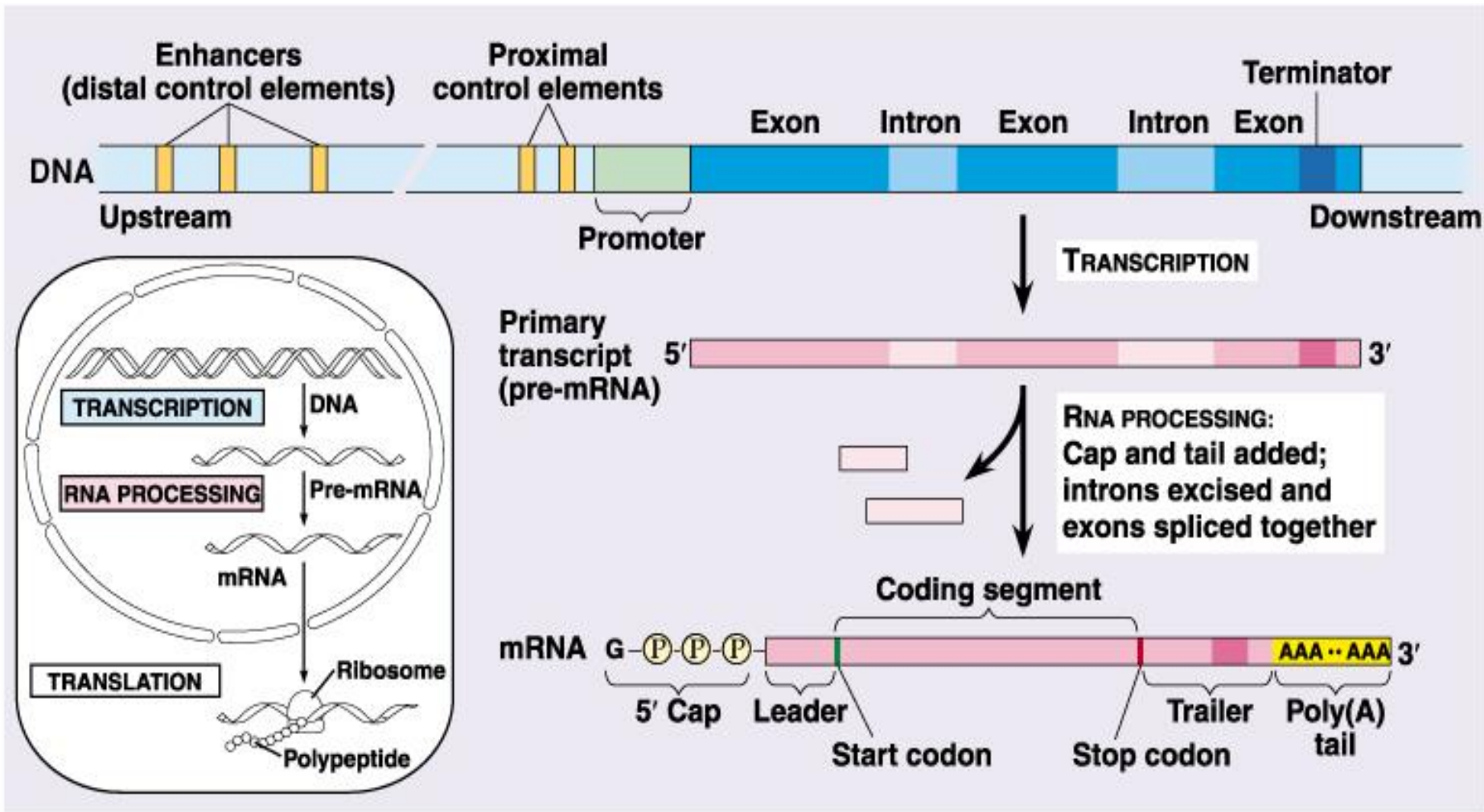


Gene Regulation in Eukaryotes

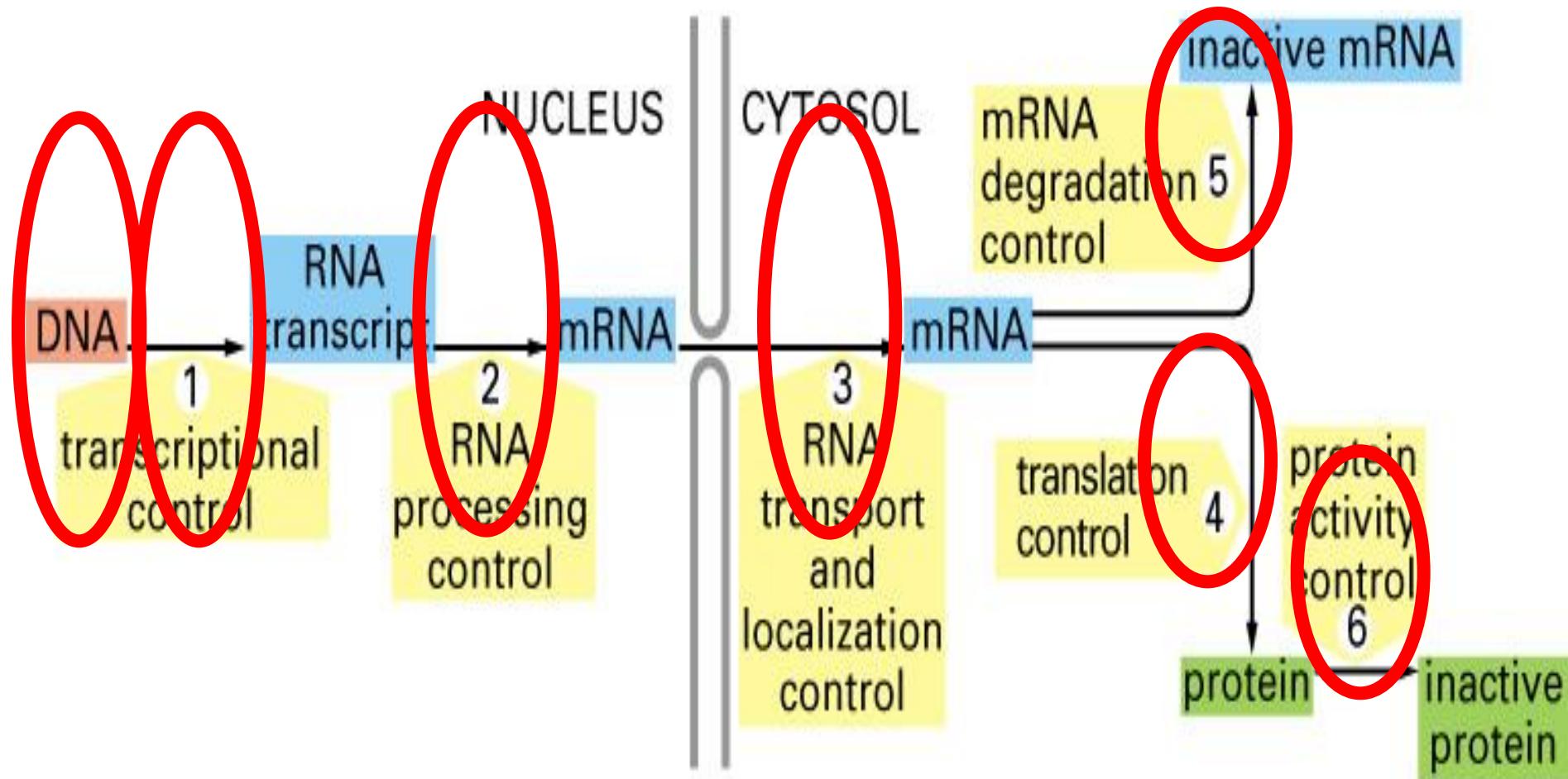


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Opportunities for the control of gene expression in the eukaryotic cell

