23 pairs. | |
| Cancer | Cells that divide and grow in an uncontrolled way to form a large mass which can break up and escape into the blood vessels. | |
| DNA Mutation | A change to the normal DNA sequence, which when found in a gene can alter the protein that it makes. | |
| Epigenetics | The study of how genes are switched on and off without changing the DNA sequence. | |
| Hypermethylation | When the DNA molecule gains too much methylation. | |
| COBRA | A technique used to analyse DNA methylation patterns. | |
| Sodium Bisulfite | A chemical used to identify where DNA is methylated. | |
| Restriction enzyme | A type of protein that cuts DNA at a specific sequence. | |
| Agarose gel electrophoresis | A laboratory method used to separate and visualise different sized DNA fragments. | |

# Tutorial 1 – The Recipe for Life

Image from Stem Cell Reports 2017

## What is the Purpose of Tutorial 1?

During this tutorial you will learn all about DNA and why this amazing molecule is so important for life. You'll also find out about what the consequences could be if the recipes it contains are changed. These changes are called mutations and scientists study them to find cures for diseases, such as cancer.

You will look at data and develop analytical techniques used by scientists to investigate DNA mutations in the laboratory.

By the end of this tutorial I will be able to…

- Define what DNA and genes are.
- Understand how genes code for proteins.
- Explain what DNA mutations are.

## Activity 1 – It's Good to Be in Control

At the last count, scientists have estimated that your body is made up of a whopping 37.2 trillion cells (37,000,000,000,000 – that's a lot of noughts!).

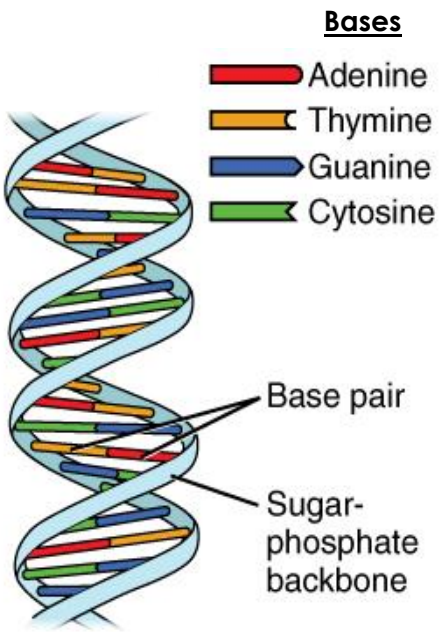
Your body works non-stop, day and night to make new cells to replace the ones that are domaged or old ones that have worn out. In the time it takes for you to read this your body has made 1 million red blood cells, 12, 000 million gut cells and 40, 000 skin cells. Whatever you do please don't use the excuse that you're too busy making new cells to do your homework or tidy your bedroom!

Why do you think it's important that the rate at which new cells are made, divide, grow and die needs to be tightly controlled? Discuss with your learning partner and write your answer below.

## Activity 2 – Make a Sweet DNA Model

It's the DNA inside your cells that contains the recipes or genes that code for the proteins that control cell growth, division and death. So, let's have a look at this very important molecule.

Examine the diagram below, showing a section of a DNA molecule and answer the following questions.




Name the three different types of chemical components in a DNA molecule?

1.

2.

3.

Which bases always pair with each other in the DNA molecule?

Now using strawberry laces, jelly babies and toothpicks make an irresistibly accurate DNA model. Make sure that you use the right colour jelly baby for each nucleotide and remember that they need to pair with the correct partner. Label your model with the key features of DNA.

Stick a picture of your fabulous DNA model in the space below.

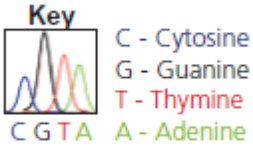
## Activity 3 – Spot the Mutations

Sometimes the DNA sequence of a gene can become damaged or mutated and this can cause the gene to code for the wrong protein. If this mutant protein promotes cell growth or prevents cell death, then it can cause a cell to grow rapidly giving rise to a lump of cells called a tumour. Theses tumours sometimes turn into a cancer.

Special machines are used to "read" the DNA sequences from normal and cancer cells from the same patient. Scientists then closely examine the DNA sequences, which are produced as a chromatogram, to identify changes or mutations to the bases. Any mutations in the cancer DNA sequence could be the reason why the person got cancer.

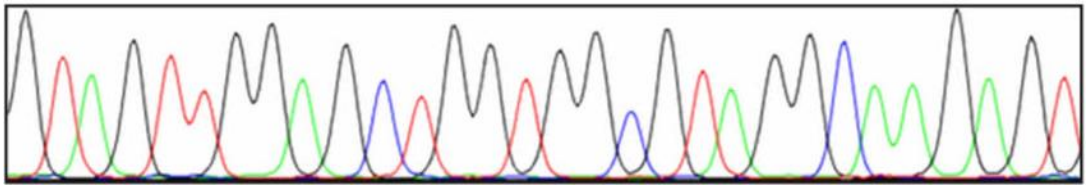
Examine the normal and cancer DNA sequence shown in the chromatograms below to see if you can detect any mutations.

Using the key, label each coloured peak on the DNA sequences from the normal and cancer cell with the correct base. Then look very carefully to identify the mutations found in the DNA sequence from the cancer cell. Draw a box around any that you find.



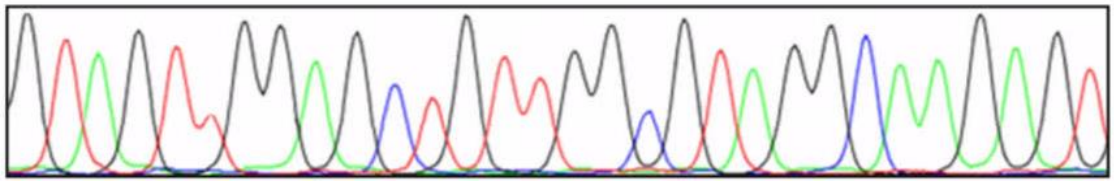

**Normal DNA Chromatogram**

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | **DNA bases** |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | **Amino acid** |



**Cancer DNA Chromatogram**

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | **DNA bases** |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | **Amino acid** |



DNA contains all the instructions to make proteins, which are made from amino acids. Each set of three bases in the DNA sequence codes for one amino acid, for example the base sequence CAG codes for the amino acid glycine. These 3 bases are called a codon.

Using the table on page 15 work out the amino acids coded for by the bases in the DNA sequence for both the normal and cancer DNA.

