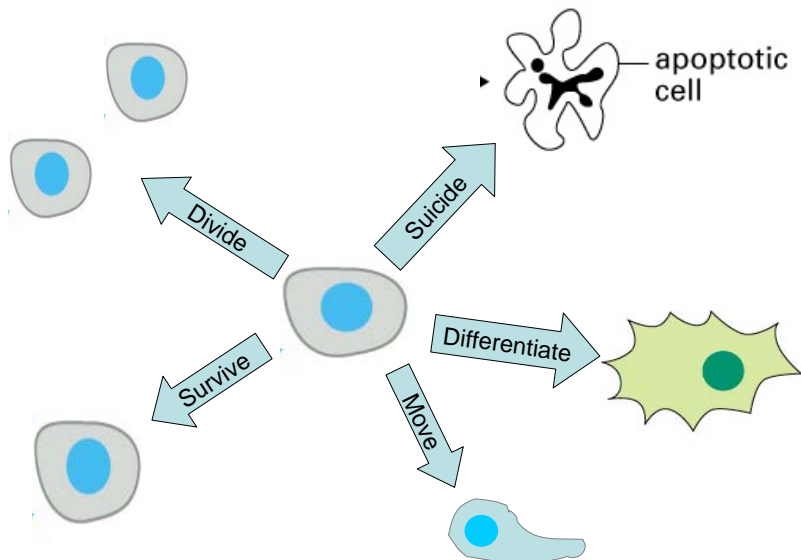


Examples of Gene Regulation

- Interferon induced genes
- Thyroid hormone receptor
- Ras pathway
- P300 as signal integrator

Communication and Cell Fate



Cell Signals

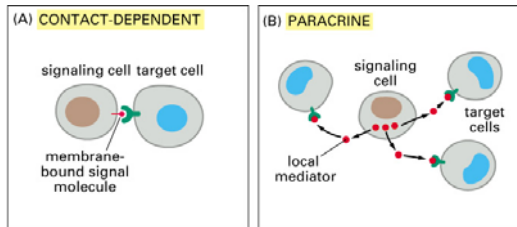


Figure 15-4 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

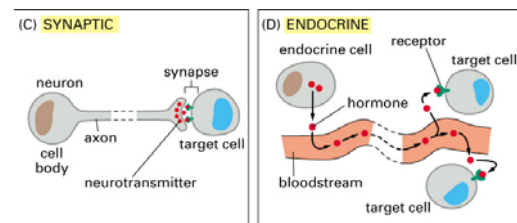


Figure 15-4 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

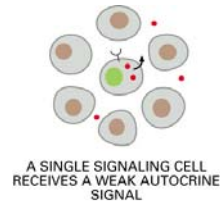
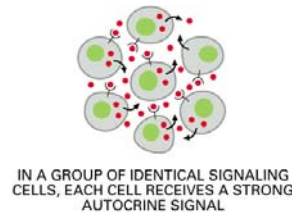


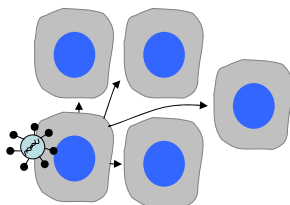
Figure 15-6. Molecular Biology of the Cell, 4th Edition.



Autocrine

Cytokines

- Secreted peptide hormones secreted by cells that can act at the paracrine, autocrine, endocrine level.
- Peptide hormones classified as cytokines are typically involved in the immune response.
- Example α Interferon – secreted by cells being infected by virus.



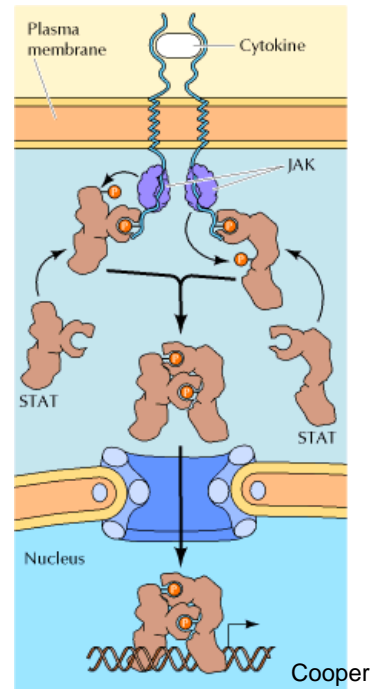
Interferon results in altered gene expression in target cells. For example it induces expression of PKR. PKR is a kinase activated by double stranded RNA. One of the substrates for PKR is the translation factor eIF2.

What is effect on target cells of induction of PKR?