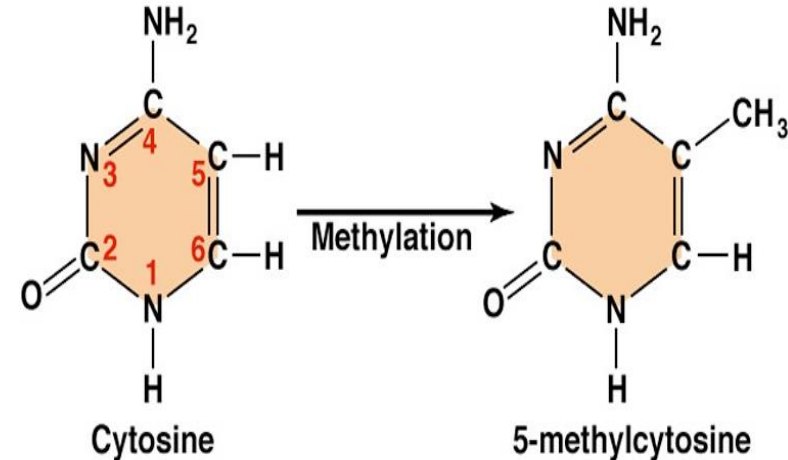


Eukaryotic gene regulation occurs at several levels



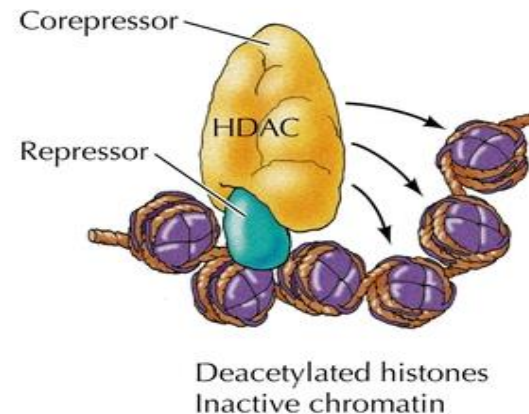
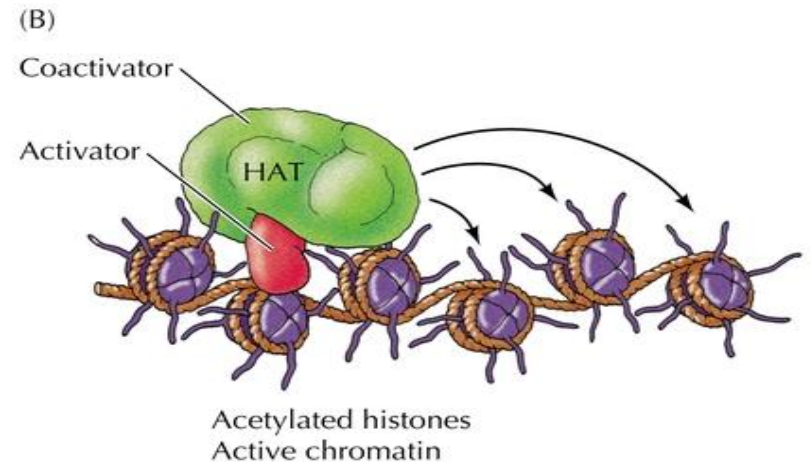
Control at DNA level by DNA methylation

- Methylation is related to the Heterochromatin formation
- Small percentages of newly synthesized DNAs (~3% in mammals) are chemically modified by methylation.
- Methylation occurs most often in symmetrical CG sequences.
