BHARATHIDASAN UNIVERSITY

Tiruchirappalli- 620024

Tamil Nadu, India

Programme: M.Sc., Biochemistry

Course Title : Biochemistry of Signal Transduction

Course Code : BC203CR

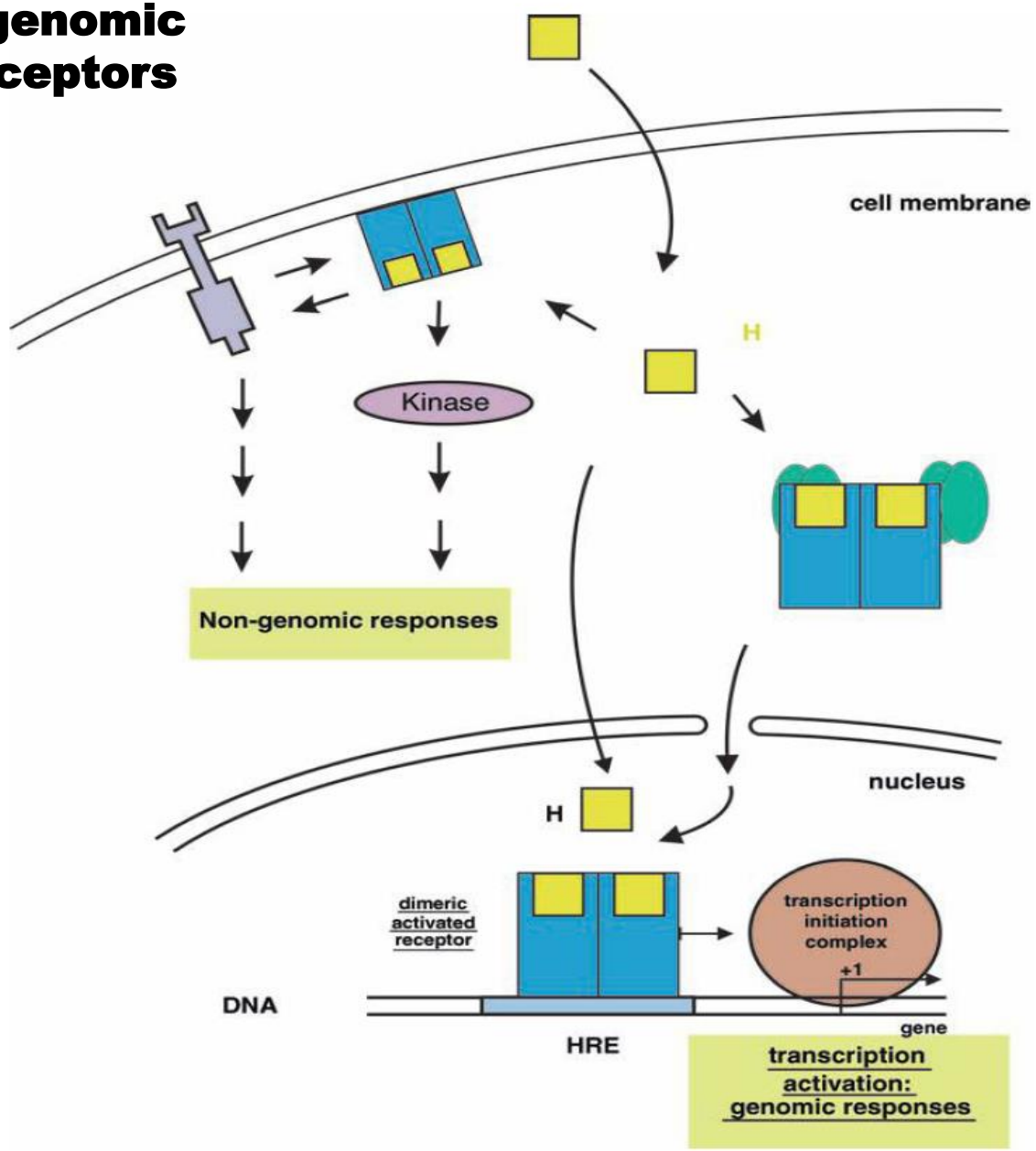
Unit-4

Nuclear and Cytokine receptor Signaling

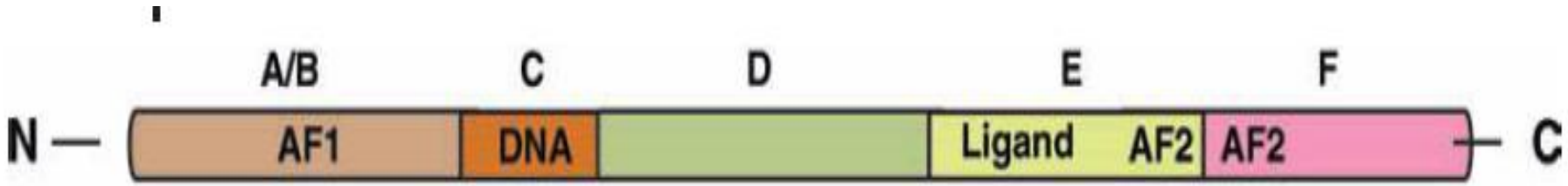
Dr. C. Prahalathan

Professor