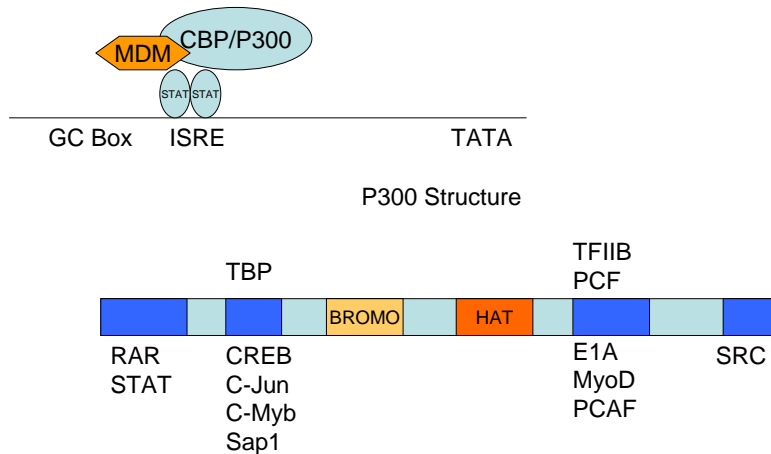
Interferon Signal Transduction Cascade

1. Interferon binds surface receptor on plasma membrane
2. Interferon binding stabilizes dimerization of receptor.
3. Dimerization results in cross phosphorylation of the receptor by a kinase called JAK (Janus Kinase).
4. The phosphorylated receptor is bound by the SH domain of STAT91 (Signal Transducers and Activators of Transcription).
5. JAK phosphorylates STAT
6. Phosphorylated STAT releases receptor and dimerizes using SH domain.
7. Dimerizes STAT moves into nucleus and binds ISRE (Interferon Stimulated Responsive Elements)
8. There is an ISRE at PKR gene
9. Binding of STAT dimer increase transcription.

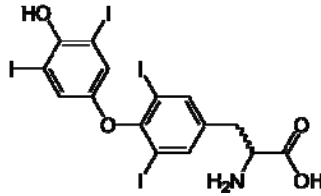
JAK-STAT Pathway



STAT Coactivators

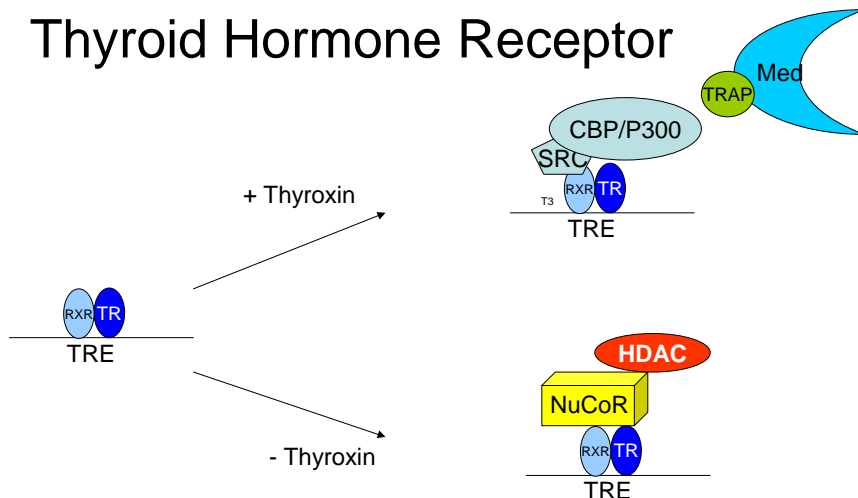


Thyroid Hormone

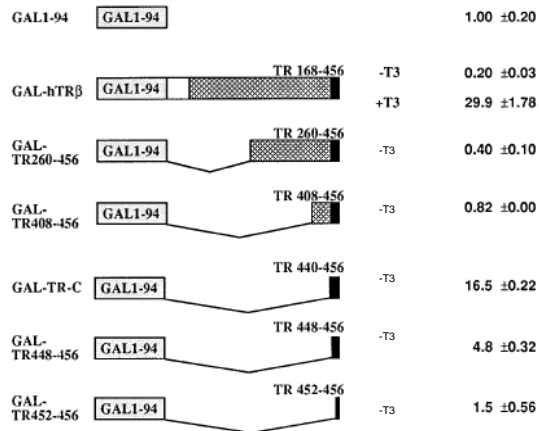


Thyroxine

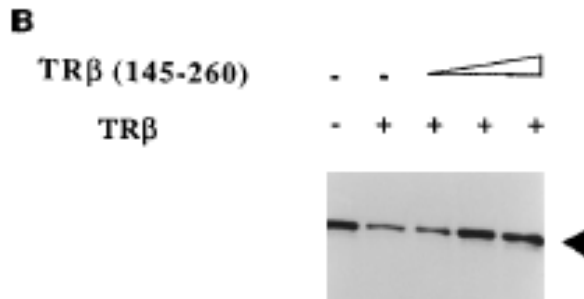
Thyroid Hormone Receptor



Activating Domain(s)

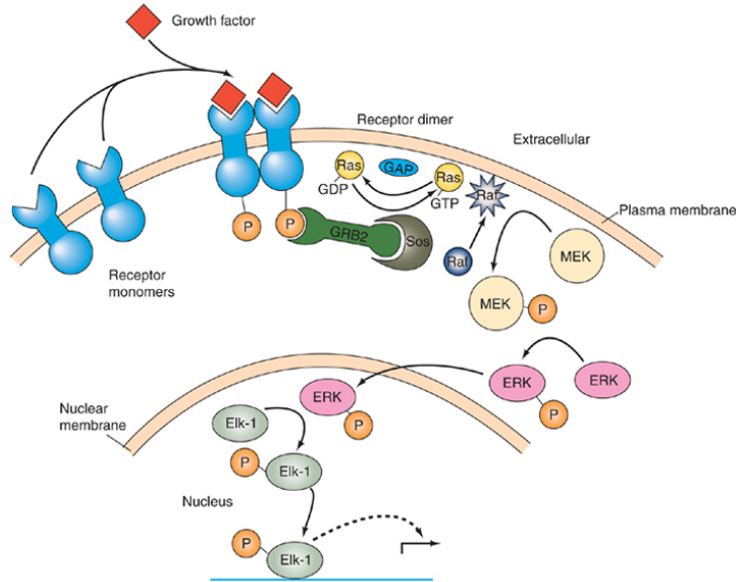


Silencing domain identified by Squelching



Ras Pathway

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Integration at CBP/p300

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