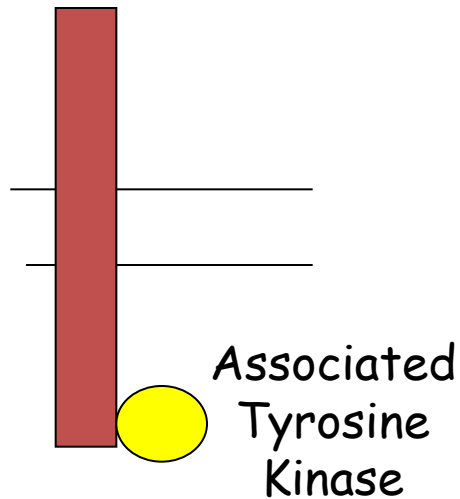


Υποδοχείς

- Κυτοκινών
- Τ- και Β-κυττάρων
- Ιντεγκρινών

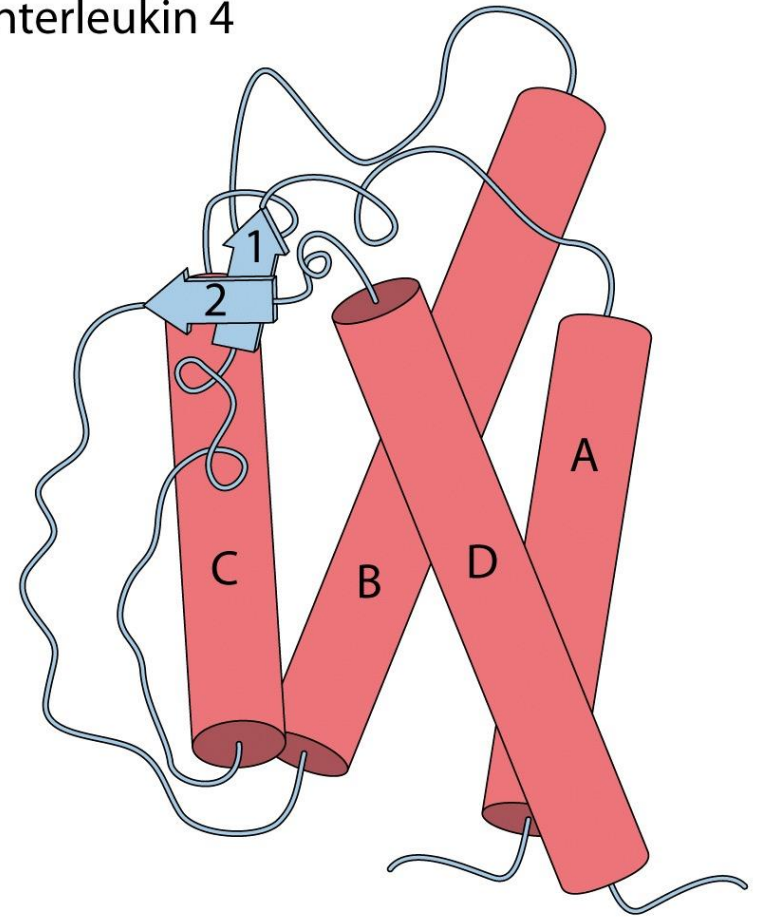


Membrane Receptors with Associated Tyrosine Kinase Activity

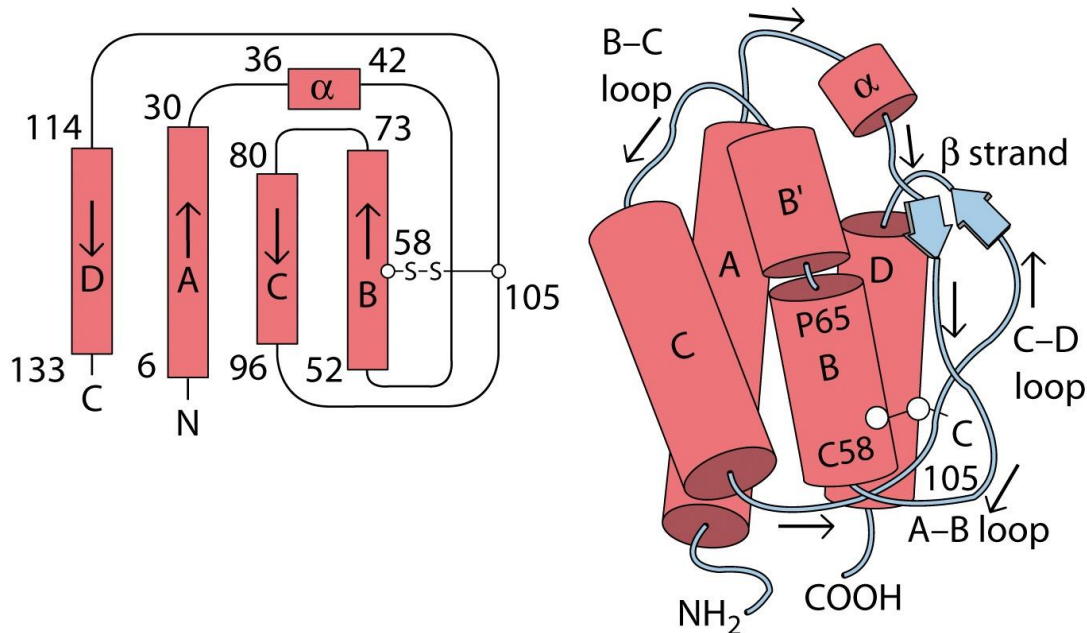
Οι κυτοκίνες και οι υποδοχείς τους

- οι ιντερλευκίνες (IL1-25),
- οι ιντερφερόνες (INF),
- η ερυθροποιητίνη,
- η αυξητική ορμόνη και
- ο παράγοντας νέκρωσης όγκων (TNF)

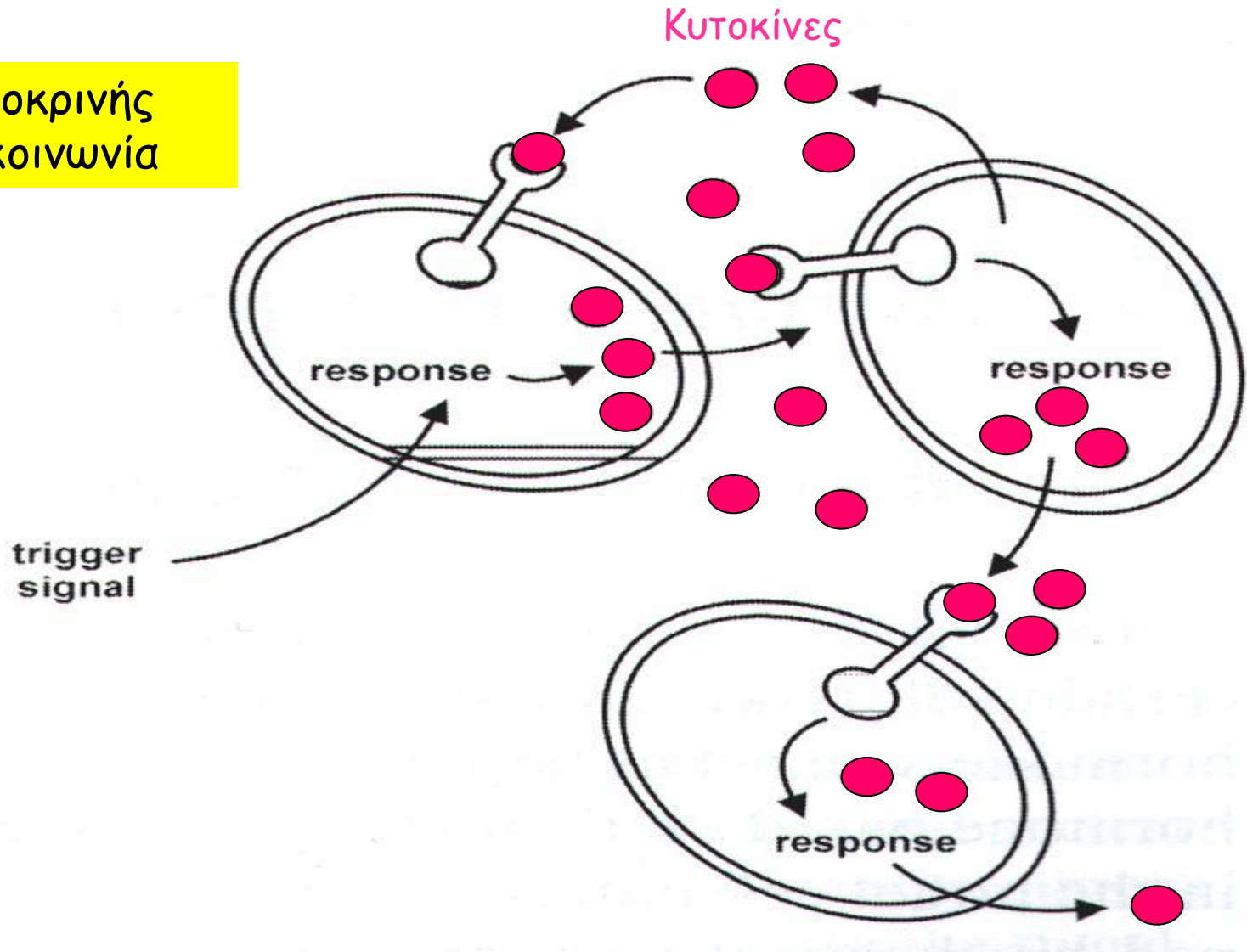
(b) Interleukin 4

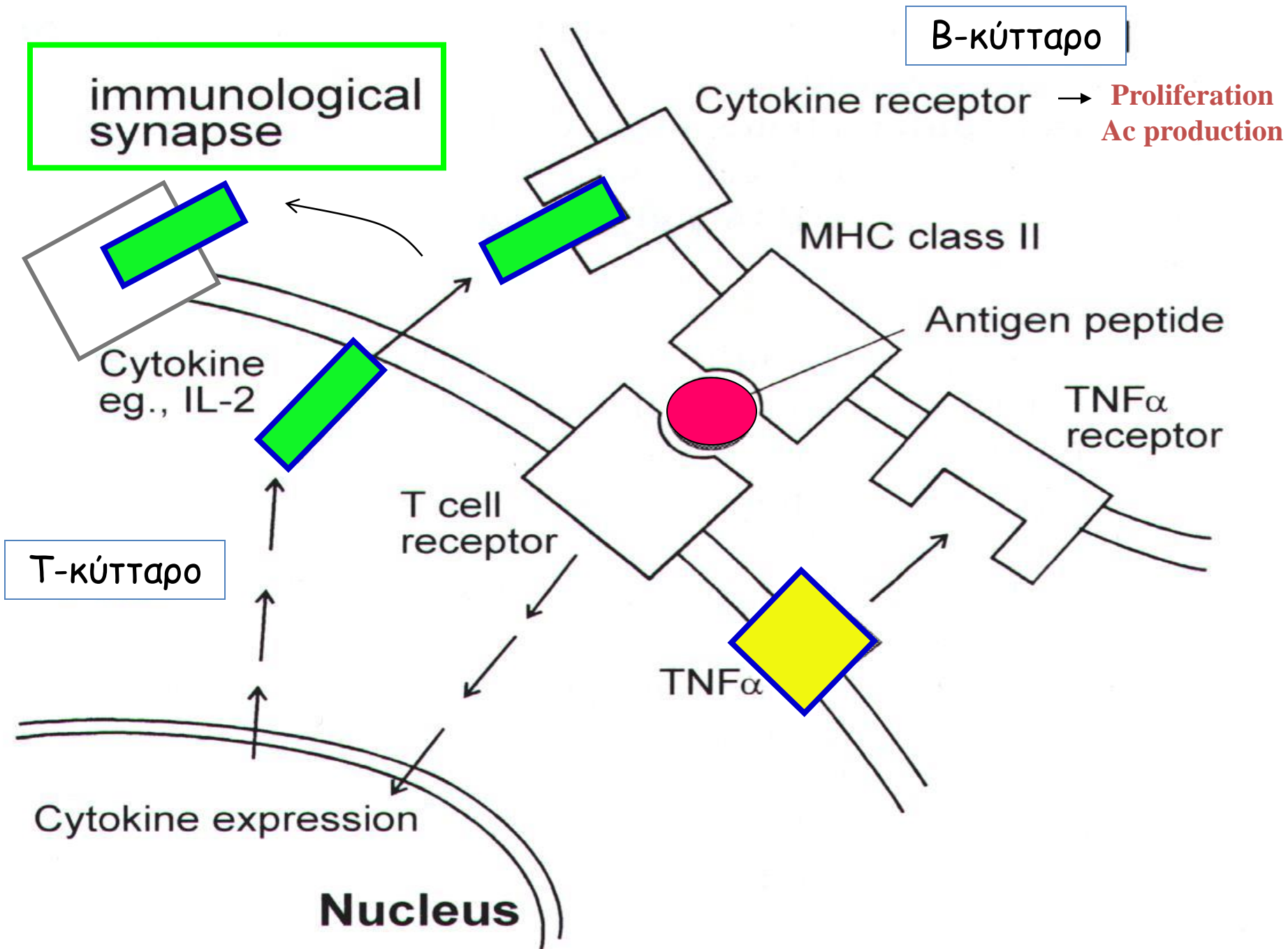


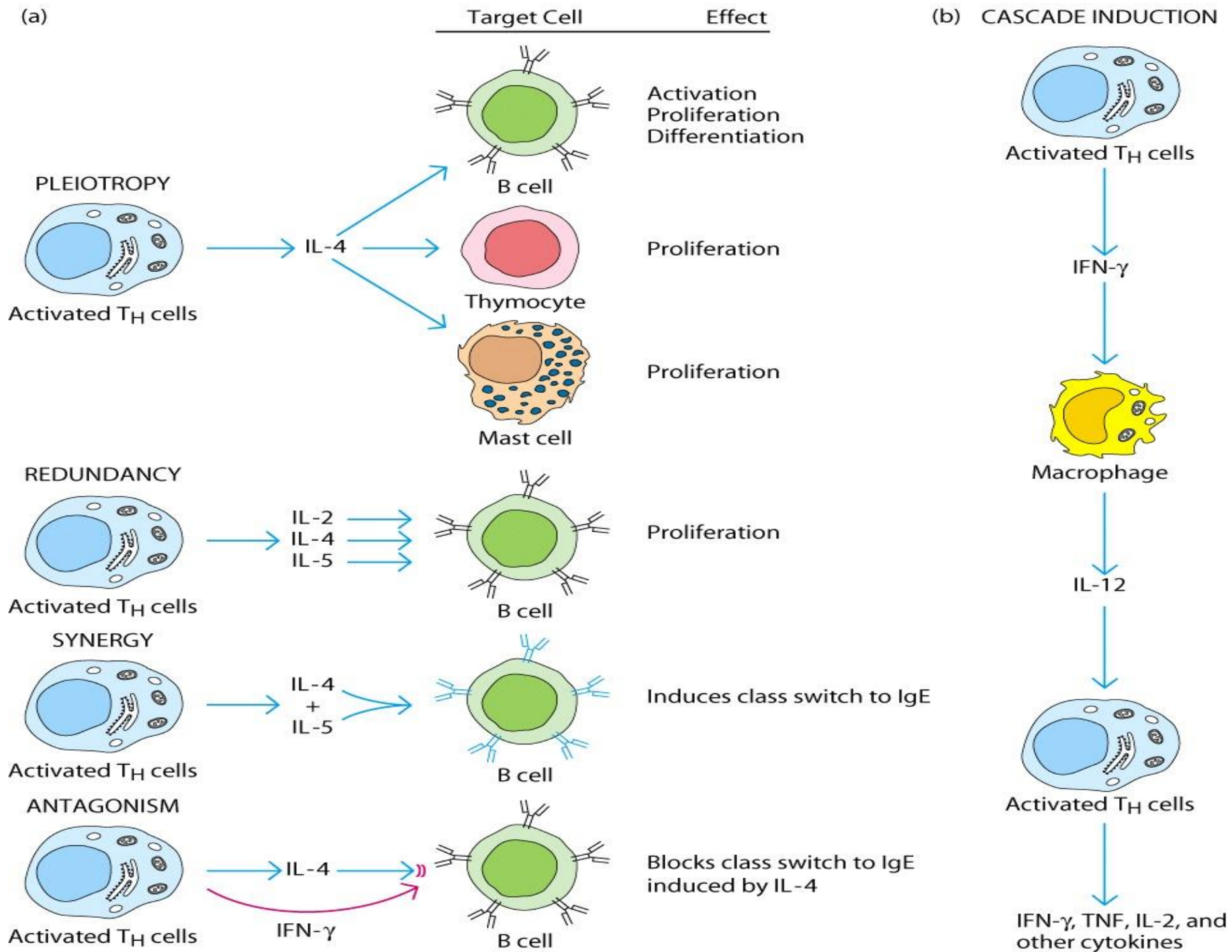
(a) Interleukin 2



**Αυτοκρινής
επικοινωνία**

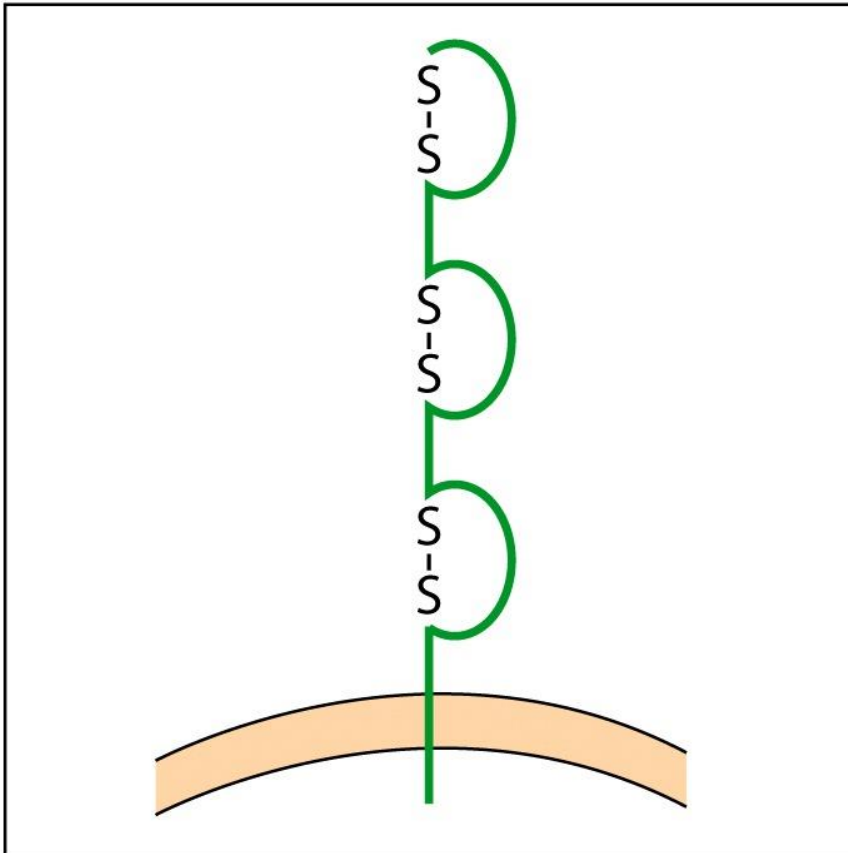






RECEPTOR FAMILY

(a) Immunoglobulin superfamily receptors



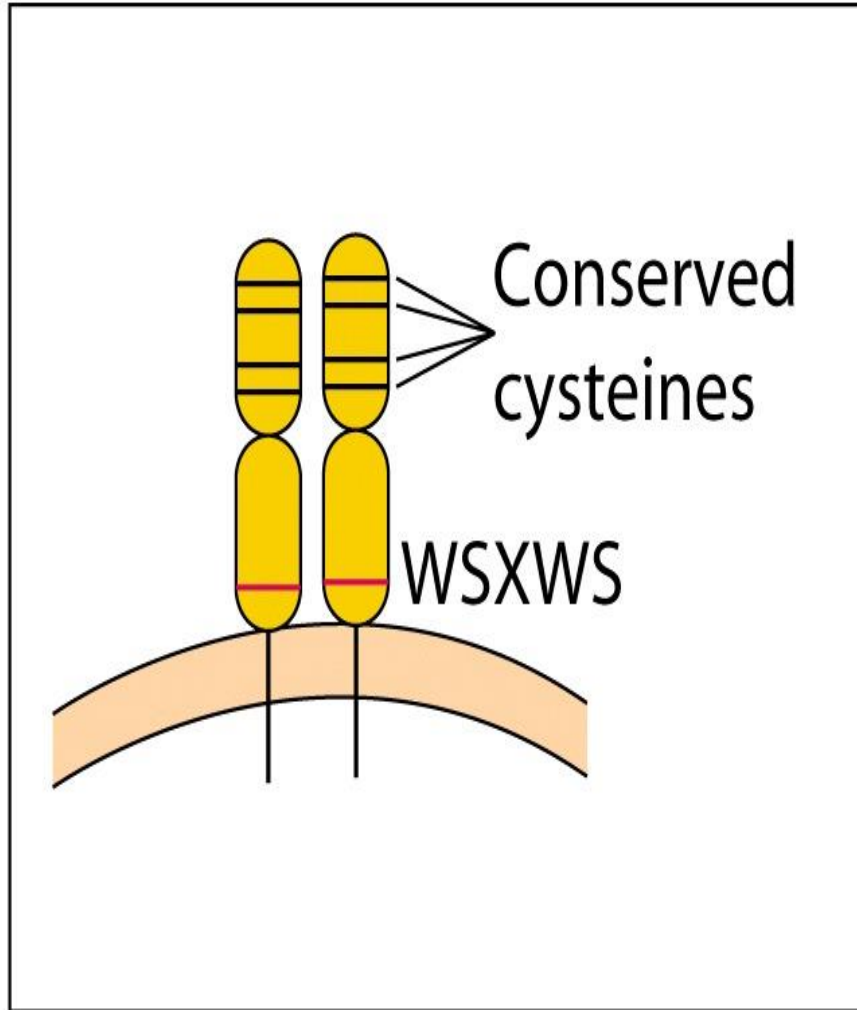
LIGANDS

IL-1

M-CSF

C-Kit

(b) Class I cytokine receptors
(hematopoietin)