- Transcriptionally active genes possess significantly lower levels of methylated DNA than inactive genes.
- Methylation results in a human disease called fragile X syndrome; FMR-1 gene is silenced by methylation.
- Hypermethylation of Tumor suppressor genes



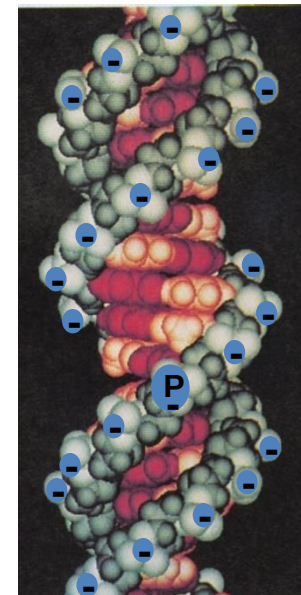
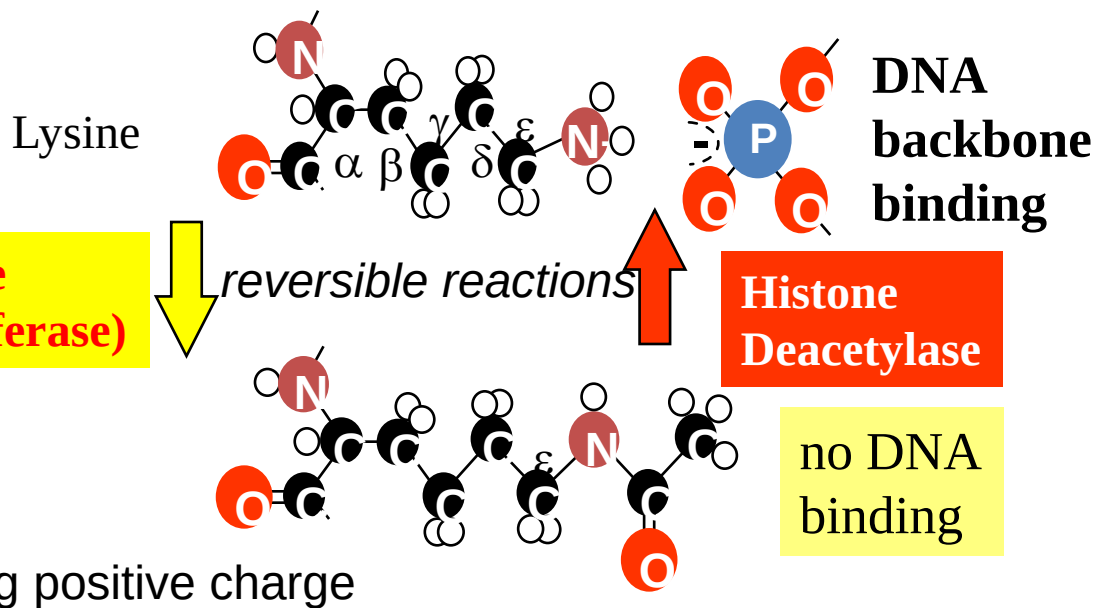
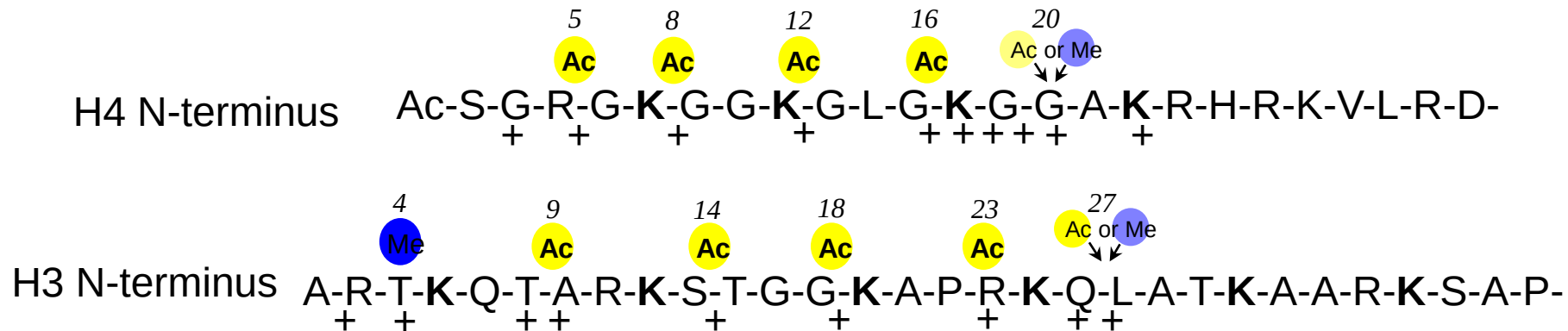
Control at DNA level by Histon modifications(Chromatin Remodeling)

