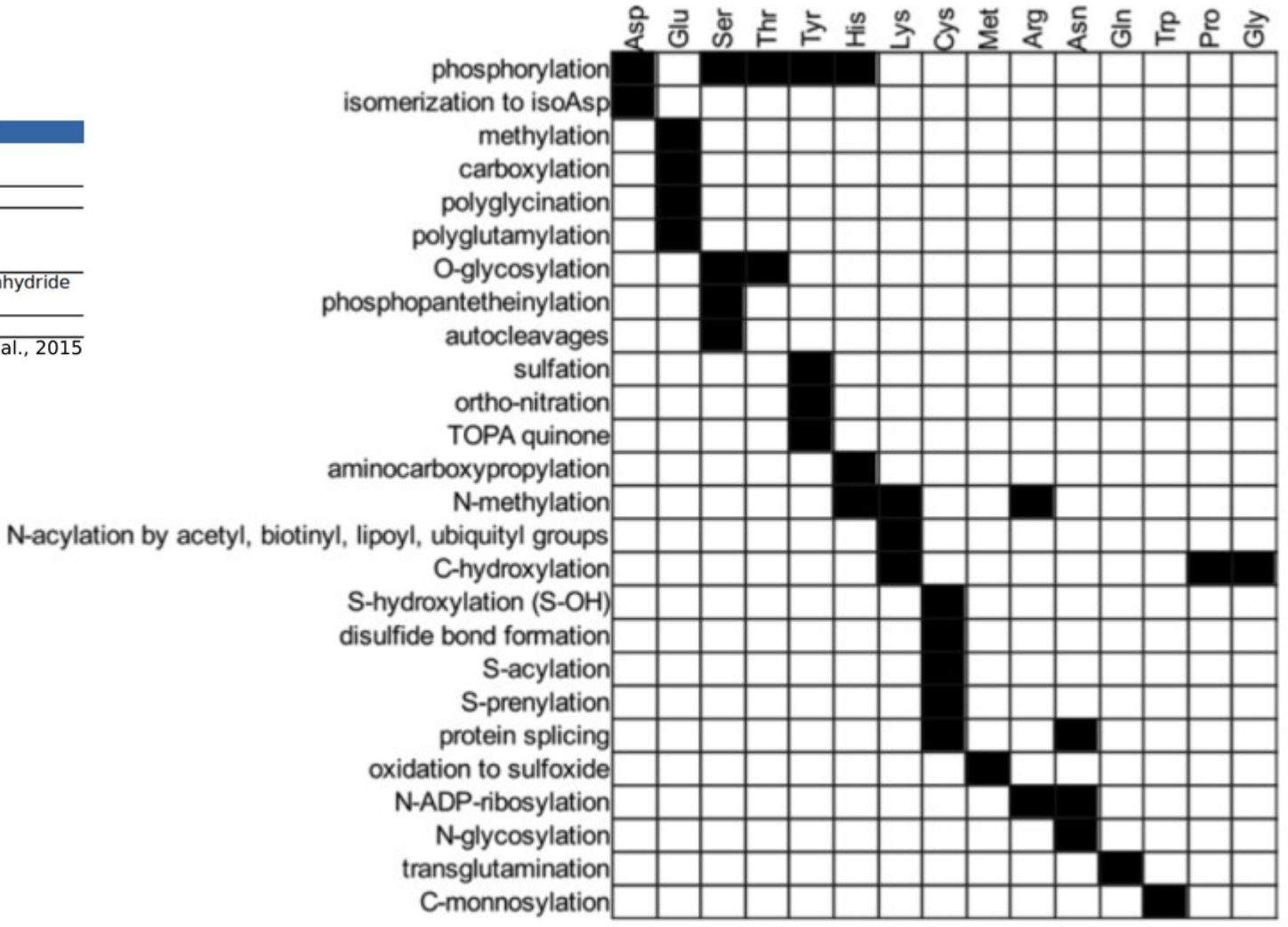
Sitokin ve kemokinler – Sinyal iletimi

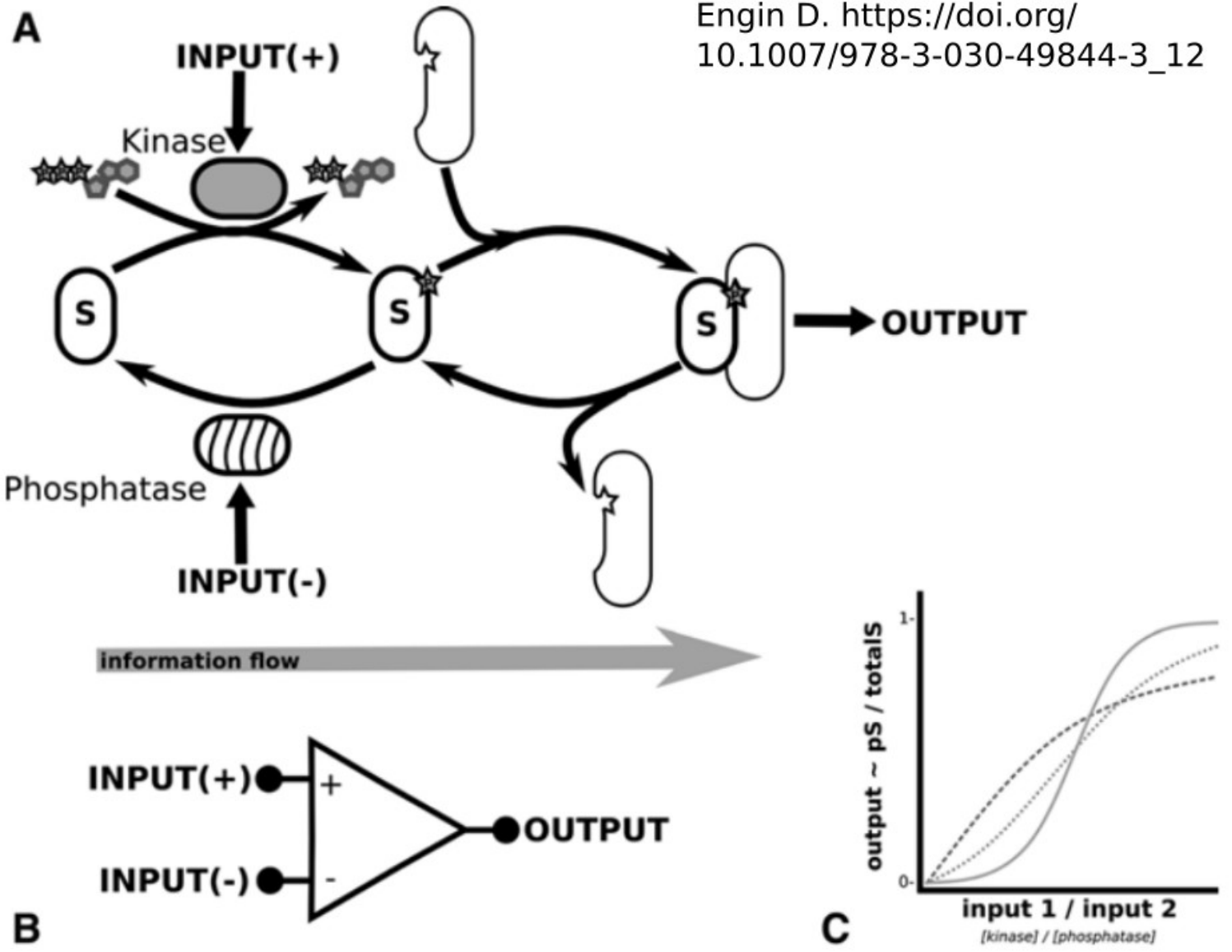
Group	Amino acid	Phospho-modification type
Alcohol	Serine Threonine	Phosphate ester
Phenolic	Tyrosine	
Basic	Histidine Arginine Lysine	Phosphoamidate
Acidic	Aspartic acid Glutamic acid	Phosphate carboxylate acid anhydride
Other	Cysteine	Phosphate thioester