Genomic and Non genomic functions by nuclear receptors

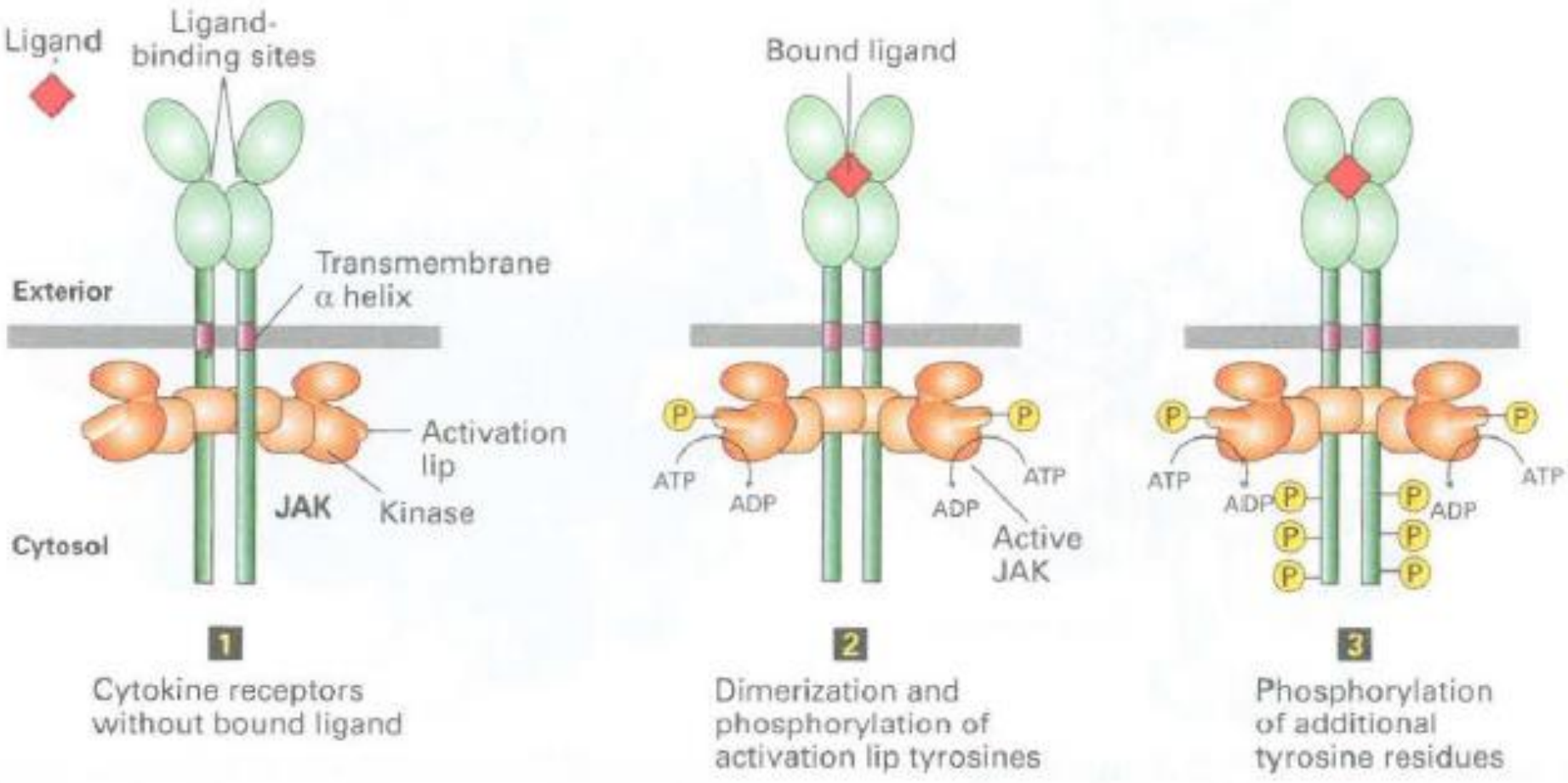


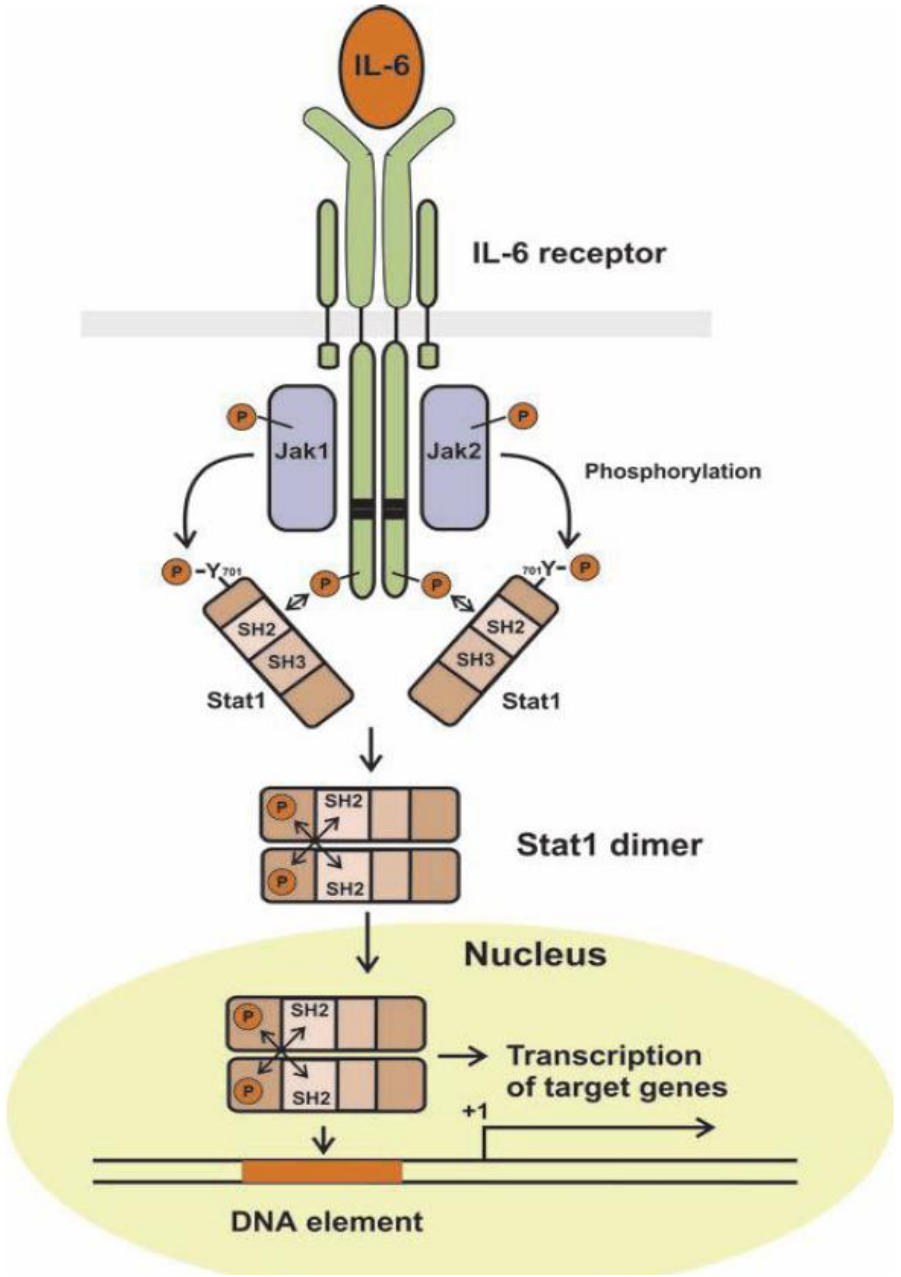
Domain structure of the nuclear receptors