## The DNA Codon Table

| 1st position | 2nd position | | | | 3rd position |
|---|---|---|---|---|---|
| | T | C | A | G | |
| T | Phe | Ser | Tyr | Cys | T |
| | Phe | Ser | Tyr | Cys | C |
| | Leu | Ser | Stop | Stop | A |
| | Leu | Ser | Stop | Trp | G |
| C | Leu | Pro | His | Arg | T |
| | Leu | Pro | His | Arg | C |
| | Leu | Pro | Gln | Arg | A |
| | Leu | Pro | Gln | Arg | G |
| A | Ile | Thr | Asn | Ser | T |
| | Ile | Thr | Asn | Ser | C |
| | Ile | Thr | Lys | Arg | A |
| | Met | Thr | Lys | Arg | G |
| G | Val | Ala | Asp | Gly | T |
| | Val | Ala | Asp | Gly | C |
| | Val | Ala | Glu | Gly | A |
| | Val | Ala | Glu | Gly | G |

**Abbreviations and full names of amino acids**

| | | | |
|---|---|---|---|
| Ala | Alanine | Leu | Leucine |
| Arg | Arginine | Lys | Lysine |
| Asn | Asparagine | Met | Methionine |
| Asp | Aspartic Acid | Phe | Phenylalanine |
| Cys | Cystine | Pra | Proline |
| Gln | Glutamine | Ser | Serine |
| Glu | Glutamic Acid | Thr | Threonine |
| Gly | Glycine | Trp | Tryptophane |
| His | Histidine | Tyr | Tyrosine |
| Ile | IsolMeucine | Val | Valine |

In learning partners, discuss whether you found any differences between the amino acid sequence coded for by the normal and cancer DNA? If you did, what is the reason for the differences and how might that effect the protein synthesised? Write your answer below.

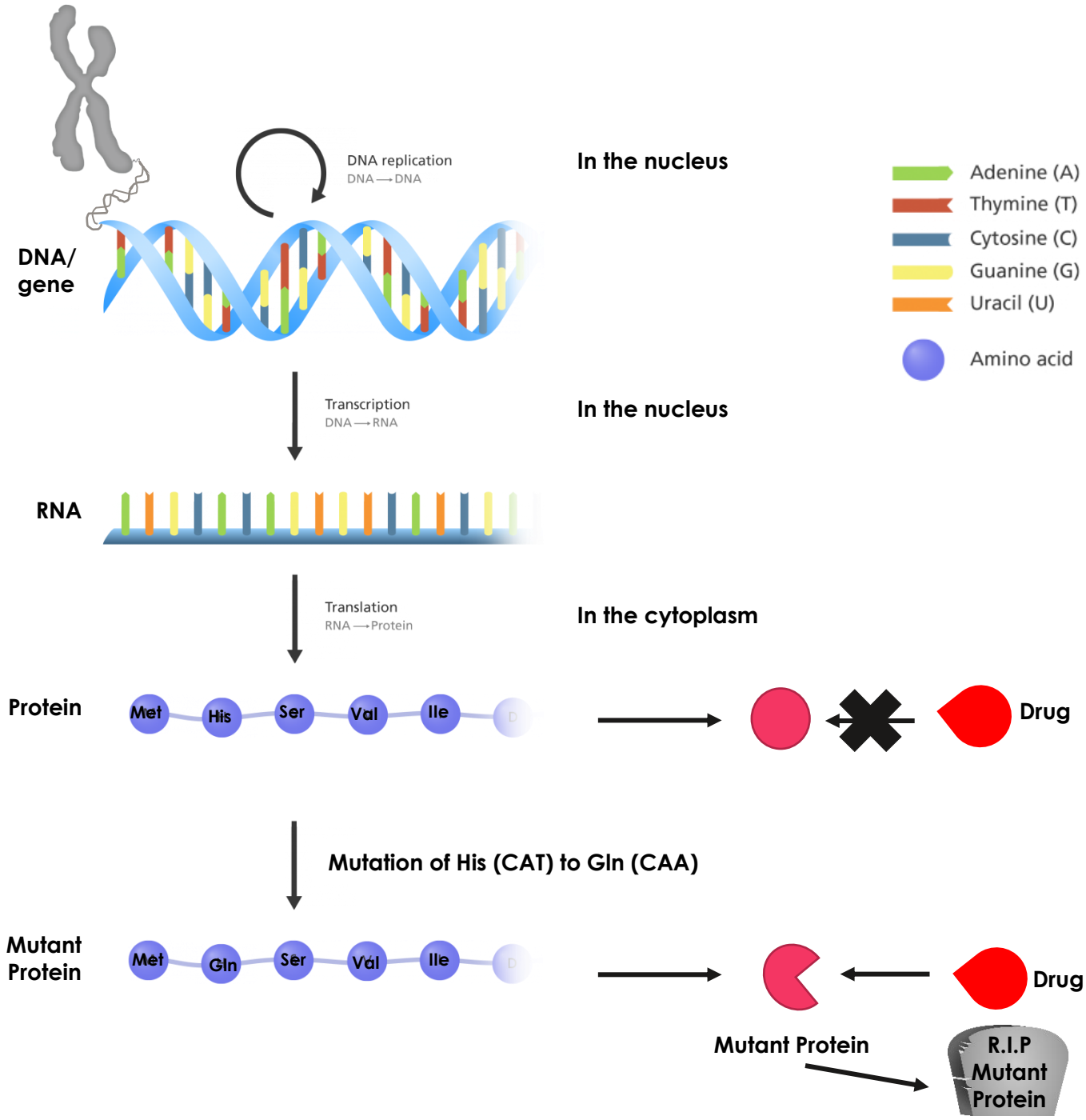
DNA can become mutated in different ways. See if you can match the name of the mutation with the DNA sequence. Circle the mutations. Which mutation did the cancer DNA have on page14?

| | |
|---|---|
| A T T T C C T G T A T C | **Unmutated DNA sequence** |
| A T T T T C C T G T A T | **Deletion** |
| A T T C C T G T A T C | **Truncation** |
| A T G T C C T G T A T C | **Duplication** |
| A T T C C T T G T A T C | **Substitution** |
| A T T C C T T G A | **Inversion** |

## Activity 4: Mutate it

Go back to your original DNA model and mutate it with one of types of DNA mutation. Explain what you did and whether that changed the amino acid sequence.

## Activity 5 – DNA Makes RNA Makes Protein



Use your knowledge from this tutorial and the diagram on page 16 to help you answer the following questions.