Sajid et al., 2015



Engin D. https://doi.org/10.1007/978-3-030-49844-3_12

Engin D. https://doi.org/
10.1007/978-3-030-49844-3_12



The Journal of Immunology

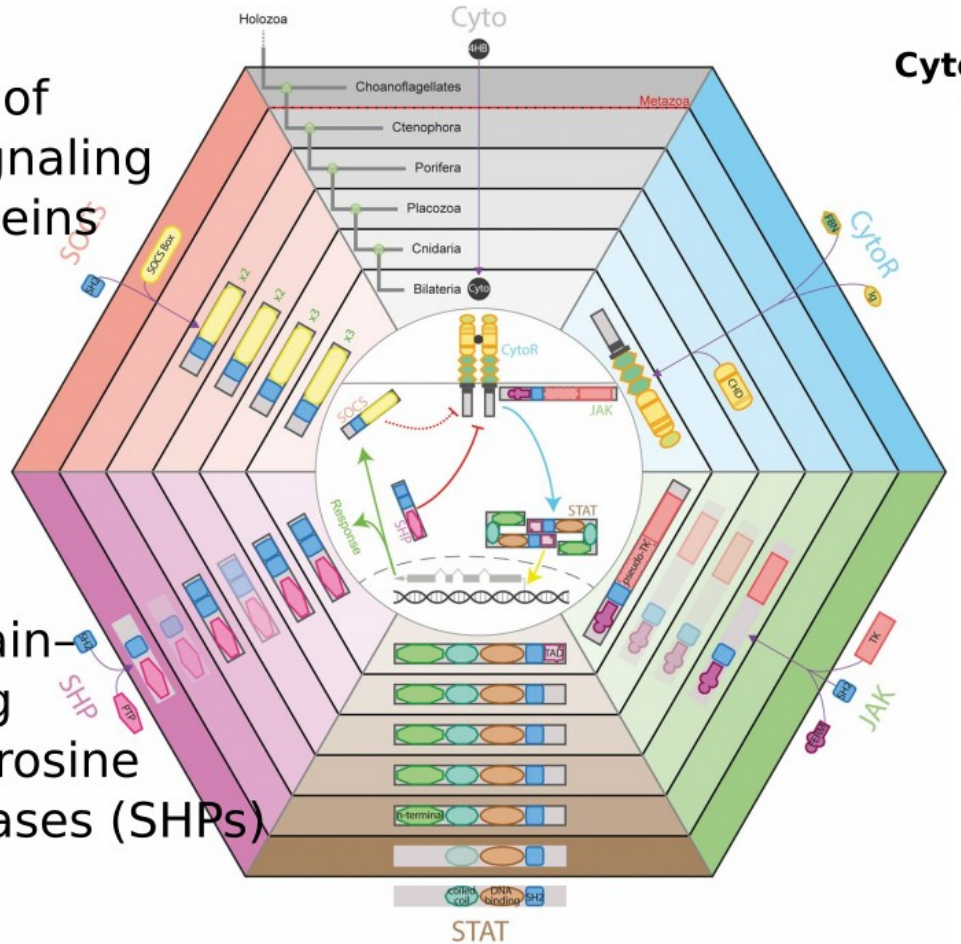
cytochromes

ferritin

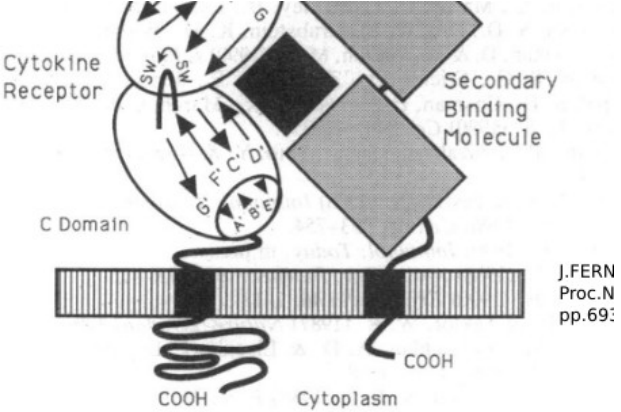
~5-25 kDa cytokine peptide

Suppressor of cytokine signaling (SOCS) proteins

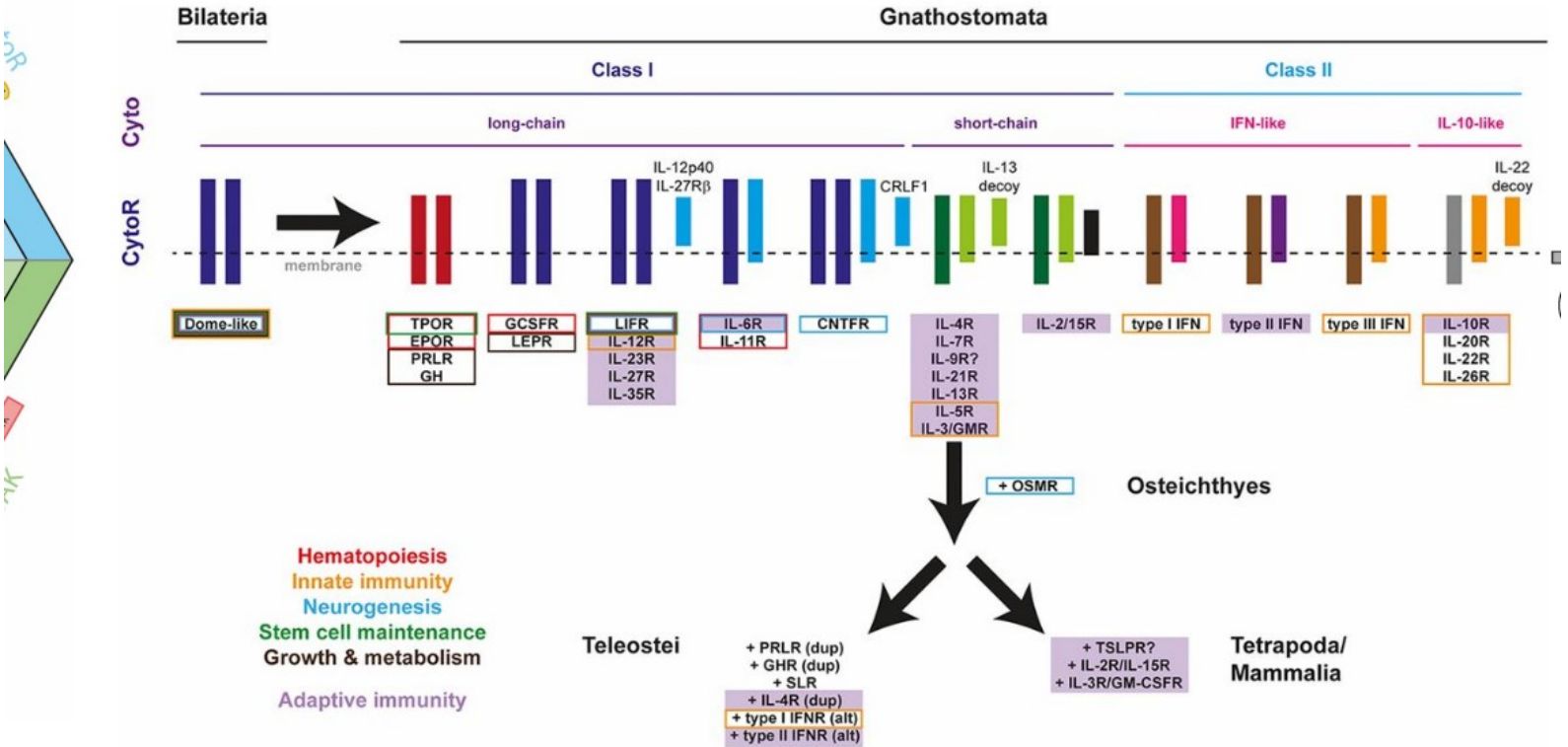
SH2 domain–containing protein tyrosine phosphatases (SHPs)

