Regulation of Gene Expression

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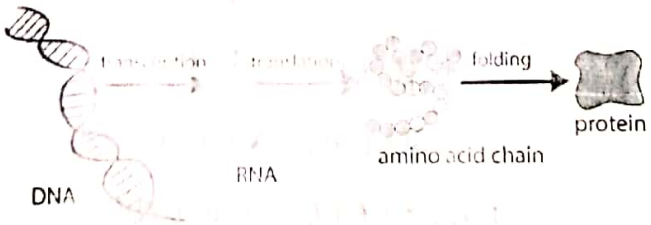
Gene Expression

- The central dogma in genetics describes the flow of genetic information in cells from DNA to mRNA to protein



- Gene expression: is the process by which information from a gene is used in the synthesis of a functional gene products: either protein or RNA such as tRNA and rRNA

functional Gene Products < 1 (protein) / 2 (RNA) < a (tRNA) / b (rRNA)

• mRNA أو اي نوع غير الـ

Non-protein couding gene (إذا كان) transcription ممكن تكون فقط عملية gene expression ~~gene~~ عملية الـ

Gene Expression

- Gene regulation control cell structure and function. It is the basis for cellular division, differentiation and morphogenesis

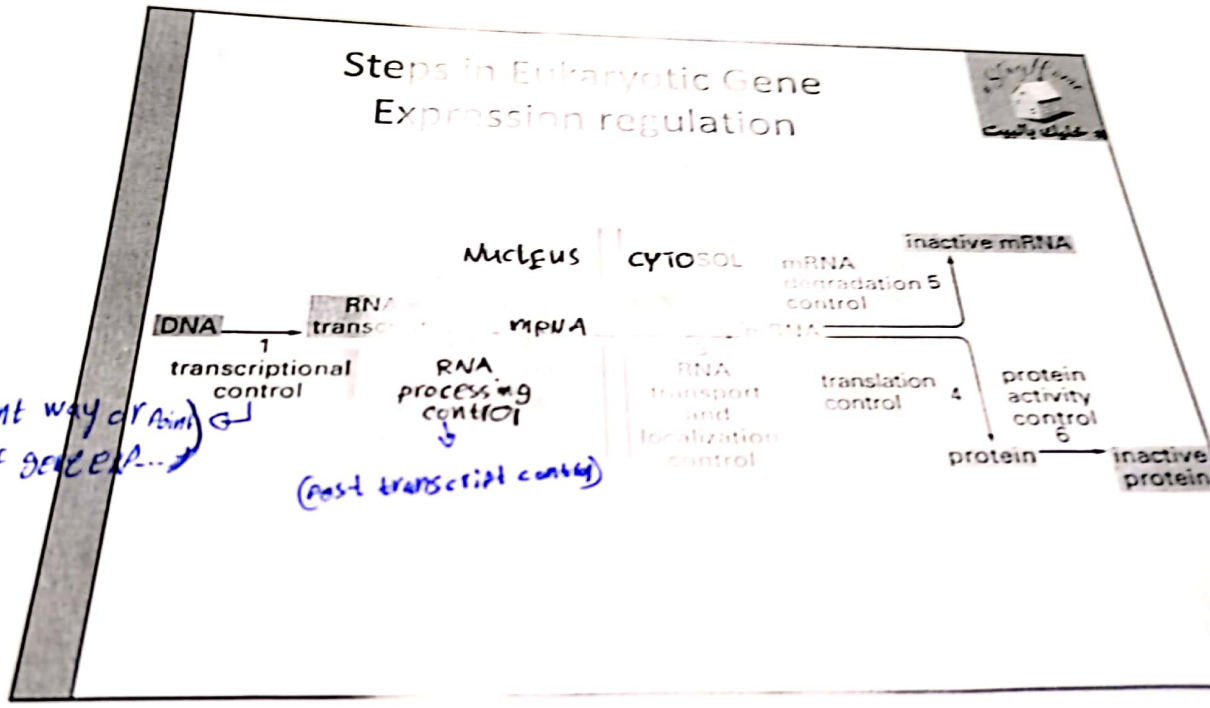
Cell Proliferation — cell specialization cell movement and morphogenesis