LIGANDS

IL-2

IL-13

IL-3

IL-15

IL-4

GM-CSF: granulocyte-macrophage colony stimulating factor

IL-5

GCSF: granulocyte colony stimulating factor

IL-6

LIF: Leukemia inhibitory factor

IL-7

CNTF: ciliary neurotrophic factor

IL-9

OSM: oncostatine

IL-11

Growth hormone

IL-12

Prolactin

(c) Class II cytokine receptors
(interferon)

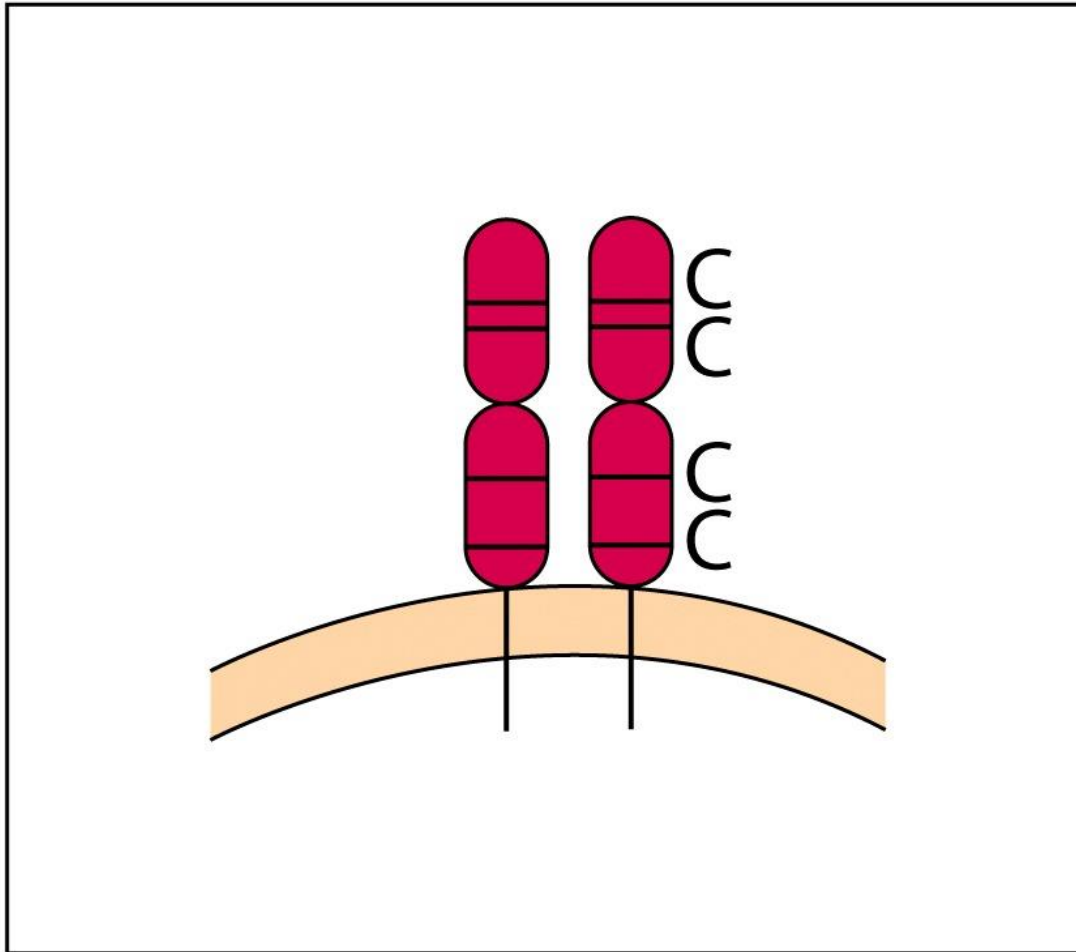
LIGANDS

IFN- α

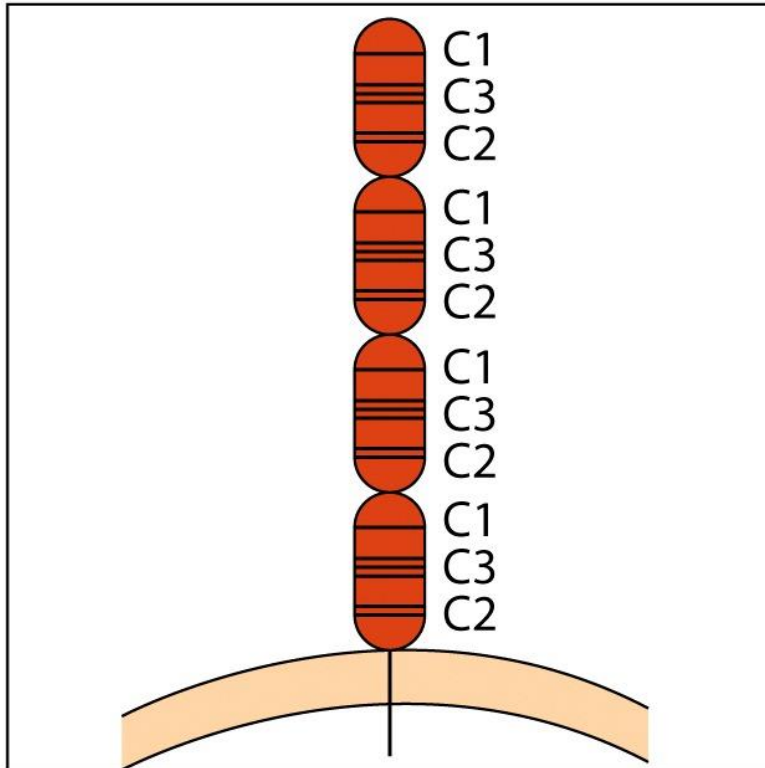
IFN- β

IFN- γ

IL-10



(d) TNF receptors



LIGANDS

TNF- α

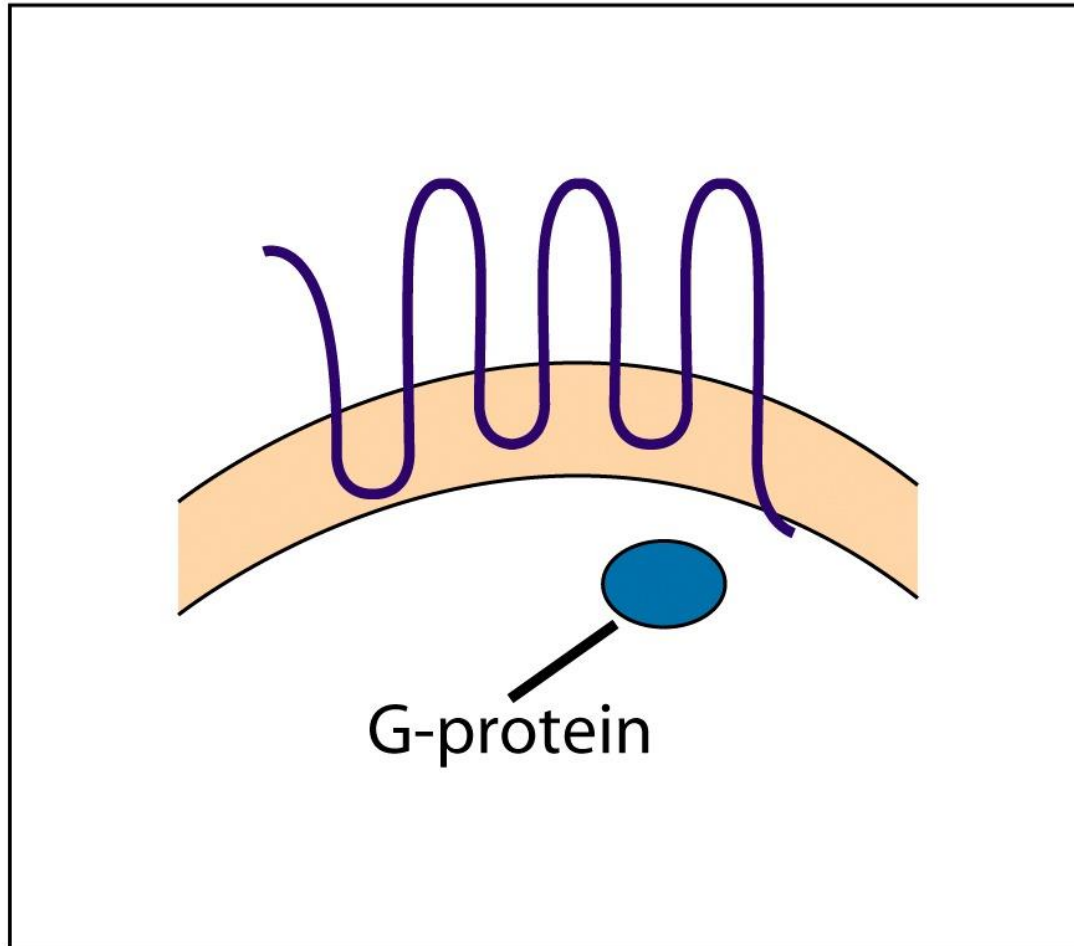
TNF- β

CD40

Nerve growth factor (NGF)

FAS

(e) Chemokine receptors



LIGANDS

IL-8

RANTES

MIP-1

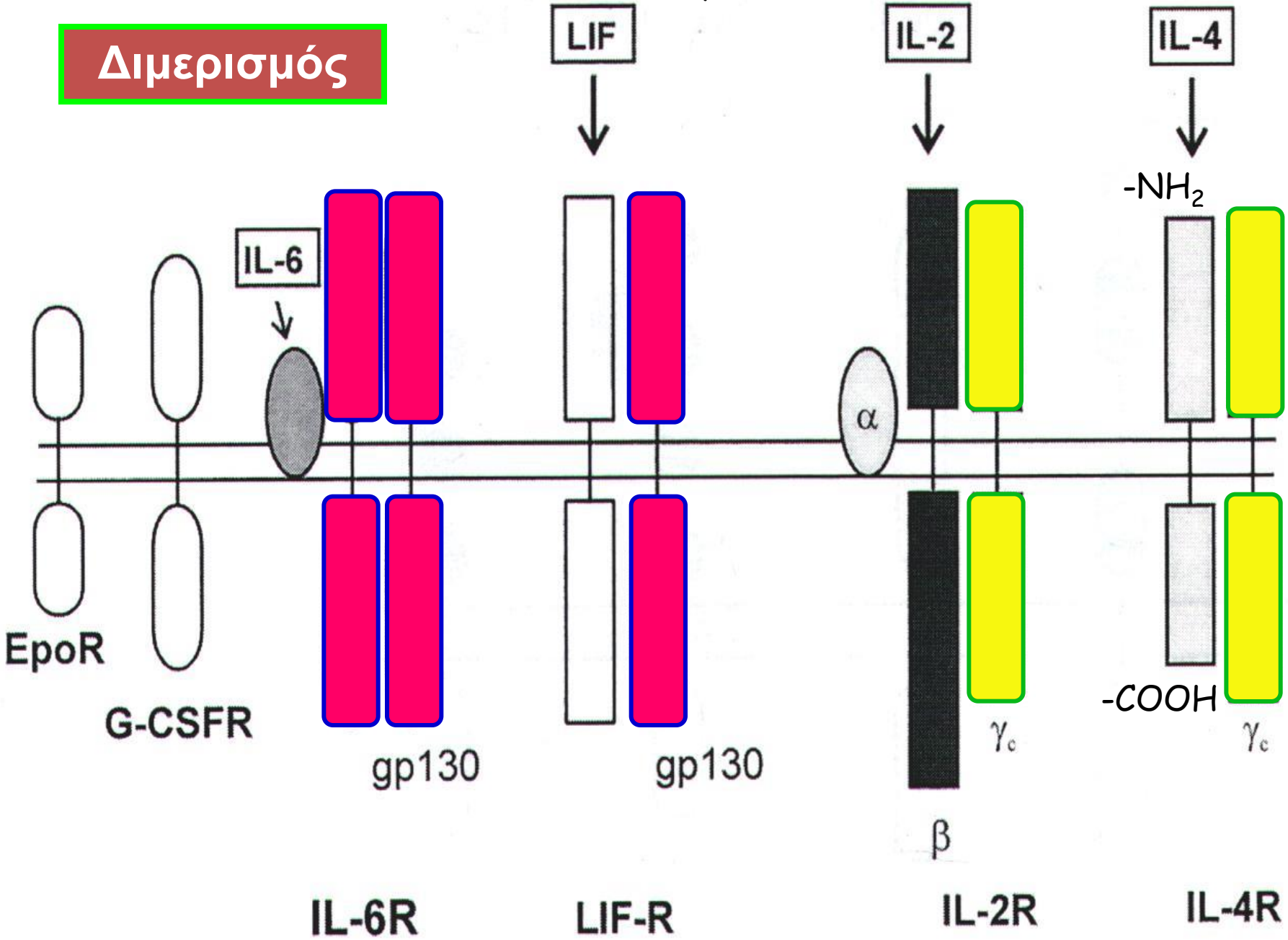
PF4

MCAF

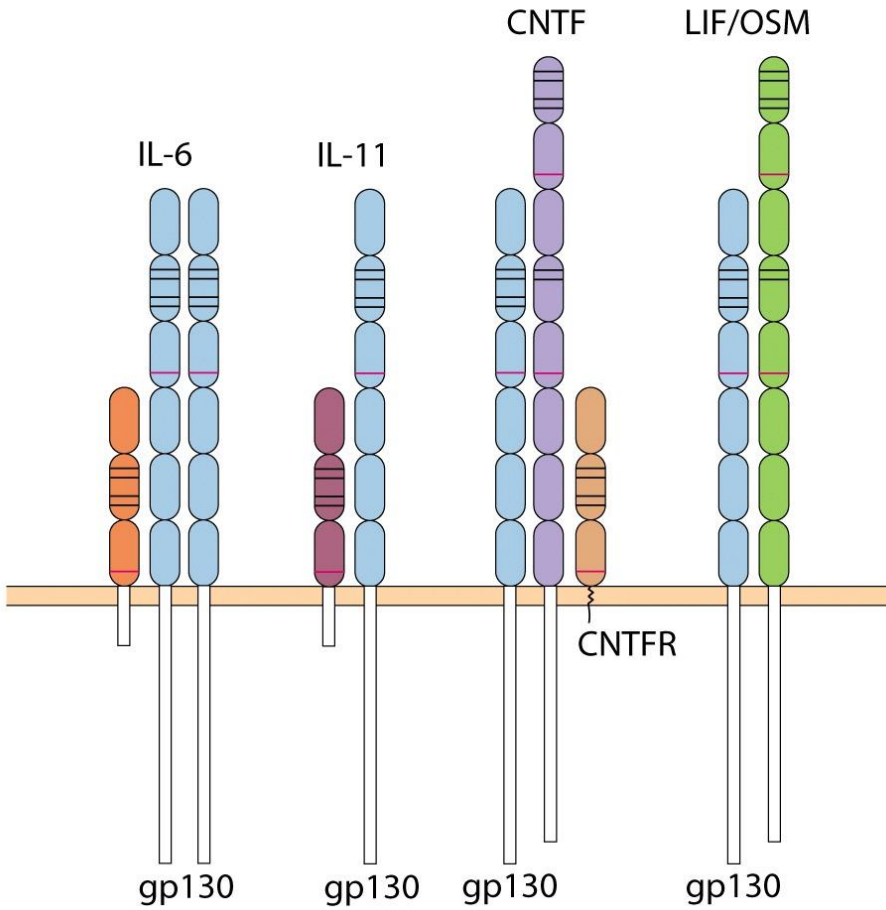
NAP-2

Leukemia inhibitory factor

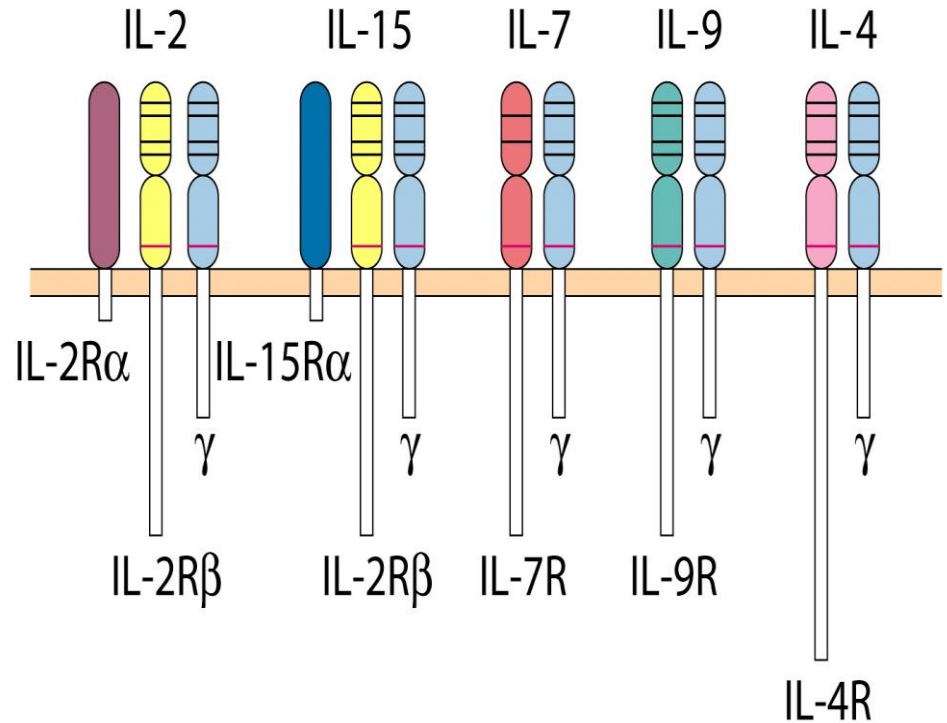
Διμερισμός

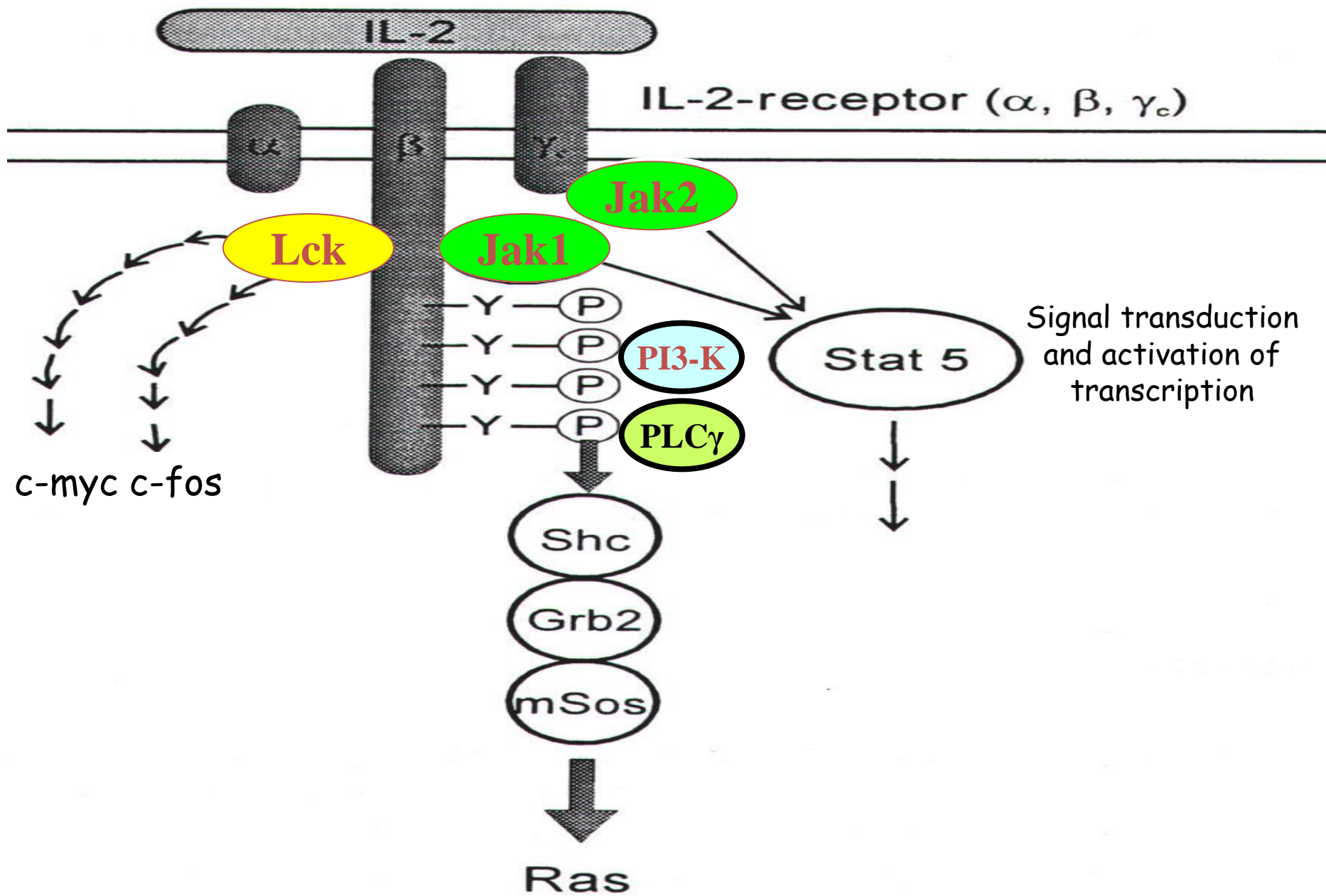


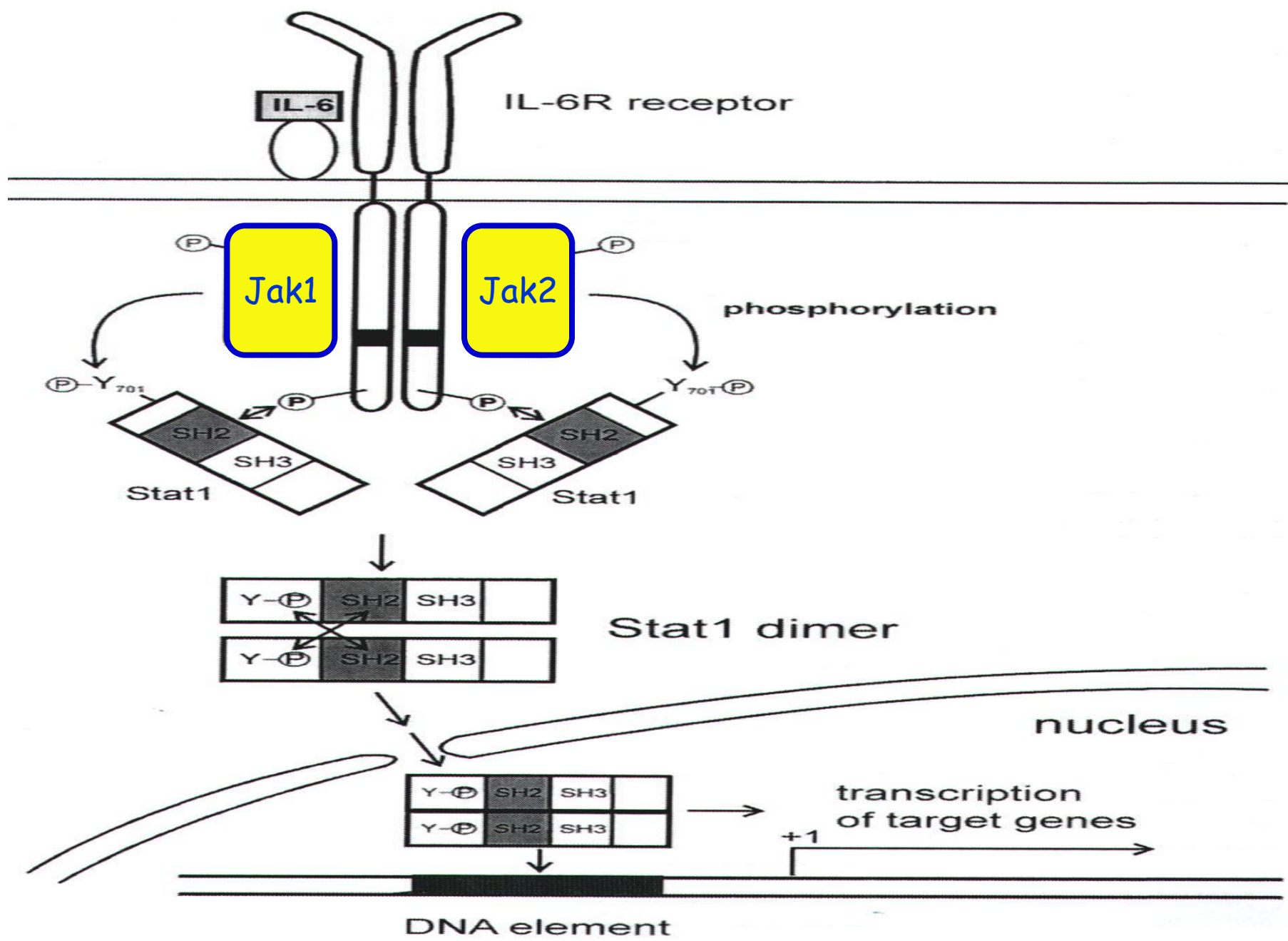
(b) IL-6 Receptor subfamily (common gp130 subunit)

