



# DP IB Biology: HL



## 7.2 Transcription & Gene Expression

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## 7.2.1 Regulation of Gene Expression by Proteins



Your notes

### The Promoter Region

#### The function of the promoter

- Only some DNA sequences code for the production of polypeptides, these are called **coding sequences**
- Non-coding sequences produce functional RNA molecules like **transfer RNA (tRNA)** or are involved in the **regulation of gene expression** such as **enhancers**, **silencers** and **promoters**
- The promoter is a non-coding sequence **located near to a gene**
  - The promoter is not itself transcribed
- The promoter acts as the **binding site for RNA Polymerase** during the **initiation of transcription**
- Binding of RNA Polymerase to the promoter is under the control of various **regulatory proteins**



Your notes

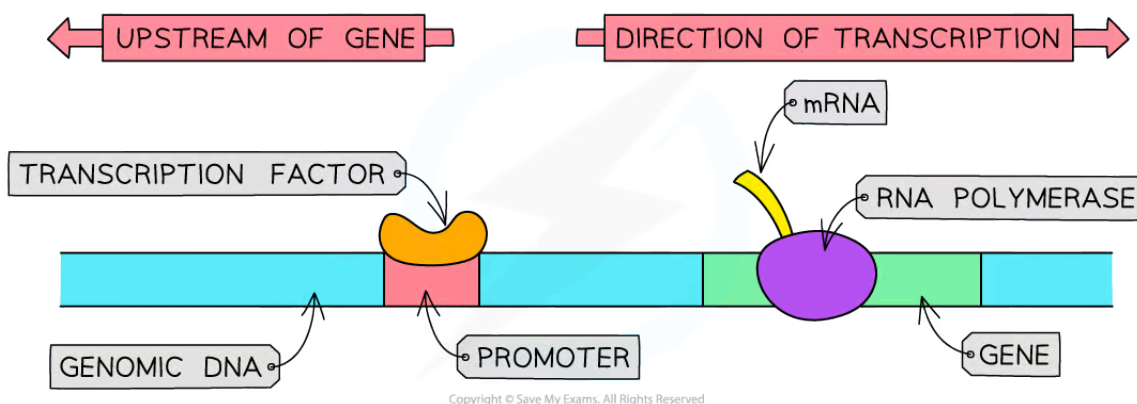
## Gene Expression Regulated by Proteins

### Gene expression varies in different cells

- Genes are **not expressed equally** in every cell
  - Essential genes** needed for the survival of an organism are **expressed all the time**
    - eg. Genes for the main enzymes in the **respiratory pathways** or ATP synthase
  - Other genes are **only expressed when needed** and at levels that make specific amounts of protein
    - eg. The gene for rhodopsin that is only expressed in light-sensitive receptor cells of the eye
- Regulatory mechanisms** exist to ensure the **correct genes are expressed at the correct time**
  - These mechanisms are different between prokaryotes and eukaryotes but both employ **transcription factors** and other proteins that bind to specific sequences in DNA

### Regulation of gene expression in eukaryotes

- Eukaryotes regulate gene expression in response to variations in their environment
- Specific proteins bind to DNA to **regulate transcription** and ensure that only the genes required are being expressed in the correct cells, at the correct time and to the right level
  - This is key to how processes of cellular differentiation and development in multicellular organisms are controlled
- Regulatory transcription factor proteins include **activators** and **repressors**, they are unique to a specific gene
  - Activator proteins bind to **enhancer** sequences and **increase** the rate of transcription
  - Repressor proteins bind to **silencer** sequences and **decrease** or **block** transcription
- General transcription factors** are a type of transcription factors that **bind directly to the promoter** to help initiate transcription
  - This helps RNA polymerase to attach to the promoter and start transcribing the gene
  - In eukaryotes, several general transcription factors are needed for transcription



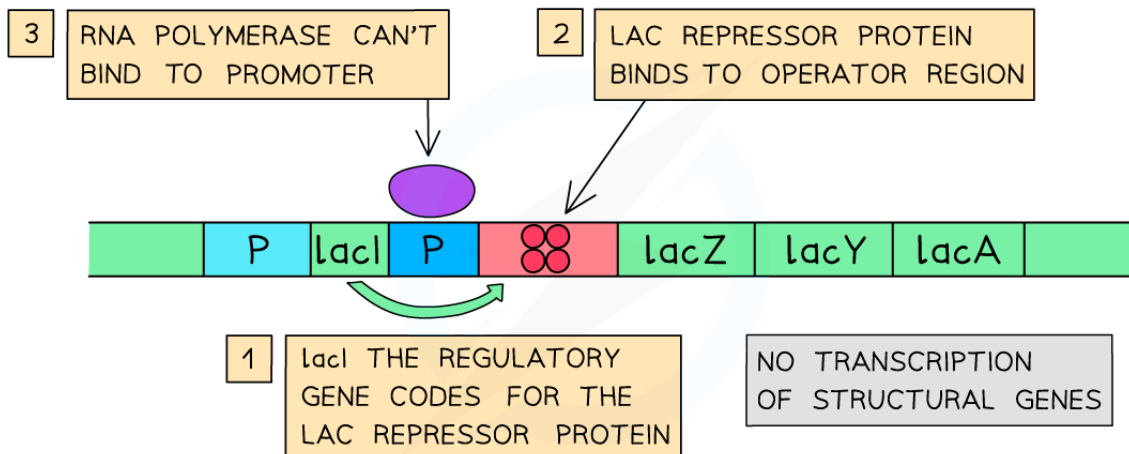
*A transcription factor binding to the promoter region of a gene which allows RNA polymerase to bind and for transcription to occur.*