- Different cell types differ in both structure and function although they contain the same genome (e.g. basophil and neuronal cell)

basophil — Neuronal cell

Gene Expression

- Different cell types synthesize and accumulate different sets of RNA and proteins (Hemoglobin in RBCs)
- Also, the level of expression of almost every active gene varies from one cell type to another
- Gene expression can be regulated at many steps:
  1. Transcriptional control (the most efficient point of gene expression regulation)
  2. RNA processing control
  3. RNA transport and localization control
  4. Translational control
  5. mRNA degradation control
  6. Protein activity control



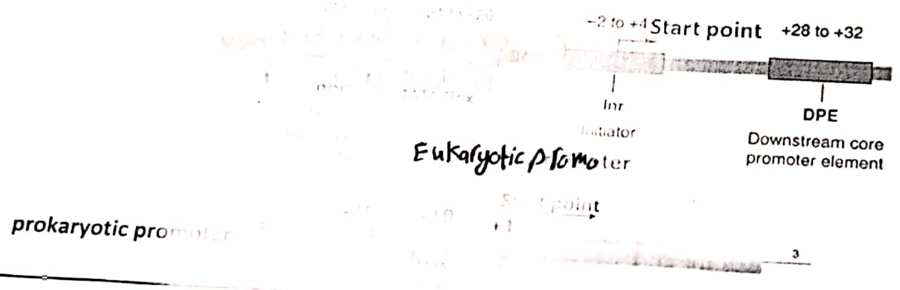
(the most efficient way of control for the regulation of gene exp...)

(post transcript control)

1. Transcription Initiation

- Steps: Initiation elongation and termination
- RNA polymerase catalyzes the synthesis of RNA strand from DNA template
- The promoter is a regulatory DNA region (100-1000 bp). In eukaryotes, it consists of consensus sequences such as TATA box, BRE INR and DPE. In prokaryotes, two consensus sequences at -10 and -35.

non couding DNA



ضروري ترجع للرسمة وتشوفهما مزبوط

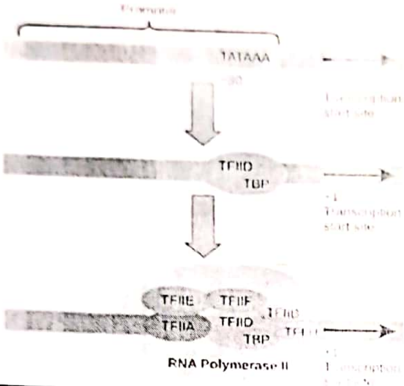
* downstream start point → couding region
* upstream // // → non // // (regulatory)

* الارقام الي بالرسمة +ve and negative بسبب حسب موقعها لل start point:
النيوكليوتيدات الي جاي قبل ال initiation site (preceding) بكونو (-ve) وبنسميه upstream
// // // بعد // // (following) // (+ve) // downstream

1. Transcription initiation

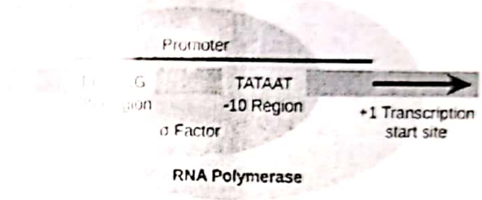
Transcription initiation in eukaryotes

1. It requires *general transcription factors* which assemble together with RNA polymerase at the promoter to form pre-initiation complex **(PIC)**
2. TFIID binds first at the TATA box via its TBP subunit