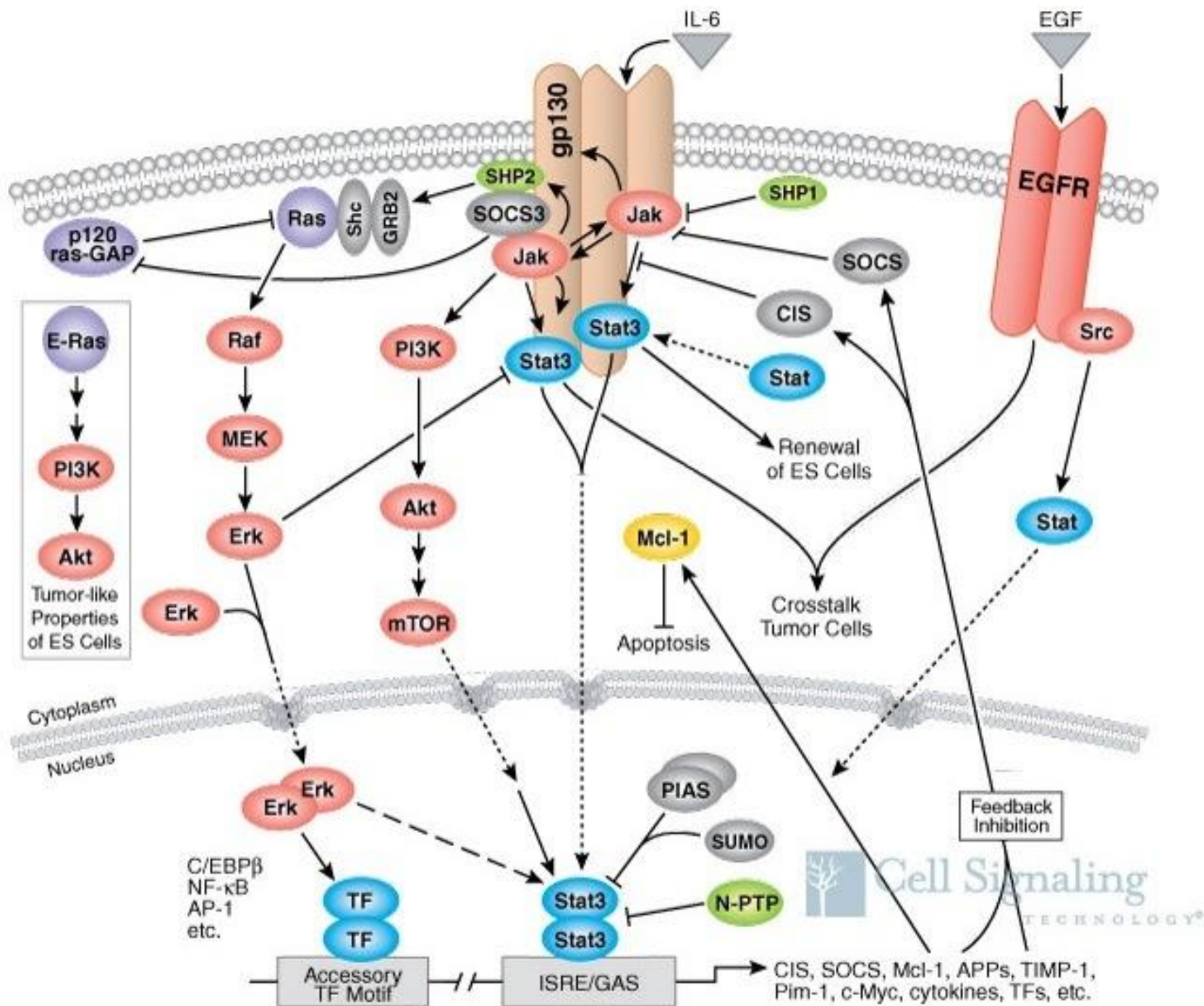


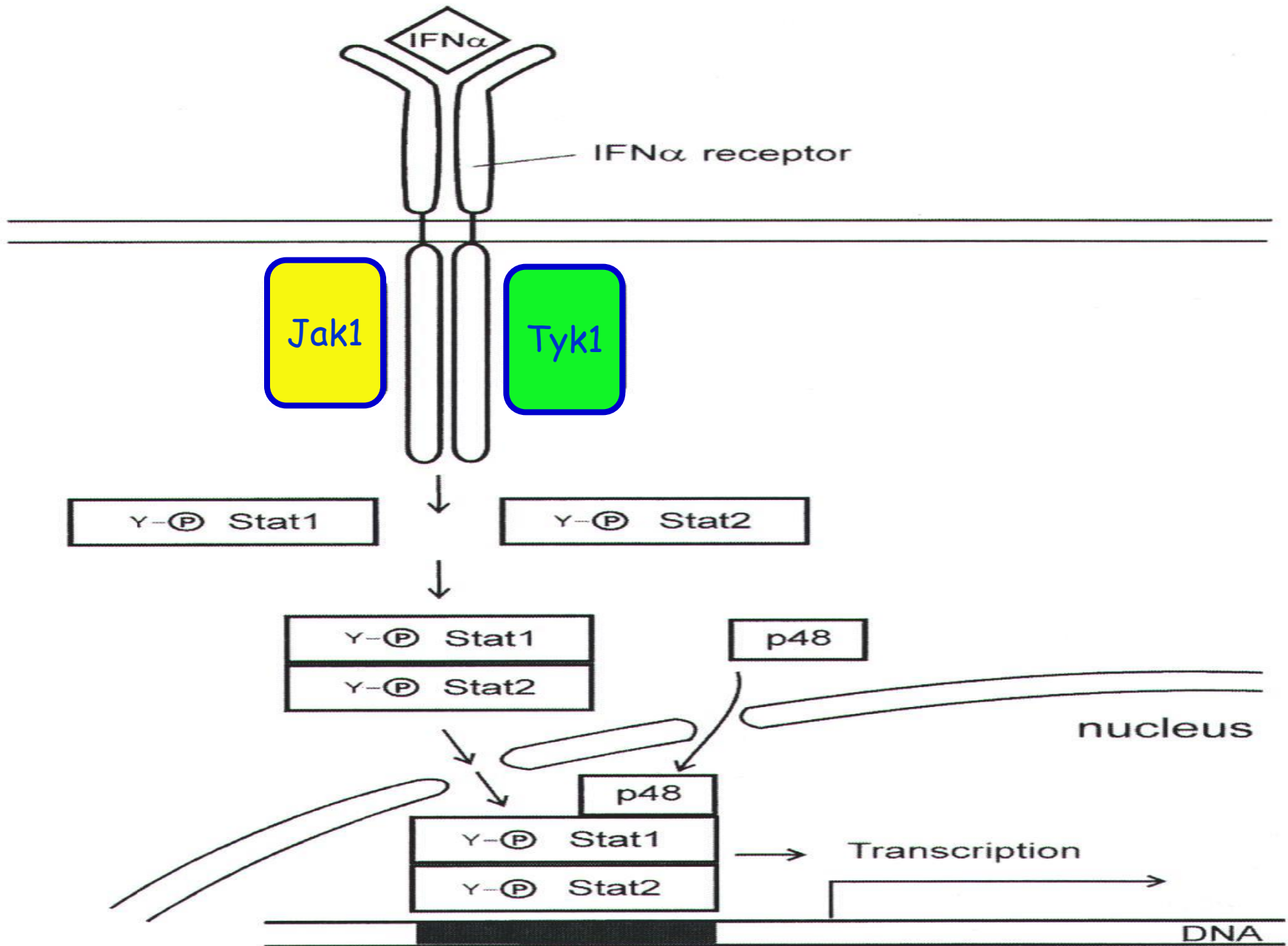
(c) IL-2 receptor subfamily (common γ subunit)



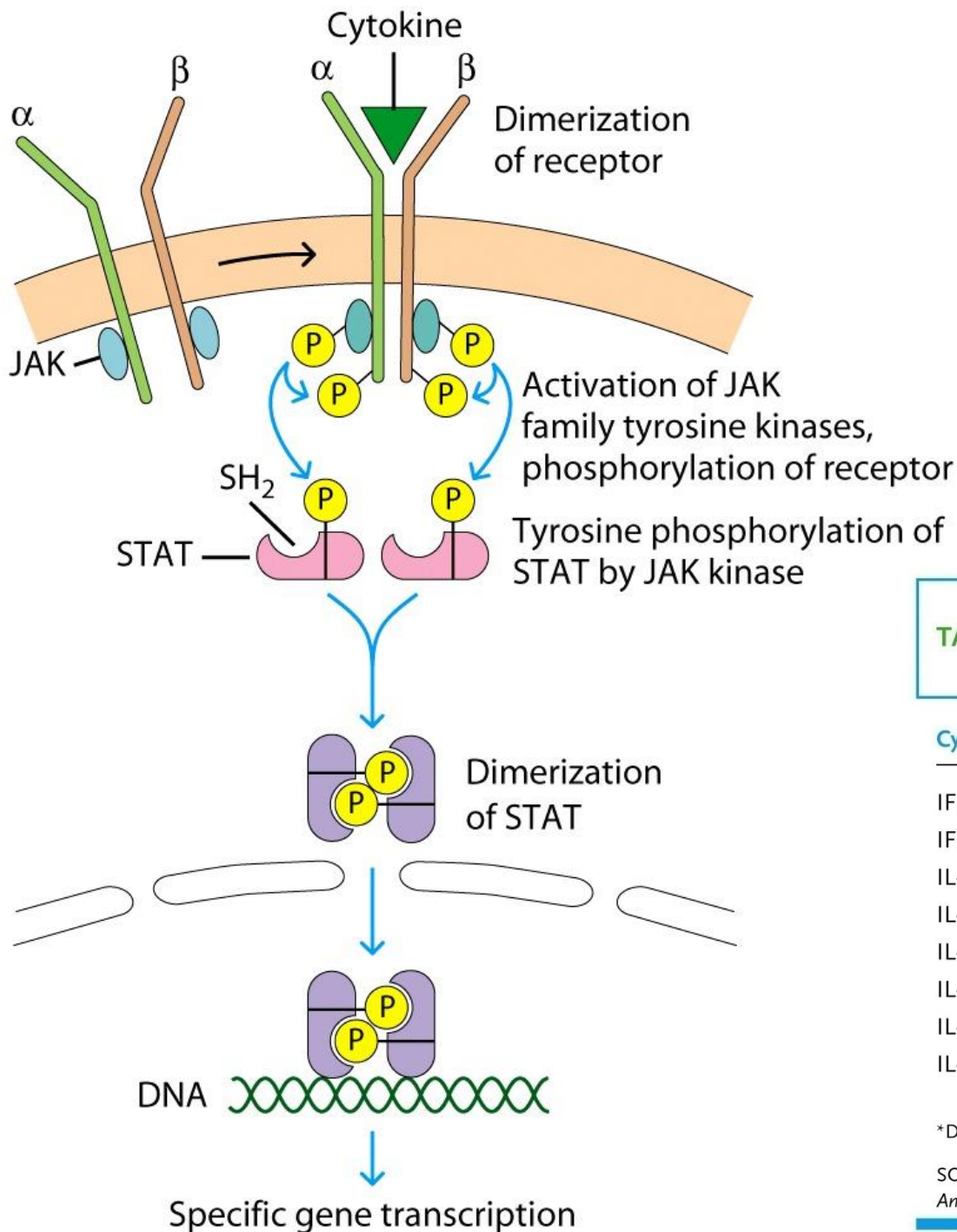








ISRE: Interferon Stimulated Response Element



Κάθε υποδοχέας είναι υπεύθυνος για διαφορετική JAK-STAT αλληλεπίδραση. Κάθε STAT ομο- ή ετεροδιμερές συνδέεται σε διαφορετικούς προαγωγείς γονιδίων. Κάθε κυτταρικός τύπος επιτρέπει την επαγωγή συγκεκριμένων γονιδίων.

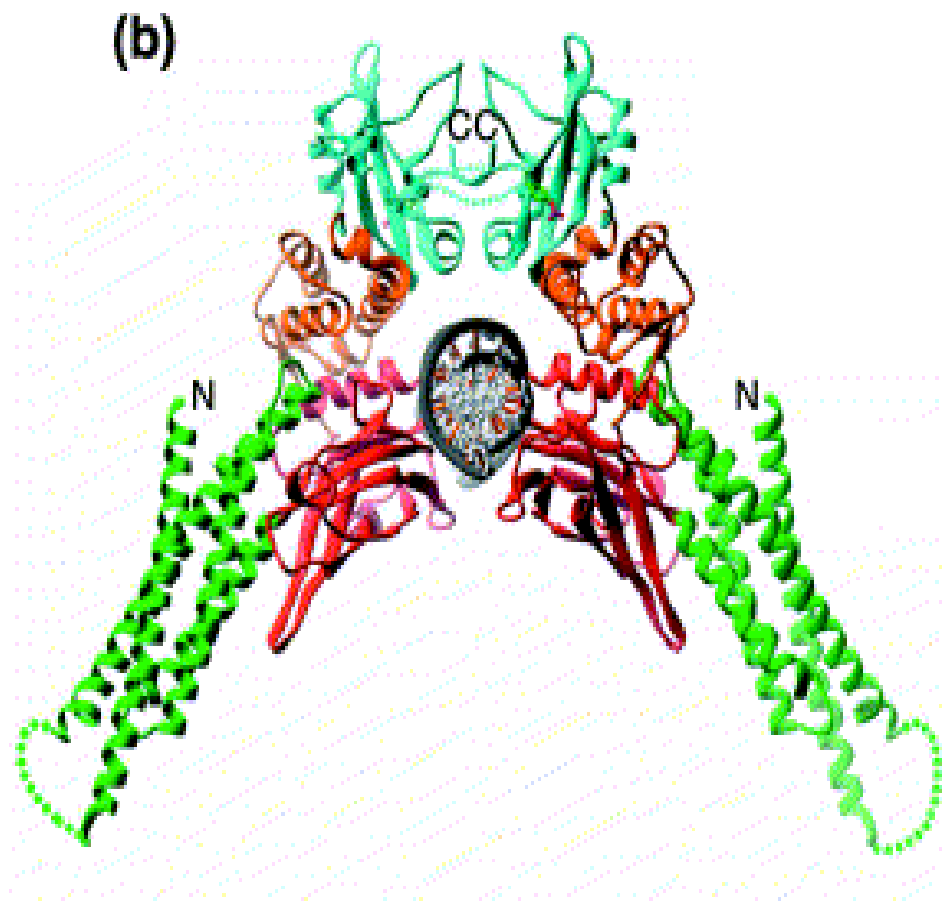
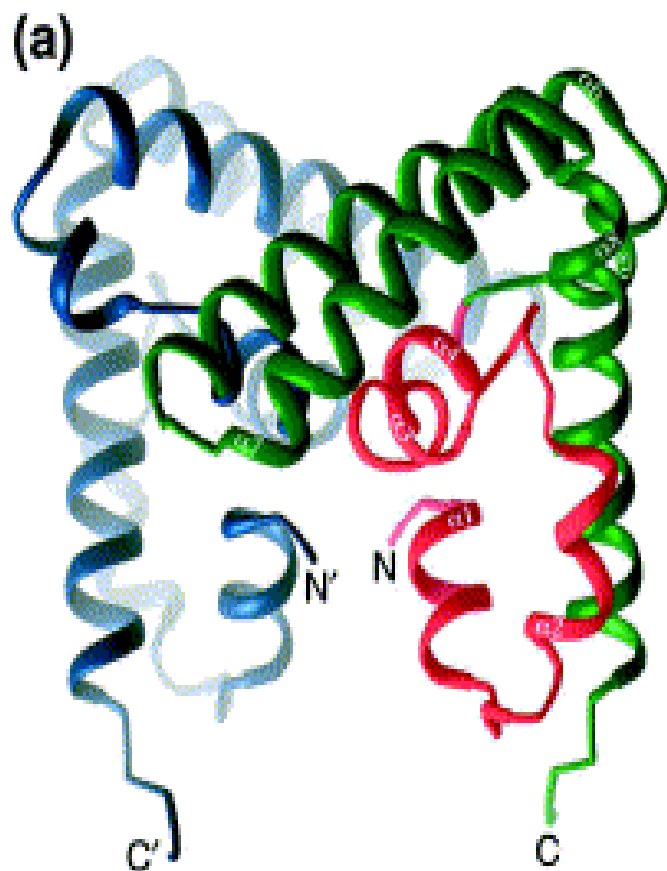
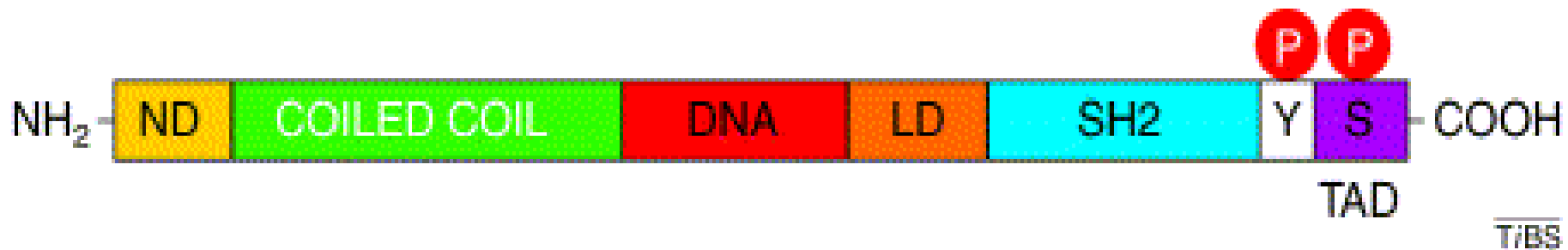
TABLE 12-2

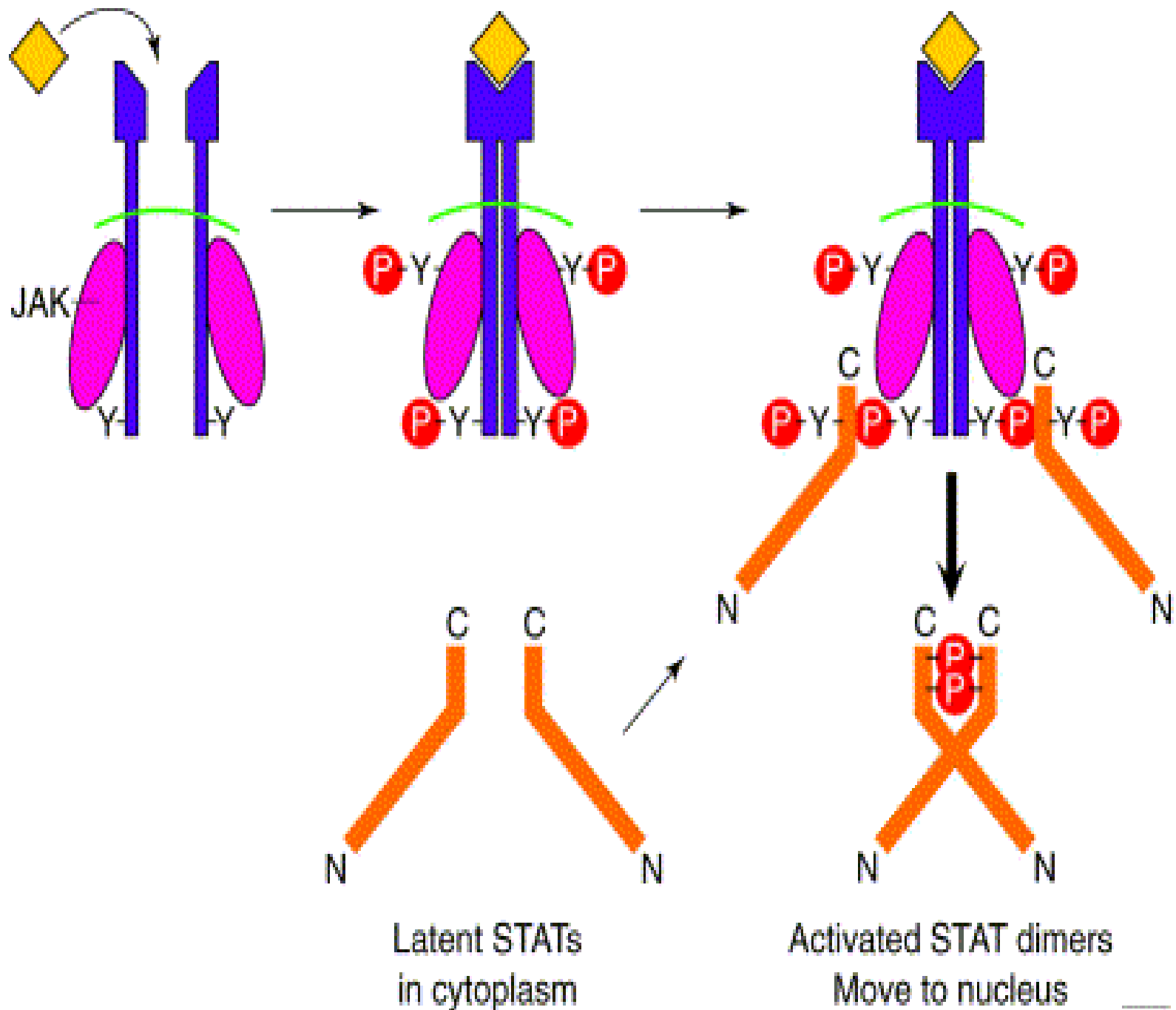
STAT and JAK interaction with selected cytokine receptors during signal transduction

Cytokine receptor	JAK	STAT
IFN- γ	JAK1 and JAK2	Stat1
IFN- α/β	JAK1 and Tyk-2	Stat2
IL-2	JAK1 and JAK3	Stat5
IL-3	JAK2	Stat5
IL-4	JAK1 and JAK3	Stat6
IL-6	JAK1 (and sometimes others)	Stat3
IL-10	JAK1 and Tyk-2*	Stat3
IL-12	JAK2 and Tyk-2*	Stat4

*Despite its name, Tyk-2 is also a Janus kinase.