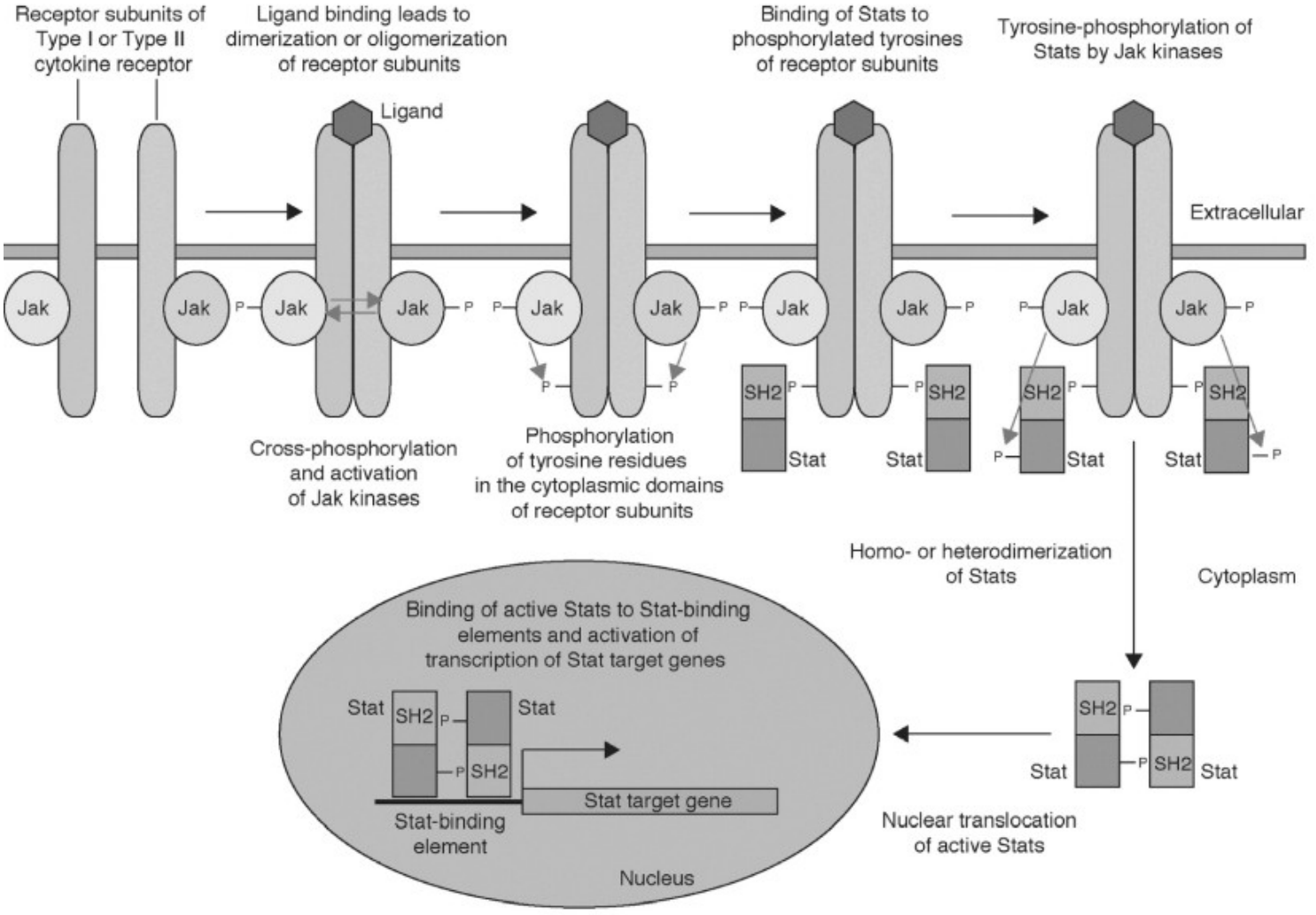


of
ology
Evolution of Cytokine Receptor Signaling
Clifford Liongue, Robert Sertori and Alister C. Ward
J Immunol July 1, 2016, 197 (1) 11-18;
DOI: https://doi.org/10.4049/jimmunol.1600372

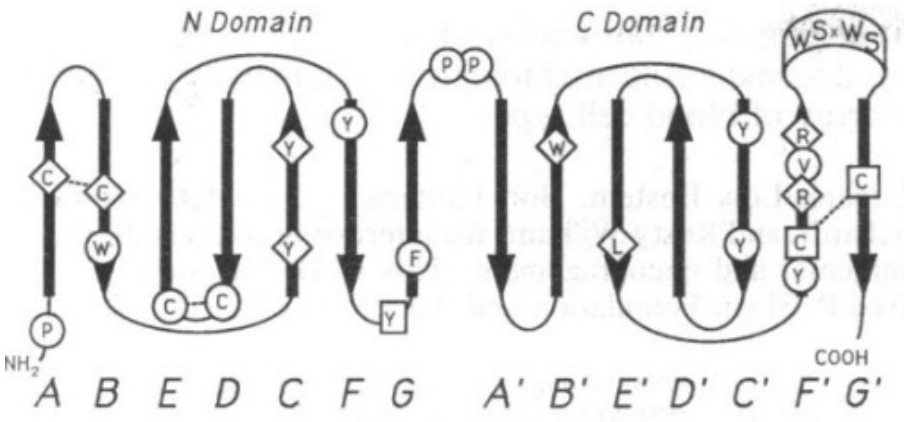


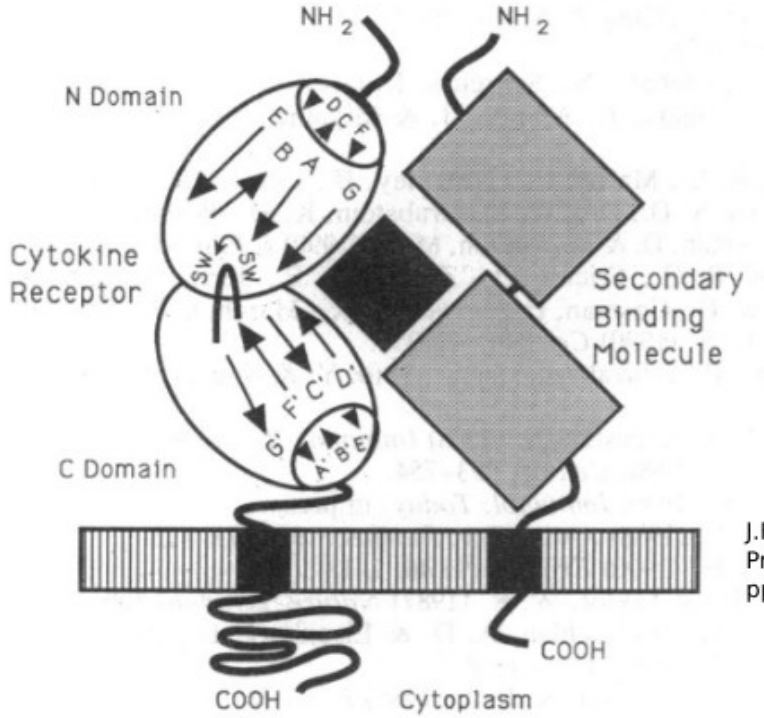
CytoR homology domain (CHD)
fibronectin (FBN) type III folds
connecting sequence <-- cytokine binding