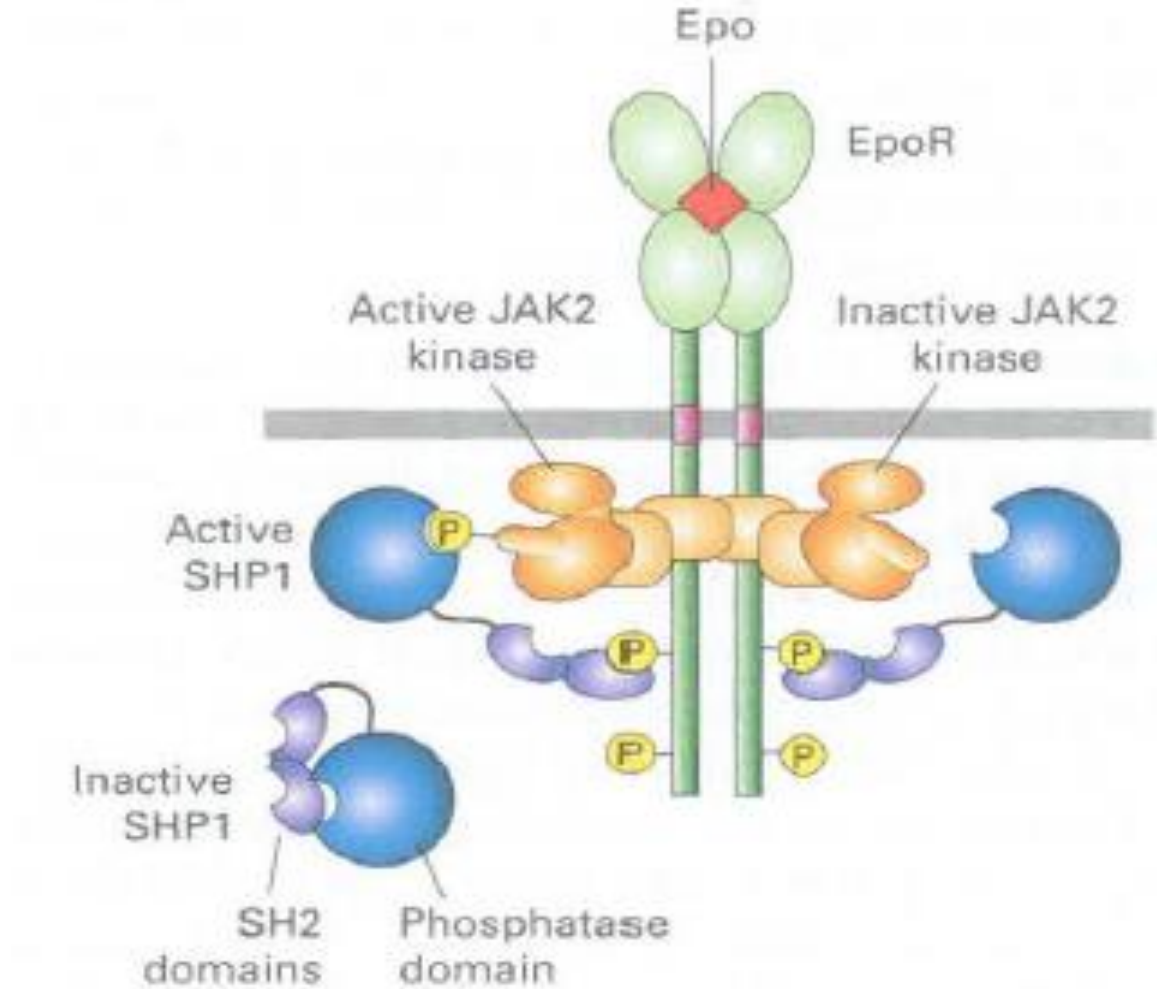
A/B : N-terminal variable region; C : DNA-binding domain
D : variable linker domain E : ligand-binding domain
F : variable C-terminal domain AF : transactivation region

General structure and activation of cytokine receptors




IL-6
IL-6 receptor
Jak1
Jak2
Phosphorylation
P
-Y701
701Y-
SH2
SH3
Stat1
Stat1 dimer
Nucleus
Transcription
of target genes
+1
DNA element