SOURCE: Adapted from E. A. Bach, M. Aguet, and R. D. Schreiber, 1997, *Annu. Rev. Immun.* 15:563.





Latent STATs
in cytoplasm

Activated STAT dimers
Move to nucleus



Figure 1

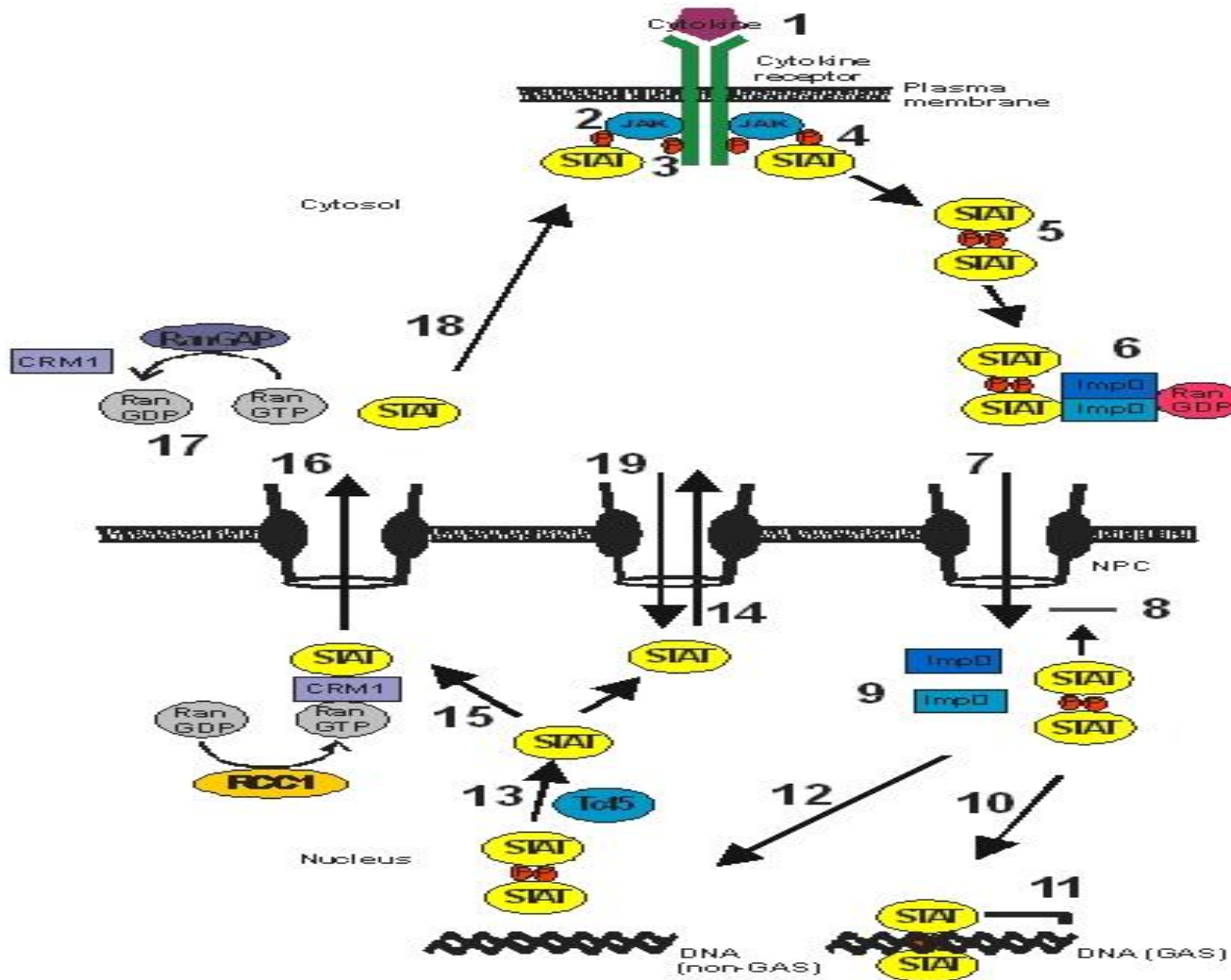
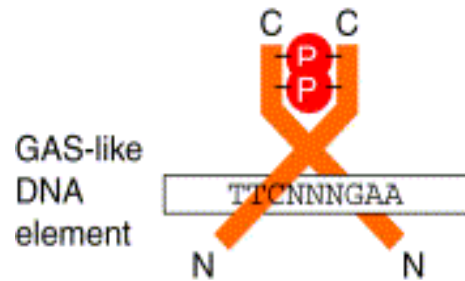


Figure 2

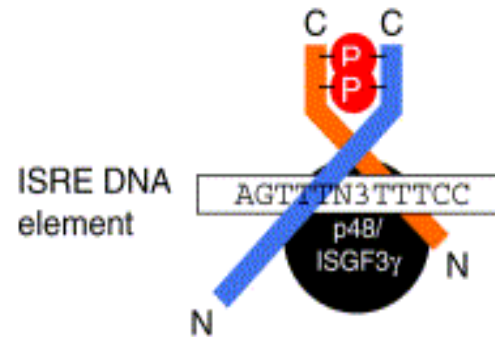
(a) GAS element preferences



STAT1-1, 1-3, 3-3, 4-4, 5-5, 6-6

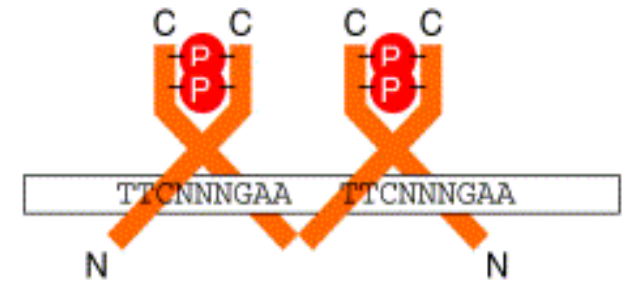
e.g. c-fos SIE
FcγR GRR
β-Cas PIE
IRF1 GAS

(b) Unique DNA recognition via protein interaction



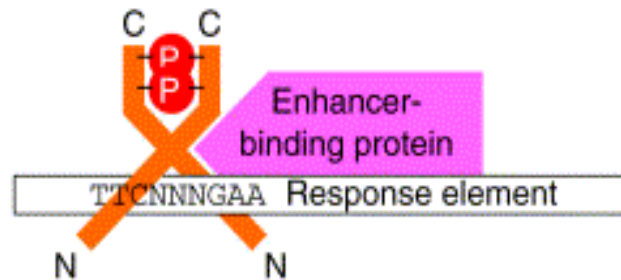
STAT1-2 + p48/ISGF3γ
ISGF3 heterotrimer

(c) Tetramer binding to tandem elements



STAT1-1/1-1, 4-4/4-4, 5-5/5-5, 1-2/1-2
Dimer/dimer interaction increases affinity

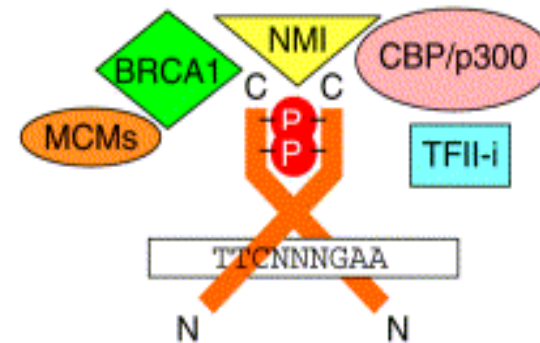
(d) Cooperative transcription regulation



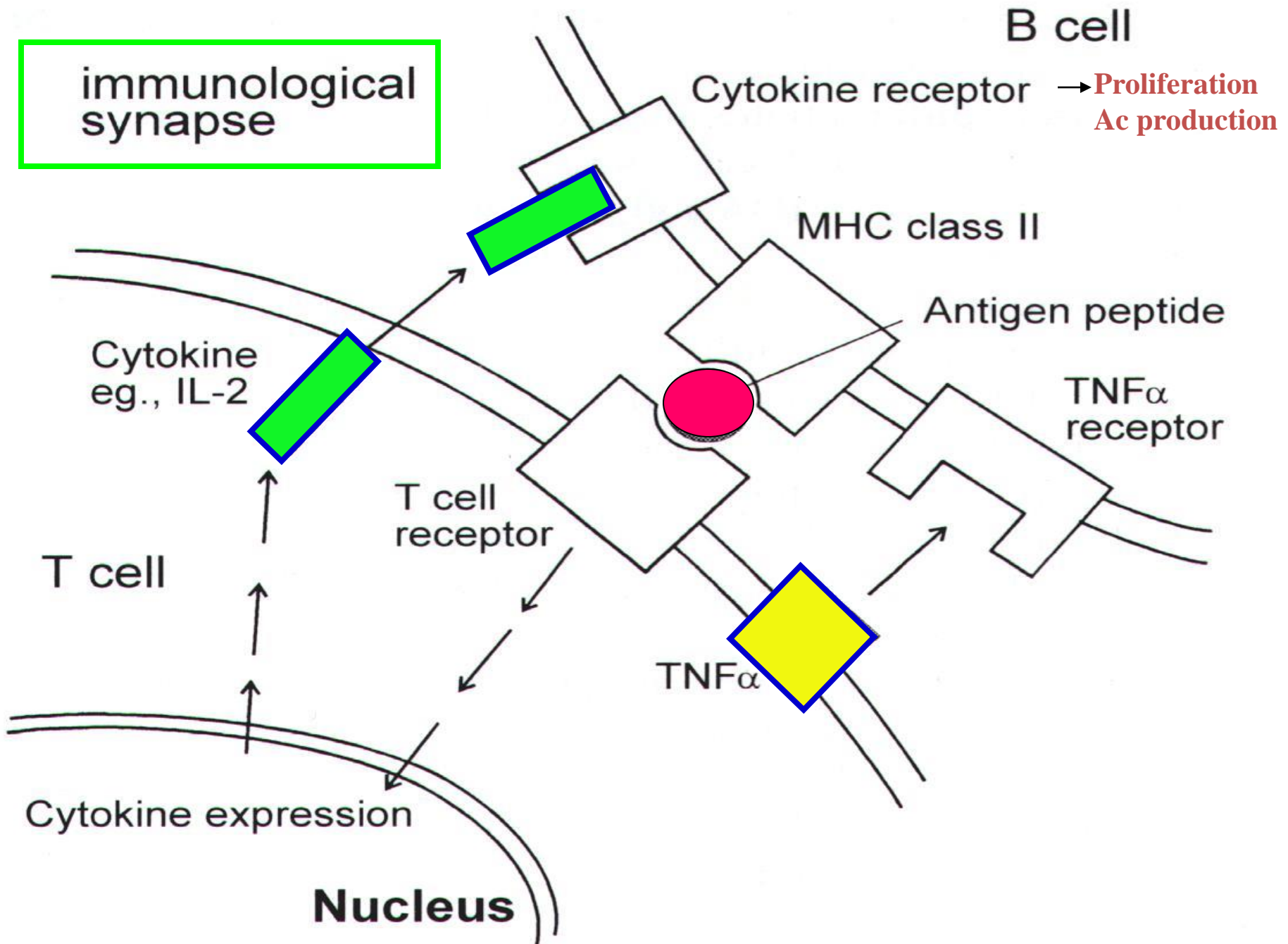
Adjacent or composite DNA elements

e.g. STAT1-SP1
STAT5-GR
STAT3-c-jun

(e) Co-activator recruitment

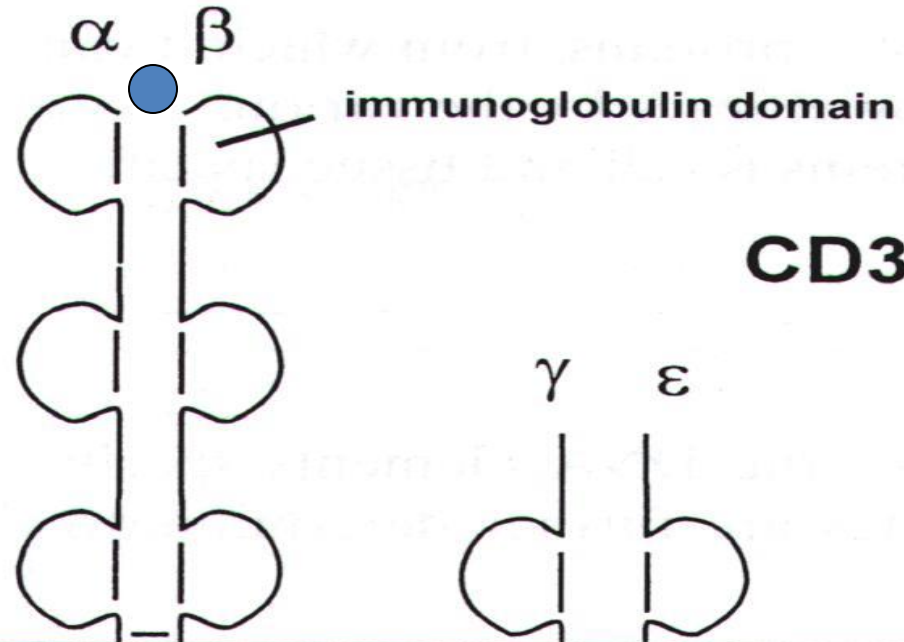


Recruit/stabilize RNA pol II complexes
Destabilize chromatin

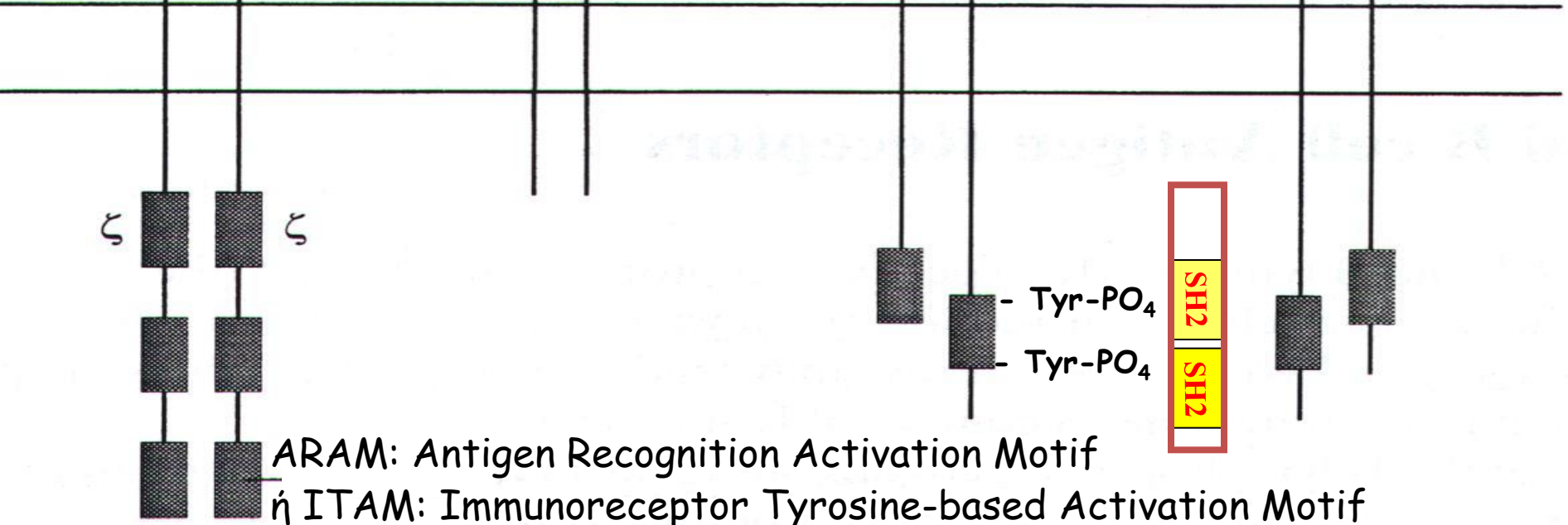
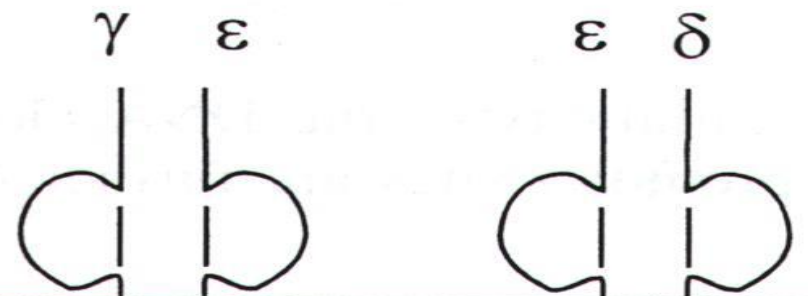