### Regulation of gene expression in prokaryotes



Your notes

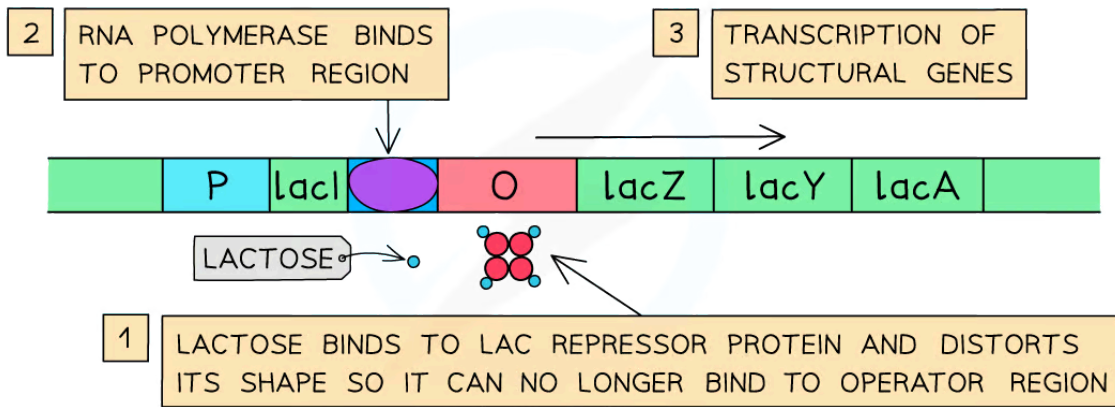
- Unlike in eukaryotes, only **one general transcription factor** and RNA polymerase is needed to initiate transcription
- When prokaryotes need to respond to environmental changes, additional proteins interact **directly with target regions of DNA** to alter the level of gene expression
- For example, the genes involved in the breakdown and metabolism of lactose by *Escherichia coli* are **repressed in the absence of lactose**
  - When no lactose is available, a **repressor protein** binds to DNA near the promoter of the genes for the proteins that degrade lactose (*lacZ*, *lacY* and *lacA*)
    - The repressor **physically blocks RNA polymerase** from accessing that section of the bacteria's genome
  - If lactose is present, the **repressor protein is released from the DNA** allowing RNA polymerase to begin transcription
  - The genes are expressed and the lactose-degrading enzymes are produced
    - Lactose can be broken down and used for energy generation in this way
  - Once all the available lactose is metabolised, the **genes are repressed again**
  - This mechanism of **negative feedback** ensures that a cell's resources are not wasted making proteins that are not needed



**In the absence of lactose the repressor protein binds which prevents RNA polymerase from initiating transcription of genes coding for enzymes used to metabolise lactose.**



Your notes



**When lactose is present it binds to the repressor protein allowing RNA polymerase to bind to the promoter and begin transcription**

 **Examiner Tip**

In your exam you may be asked to describe how the regulation of gene expression affects mRNA produced by transcription or the amount of final polypeptide that is produced. To help answer this, it is important to understand the roles of the various different sections of a gene (promoter, coding sequence, terminator) and the processes of transcription and translation.

