Common γ-chain cytokine receptors

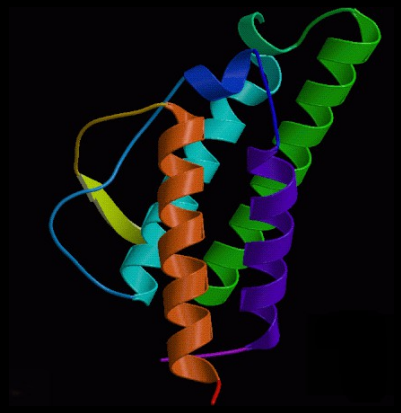
Cytokine classification

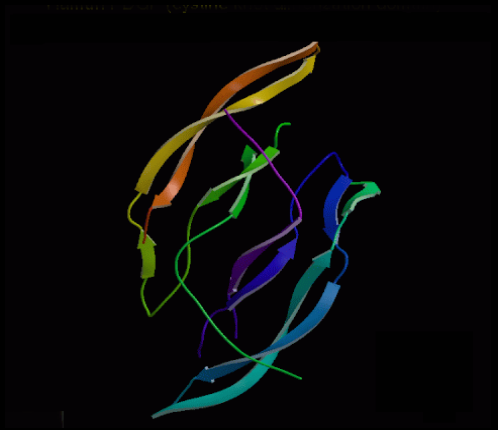
Based on structure

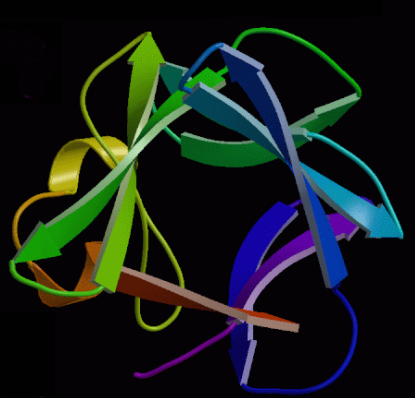
- Helical
- Cysteine knot
- Trimeric TNF family
- Beta trefoil

Based on receptor

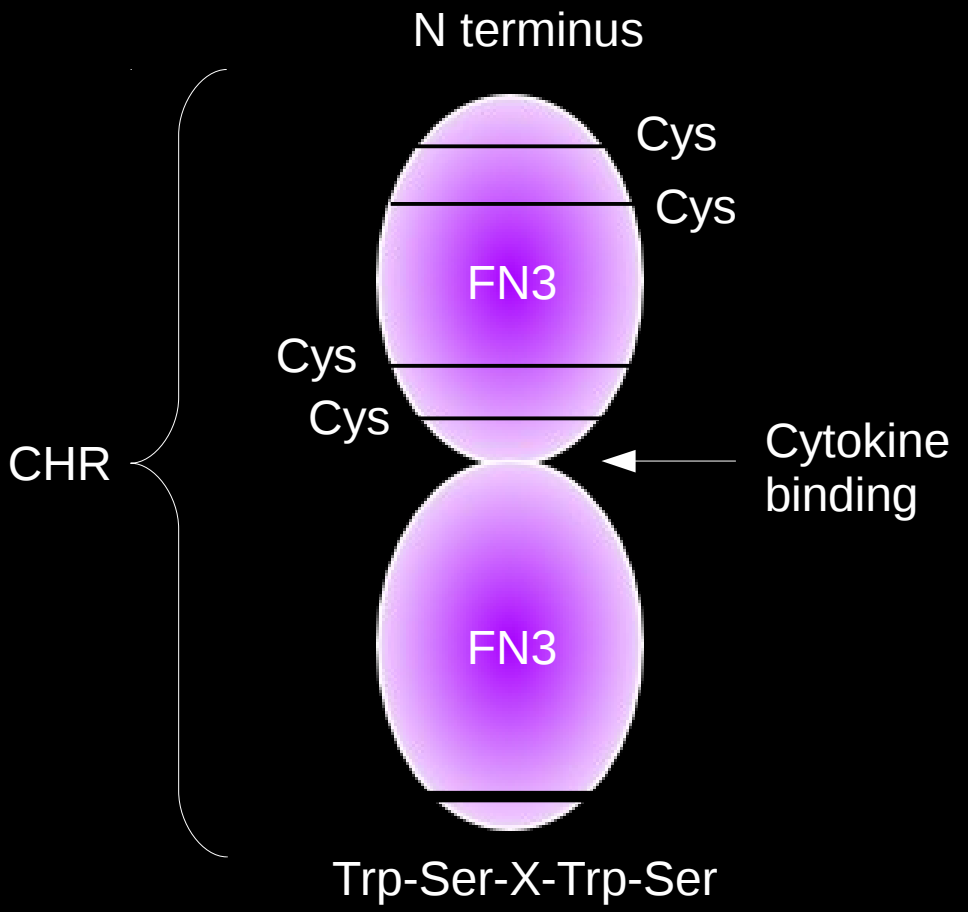
- Class I receptors
- Class II receptors
- IL-1 receptor
- PTK receptors
- Chemokine receptors