Tiα

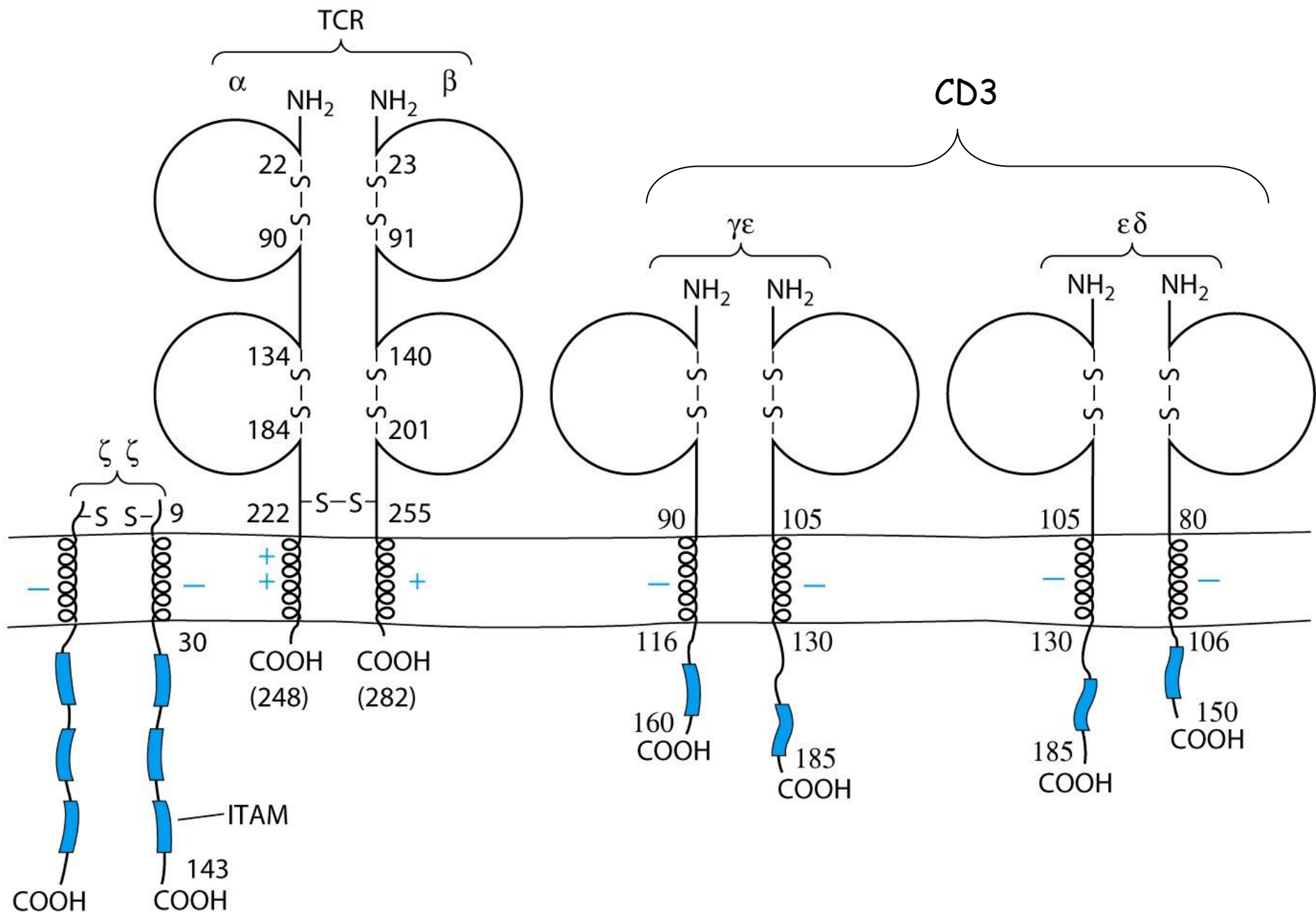
Δομή των υποδοχέων των T κυττάρων



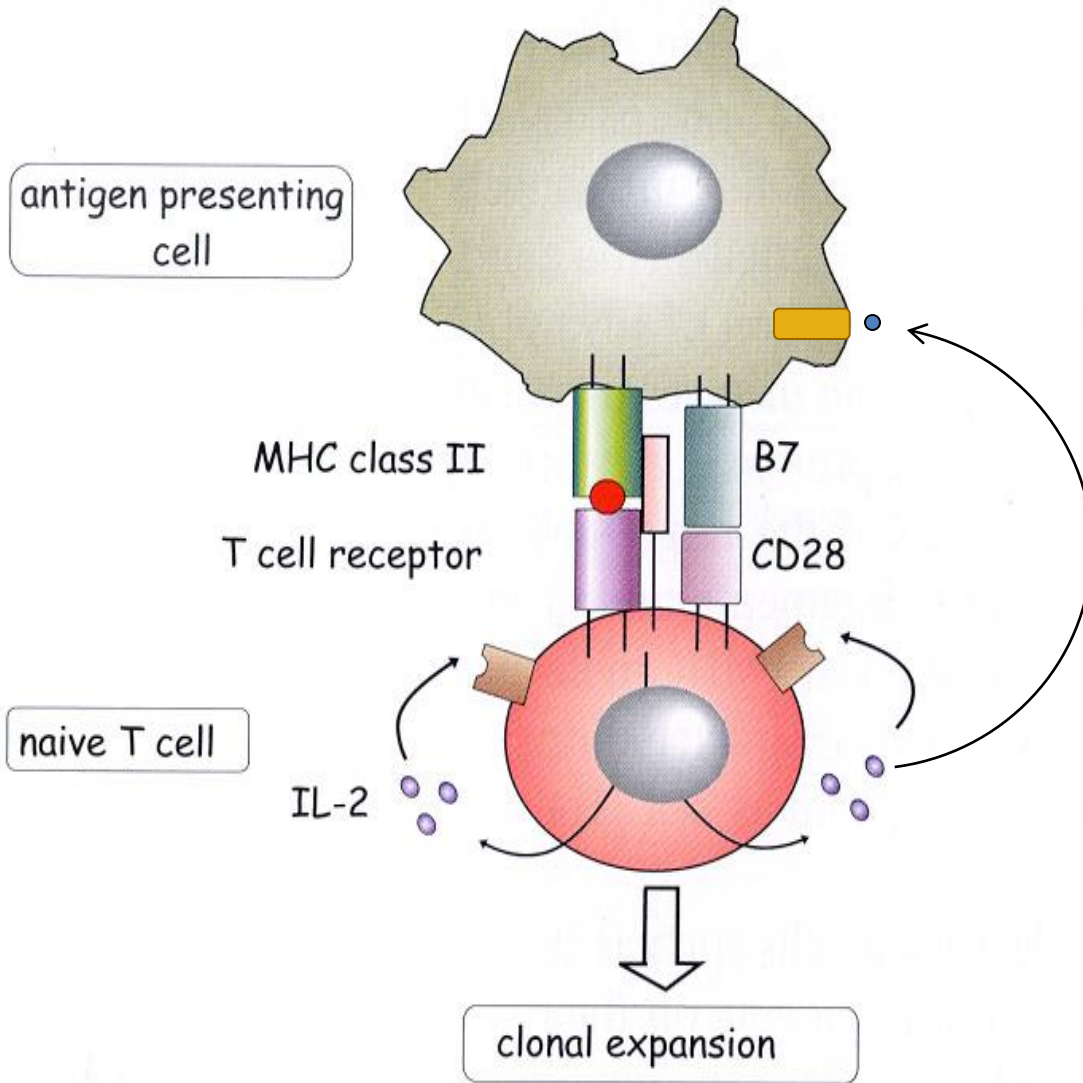
CD3



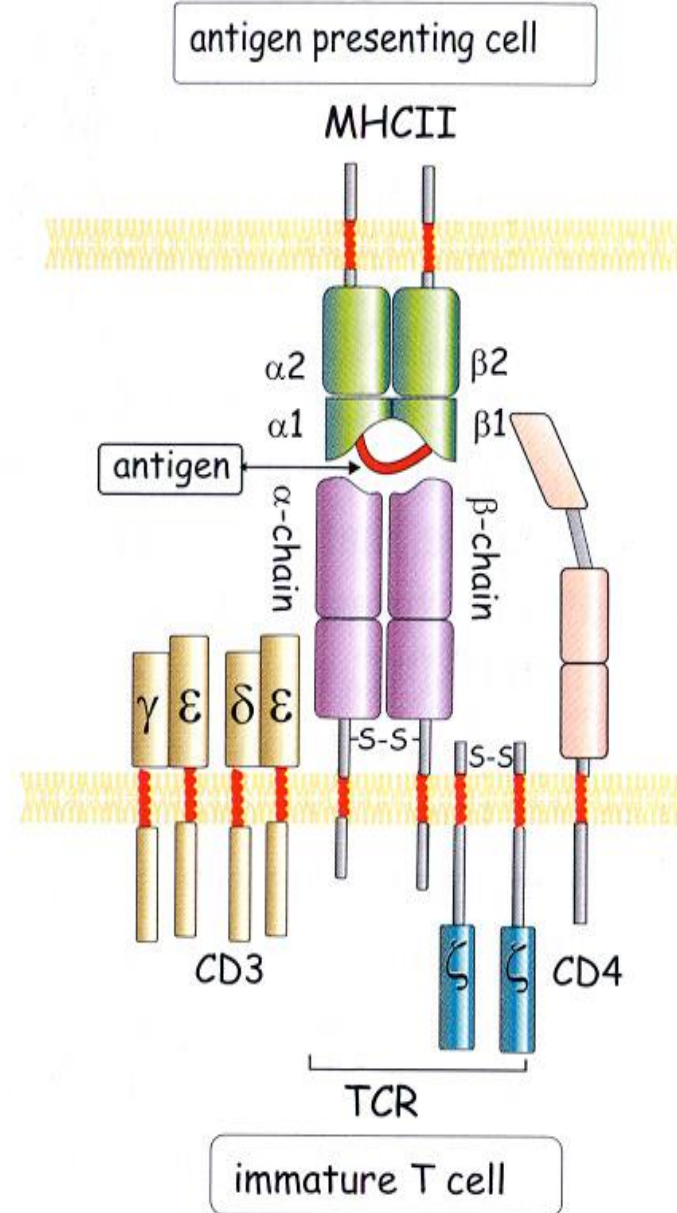
ARAM: Antigen Recognition Activation Motif
ή ITAM: Immunoreceptor Tyrosine-based Activation Motif

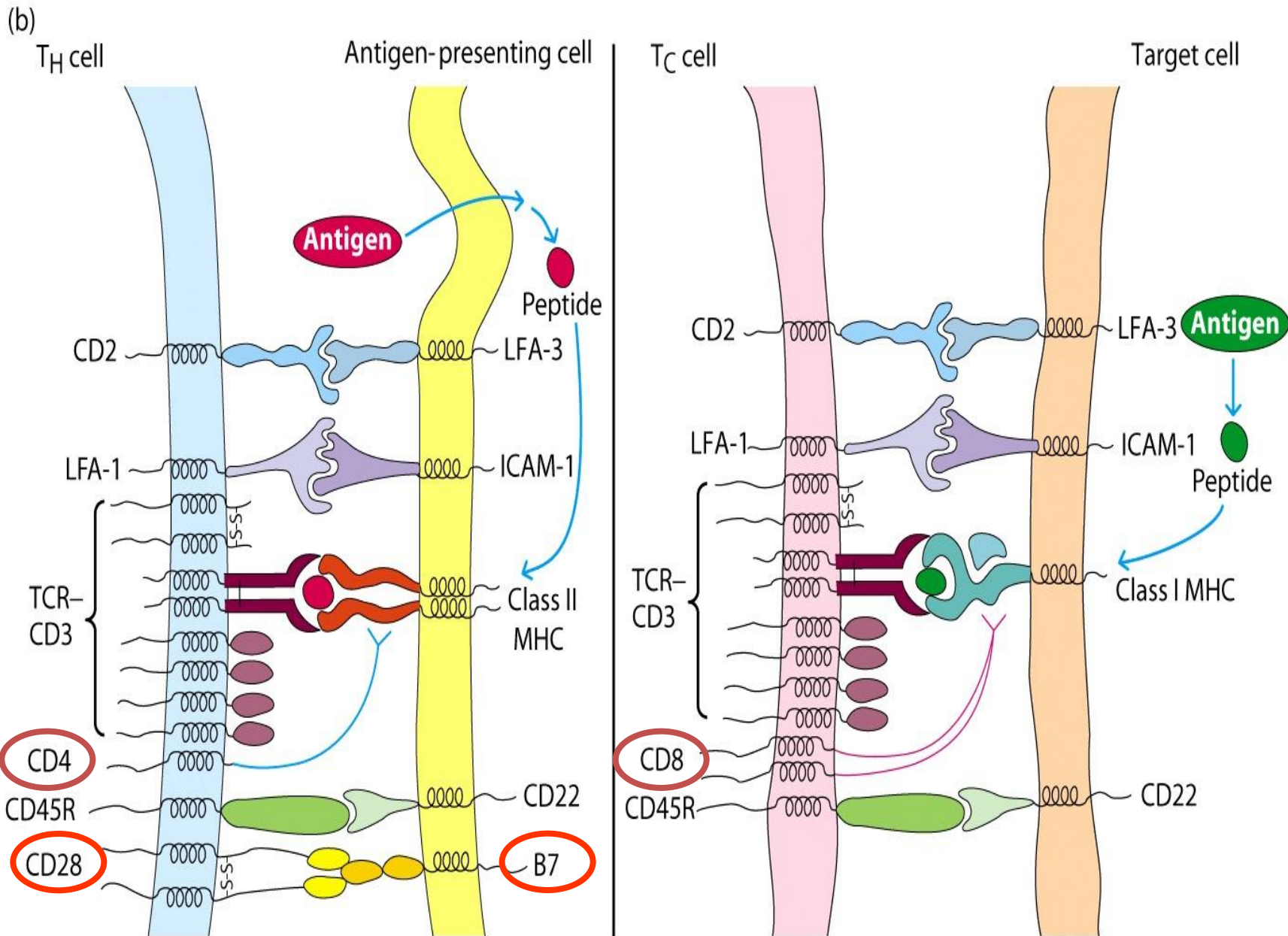


(a)



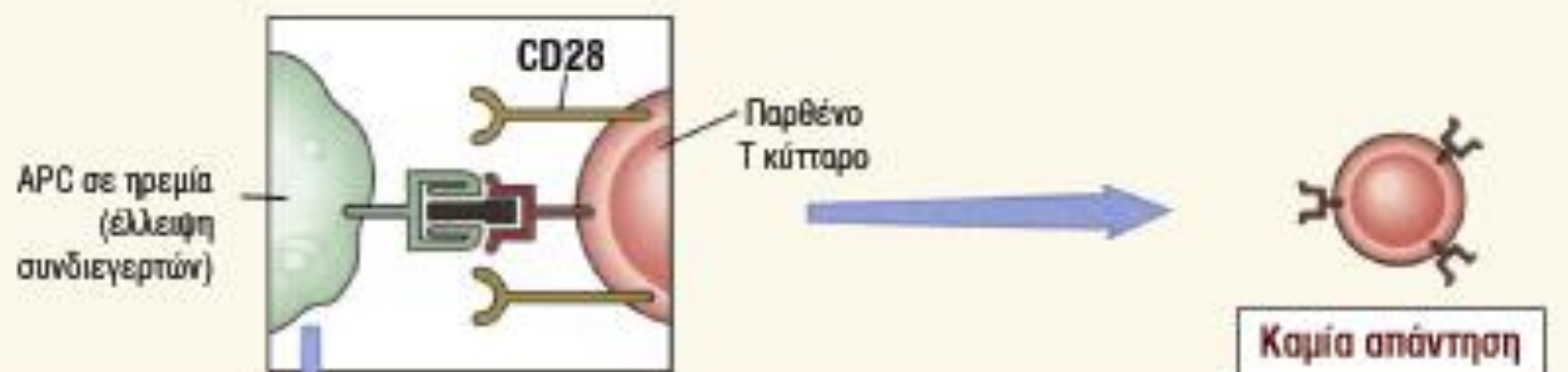
(b)