## 7.2.2 Environment & Gene Expression



Your notes

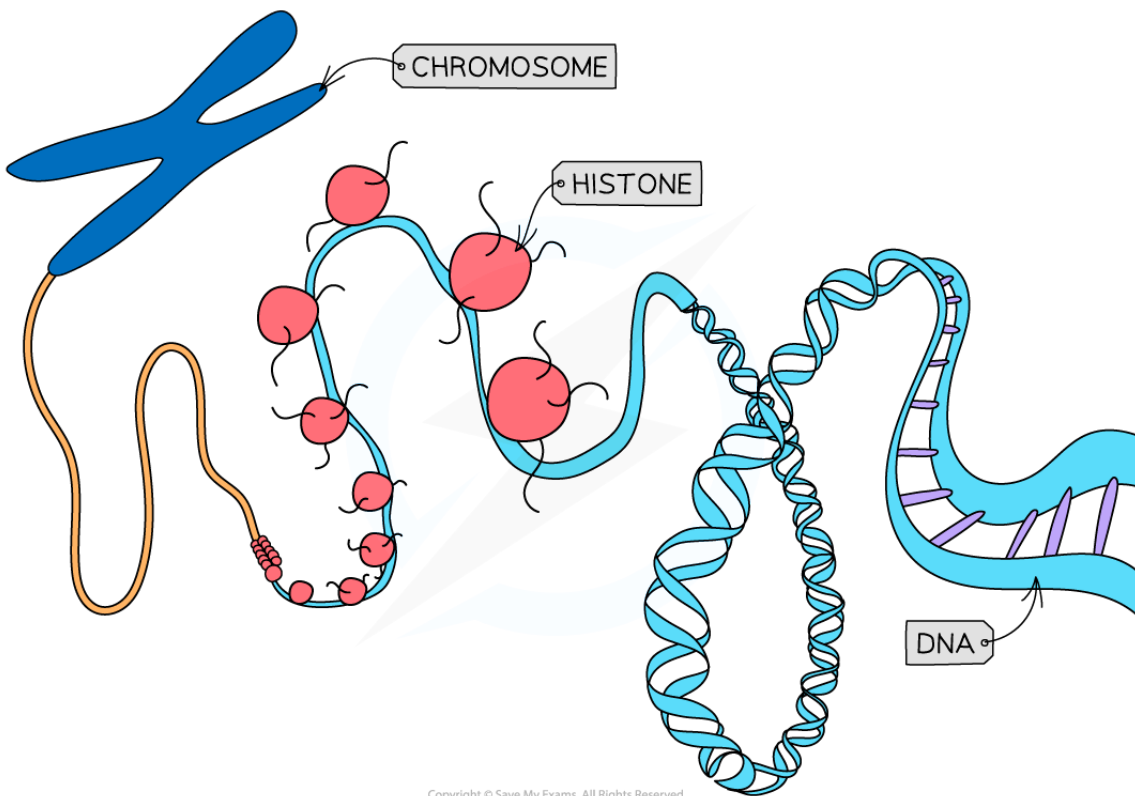
### Environment & Gene Expression

#### Environment and Gene Expression

- An organism's internal or external **environment can influence gene expression** patterns
- The levels of regulatory proteins or transcription factors can be affected **in response to environmental stimuli** such as light, and chemicals including **drugs** and **hormones**
- For example, enzymes are activated in response to ultraviolet radiation and increase the **expression and production of melanin**, leading to skin pigmentation
- **Temperature** can also influence gene expression as demonstrated by organisms
  - The Himalayan rabbit (*Oryctolagus cuniculus* L.) possesses a gene for the development of pigmentation in its fur
    - The gene is inactive above 35°C but active between 15°C and 25°C
    - In the parts of the body that are cooler such as ears, feet and nose the gene becomes active making these areas black
  - Temperature also affects the expression of the sex chromosomes in Australia's bearded dragon lizards (*Pogona barbata*)
    - Lizards raised in hot temperatures were female in appearance and were capable of bearing offspring
    - Despite having the ZZ chromosomes usually found in male lizards
- There is much debate about whether a particular phenotype or behaviour can be attributed to **inheritance** or **environment**
- Environmental factors explain the **differences** observed between **identical twins** as they age
  - Identical twins have the same DNA but their individual genomes can come under **different outside influences**
  - They can change independently, leading to **phenotypic differences** such as height
  - Twin studies have shown that **environmental factors have a greater influence** on many disease states (e.g. cancer and rheumatoid arthritis) compared to genetic influence



Your notes



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**DNA is wrapped around histone proteins which form a nucleosome. Nucleosomes coil tightly around each other to form the chromosome structure.**



Your notes

## Epigenetics

**NOS: Looking for patterns, trends and discrepancies; there is mounting evidence that the environment can trigger heritable changes in epigenetic factors**

- Epigenetics is the **genetic control by factors other than** an individual's DNA sequence
- Epigenetics is a broad term that encompasses (m)any alterations
  - That induce **switching-on** and **switching-off** of genes, but
  - **Without changing** the actual genetic code
- Epigenetics involves **heritable changes in gene function**, without changes to the DNA sequence
- In eukaryotic cells, nuclear DNA is wrapped around **proteins** called **histones** to form **chromatin**
- Chromatin can be **chemically modified** in different ways to alter gene expression
  - **Methylation** of DNA (chemical addition of a  $-CH_3$  group)
  - Histone modification via **acetylation, methylation** and **phosphorylation** of amino acid tails
- Such modifications are called **epigenetic tags** and collectively, all the epigenetic tags in an organism is called the **epigenome**
- The epigenome can undergo changes due to environmental factors
  - **Smoking, stress, exercise** and **diet** can cause epigenetic changes
  - **Internal signalling** from the body's own cells can also cause modifications to occur
- Epigenetic modification is independent, histone modification in one area is not linked to modification in another
- Like the genome, the **epigenome is heritable**
  - Mounting evidence demonstrates that modifications to the epigenome in one generation **can be passed on** to the next generation at cellular or whole organism level

### Examiner Tip

Epigenetics can be distinguished from mutations, both of which lead to changes in the expressed characteristics of genes. Whilst mutations affect the genetic code itself eg. by altered nucleotide sequences, epigenetics affect the way the code is read.