- **Acetylation** by HATs and coactivators leads to euchromatin formation
- **Methylation** by HDACs and corepressors leads to heterochromatin formation



Acetylation of conserved lysines

The N-termini of histones H4 and H3, and their acetylation patterns, are absolutely conserved.



HDAC

- 18 HDAC are in Humans
- **11 are Zinc dependent**

Class I (Nucleus): HDAC 1,2,3(cyto/nucl-membrane associated) and 8

Class II A(Nucl/Cyto): HDAC 4,5,7,and 9

Class II B : HDAC 6 (Cyto) and 10

Class IV(Nucleus): HDAC 11

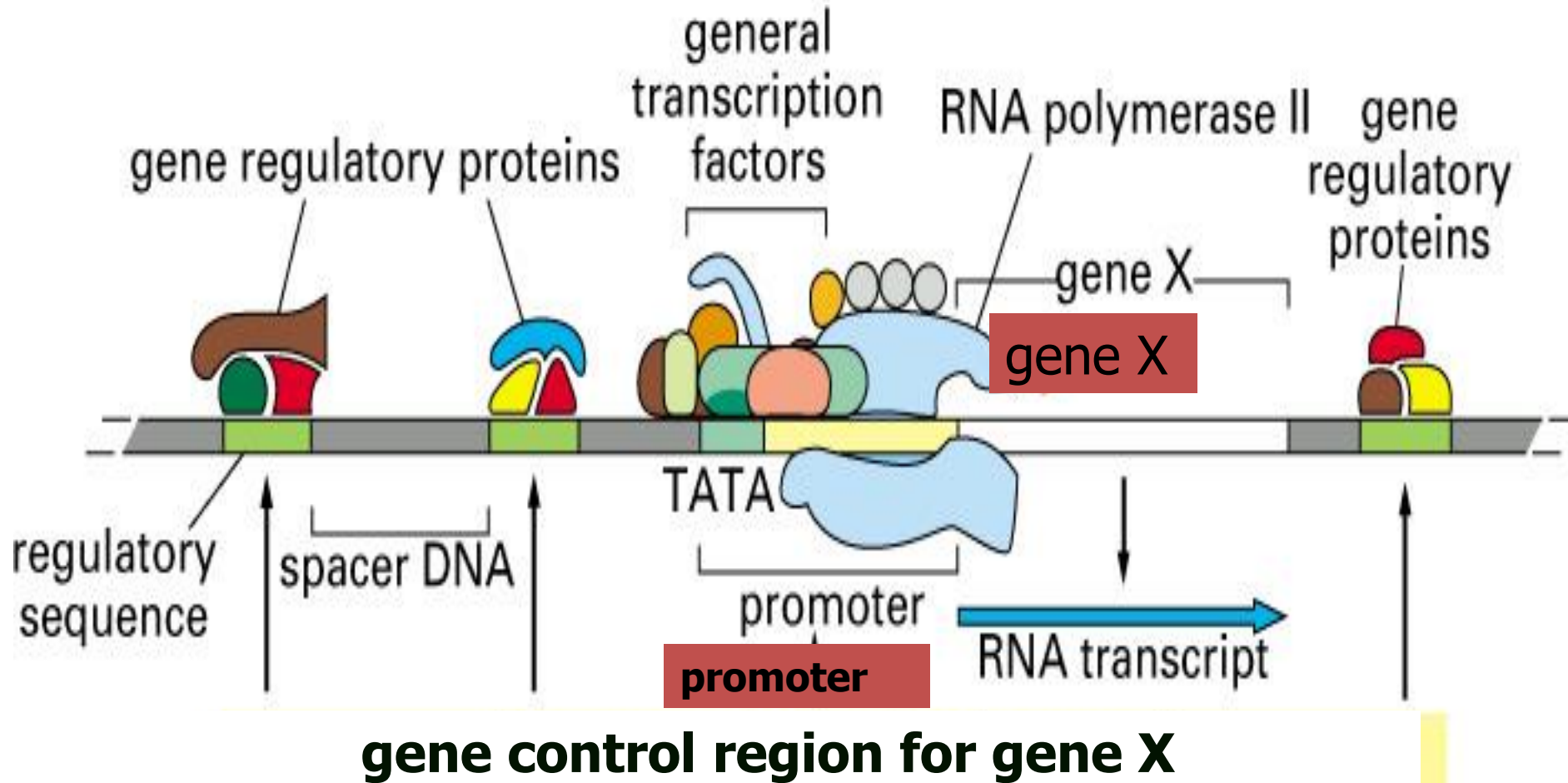
- **NAD+ dependent**

Class III-HDACs Sirutins 1-7

Class I and II enzymes and its 11 isoforms are considered as promising target for anticancer drug development (Lin H Y *et al.*, *Med Res Rev*, 2006)

Control at transcription initiation

By using different sequences (promoter, enhancer or silencer sequences) and factors, the rate of transcription of a gene is controlled



RNA Editing

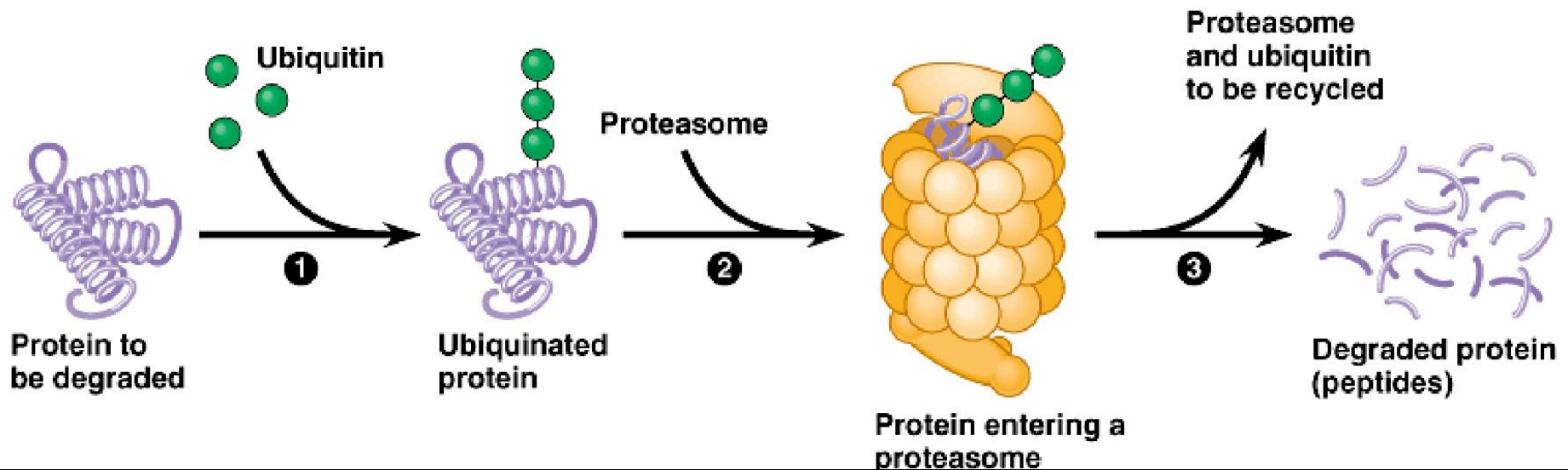
RNA editing refers to an alteration in the nucleotide sequence of an RNA (the sequence of the mRNA differs from exons encoding it).

Apolipoprotein was the first example of a mammalian RNA that undergoes editing. In apoB transcripts in the small intestine, **a cytidine in the coding region is converted to a uridine generating a premature stop codon** and a truncated version of the gene-encoded protein (the C to U change converts a glutamine codon (CAA) to a stop codon (UAA)).