Transcription initiation in prokaryotes

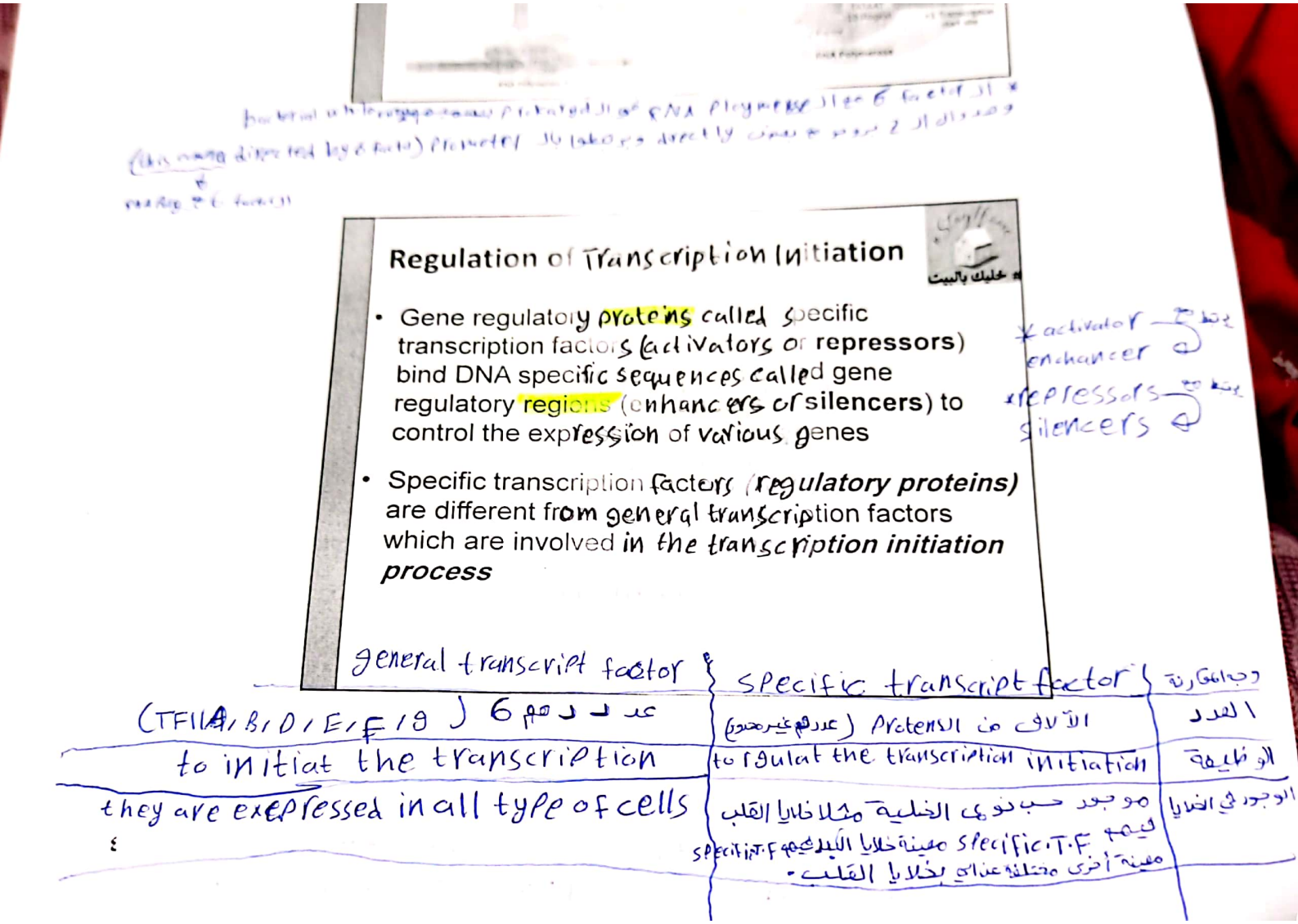
1. The σ factor recognizes the -35 region in the promoter and binds to it (RNA Polymerase وبكون معه ال)
2. Once the RNA polymerase starts the transcription, **σ factor** then dissociates to guide another enzyme to the initiation site



* ال σ factor مع ال RNA Ploymerase في ال Prokaryotic بنسميهم bacterial whole enzyme

وهدول ال 2 بروحو مع بعض directly وبرتبطوا بال Promoter (this complex directed by σ factor)