Think about an identical passage of text being read by two different people, one with perfect Queen's English and the other with a very strong regional dialect. Despite the text being the same (no mutations), the effect of the dialect (epigenetics) might alter the meaning of the piece drastically to a listener.





Your notes

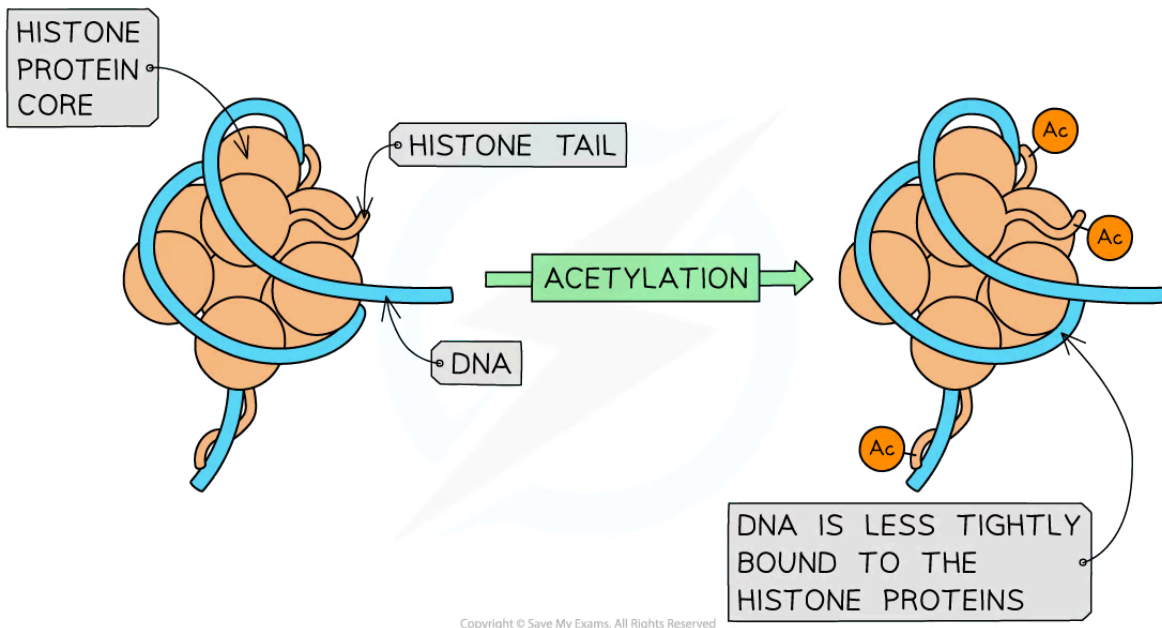
## 7.2.3 Transcription

### Nucleosomes Regulate Transcription

- Nucleosomes are the **structural unit of DNA packaging** in eukaryotes that **facilitate supercoiling**
- Within a nucleosome, DNA is wrapped around proteins called **histones**
- The tails of histones can be chemically modified which can influence **whether a gene will be expressed or not**
  - An **acetyl** group, **methyl** group or a **phosphate** group can be added
  - Chemical modifications can either **activate or deactivate genes** by making the gene more or less accessible to transcription factors
- Methyl groups can also be **directly added to DNA** to change the activity of a gene

#### Acetylation and methylation of histone tails

- Positively charged **lysine** (an amino acid) in histone tails binds to negatively charged DNA
  - This helps DNA to **coil tightly** around the histone protein core
- Adding an acetyl group (acetylation) to lysine **neutralises the charge**, causing the DNA to be **less tightly wrapped**
  - RNA polymerase and transcription factors can more easily access the DNA so **gene expression is stimulated**
- Adding a methyl group (methylation) to lysine maintains the positive charge causing the DNA to be more **tightly wrapped** and therefore **inhibits transcription/expression**



#### Acetylation of the Nucleosome

#### Methylation of DNA

- DNA methylation commonly involves the direct addition of a methyl group ( $-CH_3$ ) to cytosine bases which can influence gene expression
- Methylation of DNA suppresses the transcription of the affected gene by inhibiting the binding of transcription factors
- Cells use this mechanism to lock genes in the 'off' position
- DNA methylation can be affected by many environmental, lifestyle or age-related factors