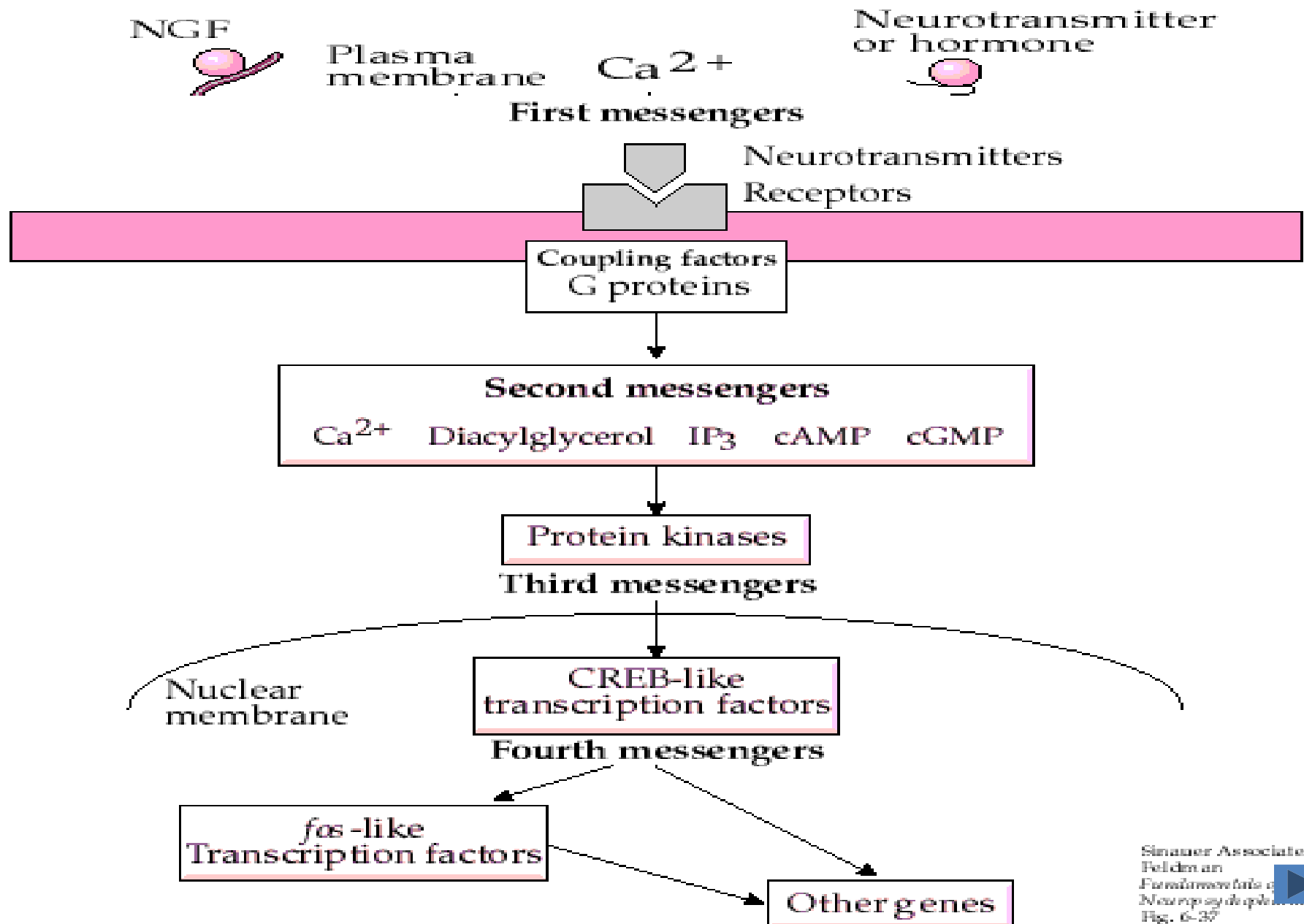
-The two apoB forms serve different physiological functions in lipid metabolism .