ال σ factor مع RNA Poly

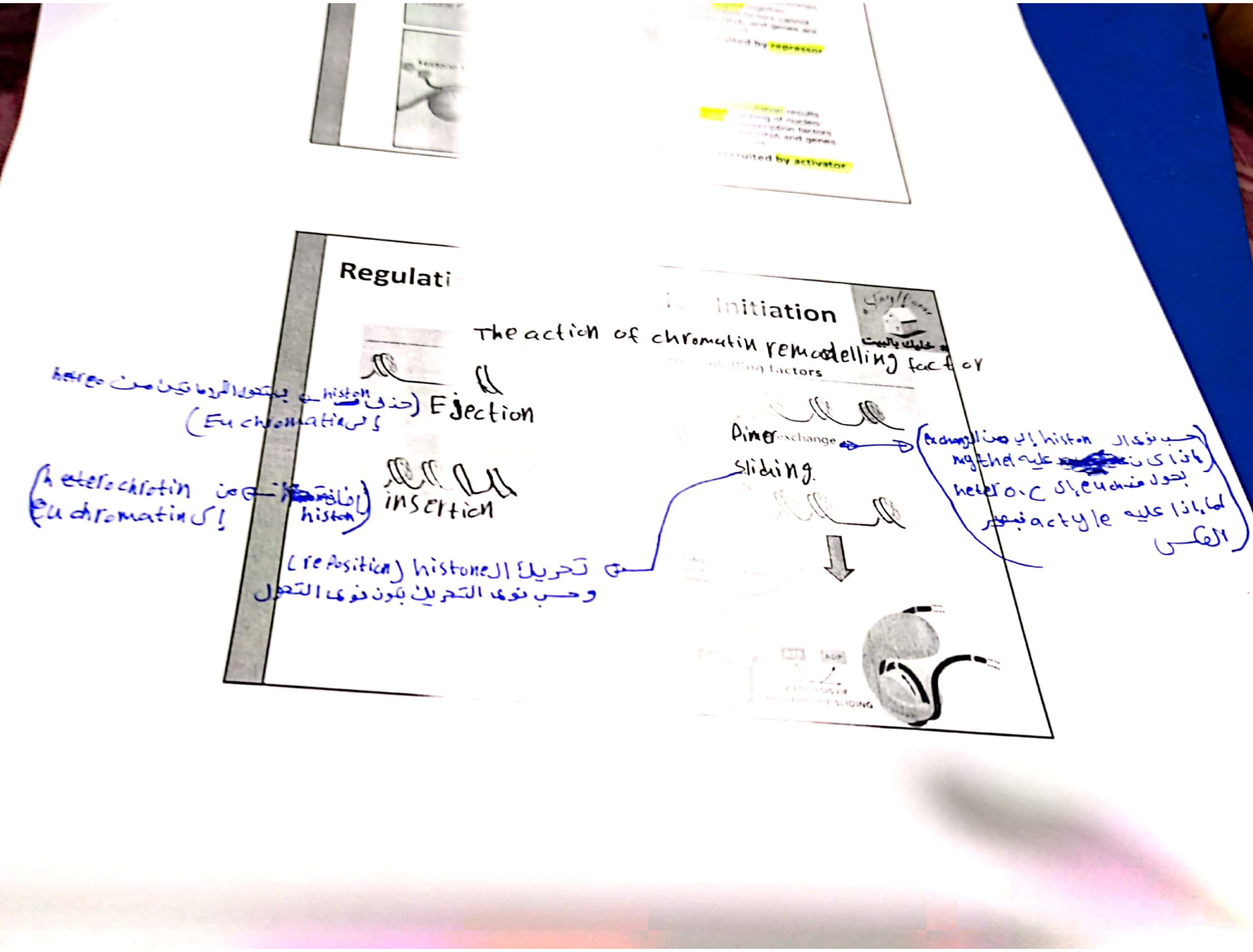


Regulation of Transcription Initiation

- Gene regulatory proteins called specific transcription factors (activators or repressors) bind DNA specific sequences called gene regulatory regions (enhancers or silencers) to control the expression of various genes
- Specific transcription factors (*regulatory proteins*) are different from general transcription factors which are involved *in the transcription initiation process*

* activator يرتبط مع enhancer
* repressors يرتبط مع silencers

	general transcript factor	specific transcript factor
مقارنة	عددهم محدود (TFIIA, B, D, E, F, H)	الآلاف من الـ Proteins (عددهم غير محدود)
الوظيفة	to initiat the transcription	to regulat the transcription initiation
الوجود في الخلايا	they are expressed in all type of cells	موجود حسب نوع الخلية مثلاً خلايا القلب فيها specific T.F معينة خلايا الكبد فيها specific T.F معينة أخرى مختلفة عن خلايا القلب.