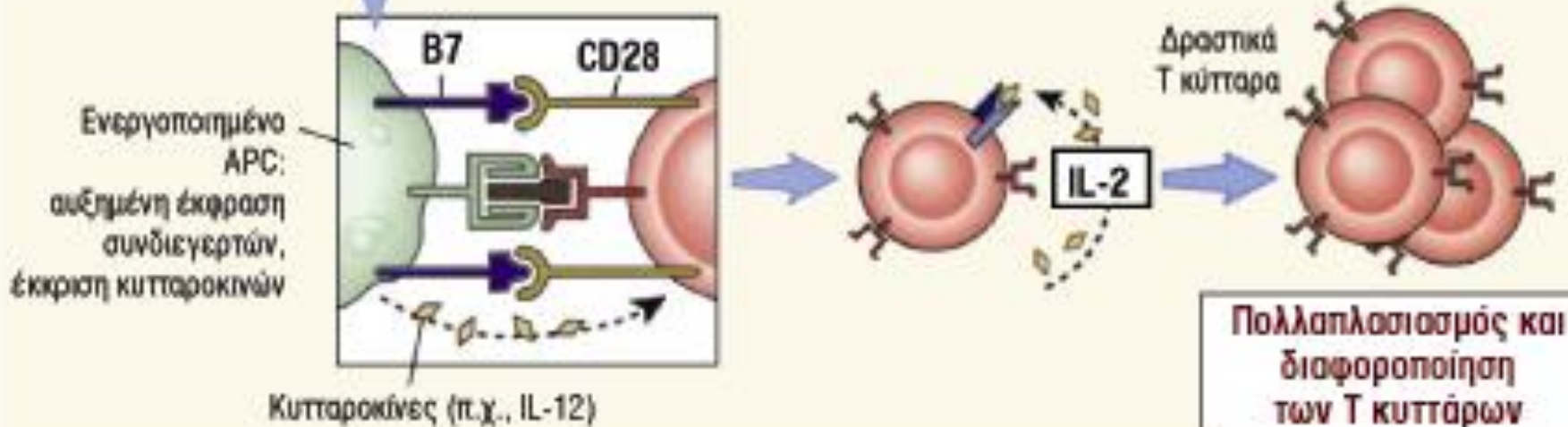


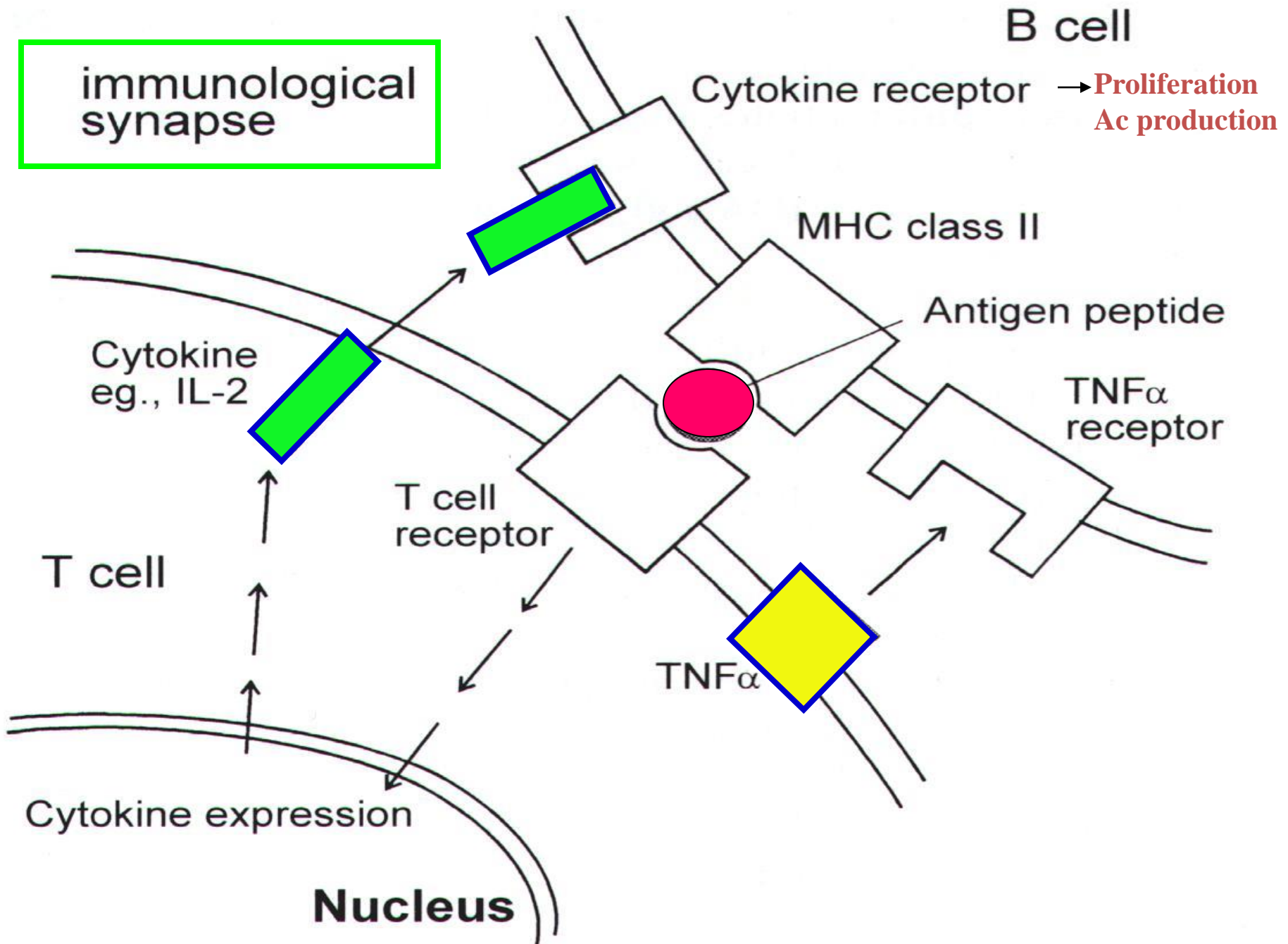
Αναγνώριση αντιγόνου

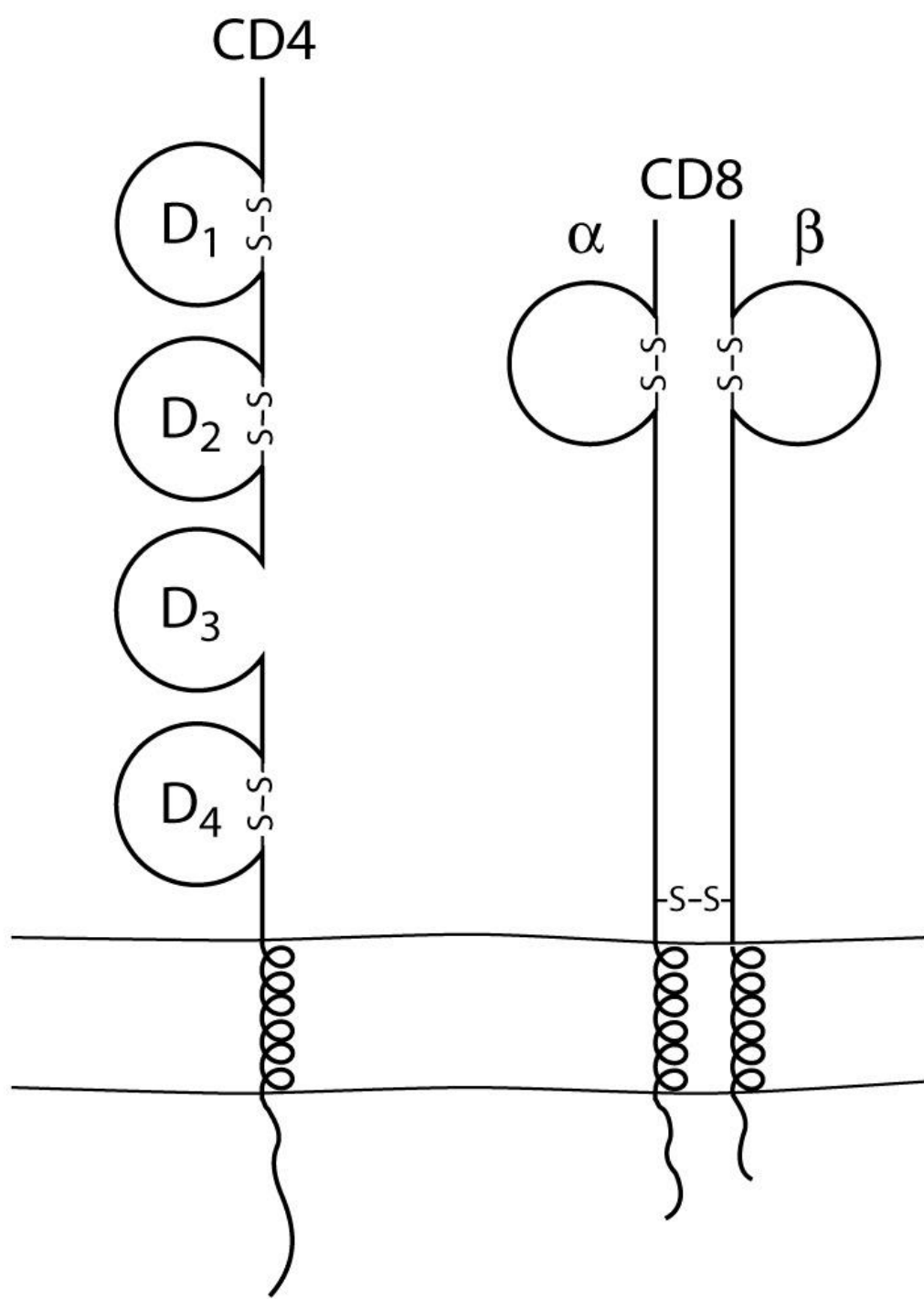
T κυτταρική απάντηση



Ενεργοποίηση των APCs από μικρόβια, απάντηση της φυσικής ανοσίας

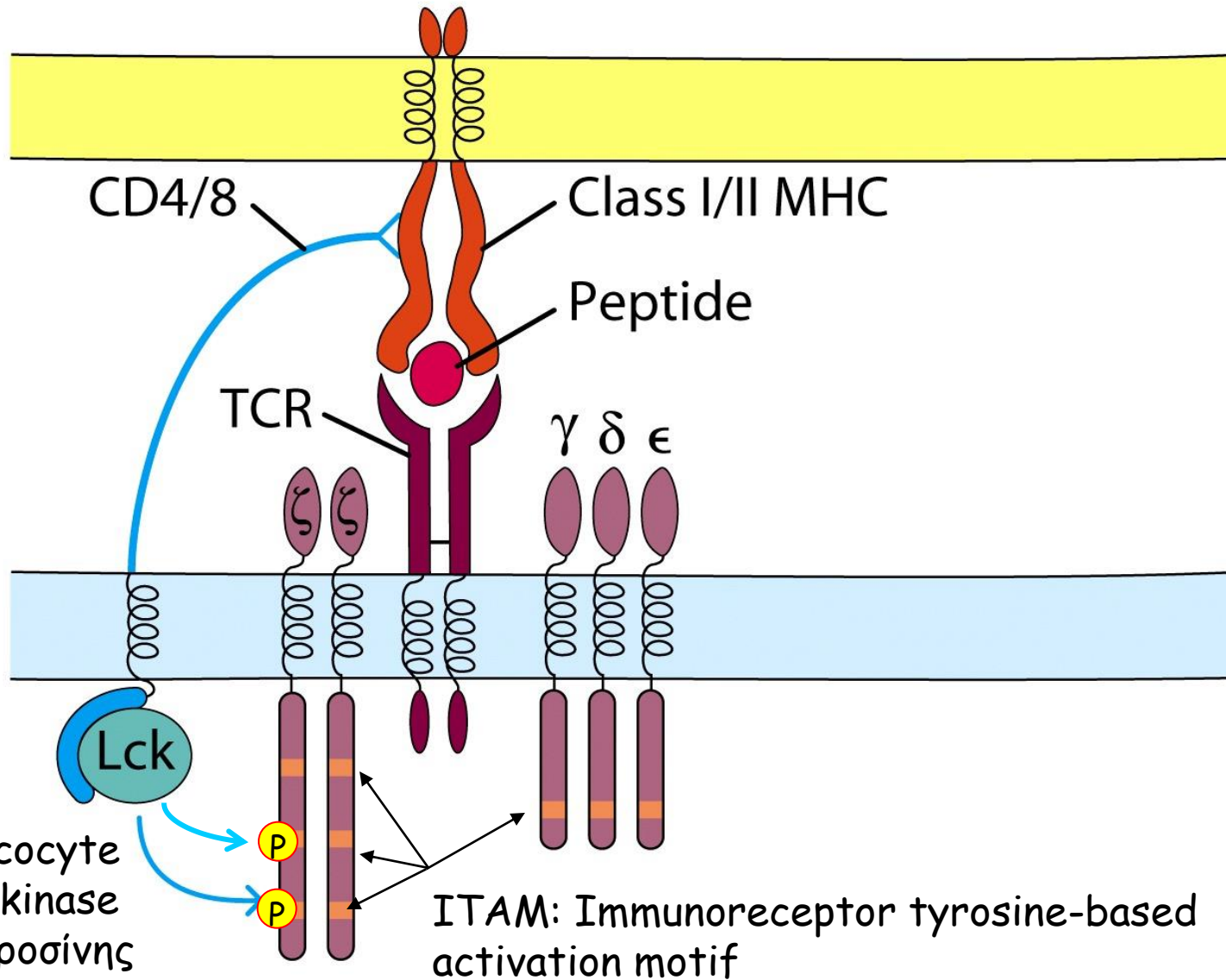






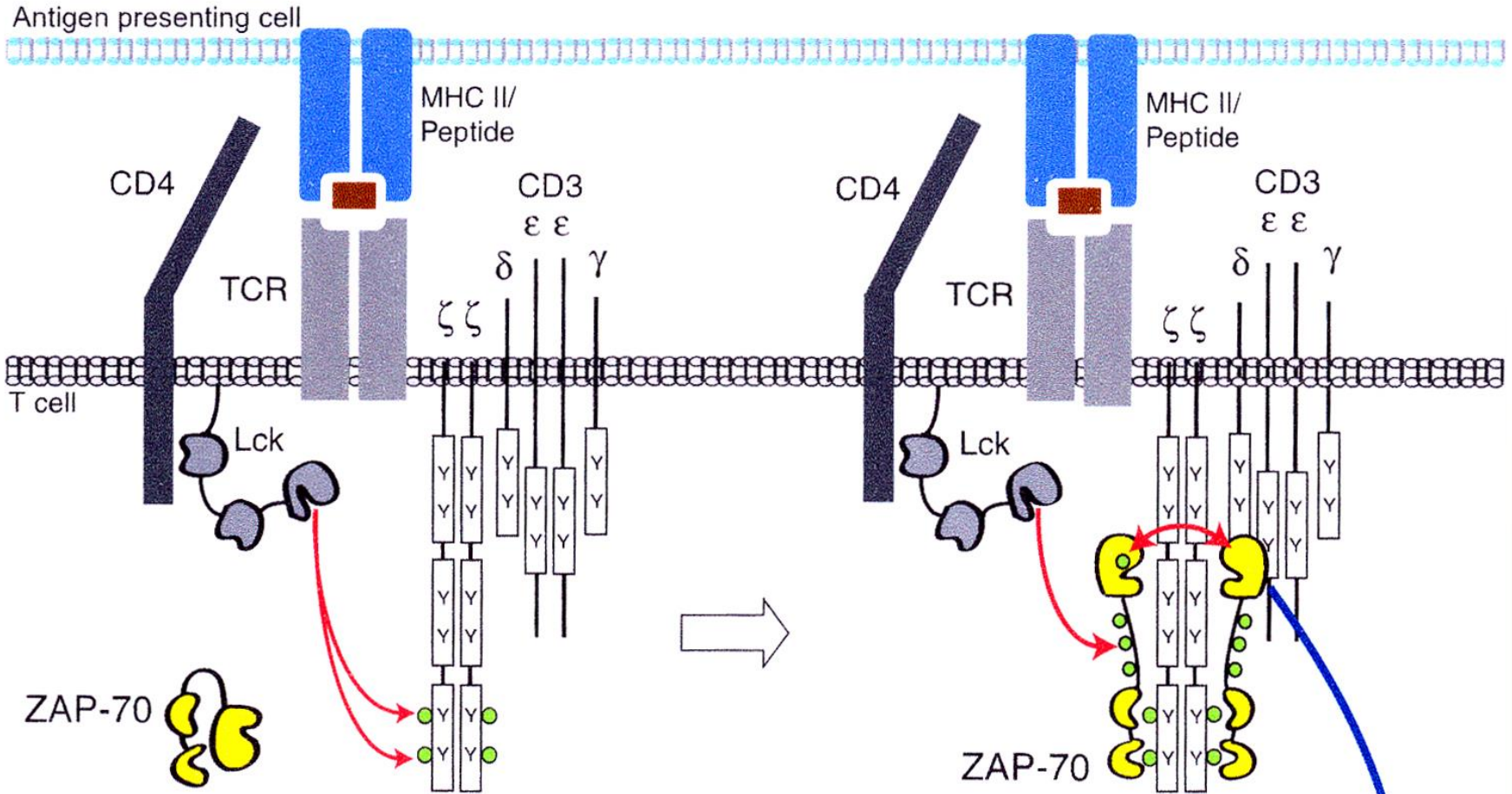
Ενεργοποίηση των T_H-λεμφοκυττάρων

Αναγνώριση του αντιγόνου - Στρατολόγηση της Lck

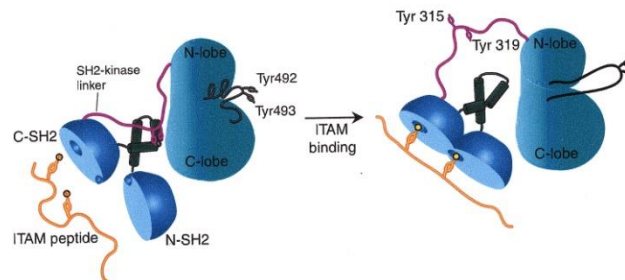


Lck: Leucocyte specific kinase
Κινάση τυροσίνης
τύπου Src

Η Lck φωσφορυλιώνει 2 Tyr του υποδοχέα. Στρατολογείται η κινάση ZAP-70 και φωσφορυλιώνεται από την Lck

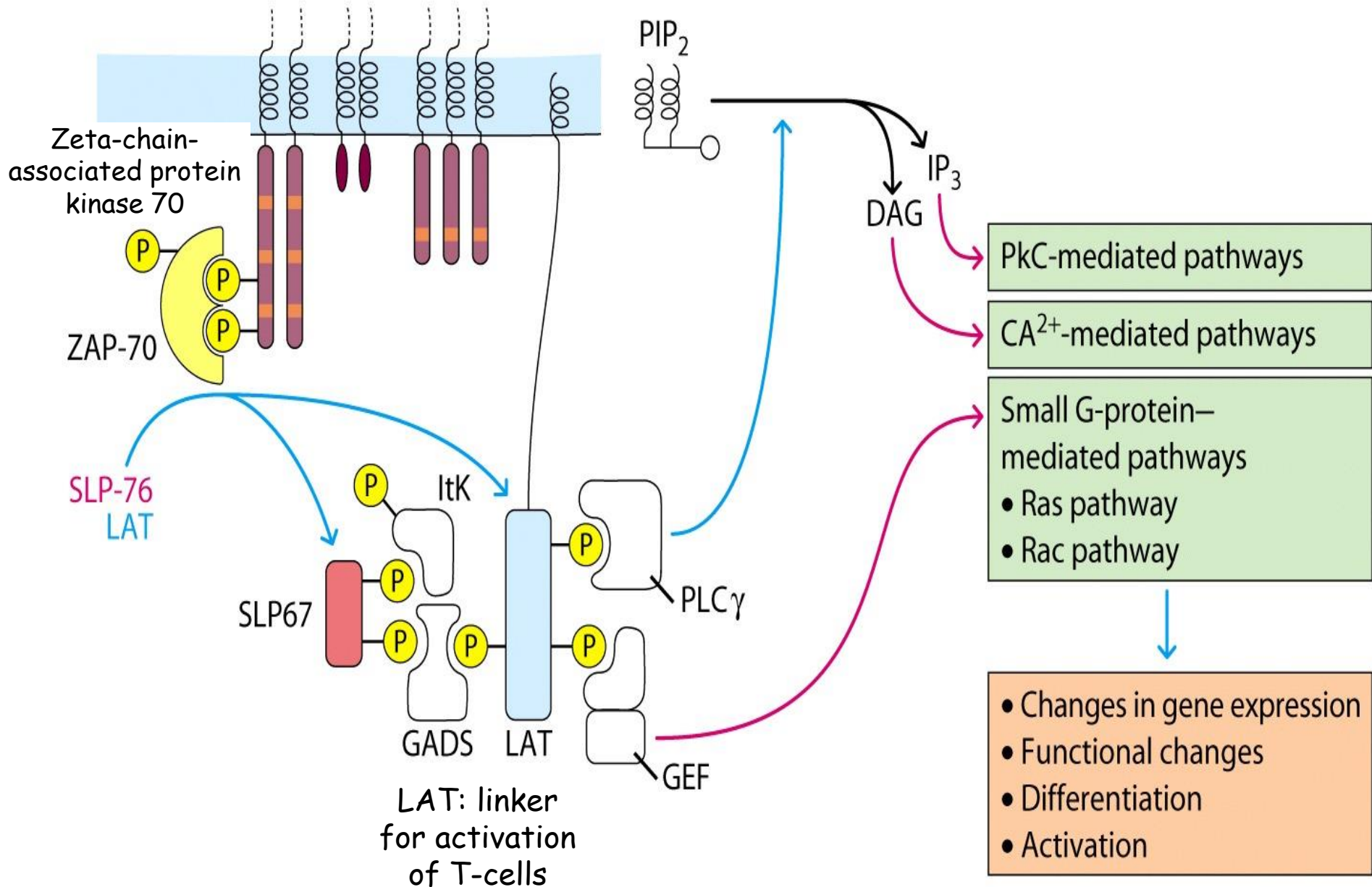


Domain organization of ZAP-70
Zeta-chain-associated protein kinase 70

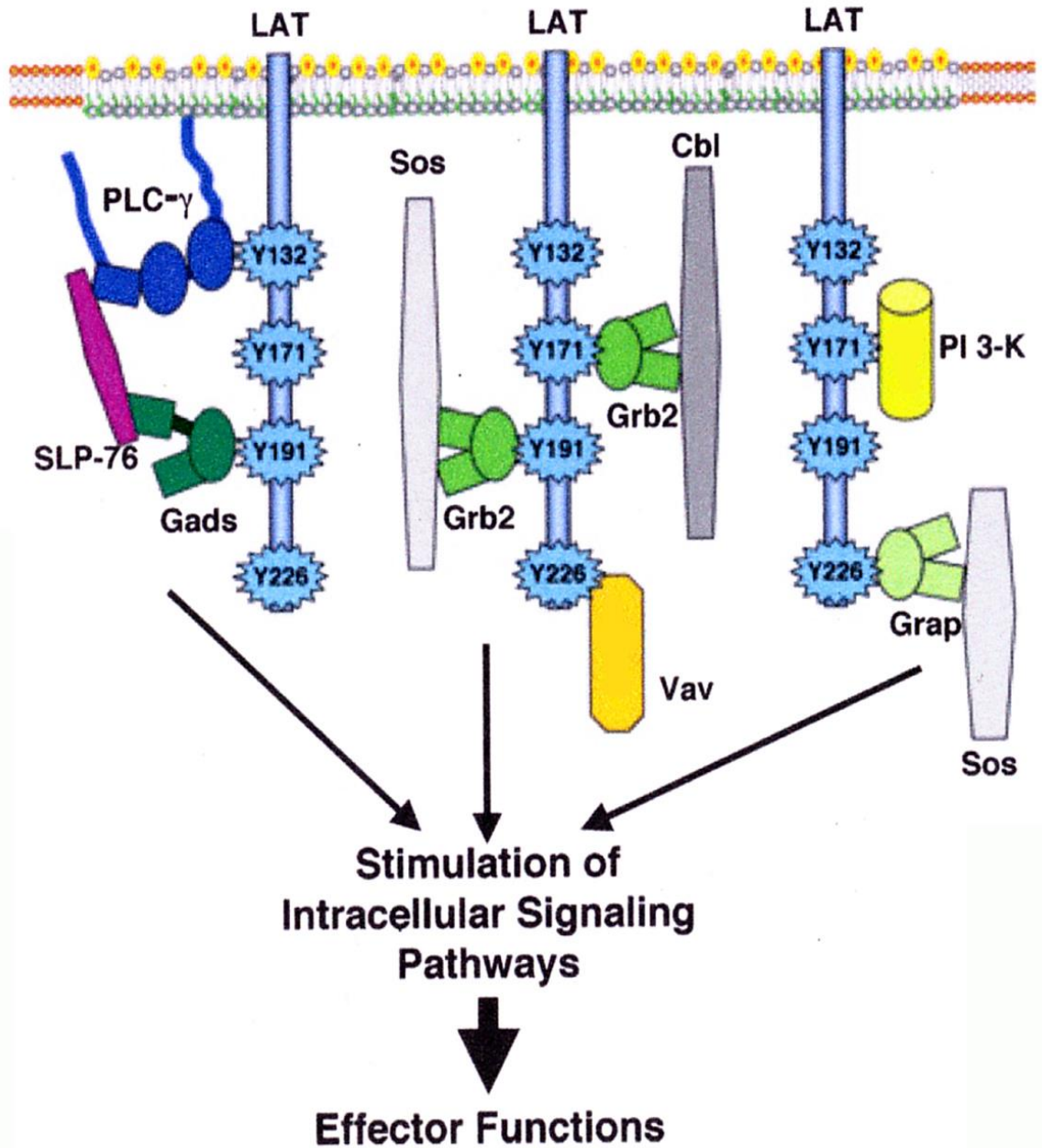
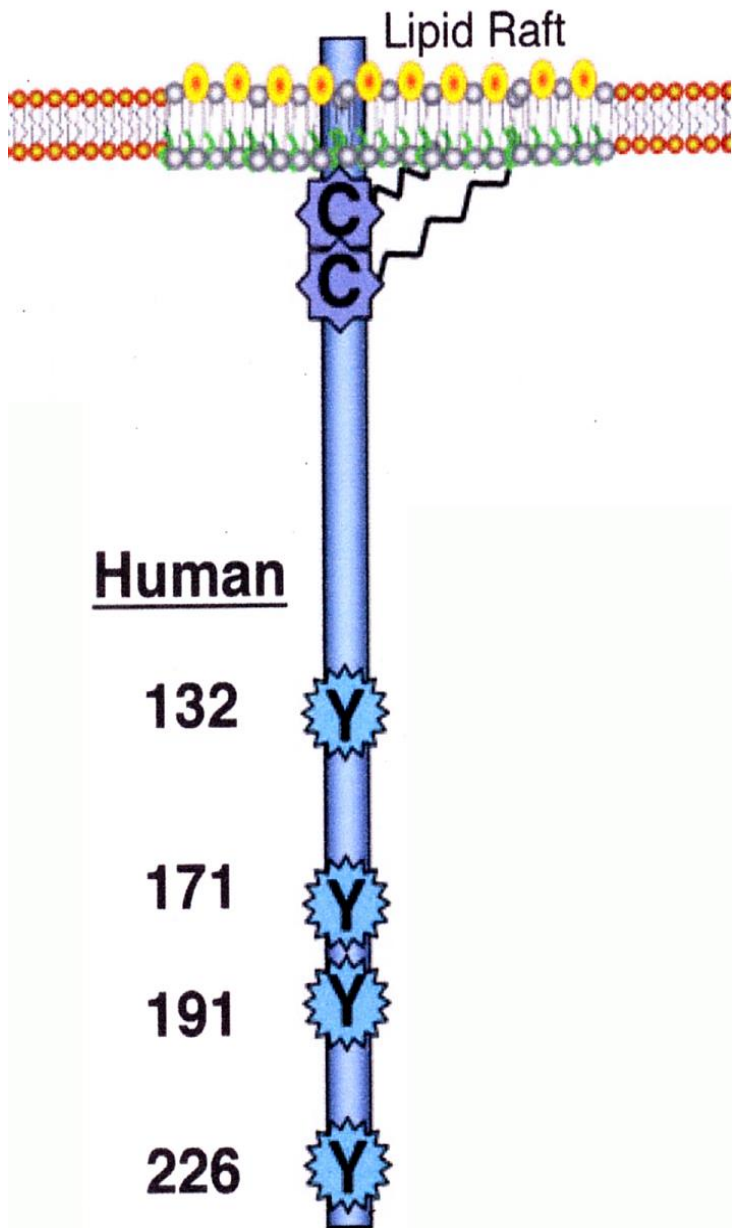


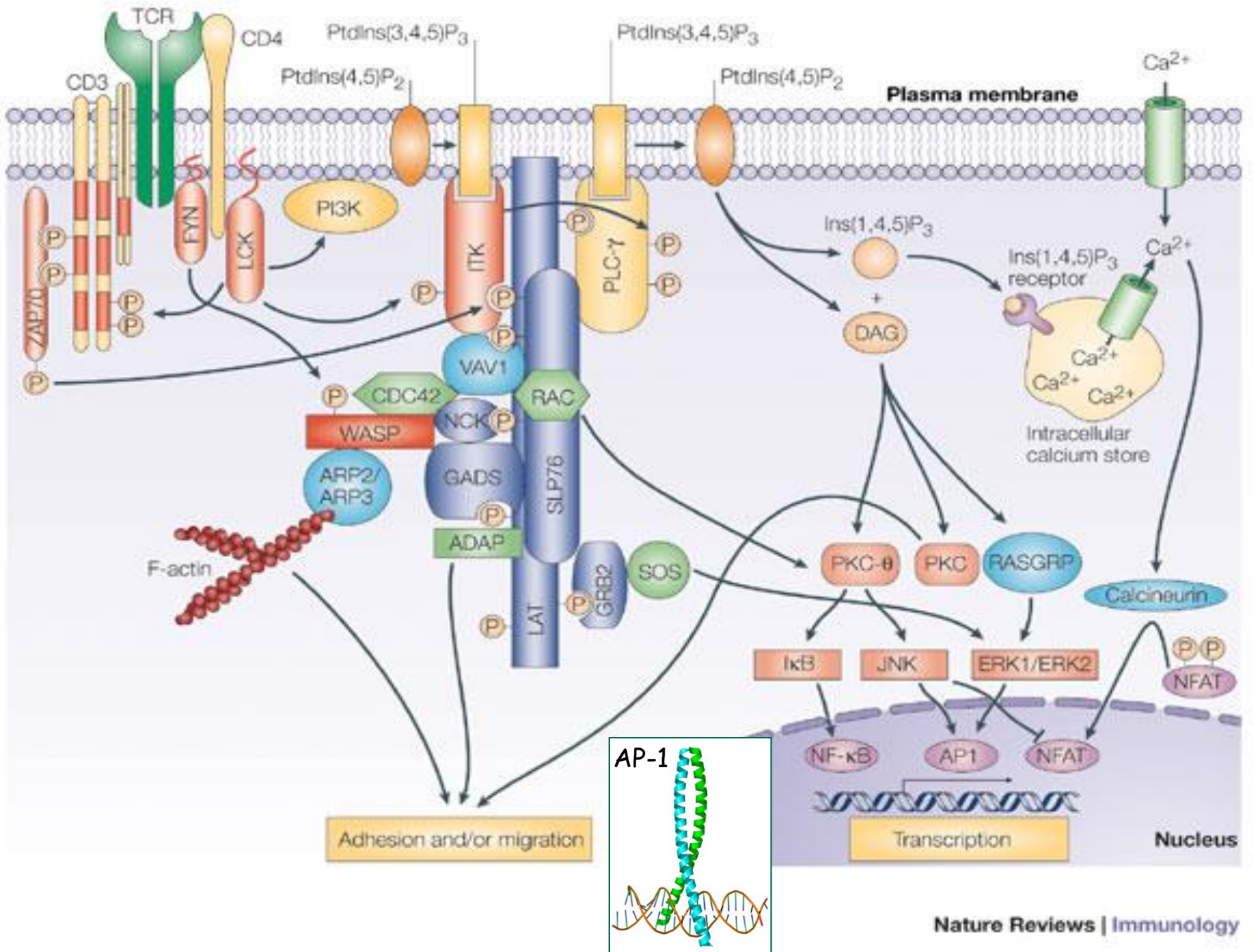
Downstream signals
gene transcription
T cell activation