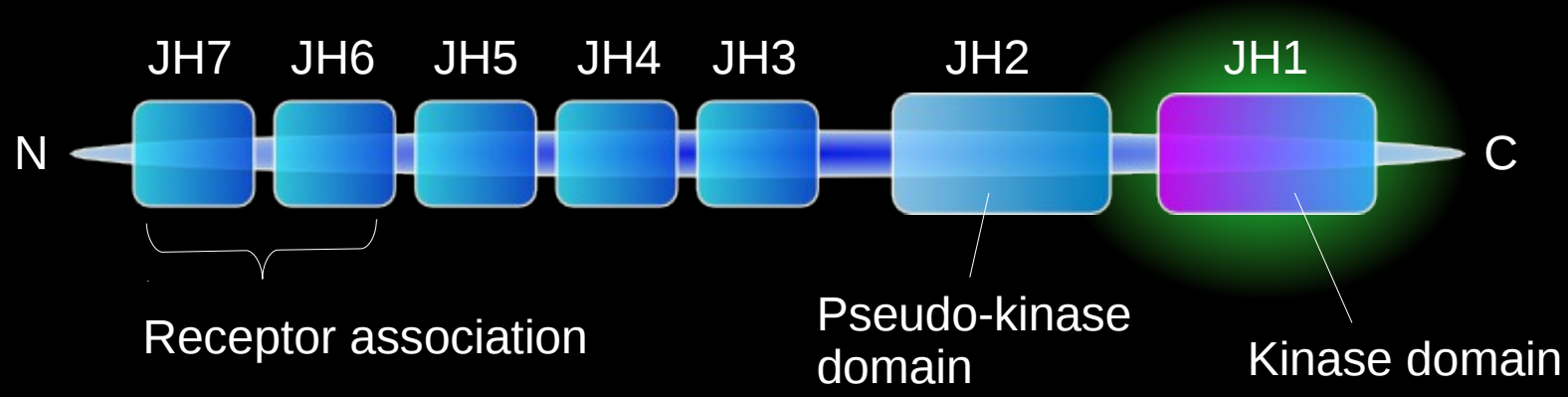
Cytokine receptor class I domains



- CHR: Cytokine-binding Homology Region
- May have additional (eg Ig-like) domains
- May have an additional membrane-proximal FN3 domain
- Some are atypical and have two SUSHI domains instead (IL-2R alpha and IL-15R alpha)