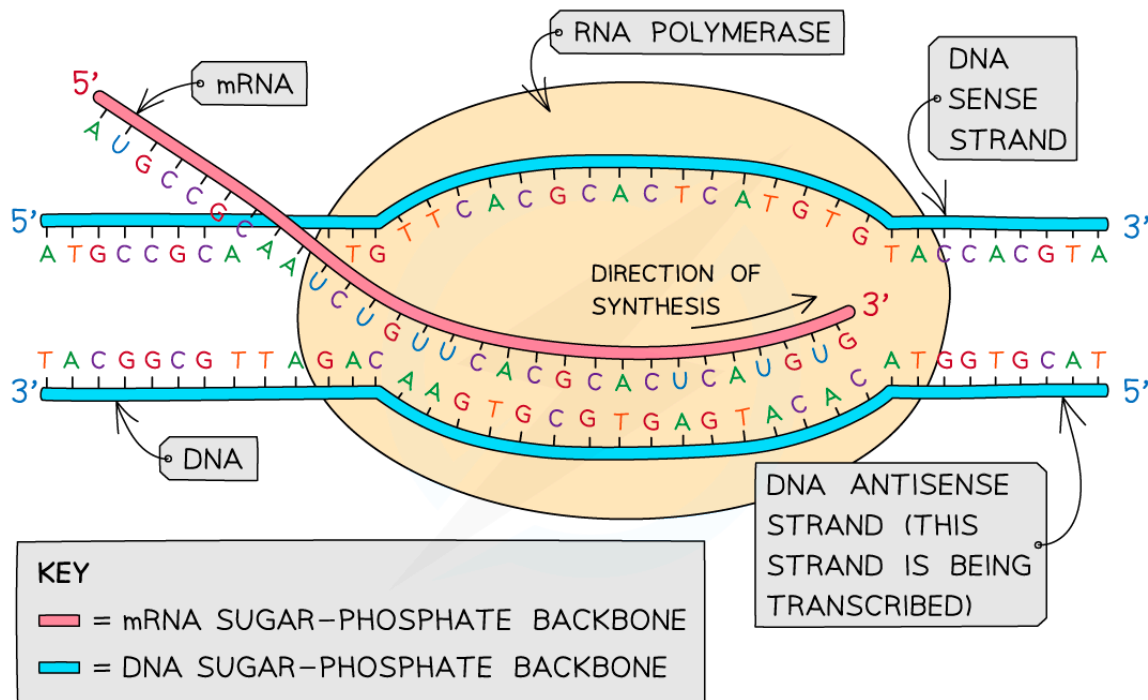
Your notes



Your notes

## Direction of Transcription

- The synthesis of mRNA occurs in **three stages**:
  - Initiation
  - Elongation
  - Termination
- During **initiation**, RNA polymerase binds near the promoter, causing the **DNA strands to separate** to form an open complex
- During **elongation**, RNA polymerase moves **along the antisense strand**
  - RNA polymerase adds the 5' end of the free RNA nucleotide to the 3' end of the growing mRNA molecule
  - Elongation occurs in a **5' to 3' direction**, synthesising a single strand of RNA
- Termination occurs when RNA polymerase reaches a **terminator sequence**
  - Which triggers the **detachment of the polymerase enzyme and mRNA strand**