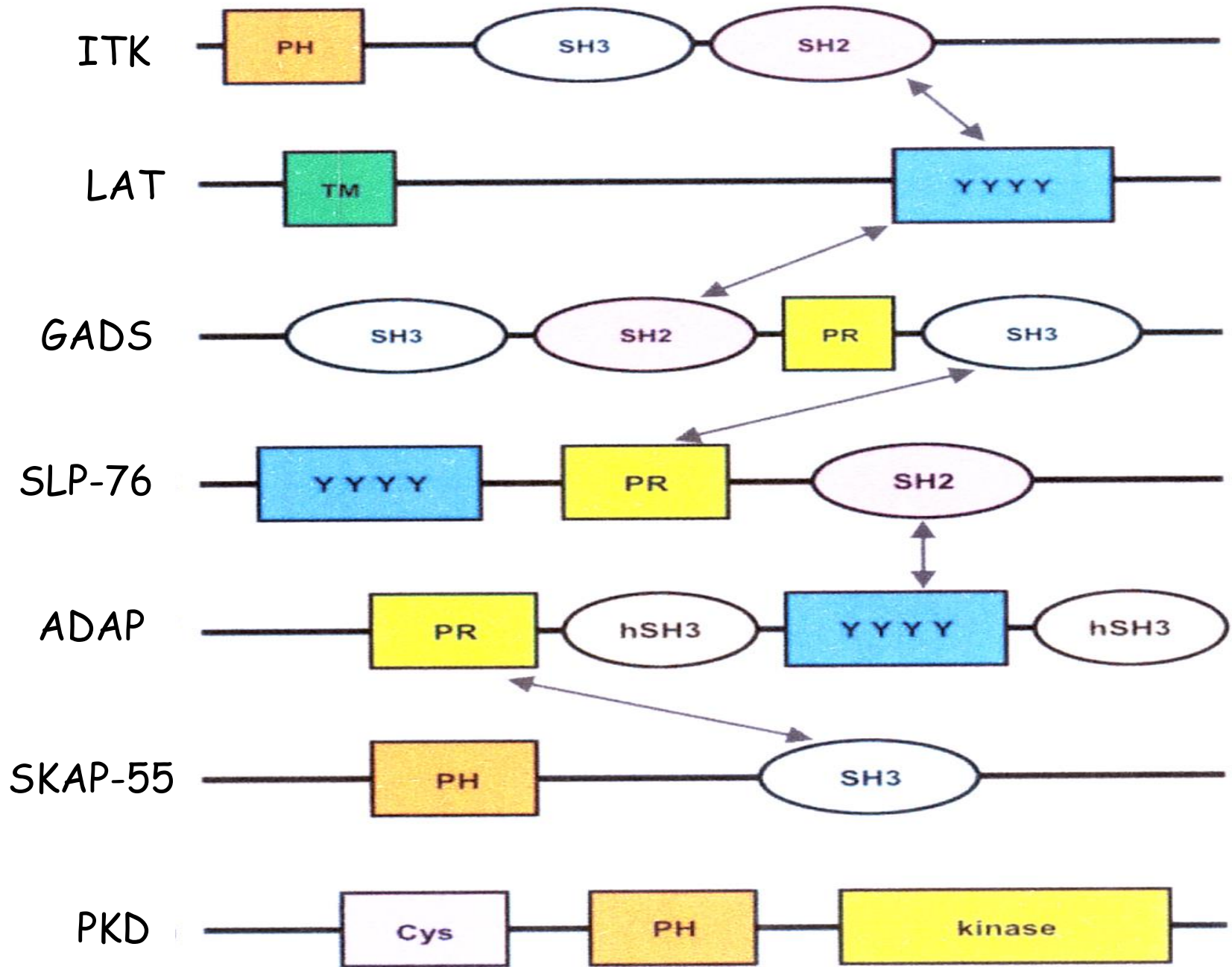
Παραγωγή πολλαπλών ενδοκυτταρικών σημάτων

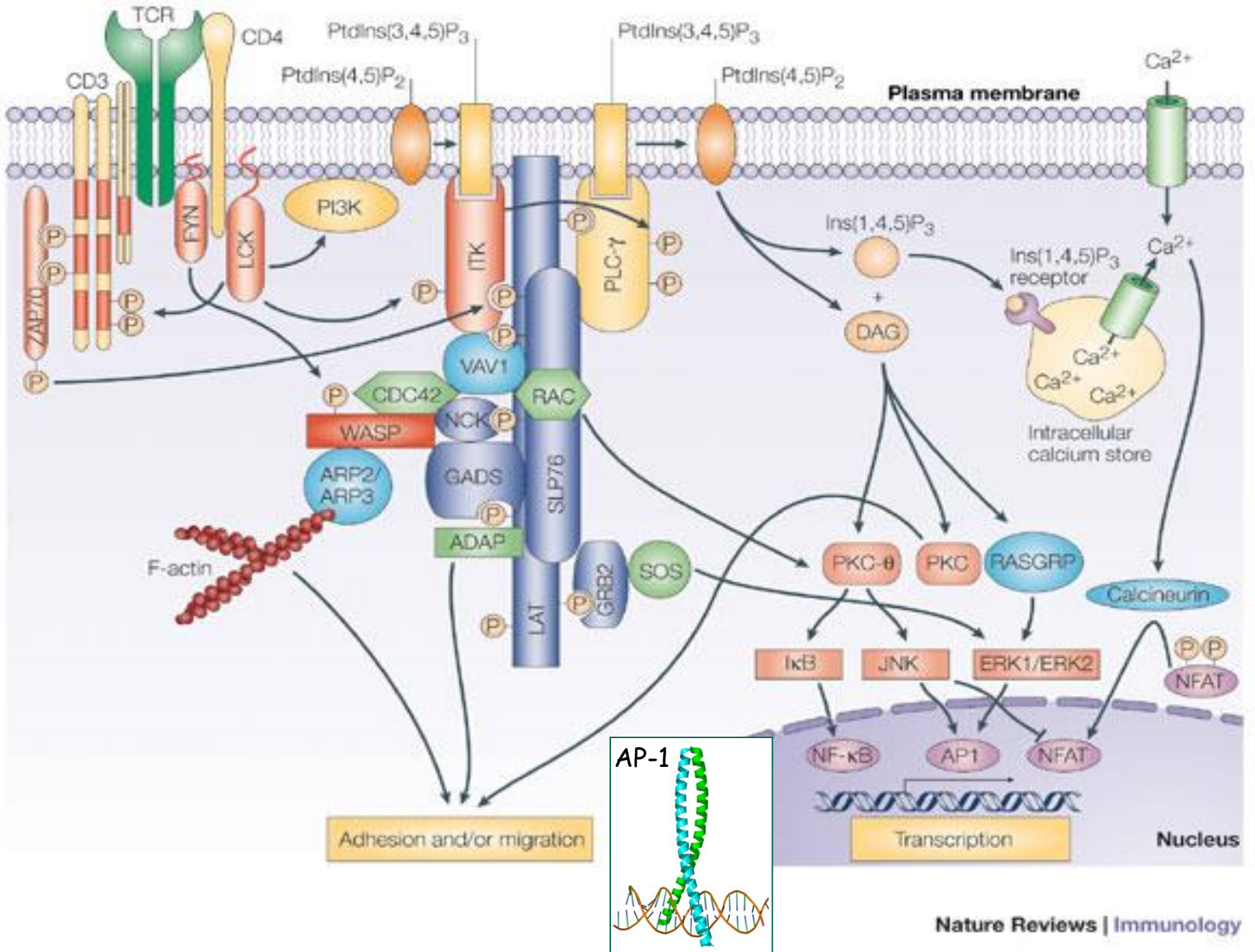


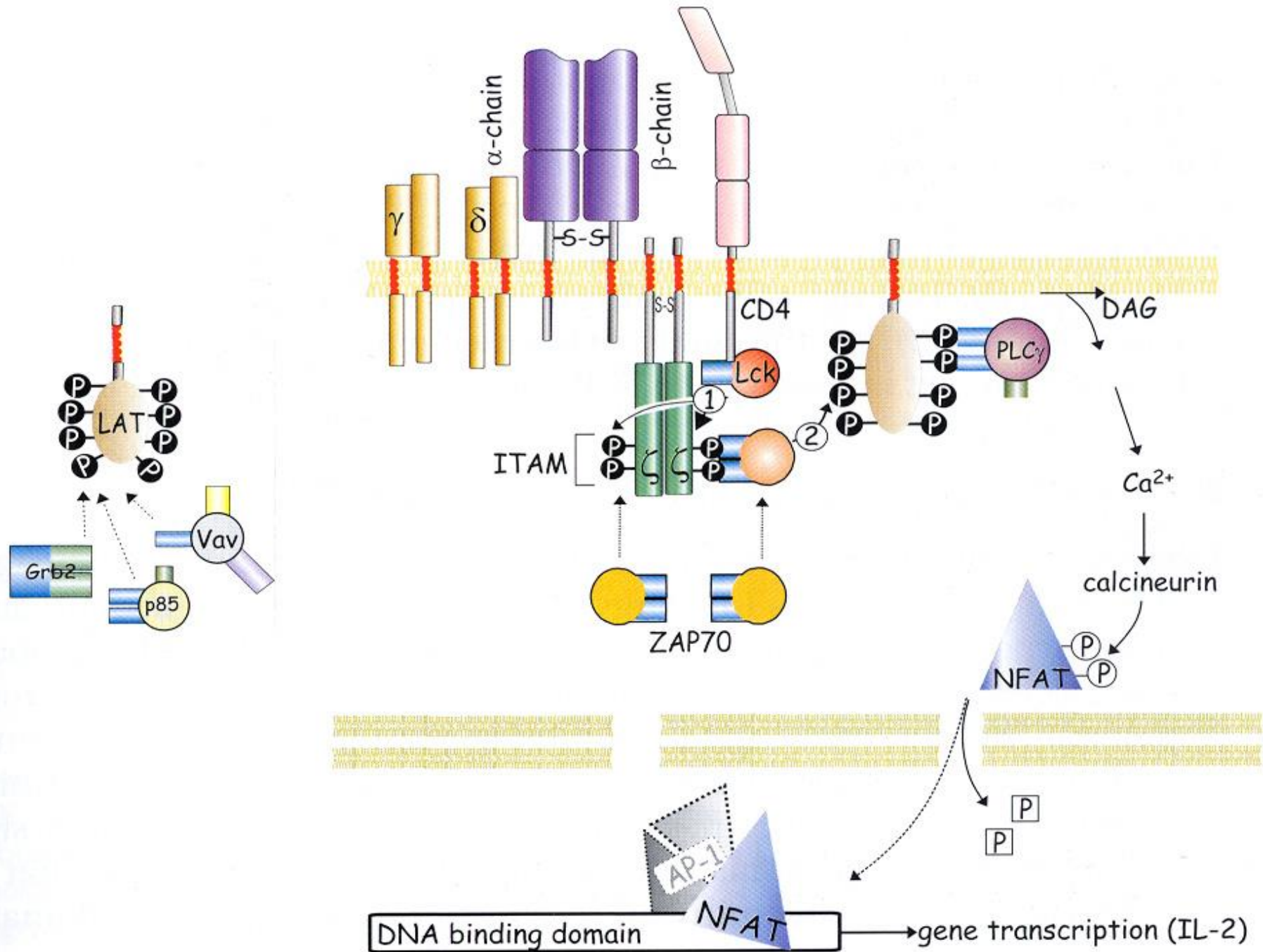
LAT adaptor protein

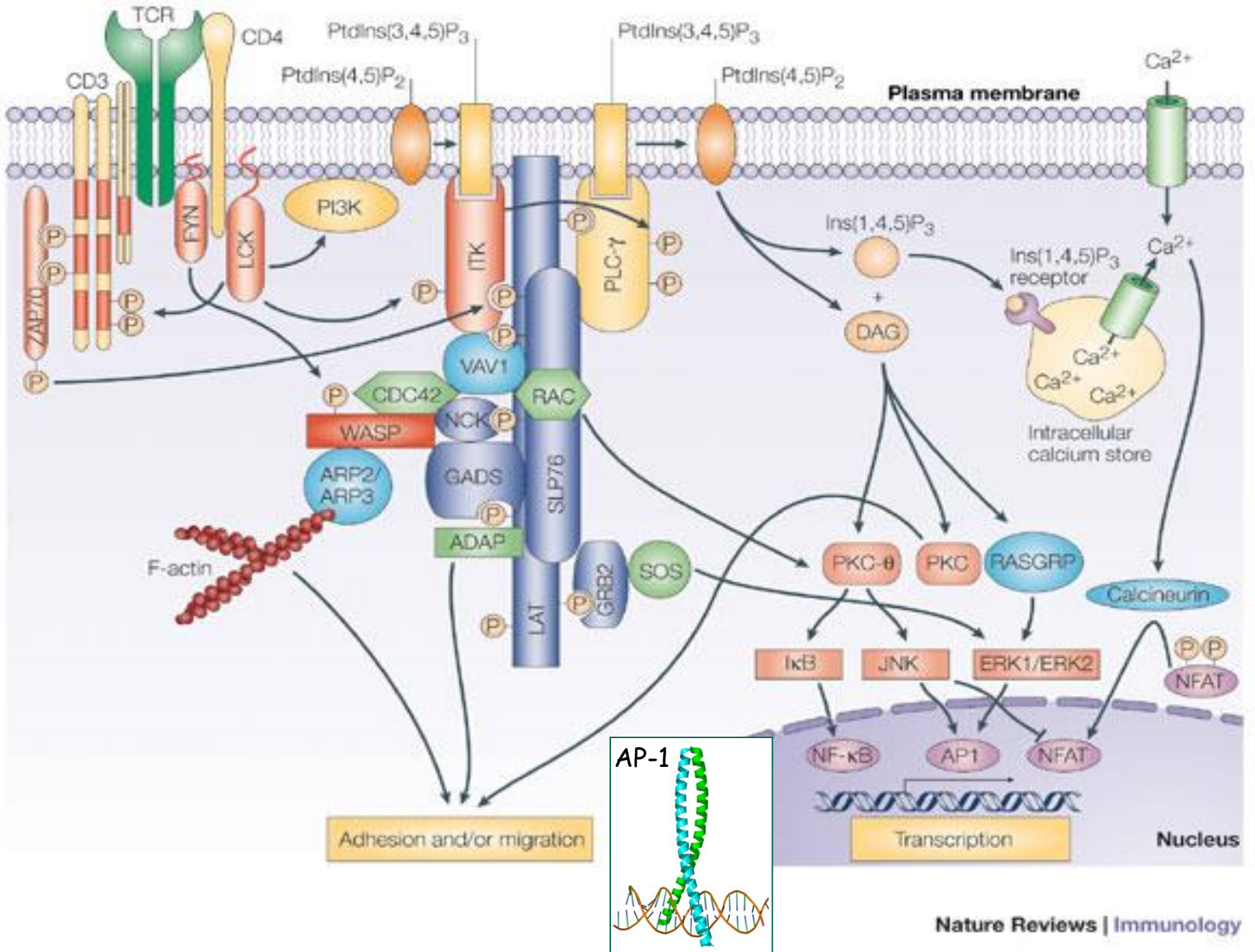




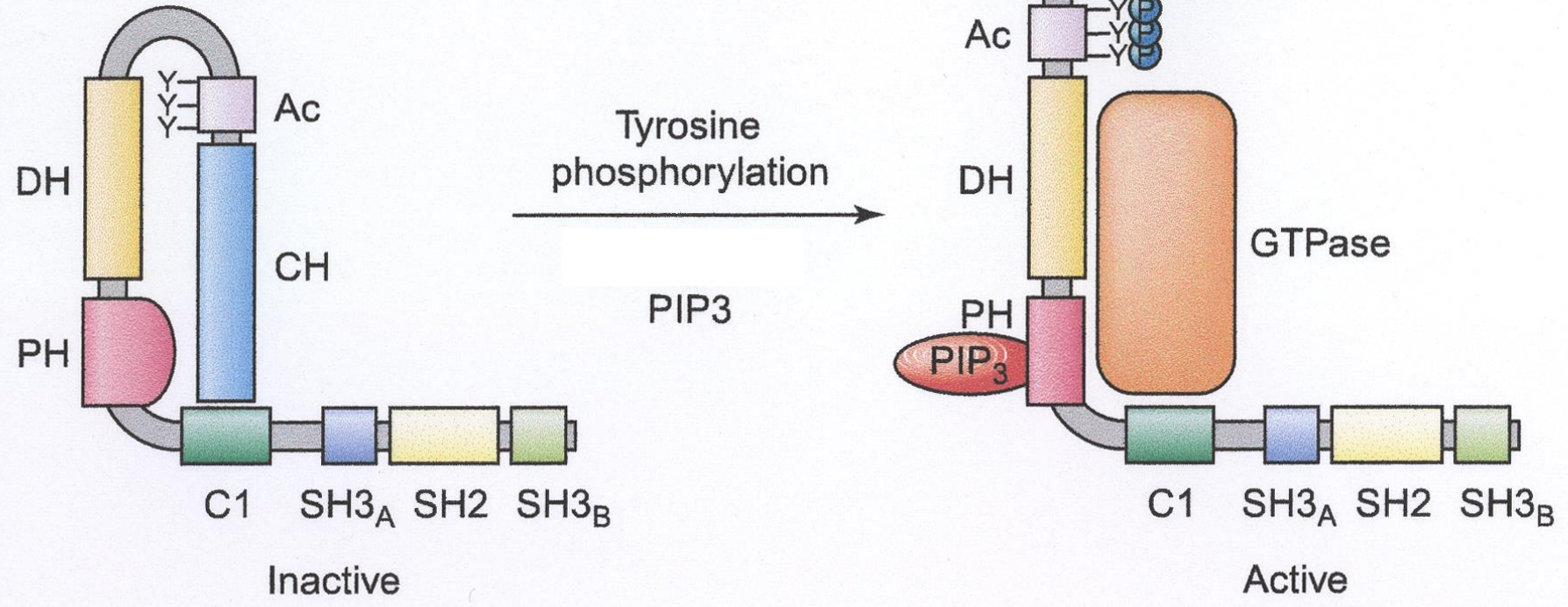
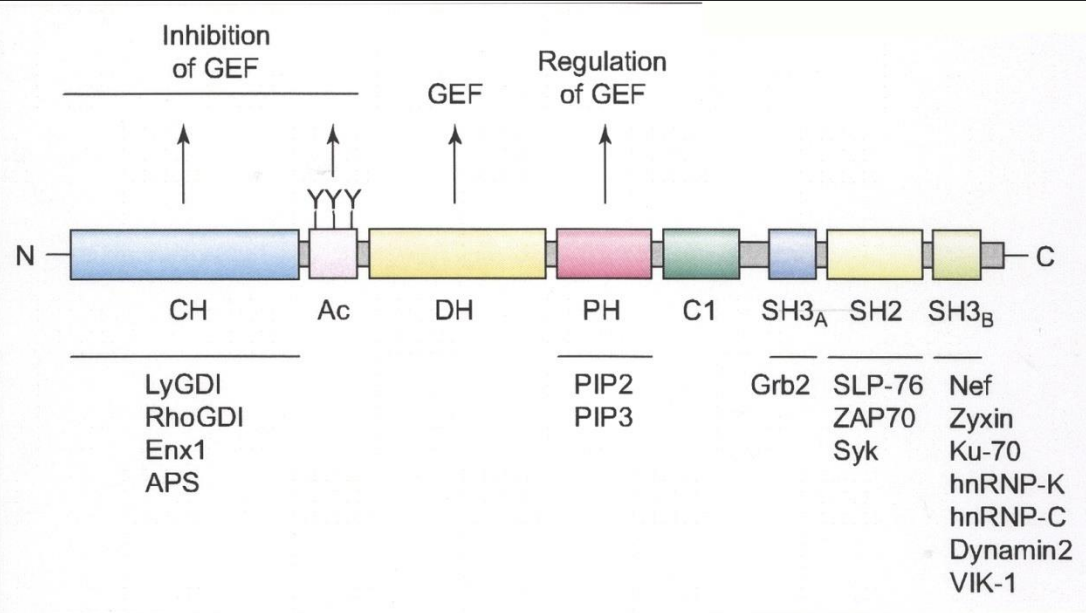