Hodaka Fujii. Mechanisms of Signal Transduction from Receptors of Type I and Type II Cytokines. https://doi.org/10.1080/15476910601154779





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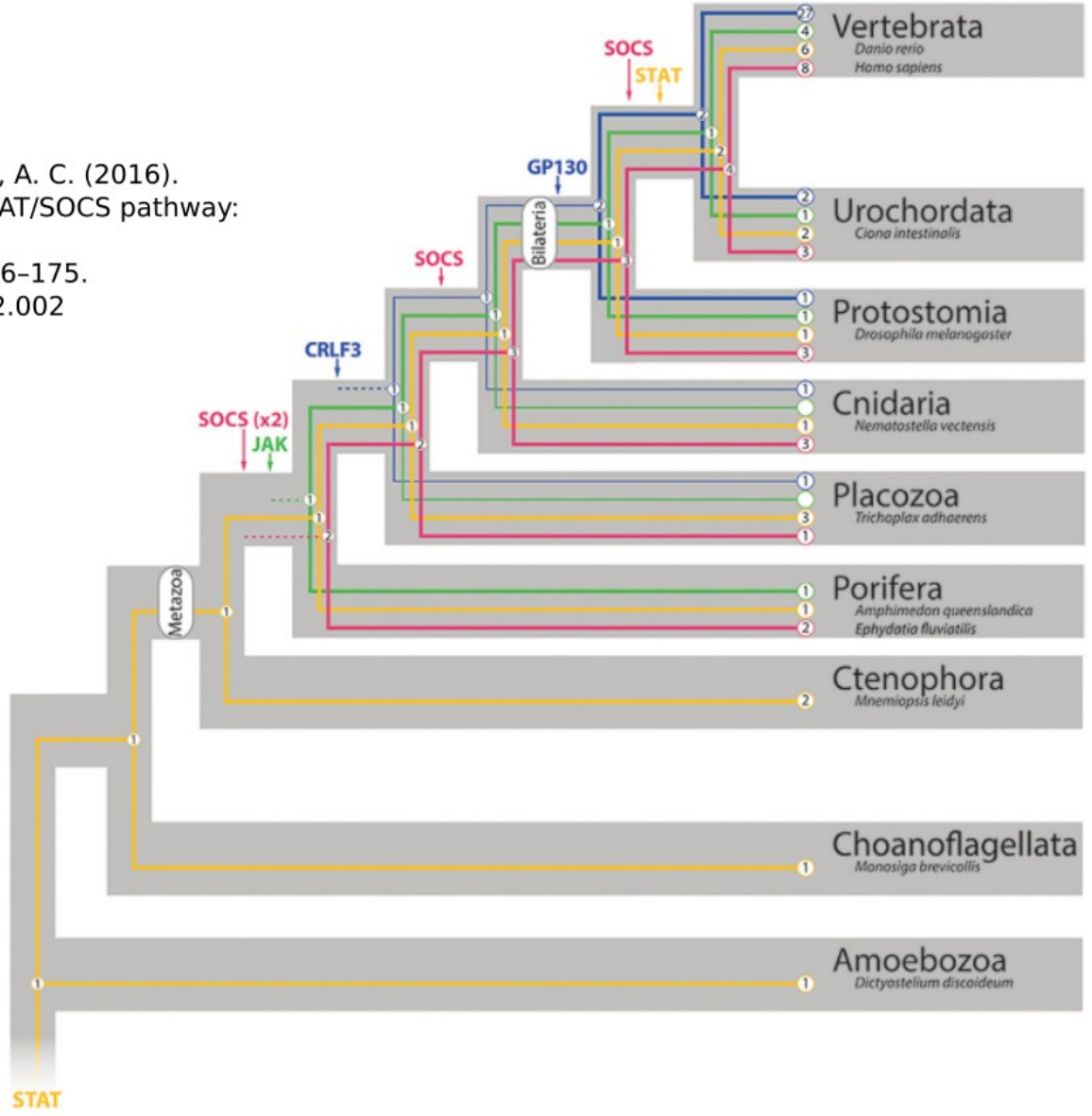
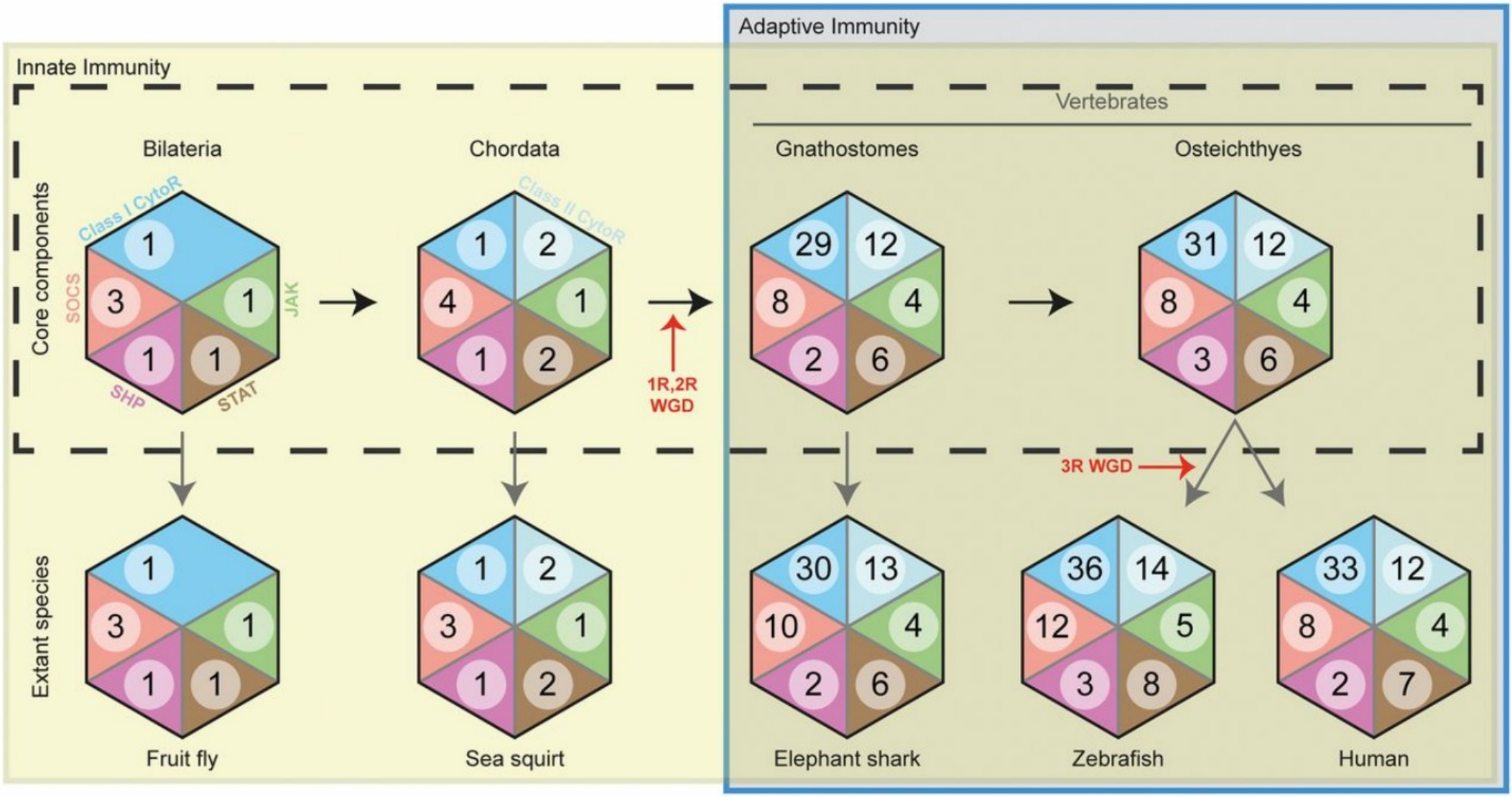
Proc.Natl.Acad.Sci.USAVol.87,
pp.6934-6938, September 1990