Regulation of Transcription Initiation

- Beside the mediator, other proteins are recruited by specific transcription factors to the promoter such as: histone modifying enzymes and chromatin remodeling complexes
- Epigenetic factors: gene expression is affected by changes in chromatin structure (Heterochromatin/ Euchromatin)

outside DNA التغيير يكون
DNA itself الـ على

Regulation of Transcription Initiation in Prokaryotes

The expression of many genes is regulated according to the available food in the environment

Operon: DNA unit consists of a cluster of related genes controlled by single promoter and transcribed together into single mRNA strand (bicistronic or polycistronic transcript)

ج جاي من جينين

Operator: a segment of regulatory DNA to which a repressor can bind to regulate the transcription of downstream target genes

The three basic DNA components of operon:

1. **Promoter**
2. **Operator**
3. **Structural genes** (downstream)

Examples in *E-coli* bacteria: ***Trp* operon** and ***Lac* operon**

الـ mRNA جاي من أكثر من جين.

Lac Operon

- *Lac* operon consists of three structural genes required for the transport and metabolism of lactose as an alternative carbon source to glucose:

1. ***lacZ***: encodes β-galactosidase which cleaves lactose into glucose and galactose
2. ***lacY*** : encodes lactose permease to transport lactose into the cell
3. ***lacA*** : encodes galactoside O-acetyltransferase which plays a role in cell detoxification

للإطلاع فقط

Lac Operon

*cap: binding site for cap protein (activator وهو عبارة عن)

binding site

DNA | | CAP | P | ram otd | oberatob | lac Z | lac Y | lac A |

RNA Playmerase

Lac Repressor (gene regulatory protein)

CAP (gene regulatory protein)

Allolactose (Co-repressor) ضد

Glucose

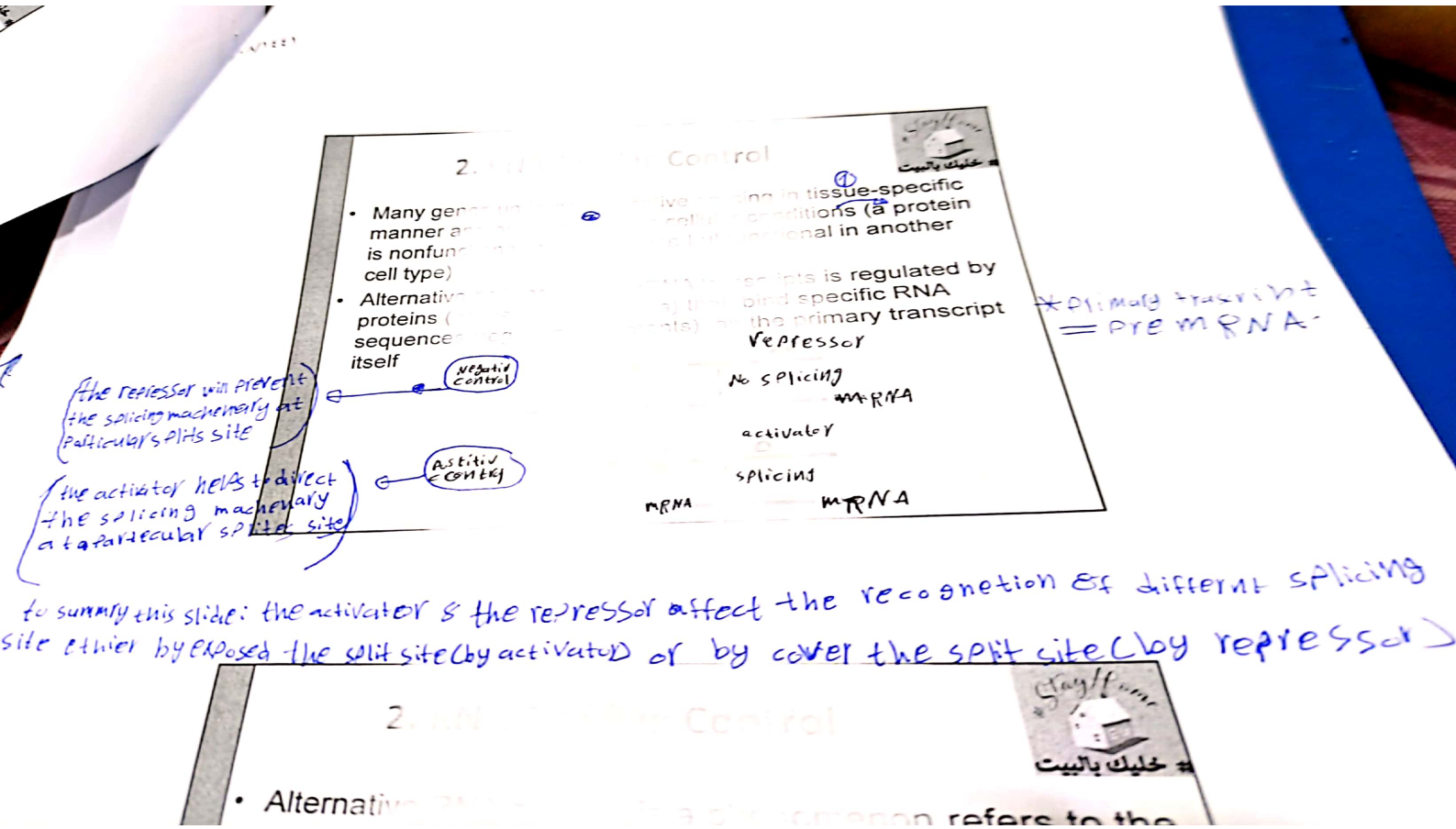
cAMP (Co-activator)