1. What is a gene?

2. How does a gene code for a protein?

3. How can drugs specifically destroy mutant proteins?

4. Getting rid of the mutant protein is beneficial for the health of the cell because……..

## Tutorial Glossary

Use this space to write down any new words that you have learned in this tutorial.

| Word | Definition |
| --- | --- |
| | |
| | |
| | |
| | |
| | |

## Notes

## Notes

## Homework – Baseline Assignment

**Q: How are chromosomes, DNA, genes and proteins related to each other and how do DNA mutations effect the protein that a gene codes for?**

Write your answer in approximately 500 words, using diagrams where necessary to illustrate your points:

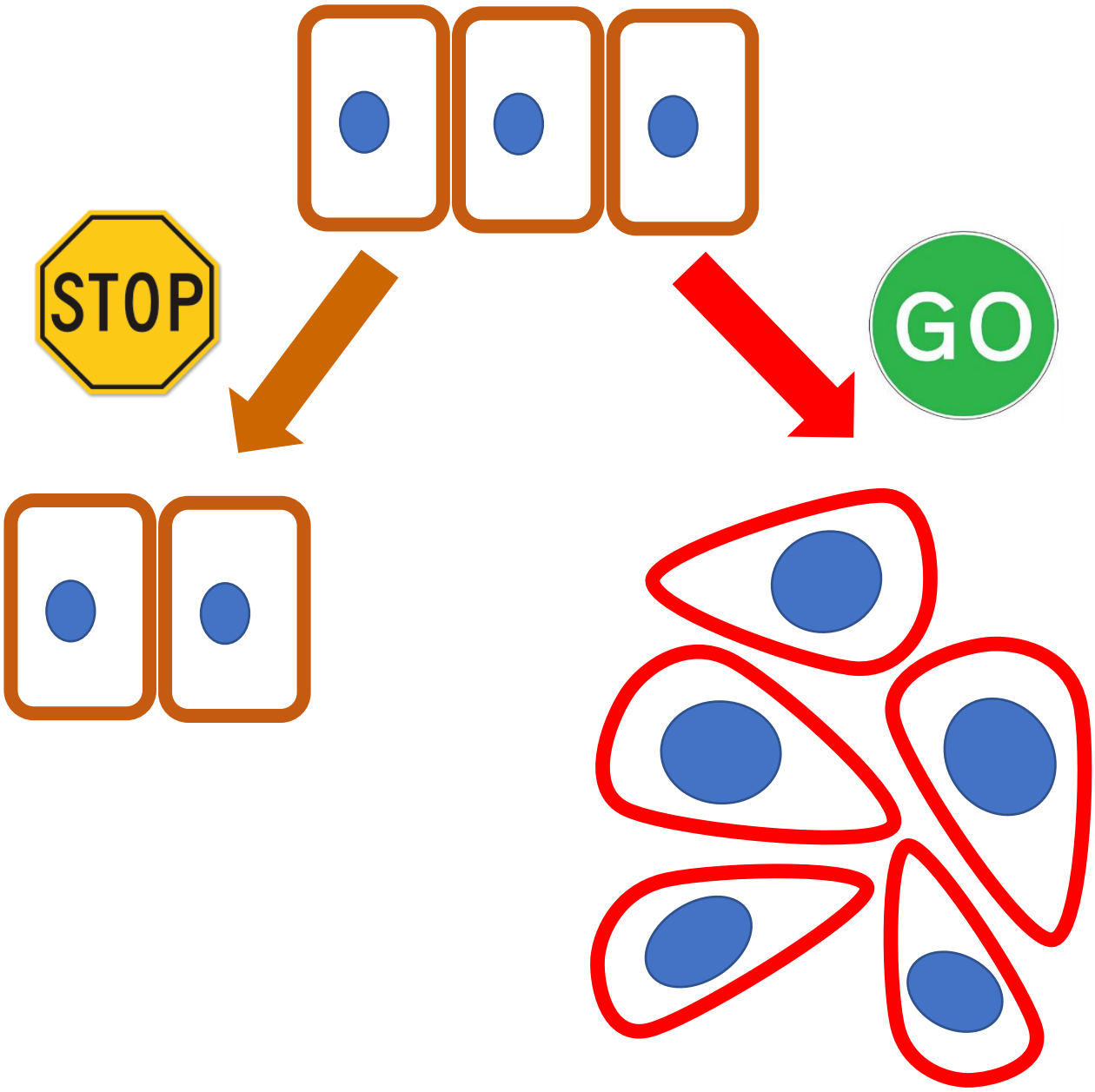
***Key Points to Discuss:***

- What is a chromosome, DNA and a gene?
- What are DNA mutations and how are they caused?
- How does a gene code for a protein?
- What can happen to a protein if the DNA sequence is mutated.

Use your tutorial notes to help you. You can also conduct your own independent research using relevant books and websites such as:

- https://kids.frontiersin.org/article/10.3389/frym.2019.00046
- http://whoami.sciencemuseum.org.uk/whoami/findoutmore/yourgenes

# Tutorial 2 – The C-Word




## What is the Purpose of Tutorial 2?

During this tutorial you will learn all about how cells lose control and start to behave very badly. This can lead to the growth of a cancer.

By the end of this tutorial I will be able to…

- Understand what cancer is.
- Distinguish between benign and malignant cancer.
- Describe the two main types of gene that are involved in cancer.
- De-bust cancer myths.

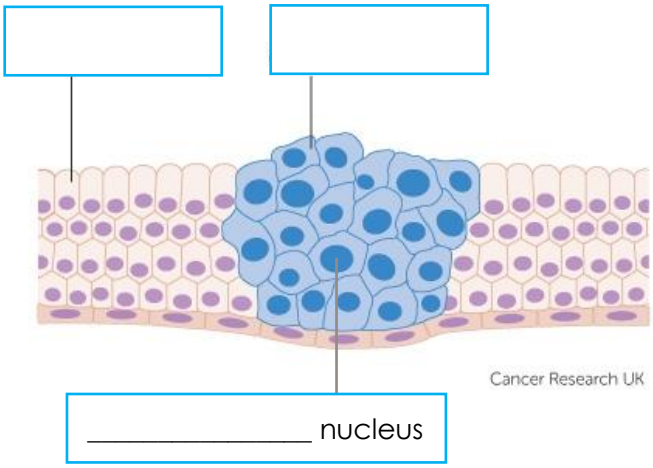
## Activity 1- What Is Cancer?

A cancer starts to grow when the DNA sequence of a gene in a healthy cell is damaged by mutations, resulting in the synthesis of too much, too little or the wrong type of protein. These proteins might be involved in the control of cell growth, repair of the mutated DNA or cause the cell to die (apoptosis) if it couldn't be repaired.

These cells then start to behave really badly by escaping the normal cell growth, division and death processes and begin to rapidly grow and divide more than a normal well-behaved cell. A benign tumour is formed however, it is not yet a fully formed malignant cancer.