*The antisense strand of the DNA molecule is the one that is transcribed*



Your notes

## 7.2.4 Post-transcriptional Modification

### Modification of RNA

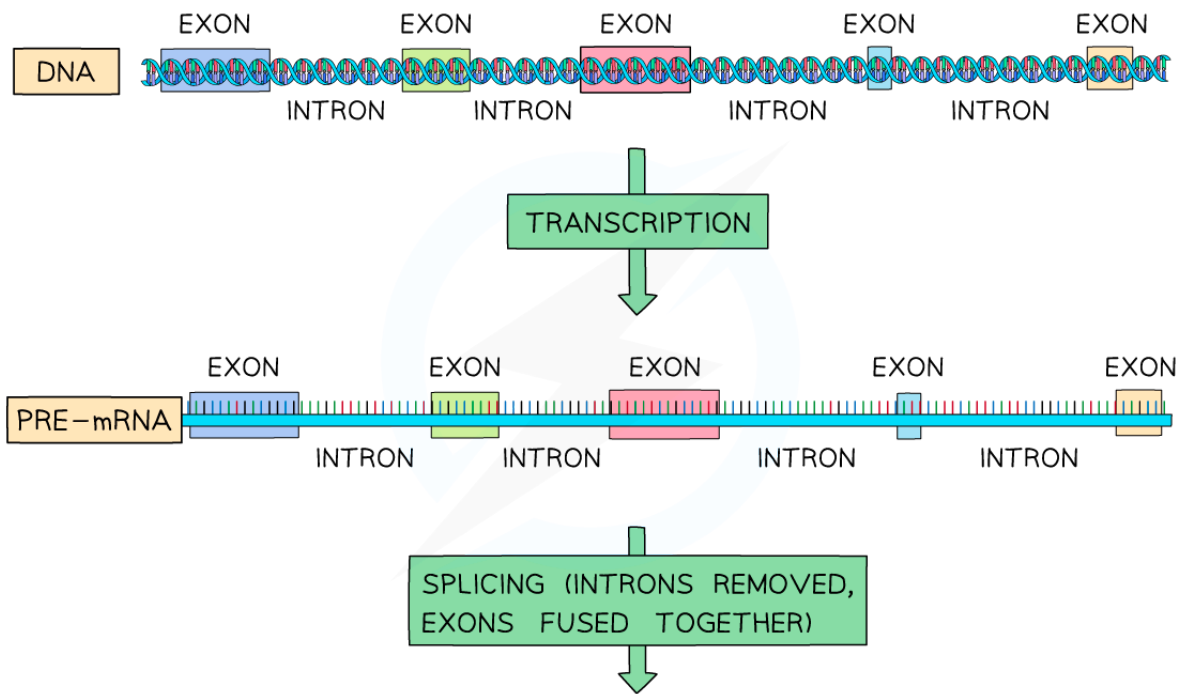
- In all kingdoms of life, **gene expression can be regulated** after an mRNA transcript has been produced
- **Post-transcriptional modification of mRNA**
  - Helps **prevent degradation**
    - mRNA is single stranded and therefore, **inherently unstable**
    - Increases the **efficiency** of protein synthesis
    - In eukaryotes, expands the complexity of the proteome
- Prokaryotic mRNA does not require any significant post-transcriptional modification as **translation can occur immediately** which prevents degradation of the mRNA
- In eukaryotes, transcription and translation occur in **separate parts of the cell**, allowing for significant post-transcriptional modification to occur
- In eukaryotes, the immediate product of an mRNA transcript is called **pre-mRNA** which needs to be modified to form **mature mRNA**
- **Three** post-transcriptional events must occur
  1. A **methylated cap** is added to the 5' end to protect against degradation by exonucleases
  2. A **poly-A tail** (long chain of adenine nucleotides) is added to the 3' end for further protection and to help the transcript exit the nucleus
  3. **Non-coding sequences are removed** through **mRNA splicing**



Your notes

## mRNA Splicing

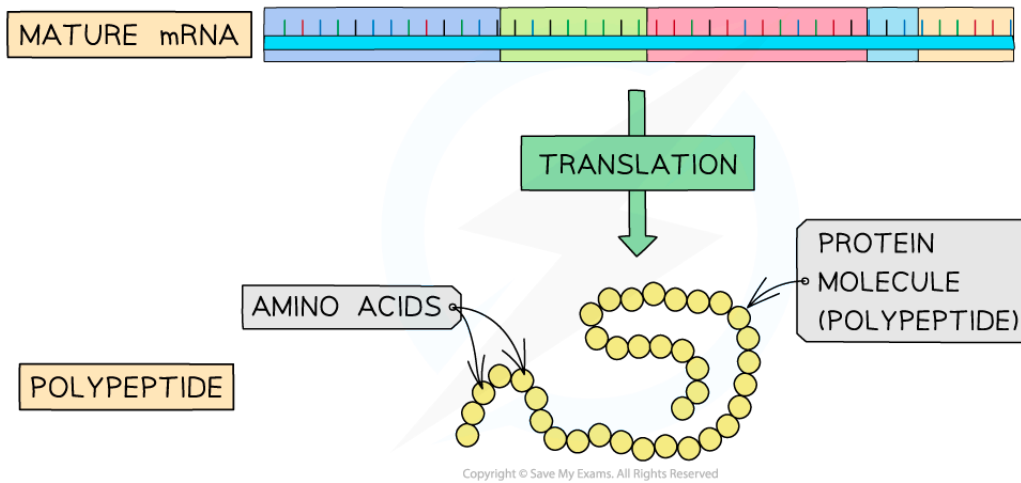
- Eukaryotic genes contain both **coding** and **non-coding sequences** of DNA
  - Coding sequences are called **exons**
  - Non-coding sequences are called **introns**
- During transcription **the whole gene is transcribed** including all introns and exons
  - Introns are not translated** as they do not code for amino acids and **need to be removed**
- Before the pre-mRNA exits the nucleus, **splicing** occurs, during which
  - Introns (non-coding sections) are removed
  - Exons (coding sections) are joined together
  - The resulting **mature mRNA molecule contains only exons** and exits the nucleus before joining a ribosome for translation