lac repressor

dual control ① ②

- It is under both negative ① & positive ② transcriptional controls (dual control) the lac repressor and the CAP activator (catabolite activator protein) respectively
- In the absence of lactose, lac repressor binds lac operator and inhibits RNA polymerase binding so genes are switched off (regardless of glucose level).
- In the absence of glucose, cAMP level is high. cAMP is co-activator of CAP
- In presence of lactose, the lac repressor is inactivated by the binding to lactose metabolite (allolactose) so the repressor dissociates from the operator with the genes are weakly transcribed in the presence of glucose but extensively transcribed in the absence of glucose
- Allolactose is an inducer of lac operon. It acts as co-repressor of lac repressor protein.

cAMP is an inducer only in present of lactose



the repressor will prevent the splicing machinery at particular splits site

negativ control

the activator helps to direct the splicing machinary at a tapartecular splits site

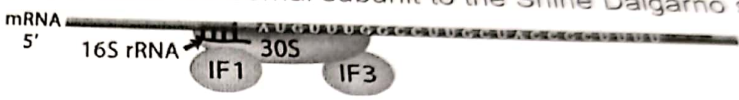
astiviy control

*primary transcript = pre mRNA

to summary this slide: the activator & the repressor affect the recognetion of different splicing site either by exposed the split site(by activator) or by cover the split site(by repressor)

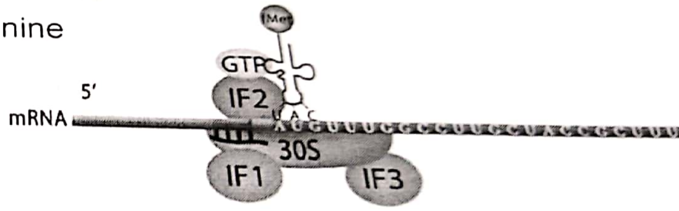
Translation Initiation in Prokaryotes

1. Binding of the small ribosomal subunit to the Shine Dalgarno sequence



2. Recruitment of initiator tRNA carrying formylmethionine

هاي الخطوة تتطلب IF 2



3. Dissociation of IFs and binding of large ribosomal subunit