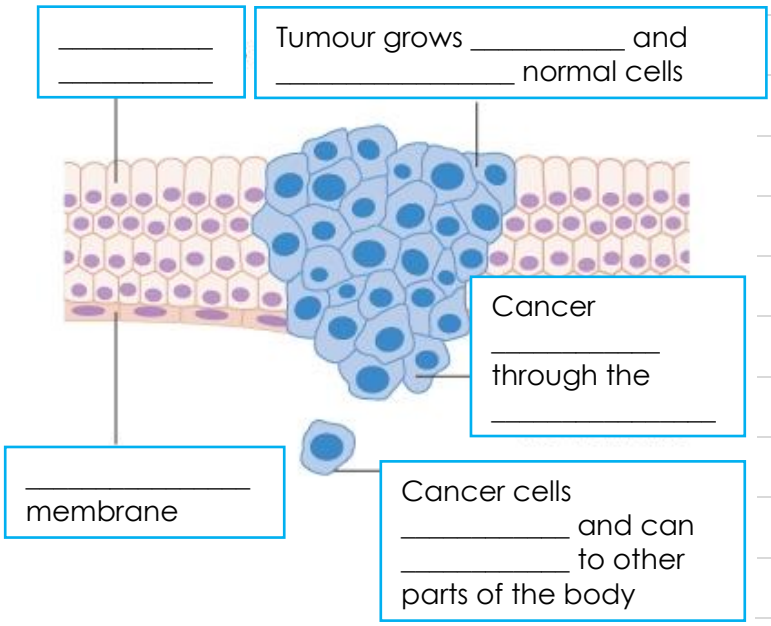
Use the diagrams below to write the story of how a cancer is formed. Choose the correct keywords to help you fill in the boxes and describe what you can see in each diagram.

### A Benign Tumour




**Keywords:** normal cell, enlarged, cancer cell

### A Malignant Cancer




**Keywords:** normal cell, breaks, rapidly, spread, invades, membrane, basement, detach.

## Activity 2 – Genes Not Jeans!

There are two main types of growth controlling genes that can cause cancer.

In your own words explain how these genes can cause cancer when their DNA sequence is mutated. You can use diagrams to illustrate your answers.

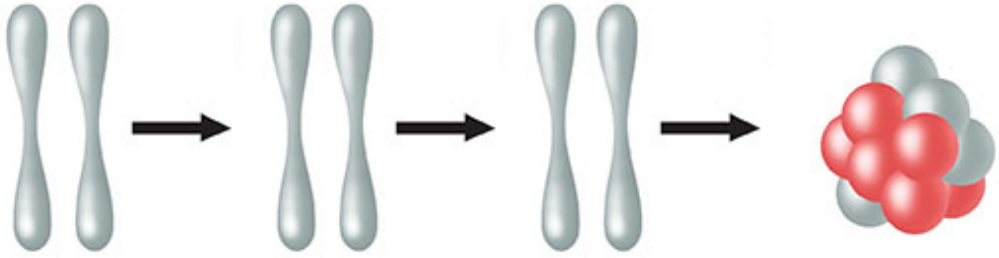
A tumour suppressor gene is

An oncogene is

## Activity 3 – It Takes Two Hits

Way back in 1971, a famous scientist called Dr Knudson found that for a cancer to form, both copies of a tumour suppressor gene (one copy inherited from either parent) need to be mutated and switched off for a cancer to form. He called this the Two-Hit hypothesis.

Mark in the two copies of a gene on the chromosome pair and then stick on a star to show the correct number of "hits".



1st Hit 2nd Hit Cancer

## Activity 4 – Fact or Fiction

There are a lot of myths surrounding the causes of cancer making it difficult to know what the culprits really are.

Work with your learning partner to test your knowledge by sorting out the facts from the fiction. Write your answers in the boxes below.

| FACT | FICTION |
| --- | --- |
| • | • |
| • | • |
| • | • |
| • | • |
| • | • |

Add any other causes of cancer that you know in the space below.

## Tutorial Glossary

Use this space to write down any new words that you have learned in this tutorial.

| Word | Definition |
|---|---|
| | |
| | |
| | |
| | |
| | |

## Notes

## Homework

In Appendix 2 there are five examples of genes that are mutated in cancer. Use this information to answer the following question, you should aim to write 200-300 words in total.

**Q: Discuss why some cancers are caused by mutated genes.**

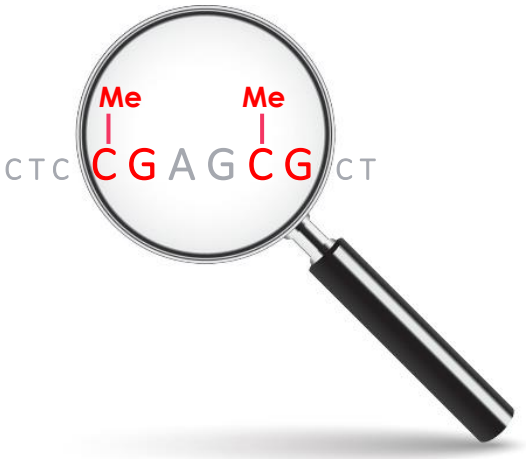
***Key points to discuss*:**

- What is cancer?
- The name of the cancer.
- The name of the gene(s) involved.
- What is the normal function of the gene(s)?
- How are the genes mutated?
- The consequences of the mutations.

You could also do your own independent research and the following websites are a good place to start:

- https://www.cancer.net/navigating-cancer-care/cancer-basics/genetics/genetics-cancer
- https://www.cancerresearchuk.org/about-cancer/what-is-cancer/genes-dna-and-cancer
- http://whoami.sciencemuseum.org.uk/whoami/findoutmore/yourgenes/whydoscientistsstudygenes/howdoscientistslookatchromosomes/arechromosomeslinkedtocancer
- http://news.bbc.co.uk/cbbcnews/hi/find_out/guides/tech/cancer/newsid_2913000/2913831.stm about cancer
- https://www.breastcancer.org/risk/factors/genetics

# Tutorial 3 – The Secret Cancer Code




## What is the Purpose of Tutorial 3?

In this tutorial we will explore the fact that the DNA sequence of some genes are not mutated but can still cause cancer. This is through the addition of a secret code that can't be seen by looking at the DNA sequence.

You will find out how this secret code can take the breaks off cell growth and division by switching off genes that stop cells from multiplying.

By the end of this tutorial I will be able to…

- Define the words epigenetics and DNA methylation.
- Understand how DNA methylation can switch off gene expression.
- Name some types of cancer that are caused by changes to the levels of DNA methylation.