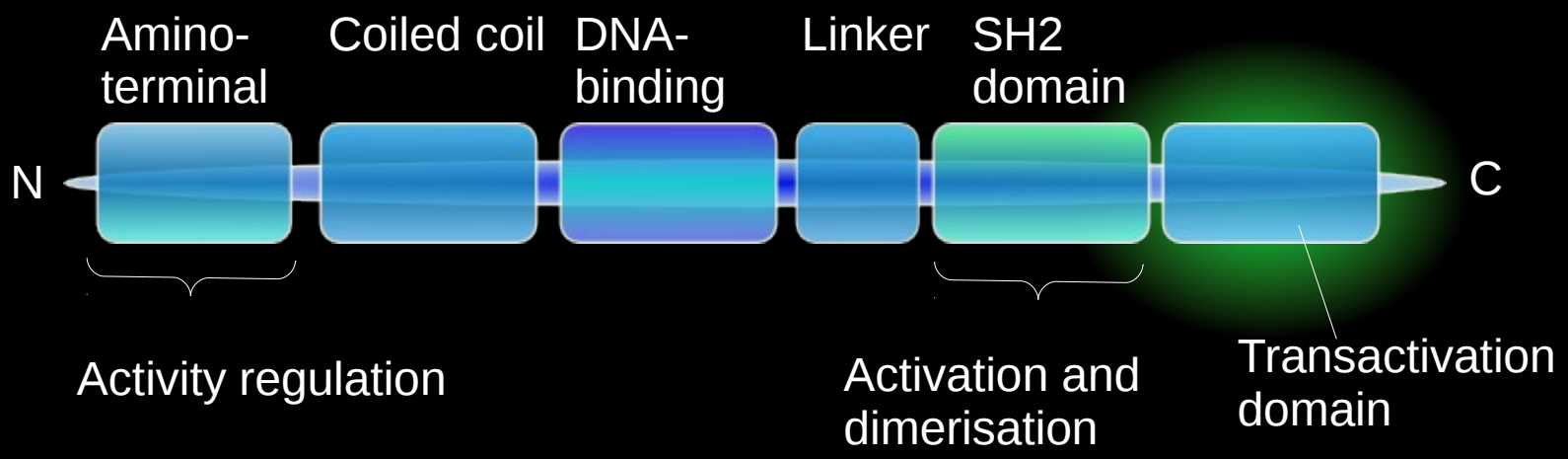
JAK

- JAK: Janus (tyrosine) kinase
- Four members: JAK1-3 and TYK2 (Tyrosine kinase)
- Seven JAK homology (JH) domains
- Two regulatory tyrosines withing the Kinase domain → activation



