CHAPTER 8 : GENE CONTROL AND CELLULAR SIGNALING PATHWAYS

- Transcription → key → gene expression is regulated to produce different cell types /allow cells to respond to specific stimuli.
- TFs need to be differentially active (in different cell types) and have activity modulated by specific stimuli.
- This allows them → turn to switch their target genes on or off in appropriate cell types or in response to specific signal → producing appropriate alterations in cellular phenotype.

REGULATION OF TRANSCRIPTION FACTORS

- TFs need to be differentially active, and have activity modulated by specific stimuli
- Method 1 (SLOW) (B): Regulation of TF synthesis
- Gene control is mediated by the transcription factor being synthesised
 dependent on the tissues and cell types
- (a) (b)

 Inactive transcription factor A

 A

 Active transcription factor A

 A

 A

 Transcription

 RNA processing

 Translation

 B
- Frequently used for expression over a long time
- ➤ Achieves this by synthesising and maintaining the expression of a TF for a certain period of time.
- ➤ E.g. cell-type specific or developmental regulated genes
- Second TF required to regulate transcription of 1st TF
- Regulated at the level of its own transcription
- > = Potentially endless hierarchy of TF genes each requiring another TF to regulate its transcription
- Solution: post-transcriptional regulation, or
- Method 2 (FAST) (A): Regulation of TF activity
- ➤ Alteration of pre-existing protein (when in an inactive form/target genes are not being expressed)
- ➤ Activates post-transcriptionally → TF is controlled and regulated by controlling the activity of its pre existing

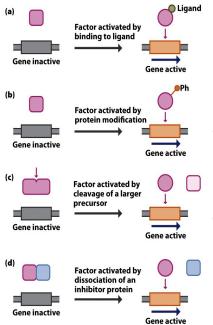
transcription factor protein.

More rapid response

EXAMPLE OF MECHANISM \rightarrow HSF \rightarrow binds -Heat shock element (HSE) \rightarrow in DNA of stress inducible genes \rightarrow plays role in induction in response to elevated temperature or other stresses.

- ➤ HSF → present in cells before exposure to heat shock and can activate heat-shock genes following exposure to elevated temp, stresses, or presence of protein inhibitors preventing its de novo synthesis.
- ➤ Heat shock activates inactive form of HSF → posttranscriptional modification involving an alteration of preexisting protein.
- This method is frequently used in the response of cells to signalling pathways (rapid change in cellular gene expression in response to signal is required)
- Exposure to a cell specific signal → change in TF activity → produce changes → expression of target genes for TF.
- Altered levels of proteins encoded by these target genes will then produce the appropriate change → cellular characteristics in response to signal change → allows signal to have biological effect

MULTIPLE MECHANISMS REGULATE TF ACTIVITY



a) **Direct binding of ligand to TF** (used in signaling molecules as they can enter the cell)

Post-transcriptional modification

- b) Phosphorylation
- **c) Proteolytic cleavage** (Signaling molecules bind to cell surfce receptors which act by inducing cleavage of a large inactive precursor =production of an active TF molecule)
- **d) Regulation of protein** protein interactions (Involved in change in post-transcriptional modifications or precursor cleavage)

Signaling pathways can regulate:

- 1. Histone modifications (role in the regulation of chromatin stucture)
- 2. Post-transcriptional processes (role in gene control)