## Activity 1 – Uncovering the Secret Code

Examine closely the DNA sequence given, and in pairs discuss what you can see. Write your answer in the space below:

The DNA sequence is made up of

Now take another look at the DNA sequence, but this time shine the lamp on the page. In pairs discuss what you can see, then write your answer in a full sentence in the space below:

After shining the UV lamp on the DNA sequence

Annotate your DNA sequence to show what you've found and stick it into the space below:

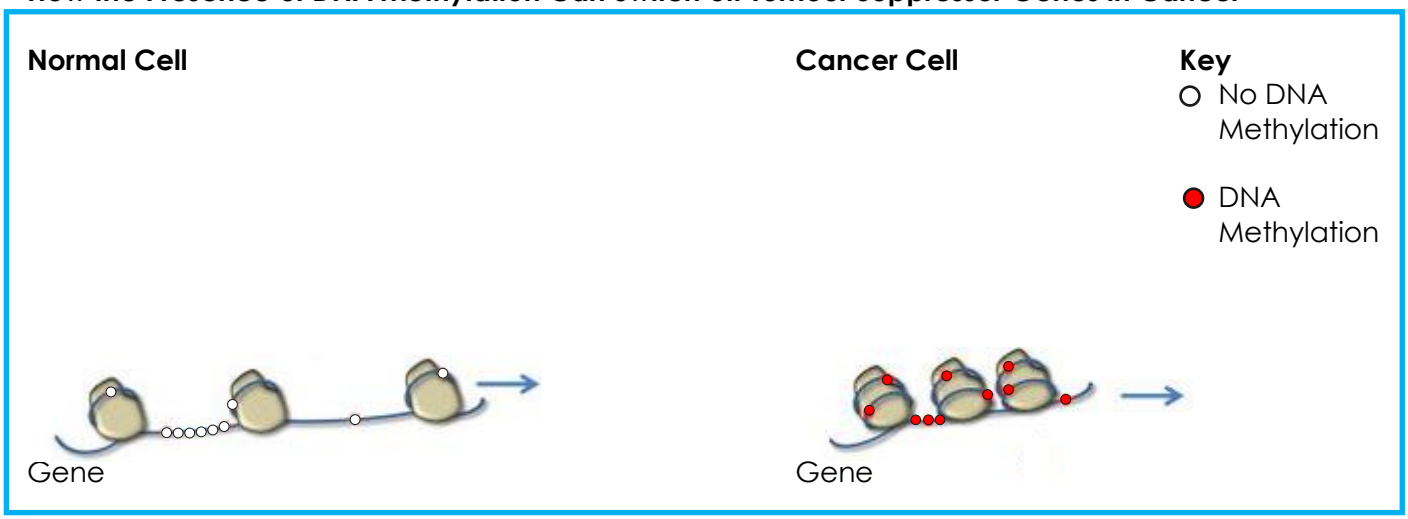
## Activity 2 – Switching Off Genes

The expression of growth limiting tumour suppressor genes can become permanently switched off in a cell causing the cell to lose its ability to control the rate at which it grows, divides and dies. This can lead to the formation of a rapidly growing cancer.

You've heard how this can happen in tutorial 1 by DNA mutations. But it can also occur by another method that doesn't change the sequence of the DNA, instead a secret code or chemical is added to some of the cytosine bases. You uncovered this secret code on page 29 and it's called DNA methylation.

Complete the diagram below and label it to show which tumour suppressor gene is expressed and which gene is switched off.

**How the Presence of DNA Methylation Can Switch off Tumour Suppressor Genes in Cancer**




Use the space below to make notes on how DNA methylation switches off genes in cancer.

## Activity 3 – Research it!

Scientists spend a lot of time in the laboratory performing experiments to examine their hypotheses, but they also spend just as much time reading about the experiments other scientist have been performing in the same or similar field of work. This information aids better understanding of what they are working on and can also give ideas of what to examine next.

Now it's your turn to do your own research of what is known about how DNA methylation can contribute to the growth of cancers. Use the information to fill in the table below.

| Name of Cancer | Genes Effected | What Happens |
|---|---|---|
| | | |
| | | |
| | | |

## Tutorial Glossary

Use this space to write down any new words that you have learned in this tutorial.

| Word | Definition |
|---|---|
| | |
| | |
| | |
| | |
| | |

## Notes

## Notes

## Homework

Prepare an A4 sized poster on one of the cancers caused by DNA methylation. You will be presenting your poster to the rest of the group next week. Be creative and make your poster eye catching.

**Key points to include:**

- What is DNA methylation and why can it lead to cancer?
- The name of the cancer.
- What gene(s) are methylated?
- What happens to the gene(s) when they are methylated?
- Diagrams to illustrate your information.

# Tutorial 4 – Detecting DNA Methylation

## What is the Purpose of Tutorial 4?

In this tutorial you will learn a technique called COBRA, but don't worry it has nothing to do with snakes! It's an acronym that stands for **Co**mbined **B**isulfite **R**estriction **A**nalysis.

Scientists use COBRA to study DNA methylation in cancer. It involves several steps, one of which uses a chemical that changes the sequence of DNA to make methylation easier to find.

By the end of this tutorial I will be able to…

- Describe all the steps of Combined Bisulfite Restriction Analysis.
- Understand how the unmethylated DNA sequence can be chemically changed.
- Explain how restriction enzymes are used to detect DNA methylation.

## Activity 1 – How to Extract Genomic DNA

The first step of COBRA is to extract genomic DNA from normal and cancer cells from the same patient, so comparisons can be made between the two samples. Any differences found could point to the reason why the cancer started to grow.

In the laboratory, scientists use a special kit to extract the DNA. Complete the boxes to explain why each stage is performed.

**Genomic DNA Extraction Protocol**

Grind the sample:

Cell lysis:

Degrade proteins:

Binding to the column:

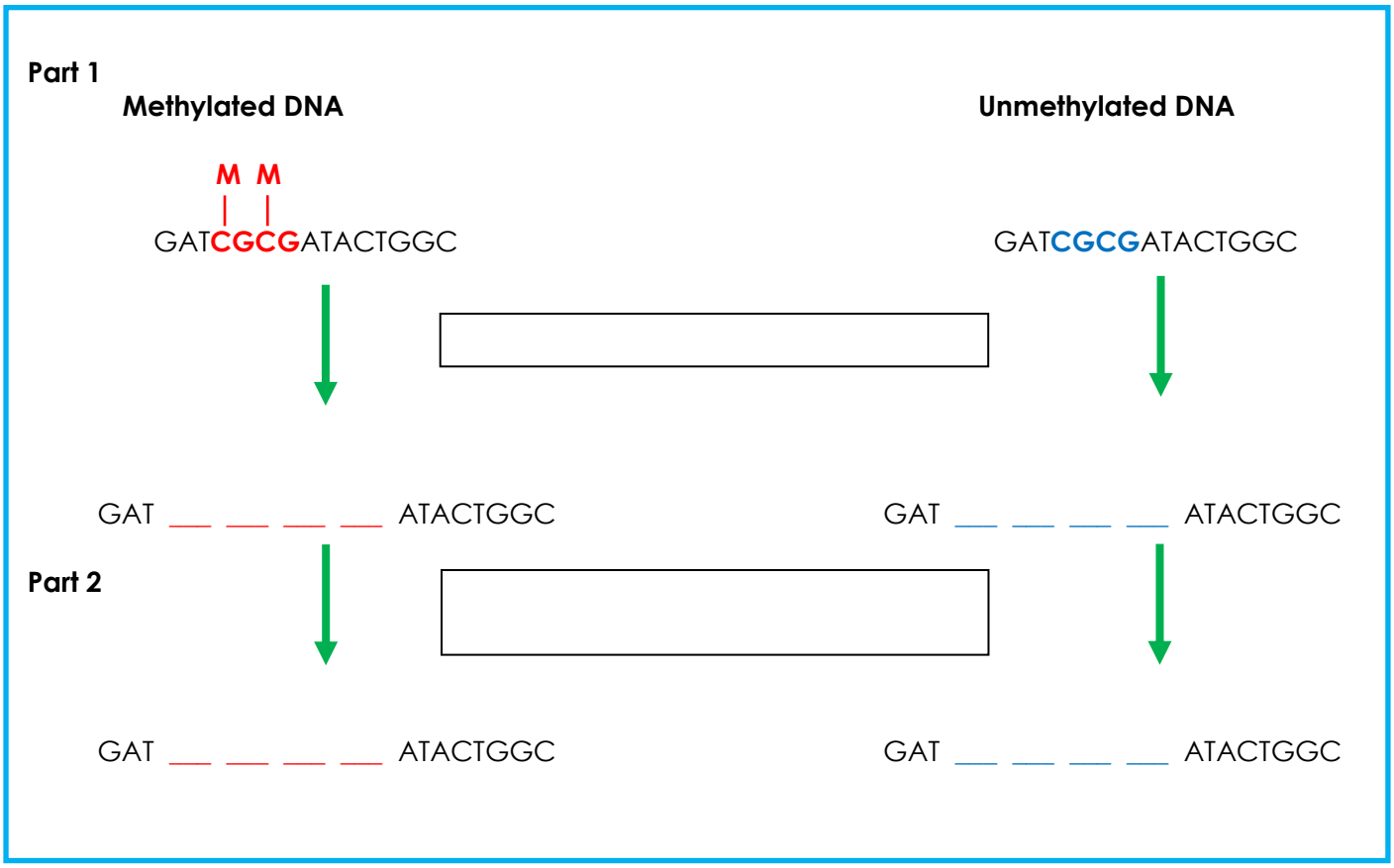
Washing the column:

Elution:

## Activity 2 – It's All in the Sequence

Once a pure sample of genomic DNA has been prepared scientists then treat the DNA with a special chemical.

In your own words explain what sodium bisulfite does to the DNA molecule. Complete part 1 of the diagram to help you explain the process.




In Part 2, scientists use restriction enzymes to identify whether the DNA is methylated or not. These enzymes recognise and cut DNA at specific sequences (recognition sequence). Think of restriction enzymes like a pair of scissors, but they can only cut at certain places.

Explain why after treating the DNA with sodium bisulfite the restriction enzyme *Bst*UI, which has the recognition sequence CGCG, is only able to cut methylated DNA. Write your answer below.

Discuss with your learning partner, why this technique is good for detecting DNA methylation in cancer. Write your answer below.

Now you know what sodium bisulfite does and what restriction enzymes are, it's your turn to have a go at investigating the methylation pattern of a real DNA sequence from a cancer.

Have a careful look at the DNA sequence on page 39, It's the same one you were studying earlier in tutorial 3. See if you can find the following restriction enzyme sites and mark them on the DNA sequence by drawing a box around the correct bases. Then fill in the table with the extra information.

| **Restriction Enzyme** | **Recognition Sequence** | **Number of Times Found** | **Converted Recognition Sequence** | **Still Cuts?** | |
|---|---|---|---|---|---|
| | | | | **Y** | **N** |
| *Bst*UI | CG ✂ CG | | | | |
| *Hpa*II | C ✂ CGG | | | | |
| *Sac*II | CCGC ✂ GG | | | | |

## Activity 3 – Predict the Pattern

Once the restriction sites have been found in the DNA sequence a scientist would then predict the restriction pattern observed after sodium bisulfite conversion and restriction enzyme digestion. They do this by drawing out all the different lengths of DNA fragments that could be produced after digesting the DNA with the restriction enzyme.

Use the DNA sequence above work out all the different restriction digest patterns that you would see after sodium bisulfite conversion and digestion with *Bst*UI and draw them out in the box. Remember to include the sizes of each of the fragments in base pairs (bp).

***Bst*UI Restriction Digest Patterns After Sodium Bisulfite Conversion**

**All Sites Unmethylated:**

**1st Site Methylated:**

**2nd Site Methylated:**

**All Sites Methylated:**

Explain why you drew these patterns.

## Activity 4 – Separating and Viewing DNA

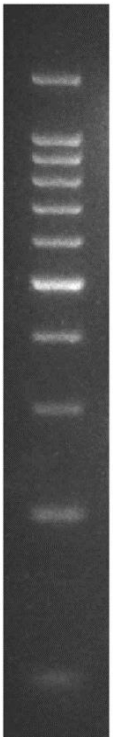
After sodium bisulfite conversion and restriction digestion there is still one more step to perform. The scientist has a problem as in the test tube is a mixture of all the different sized DNA restriction fragments that you worked out in activity 3.

Scientists use a very clever technique that enables them to separate and see all the different size fragments. This is called agarose gel electrophoresis.

In your own words, describe below how agarose gel electrophoresis works.

Draw what the bands would look like on the agarose gel, using the 100 base pair DNA ladder to help you. Label the DNA ladder with the correct sizes.

100bp
DNA ladder



## Tutorial Glossary

Use this space to write down any new words that you have learned in this tutorial.

| Word | Definition |
|---|---|
| | |
| | |
| | |
| | |
| | |

## Notes

## Homework

During this part of the tutorial you have heard all about a very important technique that scientists use in the laboratory to study DNA methylation.

To help you remember all the steps of COBRA fill in the flow chart on page 44. You can use text and diagrams to illustrate each step and make it as detailed as you can.

## **COBRA: CO**mbined **B**isulfite **R**estriction **A**nalysis

**Use the following keywords to help you:**
Genomic DNA extraction, sodium bisulfite conversion, restriction enzyme digestion of DNA, agarose gel electrophoresis.

STEP ONE

STEP TWO

STEP THREE

STEP FOUR

# Tutorial 5 – How to Write a Great Essay

## What is the Purpose of Tutorial 5?

This tutorial is dedicated to helping you develop all the important skills needed to plan and write your final assignment.

By the end of this tutorial I will be able to…

- Understand how to plan an essay using a mind map.
- Structure an essay in the correct way.
- Reference my essay with relevant sources.
- Confidently write my final assignment.

## Activity 1 – Plan it!

The most difficult part of writing an essay is knowing what to write, so it's a very good idea to prepare what you want to say.

The first thing you should always do is look at the essay question and underline or highlight the keywords. Have a go at doing this with your final assignment question, which is:

**Q: Describe how changes to the genome can contribute to the development of cancer.**

A mind map is a great way to start putting your ideas down on paper, just remember to keep referring back to the keywords in your essay question to make sure all your ideas are relevant.

Use the next page to make a mind map for your final assignment.

## MY MIND MAP

## Activity 2 – Structure it!

The next things to think about are the different parts of an essay and what to put in each of those parts.