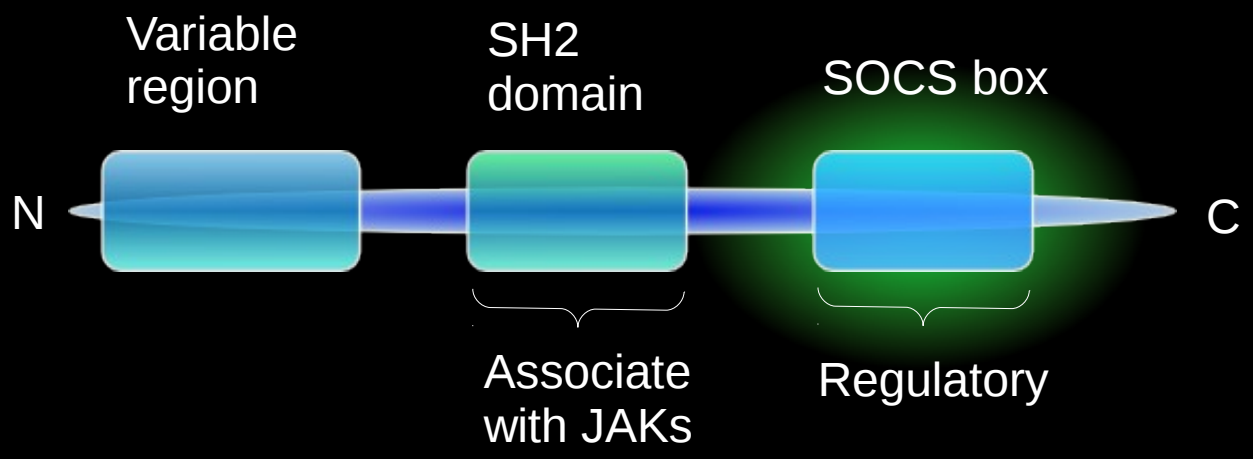
STAT

- STAT: Signal transducer and activator of transcription
- Seven members: STAT1-4, STAT5A, STAT5B and STAT6
- Two regulatory tyrosines withing the transactivation domain → associate with SH2 of other STATs



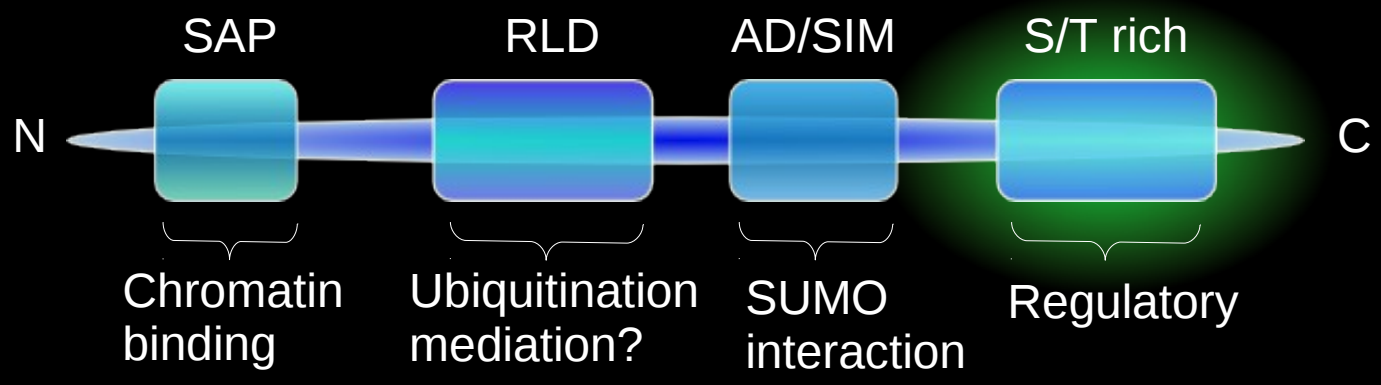
SOCS

- SOCS: Suppressor of cytokine signalling
- Eight members: SOCS1-7, CIS (cytokine inducible SH2 protein)
- Two regulatory tyrosines withing the SOCS box → target for degradation

