24: EPIGENETIC MECHANISMS

A zygote is a cell that can become any type of cell. The DNA in the nucleus contains every bit of information that every type of cell will need for the entire lifetime of the organism. A fairly large portion of the DNA contains instructions for embryonic development. Once the body has fully formed, this information is no longer necessary and will be locked away permanently. Also, bodies change and grow over time. When children begin to turn into adults, their bodies will begin to make proteins they never made before.

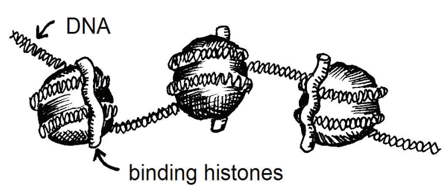
The nucleus has a way to control what sections of DNA can be opened at what times. The opening and closing of DNA is called ***epigenetics***. "Epi" means "outside of" (or "on top of") so epigenetics is on the outside of the genes. A gene is a piece of DNA that codes for one thing. The traditional understanding of a gene was a continuous strip of DNA, running along like a section from a bead necklace. New research has suggested that it is more complicated than this. A gene, even though it codes for one thing, (such as a particular protein), can be encoded as smaller sequences located in different places, not one continuous piece all in one place. The polymerase machinery has to copy the small sections then splice them together to make the mRNA. Or, a gene might be encoded in a continuous strip but using only every other base pair, or every third base pair. Genes have turned out to be a lot more complicated than anyone had imagined. However, it is okay to keep it simple for now and think of a gene as one strip, like a section snipped from a necklace.

The most permanent way to close DNA is ***methylation***. The ***methyl*** group, CH_3, can be used like clip. The methyl clip fastens to cytosines that are almost opposite each other. We have to say "almost opposite" because, of course, cytosines can't be exactly opposite because they always match up with guanine across from them. However, if you have a C-G next to a G-C, the cytosines are close enough that a methyl clip can be placed on the cytosines. This clip prevents those polymerase machines from using the DNA to create RNA. If the polymerase "sled" tries to ride along the DNA, it gets stuck on these clips and has to stop. If the polymerase can't ride along that section of DNA, no mRNA will be made. If no mRNA can be made, no proteins will be made, and the gene has effectively been silenced.

These methyl clips are put on by special enzymes designed to do that job. They have to do this every time the DNA is replicated (during mitosis, for example). DNA replication is complicated enough, but all those little methyl tags have to be added, too!

Another way to prevent gene transcription is ***histone modification***. A ***histone*** is a protein gadget that acts like a spool. DNA is very long and thin and there is a lot of it in the nucleus. It might get hopelessly tangled if it were not for the ingenious way it is wound onto "spools" and then wound again into long chains. Eight "balls" called histones stick together to make one spool. Often, the entire spool is mistakenly called a histone. The spool is properly called a ***nucleosome***, but this word seems to be harder to remember than the word histone. Therefore, many people say "histone" when they mean "nucleosome." (We can say "histone spool" and we'll know we are talking about the whole spool, not just one histone.)

The histone spool (nucleosome) has DNA wound around it—145 to 147 base pairs in length, to be exact. There is also a protein gadget that acts like a clip to keep the DNA tightly wound. The clip (or "binding histone") is called H1.



When the DNA is tightly wound, the polymerases can't get in to read the DNA. The histones must allow the DNA to loosen and relax and come unwound a bit. There are little switches (not shown in these pictures, but shown in your drawing) that control the tightening and loosening. The switches look like strings, and can be activated by three different molecules:

1) methyl (CH_3) 2) acetyl ($COCH_3$) 3) phosphate (PO_4)

Acetyl tags make the spools stay open and let the DNA be transcribed. When a gene is actively being used, we say it is being ***expressed***. ("Gene expression" is a term you should know.) If the histones are "deacetylated" (acetyls are taken off) then we say that the gene has been "turned off." Methyls and phosphates work in a similar way.

Cells have a "Plan B" for stopping genes from being expressed. Even if the DNA is open and mRNA has already been made from the DNA, it is still not too late to prevent proteins from being made. The cell can manufacture a piece of ***microRNA***, or ***miRNA***, that will prevent that mRNA from being used. A piece of miRNA is very small, usually only 20 or 22 nucleotides long. It will match one place on the mRNA. The miRNA locks on to that place and sticks there permanently. If the mRNA tries to slide through a ribosome, the miRNA will stop it from doing so. It physically prevents the mRNA from sliding through. The mRNA becomes useless and is eventually chopped up and recycled. Thus, the gene is effectively silenced.