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Your notes



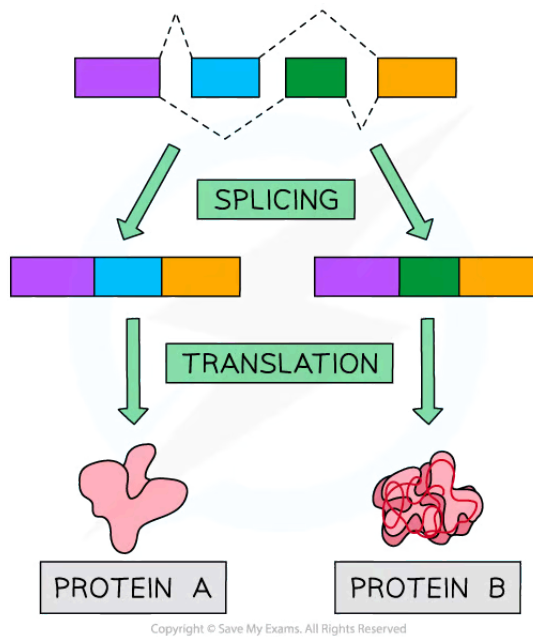
*The RNA molecule (known as pre-mRNA) produced from the transcription of a gene contains introns that must be removed (to form mature mRNA) before translation can occur*

### Alternative splicing

- The exons (coding regions) of genes can be spliced in many different ways to produce **different mature mRNA molecules** through alternative splicing
- A particular exon may or may not be incorporated into the final mature mRNA
- Polypeptides translated from alternatively spliced mRNAs may **differ in their amino acid sequence**, structure and function
- This means that a **single eukaryotic gene can code for multiple proteins**
- This is part of the reason why the **proteome is much bigger than the genome**



Your notes



*Image showing the alternative splicing of a gene to produce two different proteins*

 **Examiner Tip**

It is important you learn the terms pre-mRNA and mRNA, their location and whether they include introns as well as exons. A handy way to distinguish between introns and exons is to remember that **EX**ons are **EX**pressed.