In learning partners, sort out the instructions that you would use to write the introduction, main body and conclusion, then write them in the boxes below.

| Introduction | Main Body | Conclusion |
| --- | --- | --- |
| • | • | • |
| • | • | • |
| • | • | • |
| • | • | • |
| | • | |

## Activity 3 – Good Versus Bad!

In pairs read the short essay and use the space below to write about what "what went well" and "even better if". Make sure that you make good notes as you can use these as tips for when it comes to writing your final assignment.

What Went Well:

Even Better If:

Share what you've found out to the rest of the group.

## Activity 4 – Reference It!

Whenever you use information that someone else has written you need to acknowledge them by referencing them after the piece of information you have used.

Look back at the essay you were reading and see how the work was referenced. In learning partners, discuss how to write a reference and summarise it in a short sentence below:

To write a reference I need to include

Do some independent research using websites that you think might provide useful information to help you write your assignment. Make some notes below and don't forget to write down the reference for each website: Author, title of article, website address, [date you looked it].

## Notes

## Notes

## Homework – Final Assignment

Using all the information that you have learnt over the past five tutorials write approximately 2000 words to answer the following question:

**Q: Describe how changes to the genome can contribute to the development of cancer.**

***Key Points to Discuss:***

- What is cancer?
- What are DNA mutations?
- What is DNA methylation?
- Why can DNA mutations and DNA methylation contribute to the development of cancer?
- Use examples of different types of cancer to illustrate your answer.

Use your tutorial notes to guide you, but you can also do your own independent research.

# Tutorial 6 – Feedback tutorial

## What is the Purpose of Tutorial 6?

- To receive feedback on your final assignment
- To respond to the feedback from your Uni Pathways teacher
- To write targets for improvement on your final assignment

## Final assignment feedback from your Uni Pathways Teacher

(Remember to look at the mark scheme to help you understand what you have done well so far, and how you can do even better in your final assignment)

| Here are three things that my Uni Pathways Teacher thought I did well in my draft assignment |
|---|
| 1.<br><br>2.<br><br>3. |

| Here are three things that my Uni Pathways Teacher thinks that I could do to get a higher mark in my final assignment |
|---|
| 4.<br><br>5.<br><br>6. |

| Tasks from my Uni Pathways Teacher to do during the feedback tutorial to help me improve |
| --- |
| 7.<br><br>8.<br><br>9. |
| My response: |

| Actions I will take to improve my final assignment after this tutorial… |
| --- |
| 10.<br><br>11.<br><br>12. |

| Hand in date for my final assignment: | |
| --- | --- |

# Tutorial 7 – Final tutorial

## What is the Purpose of Tutorial 7?

- To receive feedback and a grade on your final assignment.
- To reflect on the programme including what you enjoyed and what was challenging.
- To ask any questions you may have about university.

## Final assignment feedback from my Uni Pathways Teacher

| Final mark: | University style grade: |
|---|---|
| Feedback: Here are three things that my Uni Pathways teacher thought I did well in my final assignment<br>•<br>•<br>• | |

| Here are three things that my Uni Pathways teacher thinks I should remember for when I am doing this kind of study in the future |
|---|
| •<br>•<br>• |

## University

| What questions do you still have about University after taking part in Uni Pathways? |
| --- |
| 13.<br><br>14.<br><br>15. |

## Reflecting on Uni Pathways

| What did you most enjoy about Uni Pathways? |
| --- |
| 16.<br><br>17.<br><br>18. |

| What did you find challenging about the programme? | How did you overcome these challenges? |
| --- | --- |
| 19.<br><br>20.<br><br>21. | 22.<br><br>23.<br><br>24. |

# Success Criteria – Essay-based assignments

| The Brilliant Club Mark Scheme Skills | Examples of success criteria to include in the baseline assessment, final assignment and homework guidance |
|---|---|
| Knowledge and understanding | Include content that is relevant to the topic and the specific assignment/homework title or question.<br><br>Include key words from the glossary and demonstrate that you understand them by explaining what they mean and how they relate to the topic. |
| Research and evidence | Include research findings from a wide range of sources. As well as using the sources provided, you should be discovering some sources yourself from the independent work that you do outside tutorials. |
| Developing an argument | Give reasons and evidence to back up the points that you make. You might find the PEE structure helpful:<br><br>• Point – make the key point clea.r<br>• Evidence – explain the evidence for the point.<br>• Explanation – explain why your point is relevant and important.<br><br>Make links to topics you have covered during tutorials as well as some topics that you have not discussed during tutorials. |
| Critical evaluation | Select relevant research evidence to back up your thinking. |
| Structure and presentation | Organise your ideas in paragraphs with a logical structure.<br><br>Include an introduction that clearly outlines what the assignment will contain.<br><br>Include a conclusion that summarises all the key points clearly.<br><br>Make sure that you have referenced everything correctly.<br><br>Include any diagrams that will help to illustrate your answer. |
| Language and style | Make sure your spelling, grammar and punctuation are accurate.<br><br>Use a formal style of writing that is appropriate for an academic essay. |

# Appendix 1 – Referencing Correctly

When you get to university, you will need to include references in the assignments that you write, so we would like you to start getting into the habit of referencing in your Brilliant Club assignment. This is really 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. In order to avoid losing marks in your final assignment, or even failing, you must be careful to reference your sources correctly.

## What is a reference?

A reference is just a note in your assignment which says if you have referred to or been influenced by another source such as book, website or article. For example, if you use the internet to research a particular subject, and you want to include a specific piece of information from this website, you will need to reference it.

## 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.

## How do I reference?

There are a number of different ways of referencing, and these often vary depending on what subject you are studying. The most important to thing is to be consistent. This means that you need to stick to the same system throughout your whole assignment. Here is a basic system of referencing that you can use, which consists of the following two parts:

1. **A marker in your assignment**: After you have used a reference in your assignment (you have read something and included it in your work as a quote, or re-written it your own words) you should mark this is in your text with a number, e.g. [1]. The next time you use a reference you should use the next number, e.g. [2].
2. **Bibliography**: This is just a list of the references you have used 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.

3. **Bibliography**: This is just a list of the references you have used 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.

   a. **Websites** – Author (if possible), title of the web page, website address, [date you accessed it, in square brackets].

   E.g. Dan Snow, 'How did so many soldiers survive the trenches?', http://www.bbc.co.uk/guides/z3kgjxs#zg2dtfr [11 July 2014].

   b. **Books** – Author, date published, title of book (in italics), pages where the information came from.

   E.g. S. Dubner and S. Levitt, (2006) *Freakonomics*, 7-9.

   c. **Articles** – Author, 'title of the article' (with quotation marks), *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', Guardian, 10 July 2014.