APOEC-Editosome

Regulation of Protein Stability

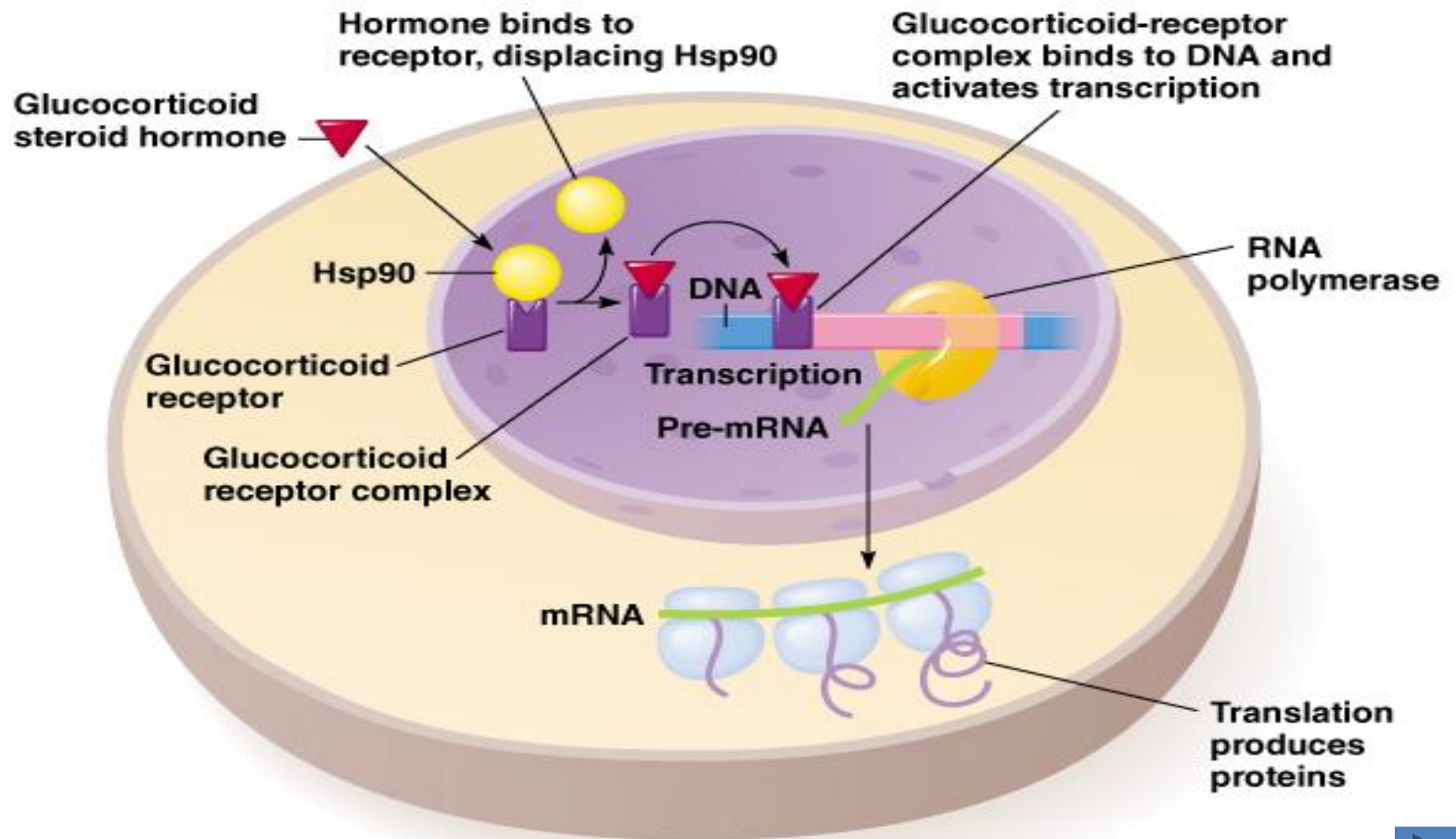


Regulation by water soluble Hormones



Regulation by lipid soluble Hormones

Steroid hormones pass through the cell membrane and bind cytoplasmic receptors, which together bind directly to DNA and regulate gene expression.

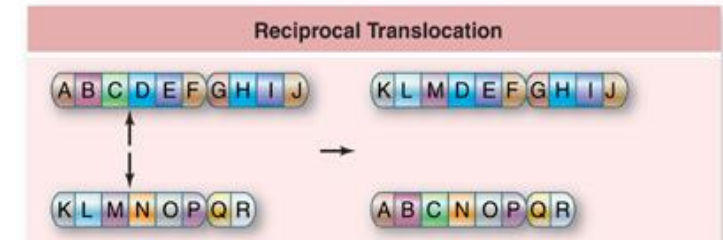
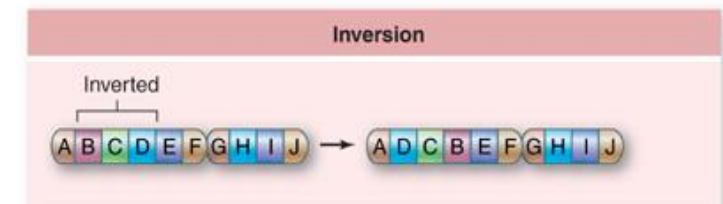
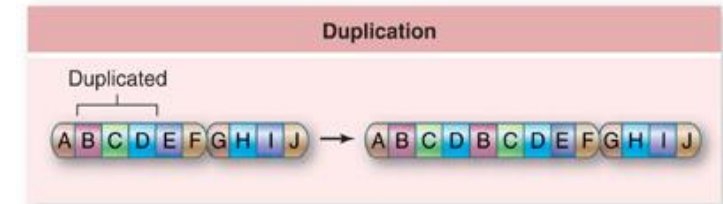
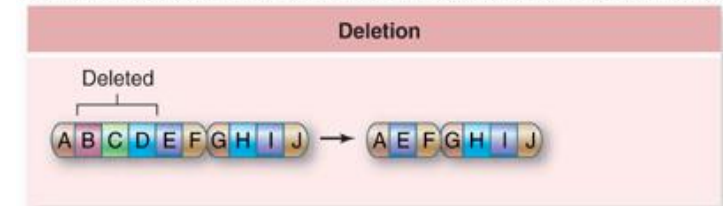


Mutation: Altered Genes

Chromosomal mutations change the structure of a chromosome.