Liongue, C., Taznin, T., & Ward, A. C. (2016).
Signaling via the CytoR/JAK/STAT/SOCS pathway:
Emergence during evolution.
Molecular Immunology, 71, 166–175.
doi:10.1016/j.molimm.2016.02.002



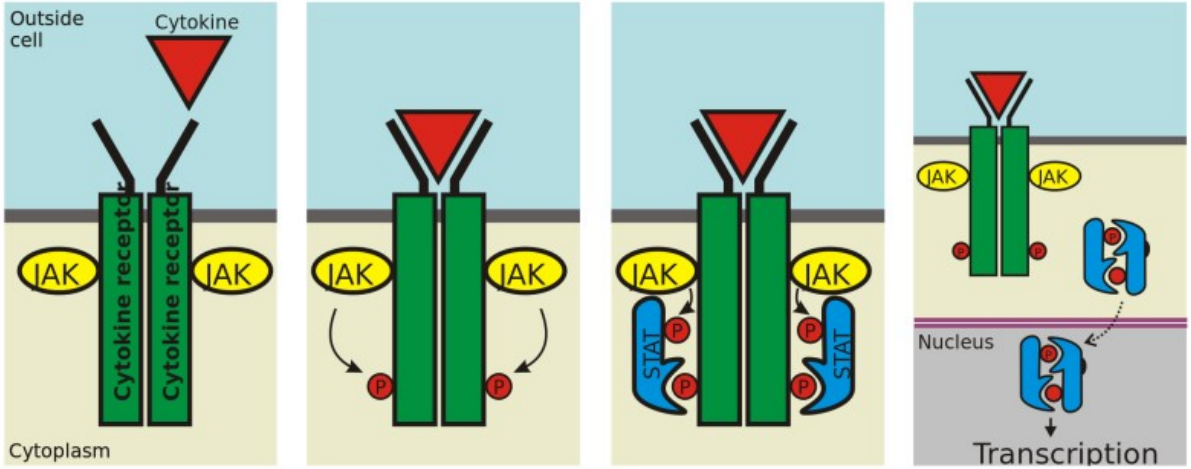

Innate Immunity
Adaptive Immunity
Vertebrates
Bilateria
Chordata
Gnathostomes
Osteichthyes
Core components
Extant species
Class I CytoR
Class II CytoR
SOCS
JAK
SHP
STAT
1R,2R WGD
3R WGD
Fruit fly
Sea squirt
Elephant shark
Zebrafish
Human

Type	Examples	Structure	Mechanism
type I cytokine receptor	Type 1 interleukin receptors Erythropoietin receptor GM-CSF receptor G-CSF receptor growth hormone receptor prolactin receptor Oncostatin M receptor Leukemia inhibitory factor receptor	Certain conserved motifs in their extracellular amino-acid domain. Connected to Janus kinase (JAK) family of tyrosine kinases. Many have a FN-III superfamily domain and an immunoglobulin-like fold.	JAK phosphorylate and activate downstream proteins involved in their signal transduction pathways
type II cytokine receptor	Type II interleukin receptors interferon-alpha/beta receptor interferon-gamma receptor		
Many members of the immunoglobulin superfamily	Interleukin-1 receptor CSF1 C-kit receptor Interleukin-18 receptor	Share structural homology with immunoglobulins (antibodies), cell adhesion molecules, and even some cytokine. Includes with the two classes above.	
Tumor necrosis factor receptor family	CD27 CD30 CD40 CD120 Lymphotoxin beta receptor	cysteine-rich common extracellular binding domain	
chemokine receptors	Interleukin-8 receptor CCR1 CXCR4 MCAF receptor NAP-2 receptor	Seven transmembrane helix, rhodopsin-like receptor[2]	G protein-coupled
TGF-beta receptor family	TGF beta receptor 1 TGF beta receptor 2	Serine/threonine kinase receptors	Dimeric TGFBR2 binds to TGFB and phosphorylates TGFBR1, which phosphorylates the SMADs. See TGF beta signaling pathway.

https://en.wikipedia.org/wiki/Cytokine_receptor

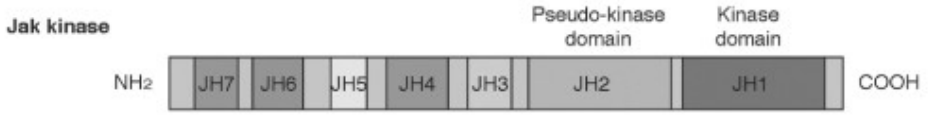
JAK/STAT signalling

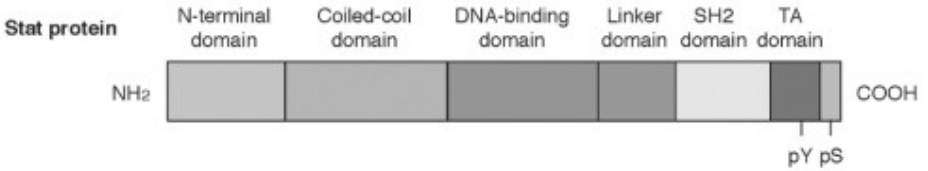
immunity
cell division
cell death
tumour formation



Peter Znamenkiy - https://en.wikipedia.org/wiki/Cytokine_receptor

Hodaka Fujii. Mechanisms of Signal Transduction from Receptors of Type I and Type II Cytokines. https://doi.org/10.1080/15476910601154779





Sitokin reseptörlerinin çoğunda *otofosforilasyon* özelliği **bulunmamakta**

Reseptör

JAK1
JAK2
JAK3
TYK2

STAT1
STAT2
STAT3
STAT4
STAT5A
STAT5B
STAT6

Tyr-phosphorylation - Sinyal iletimi

Lys/Arg-Methylation - Azalmış aktivite

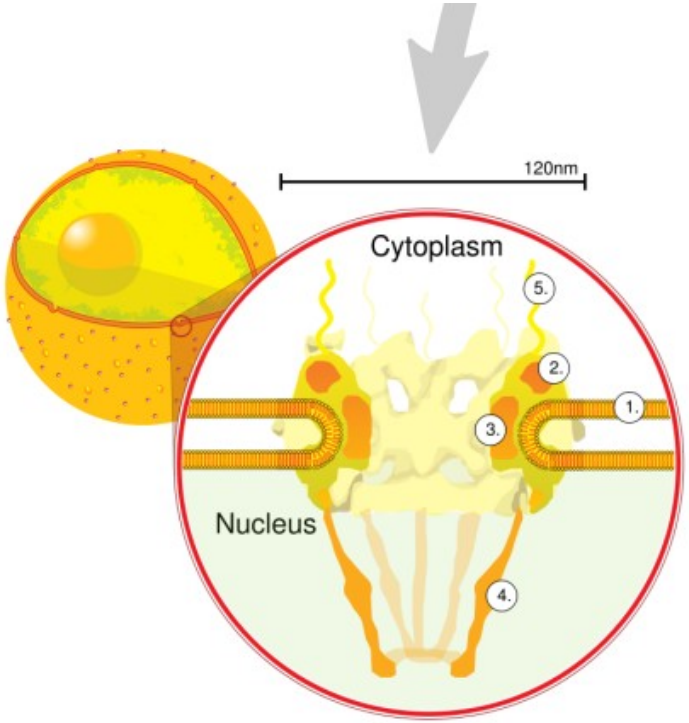
Lys-Acetylation - DNA'ya bağlanma
Apoptsis, antiviral aktivite