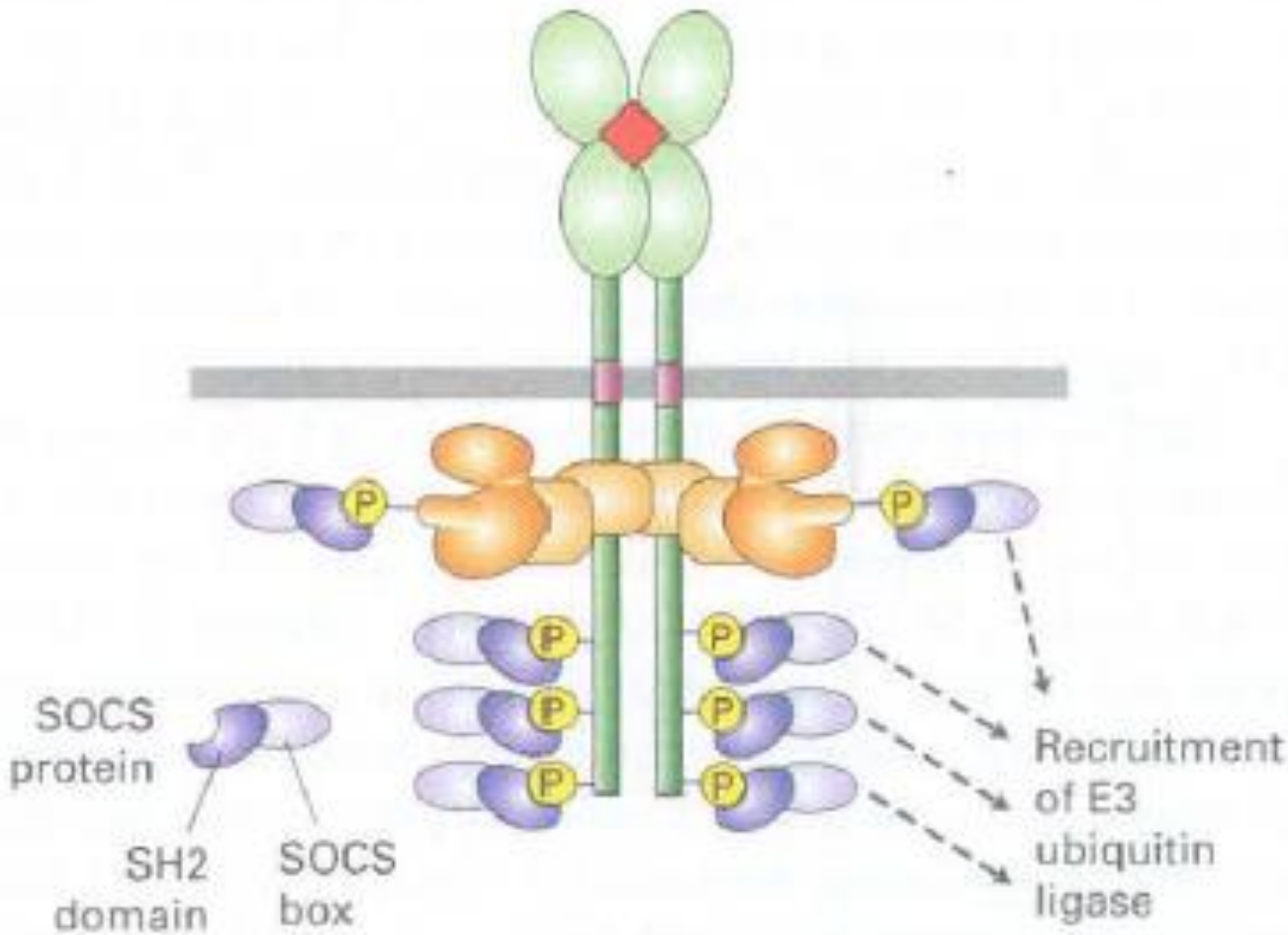
(a) Short-term regulation: JAK2 deactivation by SHP1 phosphatase



Short-term regulation

- SHPl, a phosphotyrosine phosphatase, is present in an inactive form in unstimulated cells.
- Binding of an SH2 domain in SHPl to a particular phosphotyrosine in the activated receptor unmasks its phosphatase catalytic site and positions it near the phosphorylated tyrosine in the lip region of JAK2.
- Removal of the phosphate from this tyrosine inactivates the JAK kinase.

(b) Long-term regulation: signal blocking and protein degradation by SOCS proteins



Long-term regulation

- SOCS proteins inhibit or permanently terminate signaling over longer time periods.
- Binding of SOCS to phosphotyrosine residues on EpoR or JAK2 blocks binding of other signaling proteins.
- *The* SOCS *box can also target proteins such as* JAK2 for degradation by the ubiquitin proteasome pathway