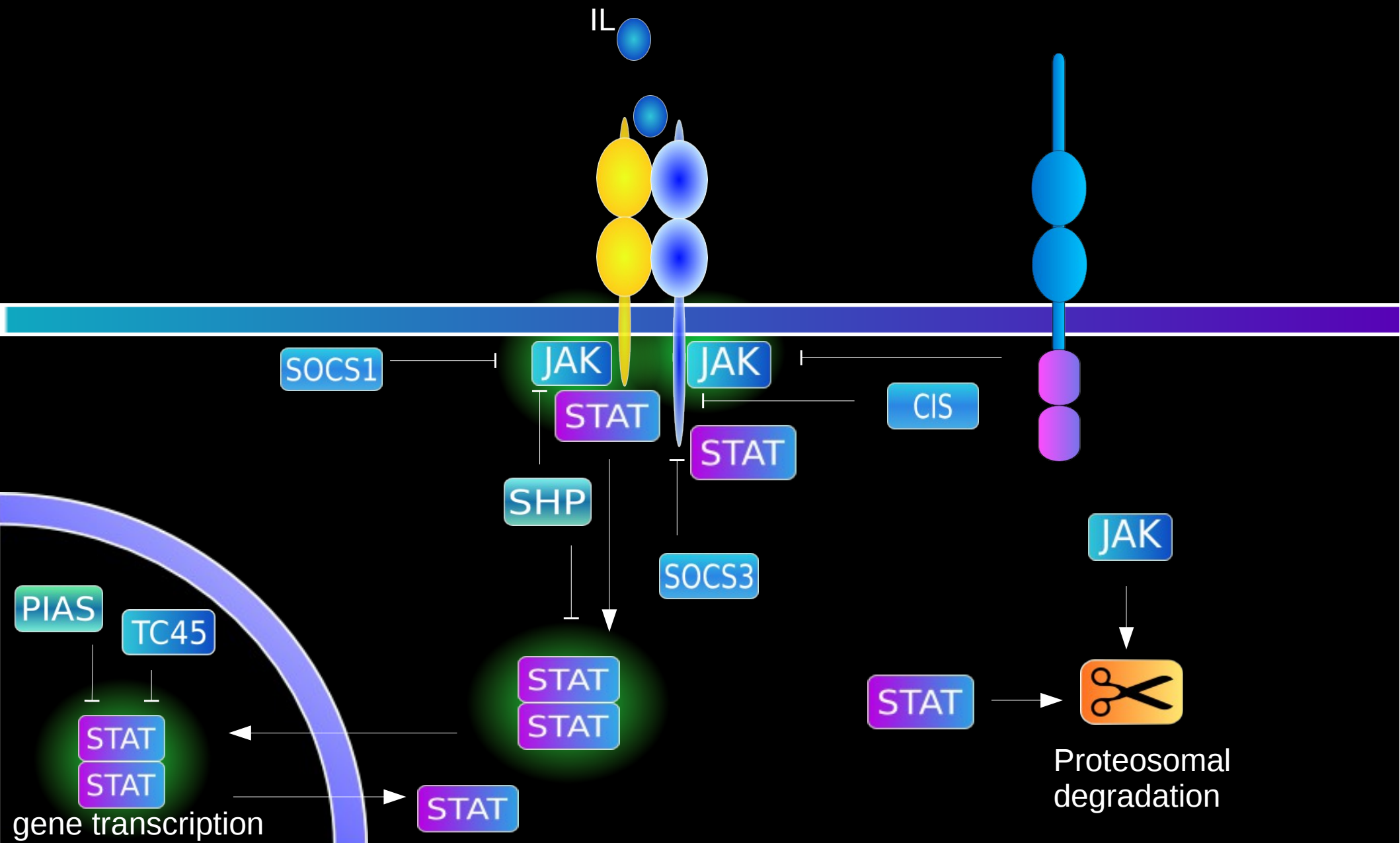


PIAS

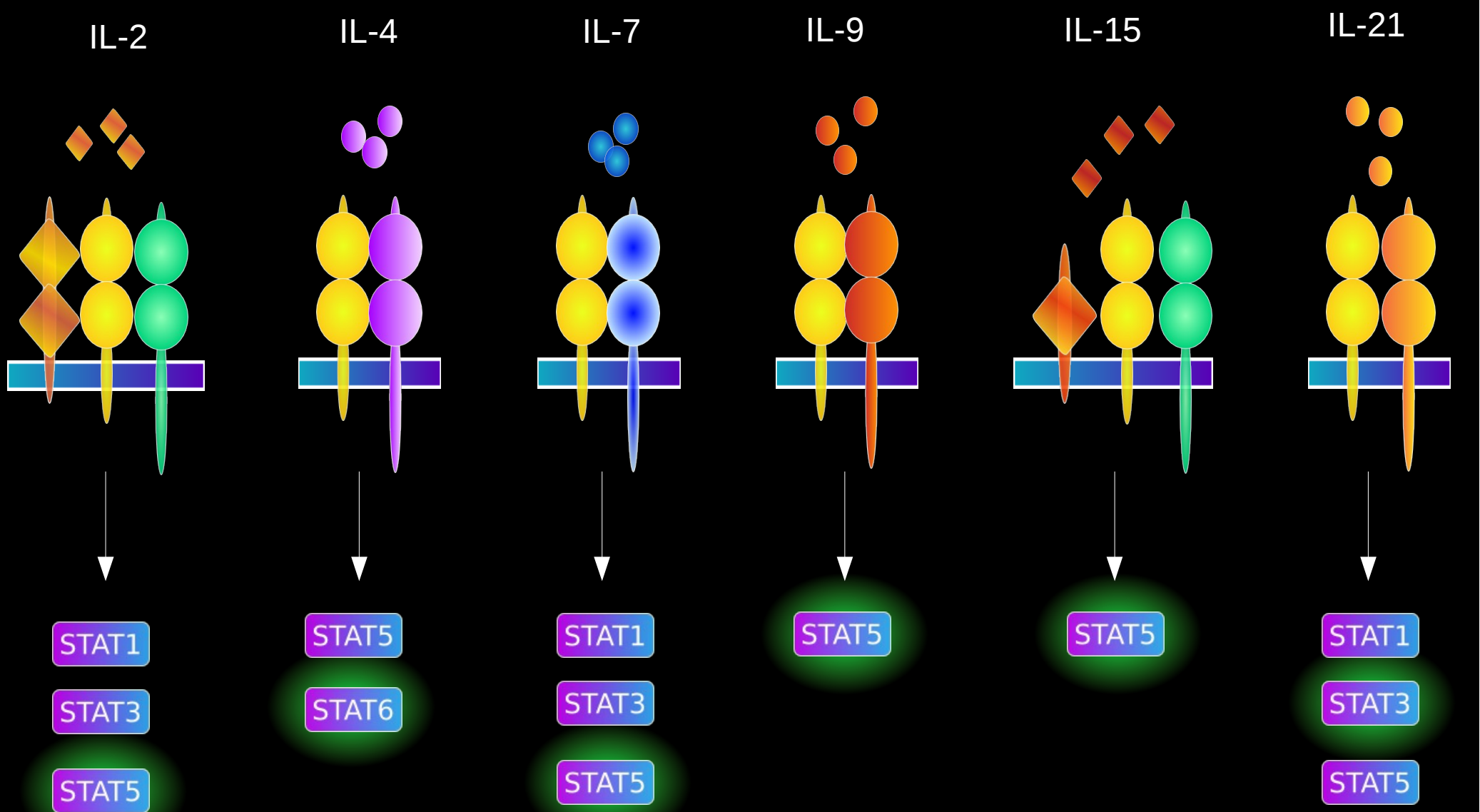
- PIAS: Protein inhibitor of activated STATs
- Four members: PIAS1, PIAS3/PIAS3β, PIASXα/PIASXβ and PIASY
- Domains: Scaffold attachment factor A/B (SAF-A/B), acinus and PIAS, RING-finger-like zinc-binding domain, acidic domain, containing SUMO interaction motif and Serine/Threonine -rich motif



