Regulation of Gene Expression

→ synthesis of a final gene pdct (protein) from the informatⁿ in gene is called gene expression.
→ mainly regulated at the level of transcriptⁿ
→ in eukaryotes, regulated at the level of post transcriptnal & post translatnal modificatns.
→ some genes are expressed at constant rates lactase enzyme (β galactosidase) is produced. genes are called constitutive genes or housekeeping genes. They're continuously expressed.
→ some genes are expressed only under certain conditions; eg:- insulin gene is expressed only in β cells of pancreas.
→ some genes are expressed only when needed. (lactose metabolising enzyme in E.coli)

Induct" & Repression

→ imp mechanisms for regulatⁿ
→ induct" is the phenomenon of ↑ed synthesis of protein or enzyme in response to certain signal (turning 'on' the switch of the gene).
→ such enzymes are said to be inducible & the signals are called inducers.
→ repression is turning "off" the gene expression.

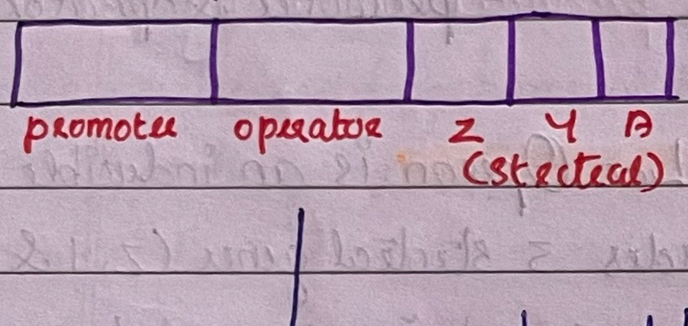
Operon Concept of Gene Regulatⁿ

→ Jacob & monod described operon model → based on studies in E.coli
→ E.coli grown in glu medium do not produce lactose metabolising enzyme. But when they're grown in lactose (& no glu) → lactose metabolism is regulated by an induct"/derepression process.
→ Operon is the unit of gene expression. → it includes :- structural genes
- control elements
- regulator/inhibitor gene
- promoter & operator areas

→ The Lac Operon is an inducible Operon
→ includes 3 structral genes (Z, Y & A) which code for 3 proteins, a regulator gene, a promoter area & an operator.
→ Z gene codes for β galactosidase
→ Y gene for permease (which transport lactose & galactose into the cell).
→ A gene for thiogalactoside transacetylase

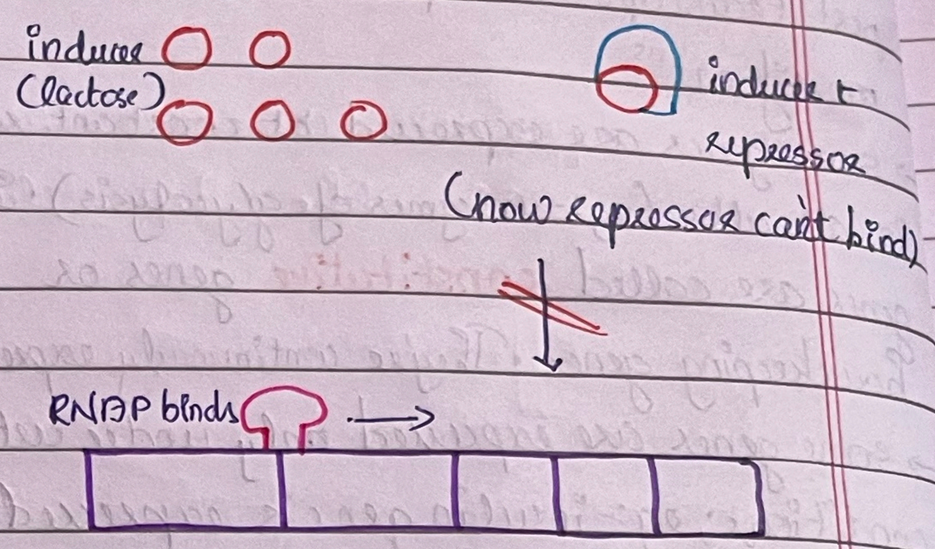
→ transcript^{n} of these 3 genes start from a common promoter located close to Z gene.
→ RNAP binds to the promoter & transcribes these 3 genes as a single mRNA.
→ When glu is available & lactose is absent, transcript^{n} is repressed.
→ regulator (inhibitor) gene produces a repressor molecule (150 kD).
→ repressor has strong affinity to the operator site & binds tightly.
→ RNAP finds the promoter & moves forward towards the structural genes, but its mvmt beyond operator is prevented

* Glu present ; Lactose absent - Operon shutoff



→ When lactose is available & glu is absent, transcript^{n} is induced or 'derepressed'.
→ lactose combines with repressor protein.
→ this lactose-repressor complex cannot bind to the operator site.
→ RNAP can move forward & transcribe the structural genes.
→ the mRNA produced will be translated to the enzymes for lactose metabolism.

* Glu absent ; Lactose present - Operon on



→ this shows that the synthesis of these proteins are normally repressed.
→ lactose is an inducer (lactose switches the genes 'on') When lactose is present, the genes are derepressed or induced.

Clinical Applicat^{ns} of Derepression

→ lactase in human intestine is an inducible enzyme.
→ eg of derepression in human beings:-

a) transaminases
b) ALA synthase
c) glucuronyl te

Regulat^{n} by

→ ALA synthase
heme synthesis
→ an aporepress
regulatory ge
with heme (c
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a) transaminases by glucocorticoids
b) ALA synthase by barbiturates
c) glucuronyl transferase by barbiturates

Regulat^{n} by Repression in Humans

→ ALA synthase (rate limiting enzyme of heme synthesis) is repressed by heme.
→ an aporepressor is produced by a regulatory gene. The aporepressor binds with heme (corepressor) to form the holorepressor.
→ holorepressor binds to the operator site & prevent the movt of RNAP
→ the transcript^{n} of ALA synthase gene is repressed.
→ when heme is not available, holorepressor is not formed, so- derepression occurs & ALA synthase is produced.

Hormone Response Elements

→ hormones or their 2nd messengers act as inducers in higher organisms
→ steroid hormones bind to cytoplasmic receptors & the complex goes into nucleus.
→ exert their effect by attaching to HRE in DNA.

Gene Switching

→ sometimes one gene is switched off while closely related gene takes up its f^{n}.
→ eg:- in fetal life, genes for α & γ chains of Hb are active. After birth, it gradually switch over to genes of α & β chains.

Role of Catabolite Activated Protein (CAP)

→ if both glu & lactose present, E.coli utilise glu. Lactose metabolising enzymes are produced if glu is absent.
→ this is bcs RNAP can attach only when CAP-cAMP complex is available.
→ cAMP accumulates only when the bacteria starves (when no glu).