**KS3/4: Discovering Epigenetics – Building a model**

**Background on DNA**

* DNA stands for Deoxyribonucleic Acid
* It is a set of instructions for every living thing (present plants, fruit, animals, bacteria etc.)
* DNA contains genes, located in exons, and a specific sequence or code of DNA will form a specific gene that can be transcribed into mRNA (messenger RNA). This is translated into a sequence of amino acids that form the proteins that are the building blocks of all living organisms. Proteins form enzymes, antibodies, and form structural components of muscle, hair, just to name a few examples.
* The proteins that form from DNA and genes are what determine the way you look, your hair colour, height, blood type.
* Our DNA is inherited 50% from your biological mother and father. When fertilized, an egg and sperm will combine their respective DNAs to develop an offspring with a unique set of DNA code (with the exception of identical twins)

**Where is DNA found?**

* DNA is found in almost every cell in ever living organisms.
  + A notable cell type without any DNA is the red blood cells, which has evolved to not have a nucleus or DNA, to give it as much room as possible to carry iron and oxygen.
* A nucleus is a cellular organelle contained within these cells, and acts like the brain of the cell, containing almost all of the DNA required to make any cell in our body.
  + Interestingly the mitochondria, another cellular organelle that acts as the powerhouse, has it’s own DNA (mitochondrial DNA, mtDNA)
* We have 46 chromosomes from a human cell (23 pairs, each pair has a copy from your mother and father).
* Our DNA is 50% similar to that of a banana, 98% similar to a chimpanzee, and 99.9% similar to other humans. That 0.1% accounts for all of the differences that we see between each other.

**Why is it important that we understand DNA?**

* Some diseases are caused by faulty DNA
  + Down syndrome, Cystic Fibrosis, Huntington’s Disease, cancer etc.
  + There are examples of those that we are born with, and those that develop in adulthood as a result of mutations to our DNA and the regulation of gene expression.
  + The more we understand about DNA in a normal situation, and the changes seen in disease, the better we can develop ways of preventing and treating the disease itself.
* Gene transfer helps to make proteins, such as the one that makes blood clot
* Genetically-modified (GM) crops can resist pest attacks or weed-killers

**What is epigenetics?**

Epigenetics is a mechanism for regulating gene activity independent of DNA sequence that determines which genes are turned on or off:

* in a particular cell type
* in different disease states
* in response to a physiological stimulus

All of your body’s roughly 50 trillion cells contain the same genetic information encoded within your DNA, but each cell type looks and functions very differently. DNA is interpreted differently in each cell type due to epigenetics, a collection of chemical marks that affect how genes behave. As such, epigenetics is part of what allows each part of your body to do different jobs.

Each cell in your body contains about 2 metres of DNA. To fit it into the cell nucleus, which is 10 times smaller than the width of a human hair, it needs to be organised: wrapped around molecules called nucleosomes like a thread around miniature reels, which are arranged into fibres and then folded into chromosomes. Epigenetic marks are attached to the nucleosomes, and from here they change how nearby DNA is used by the cell.

**What are epigenetic marks?**

Epigenetic marks can be small chemical modifications (e.g. methylation) of the DNA or the histone proteins that make up the nucleosomes. They do not alter the DNA sequence, but affect how it is read to make RNA. Different histone marks affect how strongly DNA sticks to histones, making it more or less accessible. This in turn affects whether the gene is switched on or off. Each cell type has its own set of epigenetic marks, which act like a set of instructions to determine which genes are active and what the cell will do.

**What is a nucleosome?**

Each nucleosome is constructed from eight histone proteins. Each histone has a globular ‘blobby’ shape with a ‘tail’ extending away from it. These tails can be modified with epigenetic marks - methyl (CH3) or acetyl (CH3CO) groups. The DNA is wrapped around the nucleosomes.

Methylation attaches methyl groups to histones, this can result in nucleosomes packing tightly together. This makes it hard for the cell to read the DNA and so genes near methylated nucleosomes are repressed

(switched off).

Histone acetylation results in loose packing of nucleosomes, making it easier for other proteins to get to the DNA, so nearby genes are expressed (switched on). In this way cells can ‘differentiate’ i.e. specialise to become different cell types such as blood, skin, muscle or brain cell

To further understand the role that methylation and acetylation may play in controlling the transcription of genes, we want to know which marks are found near which genes in different cells.

**Why do scientists want to understand epigenetics?**

Epigenetic marks are changed in:

* Different cell types
* Disease states
* Response to physiological stimuli
* Over time with age

Scientists at the Babraham Institute are investigating how epigenetics can control our DNA to switch genes on and off at the right time in response to the right signals. This can have important consequences for our development, growth and long-term health.

**How do scientists study epigenetics?**

We use a technique called Chromatin Immuno Precipitation Sequencing (ChIP-Seq) in which the DNA is broken apart and specialised proteins called antibodies are used to filter out particular epigenetic marks. The DNA wrapped around the marked histones is collected and we can then analyse these sections of DNA on a sequencing machine. The machine reads the genetic code of A’s, T’s, G’s and C’s that each piece contains. We use the code to identify where each piece of DNA came from and the gene it is part of.

We have to break DNA into pieces so that we can sequence it and find out where epigenetic marks are. When we get the sequencing results back, we have to compare the sequences of these DNA fragments to how we know the DNA of a mouse or human (for example) looks. We then work out where our DNA fragments came from in the DNA, a bit like using the picture on a puzzle box to help us complete a jigsaw.