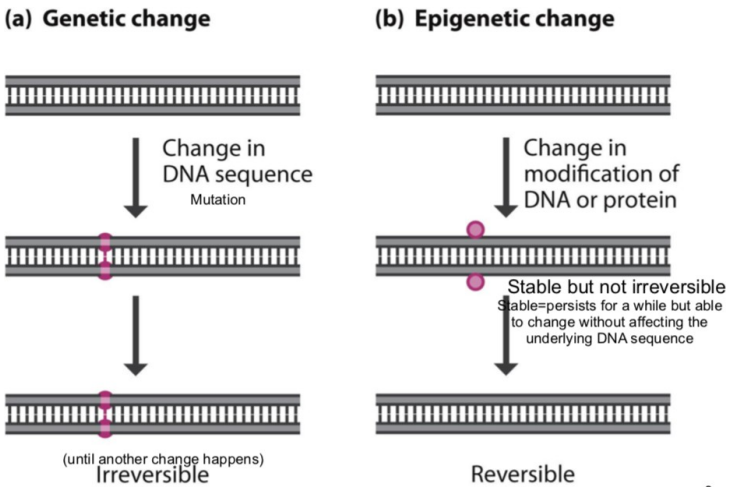
Chapter 3 : The Epigenome

Role of Chromatin Structure in Gene control

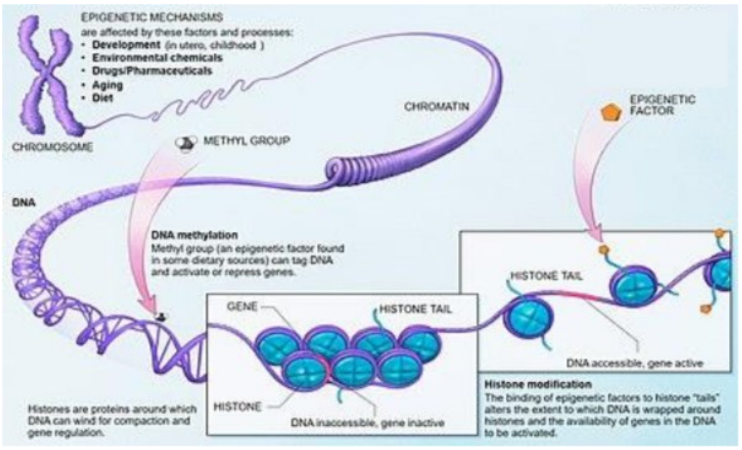
Introduction

- Under certain conditions one type of differentiated cell can give rise to a different differentiated cell type.
  - Seen in Amphibia: Wolffian lens regeneration / **Transdifferentiation**
  - If the lens of a frog's eye is surgically removed, the adjacent iris cells lose their differentiated characteristics, proliferate and differentiate into lens cells to replace those that are lost.
  - Differentiation is inherited by daughter cells.



- Stable but reversible nature of long-term regulatory processes has lead to the idea that they involve changes in chromatin structure. These changes facilitate transcription of certain genes and occur before the process of transcription itself.
- **Epigenetics:** potentially heritable modifications to chromatin that do not change the DNA sequences
  - Mitotically heritable, rarely meiotically heritable
  - Mechanisms? – DNA methylation, modifications that alter chromatin structure (eg histone mod)
  - These changes are superimposed on the DNA rather than representing genetic changes in the DNA itself.
  - Modifications to the DNA and/or the proteins associated with it result in an **epigenome** which is subject to variation in different cell type of the same organism under different conditions.
  - Epigenetic changes are potentially reversible=can account for the stable and reversible nature of long-term gene control processes.

- Changes in epigenetic modifications require cell division to replicate the DNA, which then allows alterations in the modification of the DNA itself or proteins associated with it.

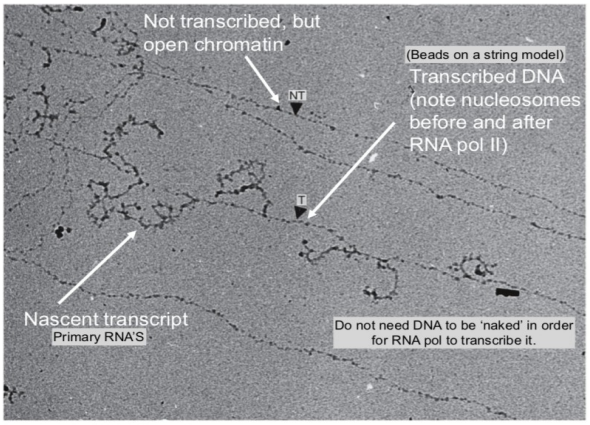


- Epigenetic changes occur before a gene becomes active: Alters chromatin structure from the 30nm fiber to the open 10nm beads-on-a-string involves modifications to genomic DNA and histones.

3.1) CHANGES IN CHROMATIN STRUCTURE IN ACTIVE OR POTENTIALLY ACTIVE GENES

Active DNA is organized in nucleosomal structure

- Actively transcribed genes are still organized into nucleosomes.
  - In an electron microscope the beads-on-a-string structure is observed with nucleosomes before and after RNA pol molecules transcribing the gene.
  - This structure may break down in genes being highly actively transcribed (eg genes for rRNA during oogenesis)



- If DNA organized into nucleosomes is isolated as a ladder of fragments once digested with Micrococcal nuclease, the DNA from the active fragments is in the same proportions as the total DNA.
  - Similarly, no enrichment or depletion in the amount of DNA is observed in tissues that do and do not transcribe the gene.