Ser-phosphorylation - Azalmış gen ekspresyonu

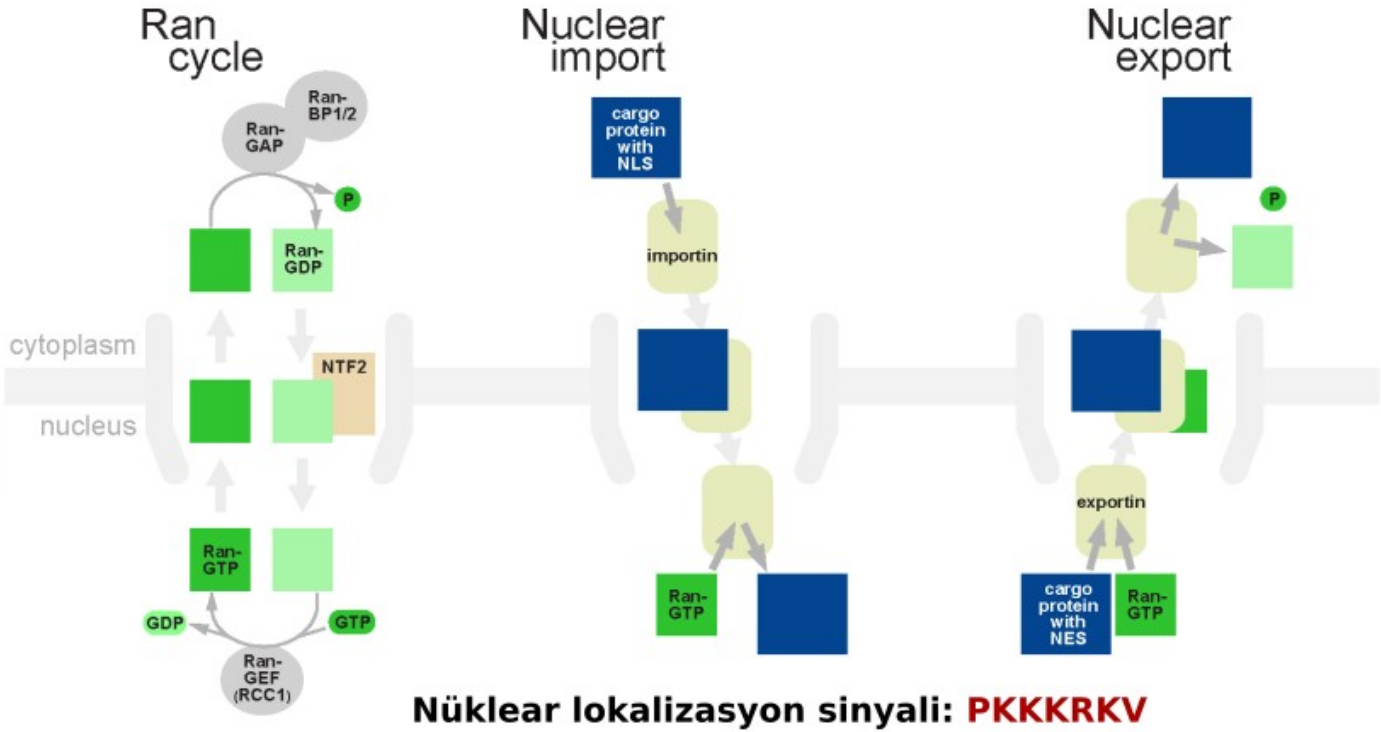
SH2 domain

Src Homology 2

Negative regulator	*Site of action*	*Inhibition mechanism*
Cytoplasmic tyrosine phosphatases	Cytoplasm	Dephosphorylation of the cytoplasmic domains of cytokine receptors, Jaks and Stats
SOCS proteins	Cytoplasm	Binding to the cytoplasmic domains of cytokine receptors and/or Jak kinases
Nuclear phosphatases	Nucleus	Dephosphorylation of Stats
PIAS proteins	Nucleus	Binding to tyrosine-phosphorylated Stats
Truncated forms of Stats	Nucleus	Dominant negative forms
SLIM proteins	Nucleus	Degradation of Stats by ubiquitin-dependent degradation