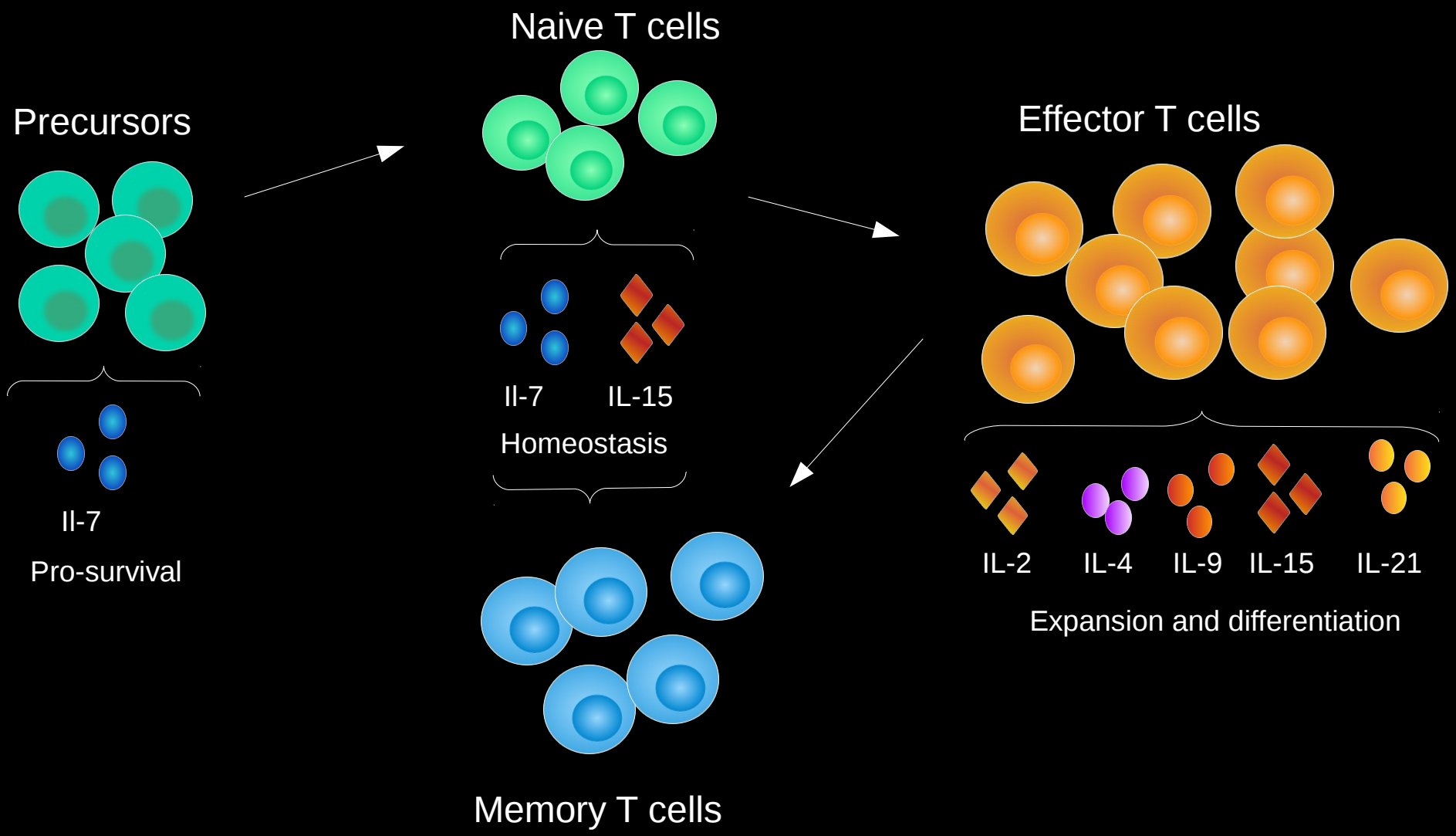
Signalling


IL
SOCS1
JAK
JAK
STAT
STAT
CIS
SHP
SOCS3
JAK
PIAS
TC45
STAT
STAT
STAT
STAT
STAT
STAT
gene transcription
Proteosomal
degradation

Family


IL-2
IL-4
IL-7
IL-9
IL-15
IL-21
STAT1
STAT3
STAT5
STAT5
STAT6
STAT1
STAT3
STAT5
STAT5
STAT5
STAT1
STAT3
STAT5

Effect on T cells



Summary

- Common CHR structure, with exception of the atypical IL-2Ra and IL-15Ra
- Form hetero dimers or trimers
- Associated JAKs interact with STATs
- STATs translocate to nucleus to upregulate gene expression
- Tight regulation of the signalling: SOCS, PIAS, PTPs, proteosomal degradation
- Different cocktail of cytokines have survival and proliferative roles at the different stages of cell development