- **deletions** – part of chromosome is lost
- **duplication** – part of chromosome is copied
- **inversion** – part of chromosome in reverse order
- **translocation** – part of chromosome is moved to a new location

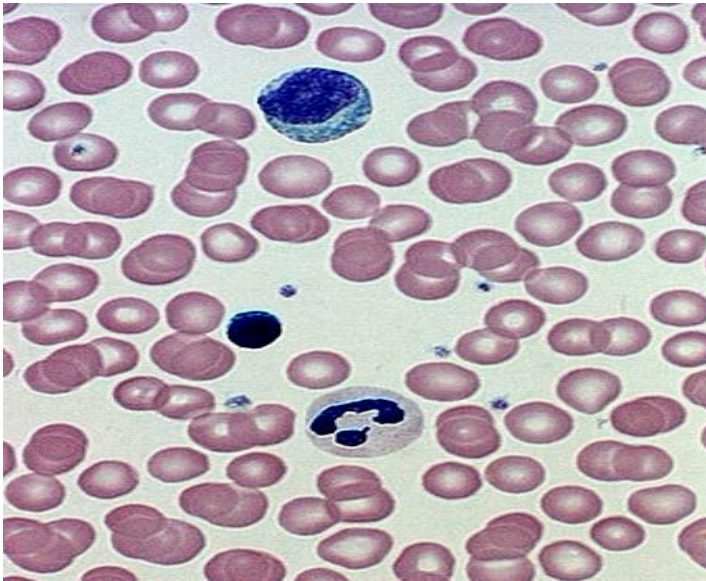
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Mutations of haemoglobin

- Haemoglobin is a tetramer = 2 α and 2 β -chains
- The genes for these polypeptides are found on different chromosomes
- The β -chain gene is found on chromosome 11
- The α -chain gene is found on chromosome 16
- The nucleotide sequences have been worked out
- Several inherited diseases occur on the β -chain, which contains 146 amino acids.

Sickle Cell Anaemia



Blood smear (normal)

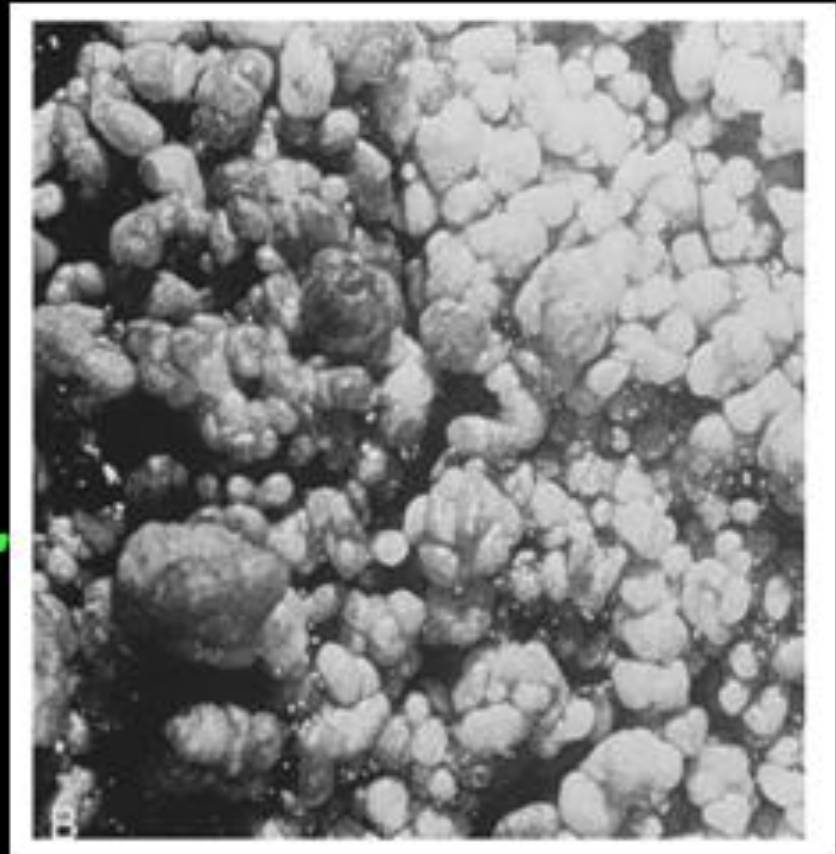


Sickle cell anemia

Mutation	Codon	Change to DNA sense strand	Change in Amino Acid
S (sickle cell anaemia)	6	GAG to GTG	Glu to Val

Adenomatous Polyposis Coli (APC)

- *tumor suppressor*
- *mutated in FAP
and in 70% of
sporadic
cases of colon cancer*



colon polyps

Thanks

Thanks

Acknowledgement

- ❖ **The Presentation is being used for educational and non commercial purpose**
- ❖ **Thanks are due to all those original contributors and entities whose pictures used for making this presentation.**