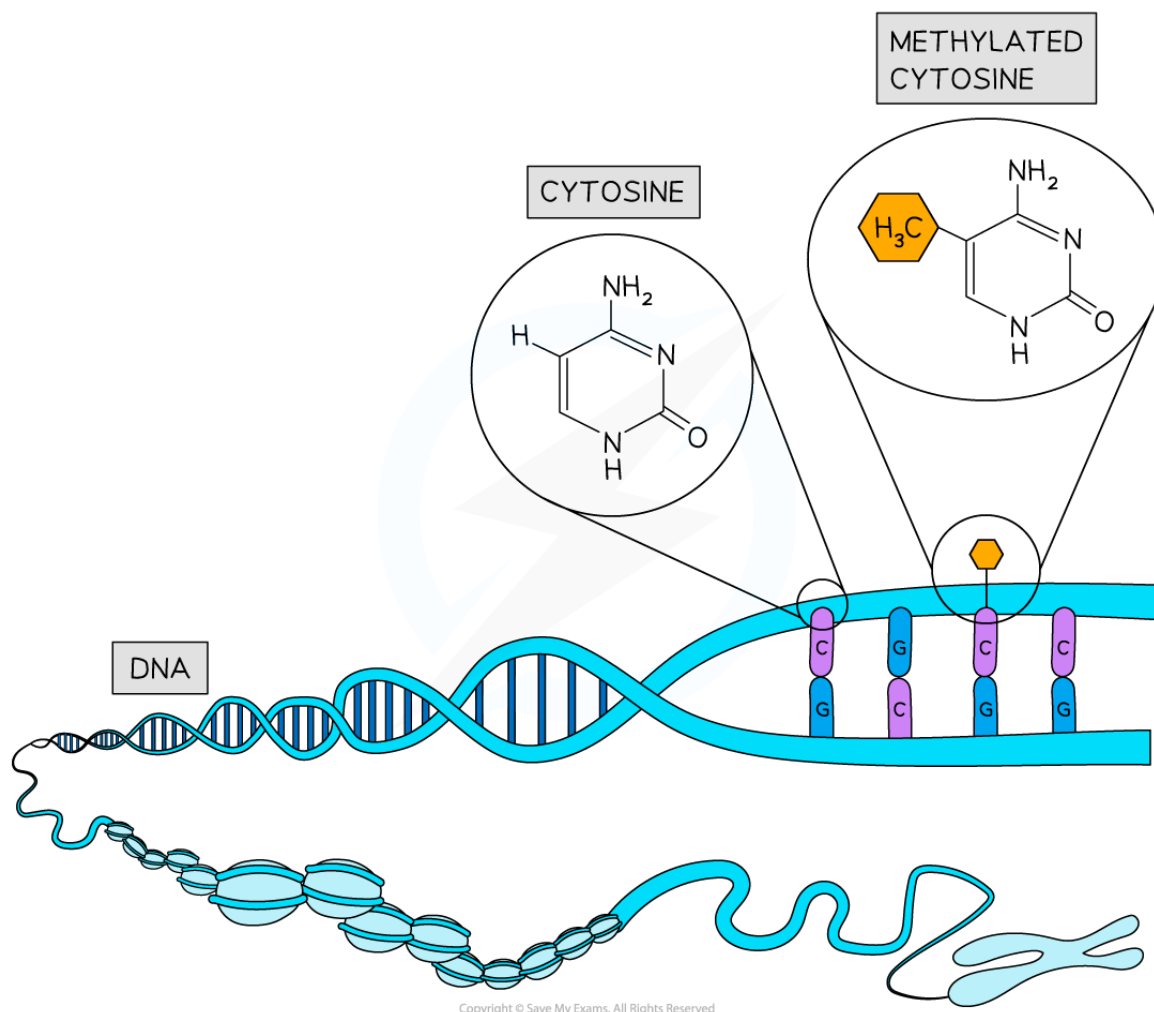
Your notes

## 7.2.5 Skills: Analysing DNA Methylation Patterns

### Skills: Analysing DNA Methylation Patterns

#### Methylation of DNA

- **Methyl groups** ( $-\text{CH}_3$ ) can be directly added to DNA to **change the activity** of a gene
- DNA methylation commonly involves the direct addition of a **methyl group to cytosine bases** which can influence gene expression
- Methylation of DNA **suppresses the transcription** of the affected gene by **inhibiting the binding** of transcription factors
  - Cells use this mechanism to **lock genes in the 'off'** position



**DNA methylation involves the addition of a methyl group to a cytosine nucleotide**

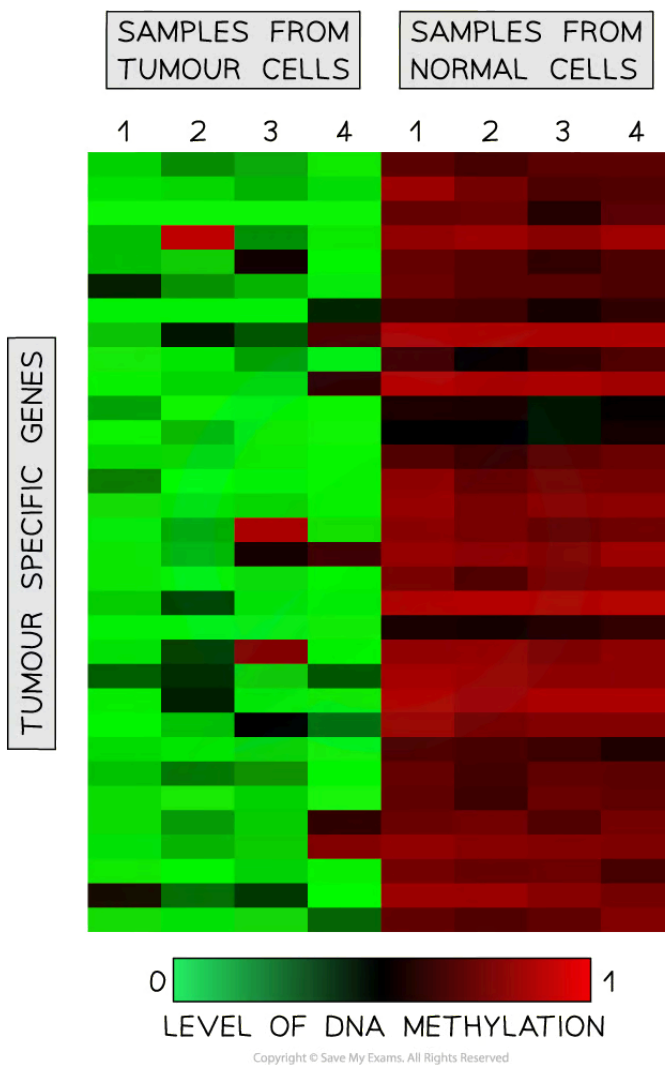




Your notes

## Analysing DNA Methylation Patterns

- DNA methylation **varies throughout a lifetime** and can be affected by environmental, lifestyle or age-related factors
- Changes in DNA methylation are observed in genetic diseases like **cancer**
- DNA methylation can be used as a **biomarker** to identify cancer related genes
  - This could help **develop therapeutics** to improve early diagnosis of disease
- Numerous methods are available to identify **which cytosine bases** have been methylated
- **Analysis of methylation patterns** between a disease and non-disease state can help identify disease marker genes



**DNA Methylation analysis showing reduced methylation of tumour-specific genes in cancerous cells. Reduced methylation results in genes always being 'switched on' which can lead to cancer**