# Appendix 2 – Cancers Caused by DNA Mutations

https://www.cancer.net/navigating-cancer-care/cancer-basics/genetics/genetics-cancer
https://www.cancerresearchuk.org/about-cancer/what-is-cancer/genes-dna-and-cancer
https://ghr.nlm.nih.gov/condition (This website is useful for the genetics of different cancers)

**Lung Cancer**
Mutations in the *TP53*, *EGFR*, and *KRAS* genes are common in lung cancers.

The *TP53* tumour suppressor gene provides instructions for making a protein, called p53, that is located in the nucleus of cells throughout the body, where it attaches (binds) directly to DNA. The protein controls cell growth and division by monitoring DNA damage (mutations). When DNA becomes damaged, by agents such as toxic chemicals (tobacco smoke), radiation, or ultraviolet (UV) rays from sunlight, this protein plays a critical role in determining whether the DNA will be repaired or the damaged cell will self-destruct, a process known as apoptosis. If the DNA can be repaired, p53 activates other genes to fix the damage. If the DNA cannot be repaired, this protein prevents the cell from dividing and signals it to undergo apoptosis. By stopping cells with mutated or damaged DNA from dividing, p53 helps prevent the development of tumours.

*TP53* gene mutations result in the production of an altered p53 protein that cannot bind to DNA. The altered protein cannot regulate cell growth effectively and allows DNA damage to accumulate in cells. Such cells may continue to divide in an uncontrolled way, leading to tumour growth.

*TP53* is the most commonly mutated gene in people with cancer, with more than 50% of cancers involve a missing or mutated *TP53* gene. Because p53 is essential for regulating cell division and preventing tumour formation, it has been nicknamed the "guardian of the genome."

The *EGFR* and *KRAS* genes each provide instructions for making a protein that is embedded within the cell membrane, known as a receptor. When these proteins are turned on (activated) by binding to other molecules, signaling pathways are triggered within cells that promote cell growth. Mutations in the *EGFR* or *KRAS* gene lead to the production of a protein that is constantly turned on. As a result, cells constantly receive signals to divide, leading to tumour formation. When these genetic changes occur in cells in the lungs, lung cancer develops.

Researchers have identified many lifestyle and environmental factors that expose individuals to cancer-causing compounds (carcinogens) and increase the rate at which mutations occur, contributing to a person's risk of developing lung cancer. The greatest risk factor is long-term tobacco smoking, which increases a person's risk of developing lung cancer 25%. Other risk factors include exposure to air pollution, radon, asbestos, certain metals and chemicals, or second-hand smoke; long-term use of hormone replacement therapy for menopause; and a history of lung disease such as tuberculosis, emphysema, or chronic bronchitis. A history of lung cancer in closely related family members is also an important risk factor; however, because relatives with lung cancer are frequently smokers, it is unclear whether the increased risk is the result of genetic factors or exposure to second-hand smoke.

**Breast Cancer**
Some breast cancers that run in families are associated with inherited mutations in particular genes, such as *BRCA1* or *BRCA2*. Inherited mutations are those which occur in the DNA of the sperm or egg and are passed on to your children.

Whilst most people associate breast cancer with women, men with mutations in these genes also have an increased risk of developing several forms of cancer, including breast cancer. The proteins produced from the *BRCA1* and *BRCA2* genes are involved in fixing mutated DNA, which helps to maintain the stability of a cell's genetic information. They are described as tumour suppressors because they help keep cells from growing and dividing too fast or in an uncontrolled way. Mutations in these

genes impair DNA repair, allowing potentially damaging mutations to persist in DNA. As these defects accumulate, they can trigger cells to grow and divide without control or order to form a tumour.

**Prostate Cancer**
Prostate cancer is a common disease that affects men, usually in middle age or later. In this disorder, certain cells in the prostate become abnormal and multiply without control or order to form a tumour. The prostate is a gland that surrounds the male urethra and helps produce semen, the fluid that carries sperm. As the tumour grows larger, signs and symptoms can include difficulty starting or stopping the flow of urine, a feeling of not being able to empty the bladder completely, blood in the urine or semen, or pain with ejaculation.

Inherited mutations in particular genes, such as *BRCA1*, *BRCA2*, and *HOXB13*, account for some cases of hereditary prostate cancer. Men with mutations in these genes have a high risk of developing prostate cancer and, in some cases, other cancers during their lifetimes. In addition, men with *BRCA2* or *HOXB13* gene mutations may have a higher risk of developing life-threatening forms of prostate cancer.

The *HOXB13* gene provides instructions for producing a protein that attaches (binds) to specific regions of DNA and controls the switching on/expression of other genes. These types of proteins are called a transcription factors. Like BRCA1 and BRCA2, the HOXB13 protein is thought to act as a tumour suppressor. *HOXB13* gene mutations may result in impairment of the protein's tumour suppressor function, resulting in the uncontrolled cell growth and division that can lead to prostate cancer.

**Neuroblastoma**
Neuroblastoma is a type of cancer that most often affects young children, mostly under the age of 5 years old. Neuroblastoma occurs when immature nerve cells called neuroblasts become abnormal and multiply uncontrollably to form a tumour. Most commonly, the tumour starts in the nerve tissue of the adrenal gland located above each kidney. Other common sites for tumours to form include the nerve tissue in the abdomen, chest, neck, or pelvis. Neuroblastoma can spread (metastasise) to other parts of the body such as the bones, liver, or skin.

It is thought that mutations in at least two genes are required to cause sporadic (not inherited) neuroblastoma. Less commonly, gene mutations that increase the risk of developing cancer can be inherited from a parent. When the mutation associated with neuroblastoma is inherited, the condition is called familial neuroblastoma. Mutations in the *ALK* gene has been shown to increase the risk of developing sporadic and familial neuroblastoma.

Several mutations in the *ALK* gene are involved in the development of sporadic and familial neuroblastoma. The *ALK* gene provides instructions for making a protein called ALK receptor tyrosine kinase. It is thought that this protein plays an important role in cell division and growth. Mutations in the *ALK* gene result in an abnormal version of ALK receptor that is constantly turned on. This can result in the abnormal division and growth of immature nerve cells and lead to neuroblastoma.

**Wilms' Tumour**
Mutations in the oncogene, *CTNNB1* gene have been found in Wilms' tumour which is a rare form of childhood kidney cancer. These mutations are somatic (non-inherited) and occur only in kidney cells that give rise to the tumour.

Normally, the *CTNNB1* gene codes for a protein called beta-catenin which promotes the growth and division (proliferation) of cells and helps determine the specialised functions a cell will have (differentiation). Certain proteins attach (bind) to beta-catenin, allowing it to move into the cell nucleus from the cytoplasm. Once in the nucleus, beta-catenin acts as a transcription factor protein and interacts with other proteins to switch on the expression of particular genes involved in growth promotion.

In Wilms' tumour, mutations to *CTNNB1* result in an over-active beta-catenin protein which switches on other genes involved in promoting the growth of kidney cells and cancer growth.

# Notes

# Notes

# Notes

UNI PATHWAYS

UNI PATHWAYS

researchersinschools.org