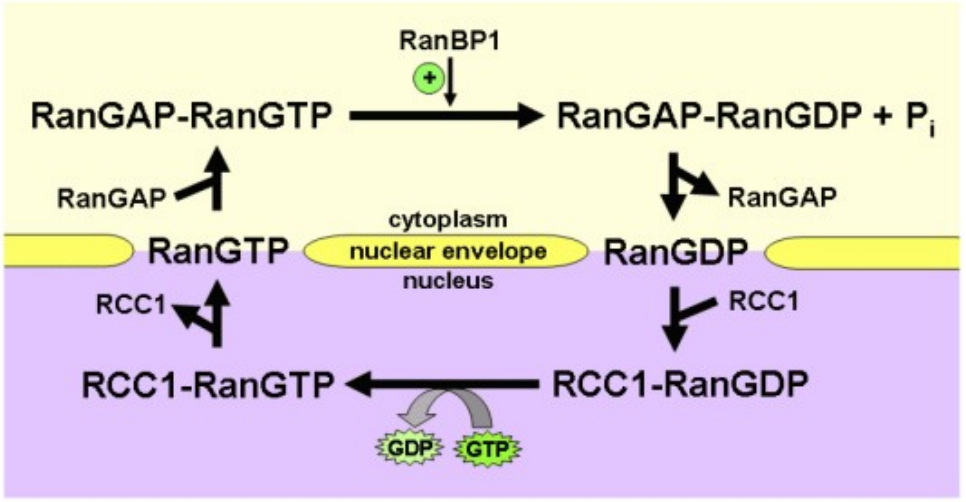
~110 MDa

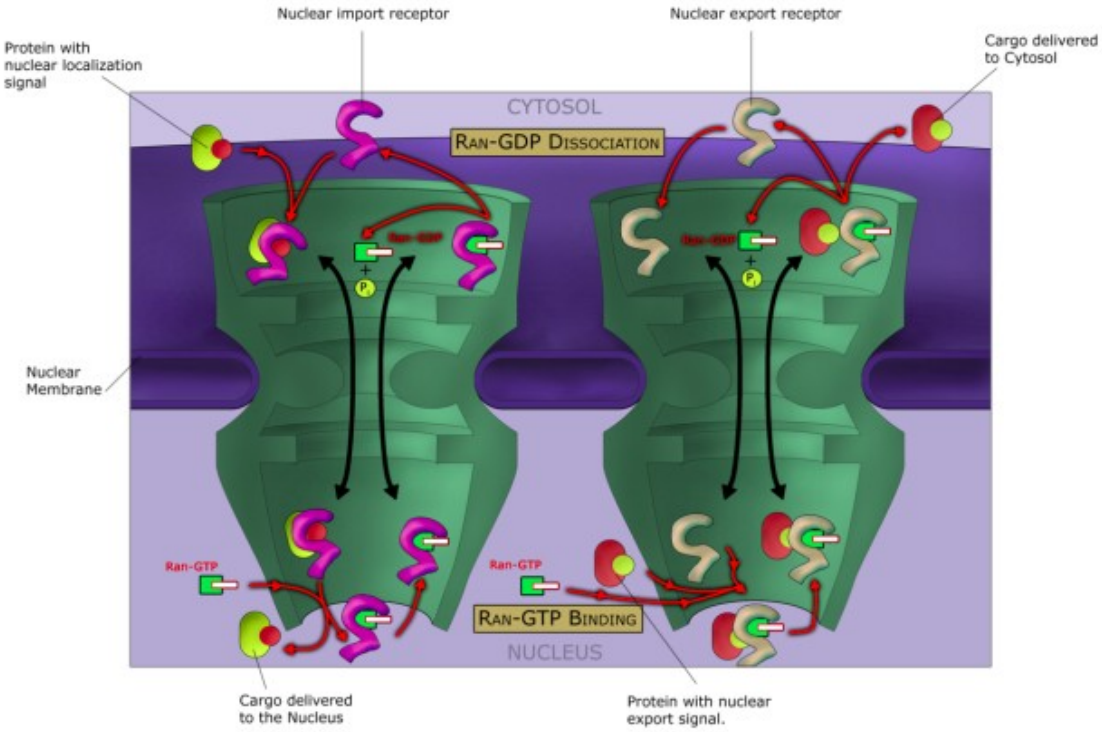


Nüklear lokalizasyon sinyali: PKKKRKV

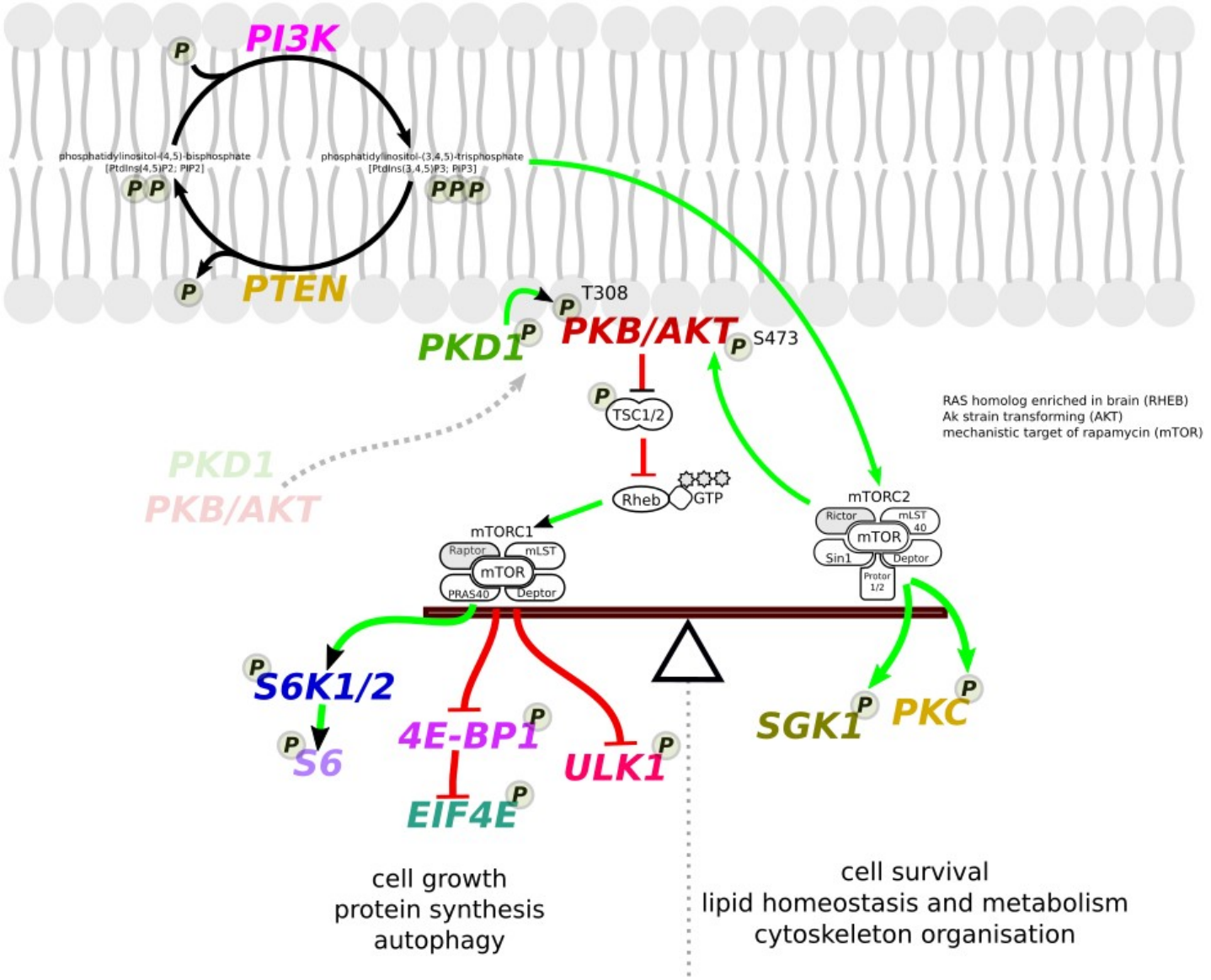
https://en.wikipedia.org/wiki/Nuclear_pore

RAs-related Nuclear protein)
GTP-binding nuclear protein Ran

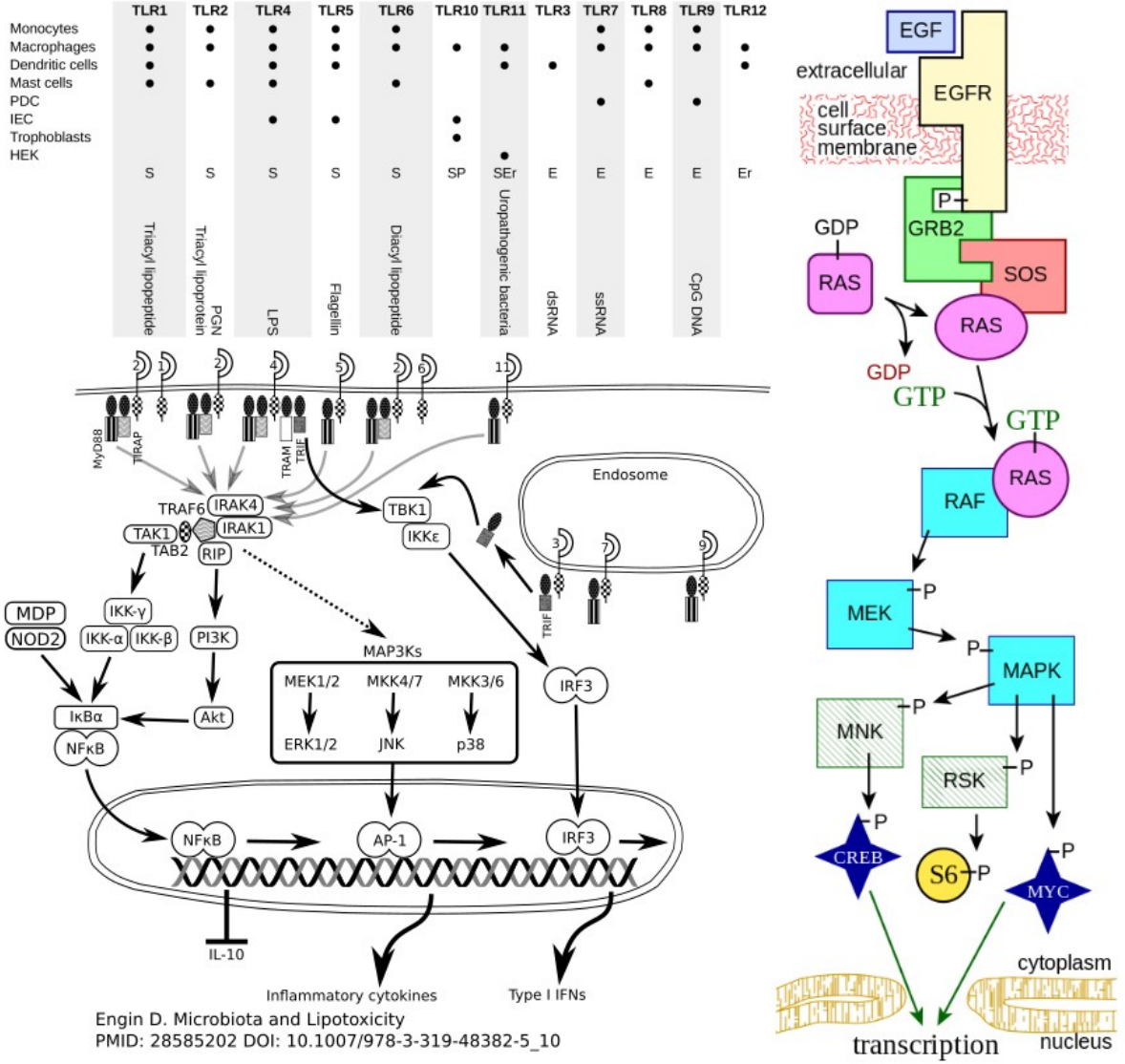




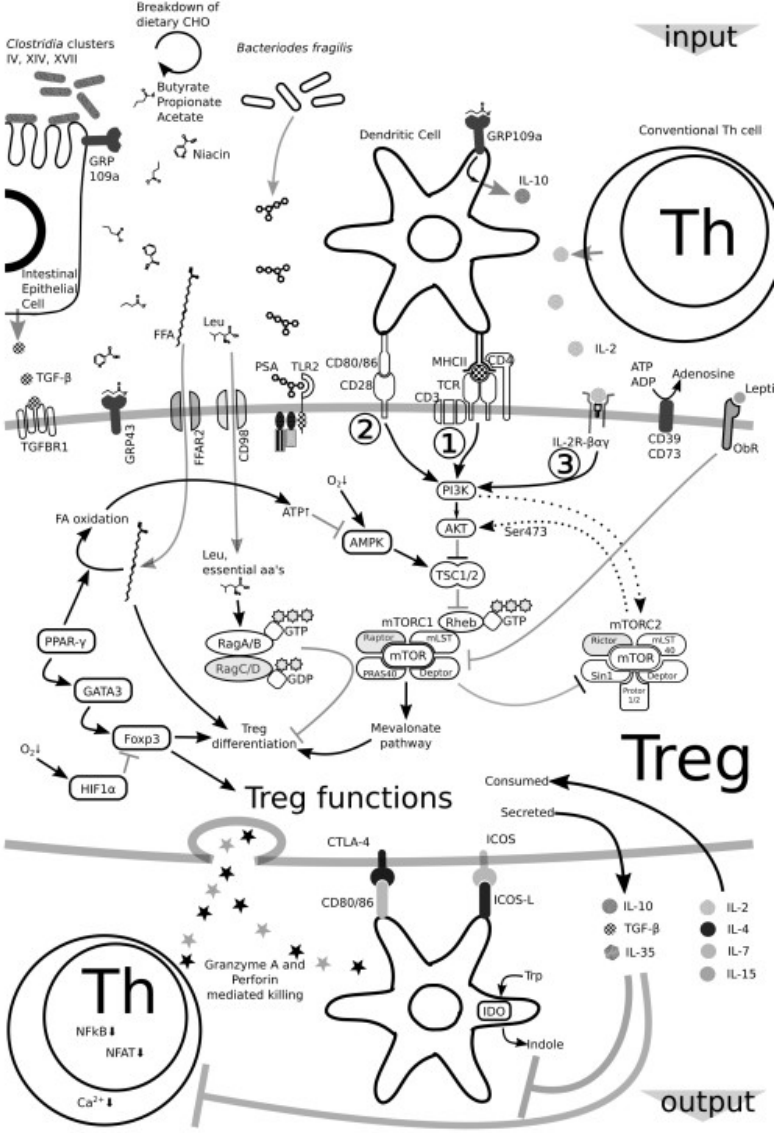
https://en.wikipedia.org/wiki/Ran_(protein)


PI3K
phosphatidylinositol-(4,5)-bisphosphate
[PtdIns(4,5)P2; PIP2]
phosphatidylinositol-(3,4,5)-trisphosphate
[PtdIns(3,4,5)P3; PIP3]
PTEN
T308
PKD1
PKB/AKT
S473
TSC1/2
Rheb
GTP
mTORC1
Raptor
mLST
mTOR
PRAS40
Deptor
mTORC2
Rictor
mLST 40
mTOR
Sin1
Deptor
Protor 1/2
RAS homolog enriched in brain (RHEB)
Ak strain transforming (AKT)
mechanistic target of rapamycin (mTOR)
PKD1
PKB/AKT
S6K1/2
S6
4E-BP1
EIF4E
ULK1
SGK1
PKC
cell growth
protein synthesis
autophagy
cell survival
lipid homeostasis and metabolism
cytoskeleton organisation

Ras-Raf-MEK-ERK pathway



Engin D. Microbiota and Lipotoxicity
PMID: 28585202 DOI: 10.1007/978-3-319-48382-5_10



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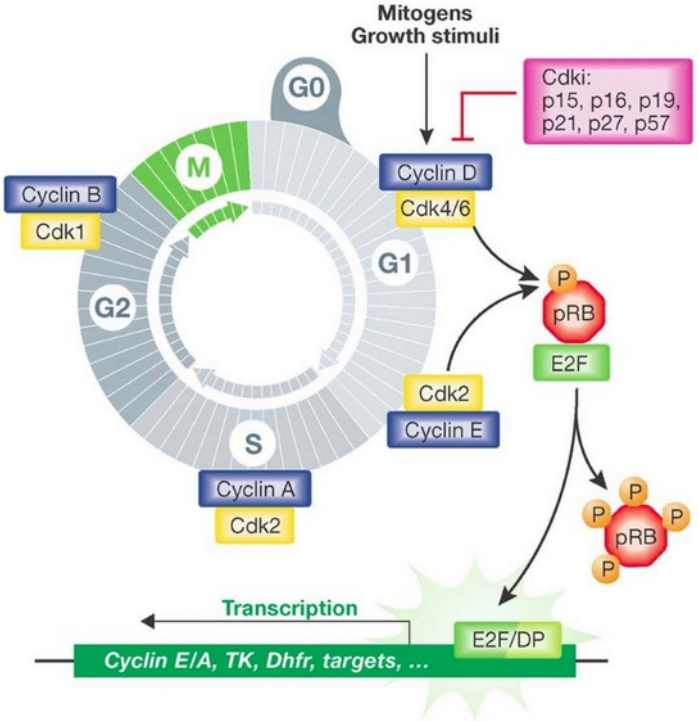

Cycling through metabolism
Victor Aguilar, Lluis Fajas
DOI 10.1002/emmm.201000089