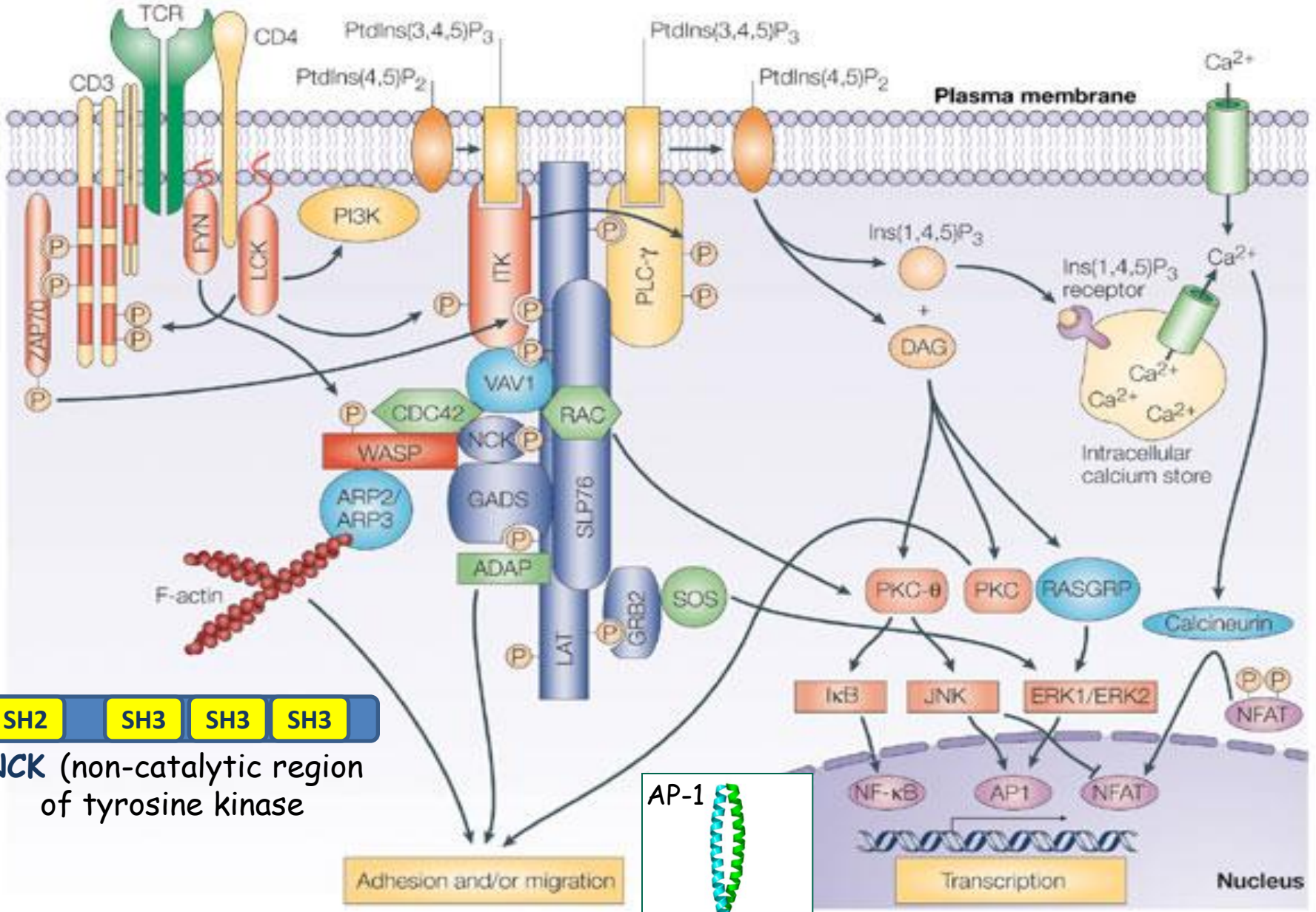






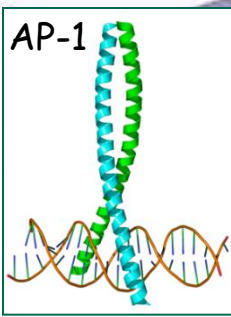
Παράγοντας ανταλλαγής νουκλεοτιδίων Van1



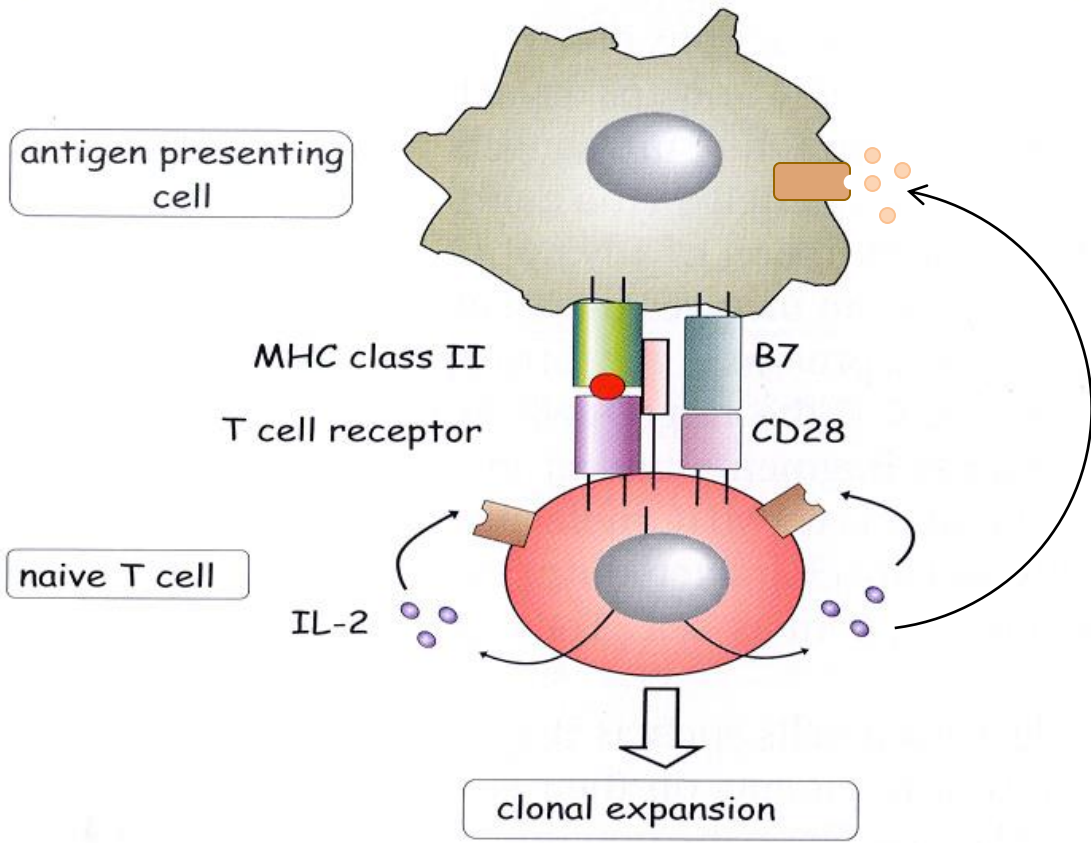


SH2 SH3 SH3 SH3

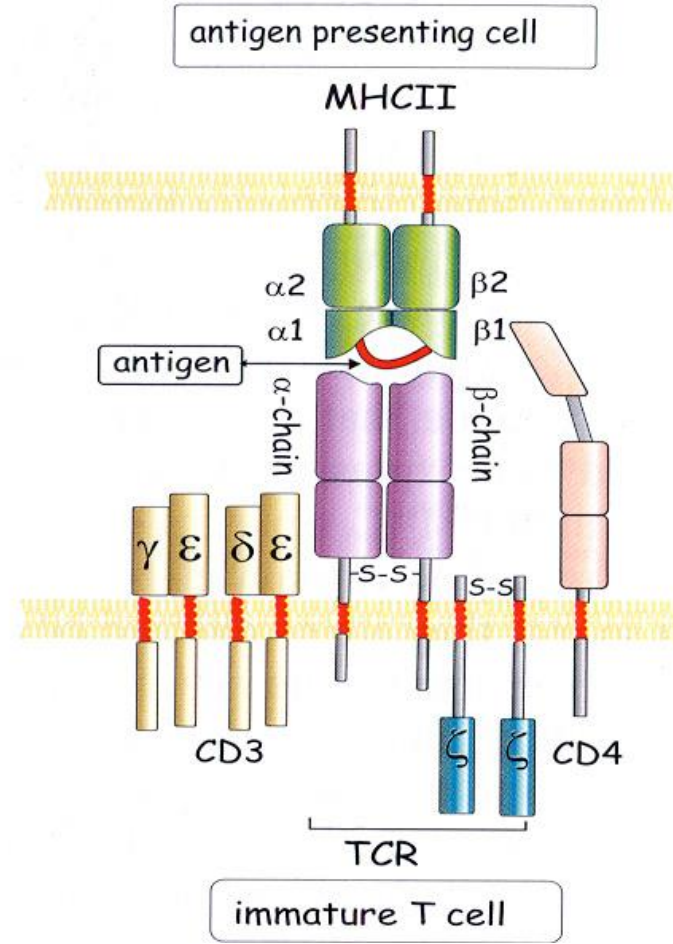
NCK (non-catalytic region of tyrosine kinase)



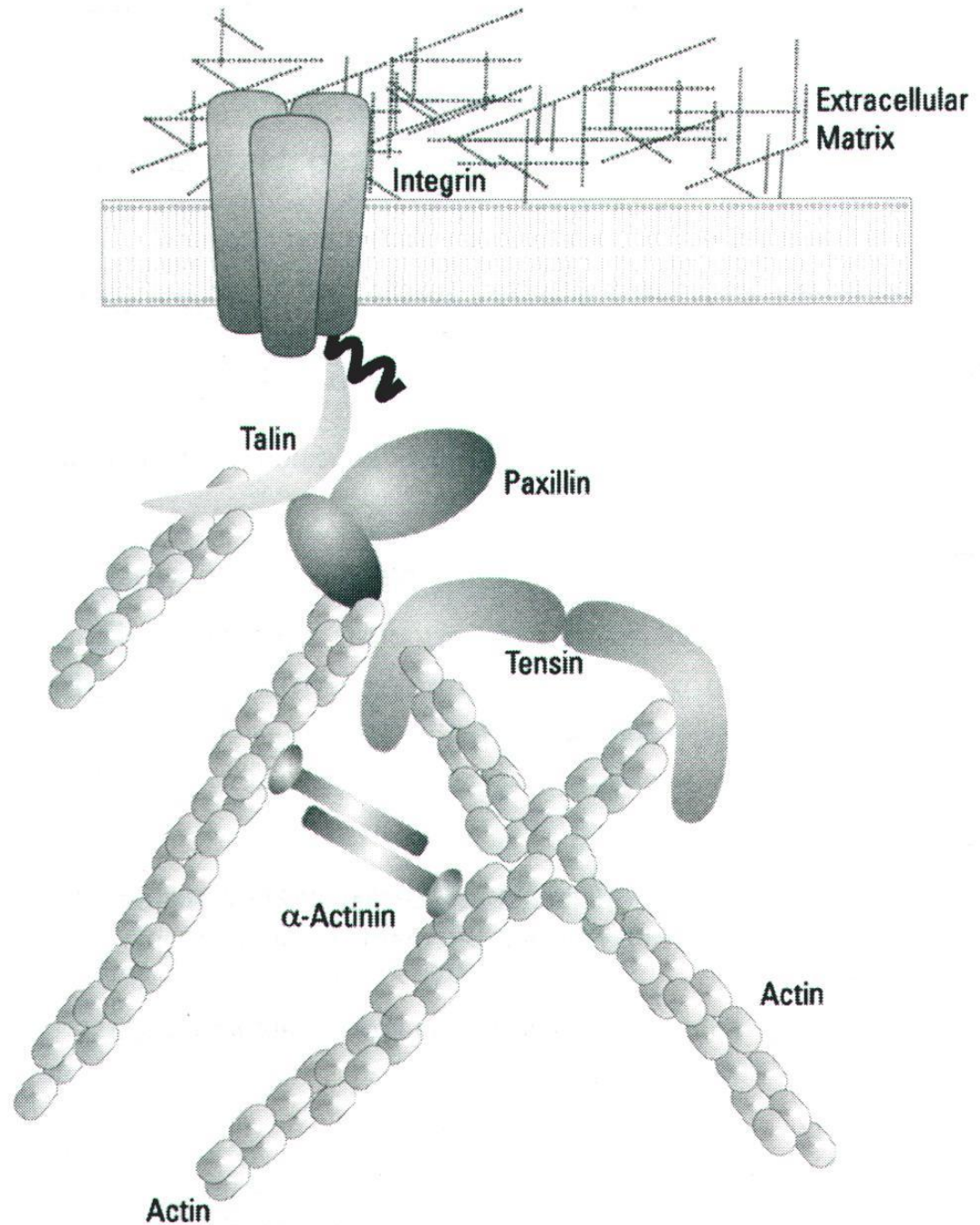
(a)



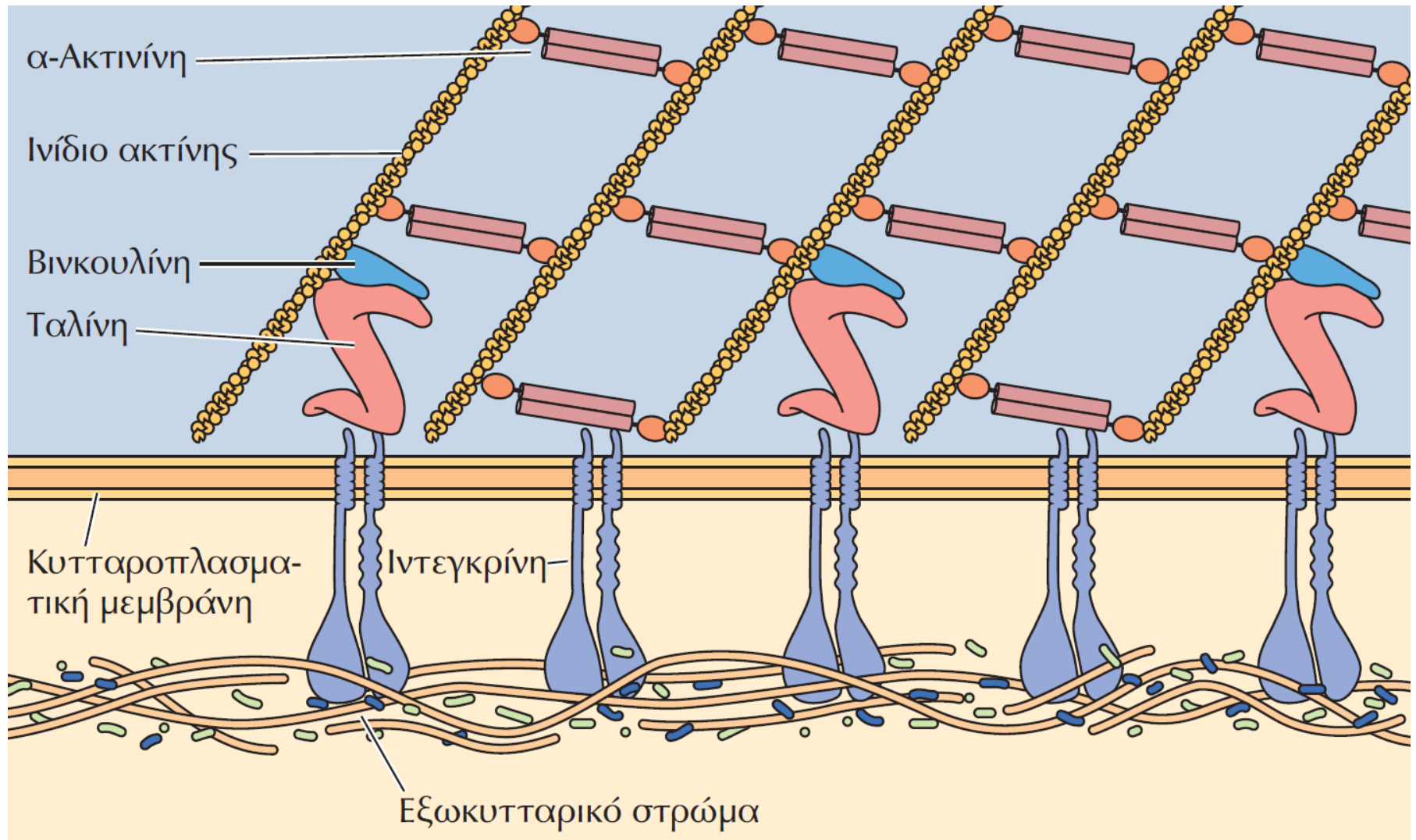
(b)



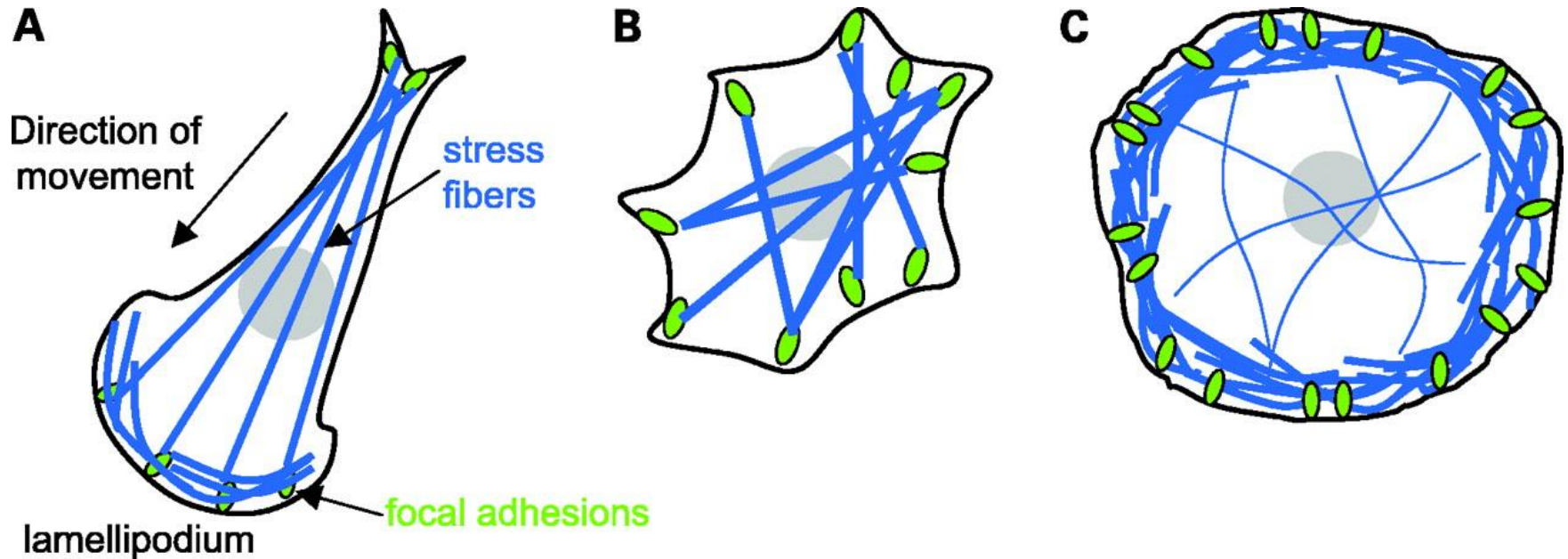
Σηματοδότηση μέσω
ιντεγκρινών



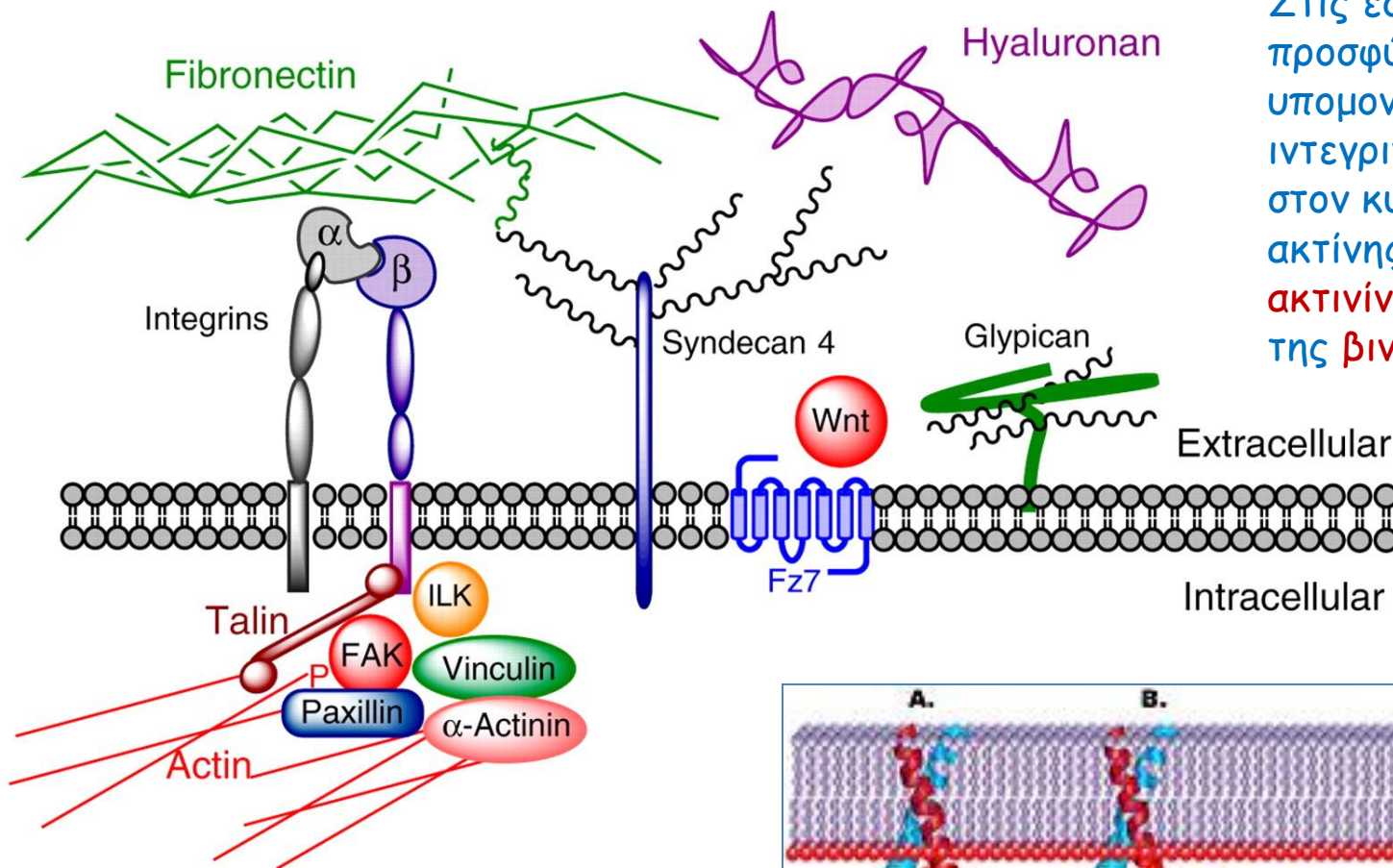
Τα ινίδια απόκρισης στο κυτταρικό στρες (stress fiberrrs) είναι συσταλά δεμάτια ινιδίων ακτίνης, τα οποία συγκρατούν αγκυροβολημένο το κύτταρο και ασκούν τάση στο υπόστρωμα.



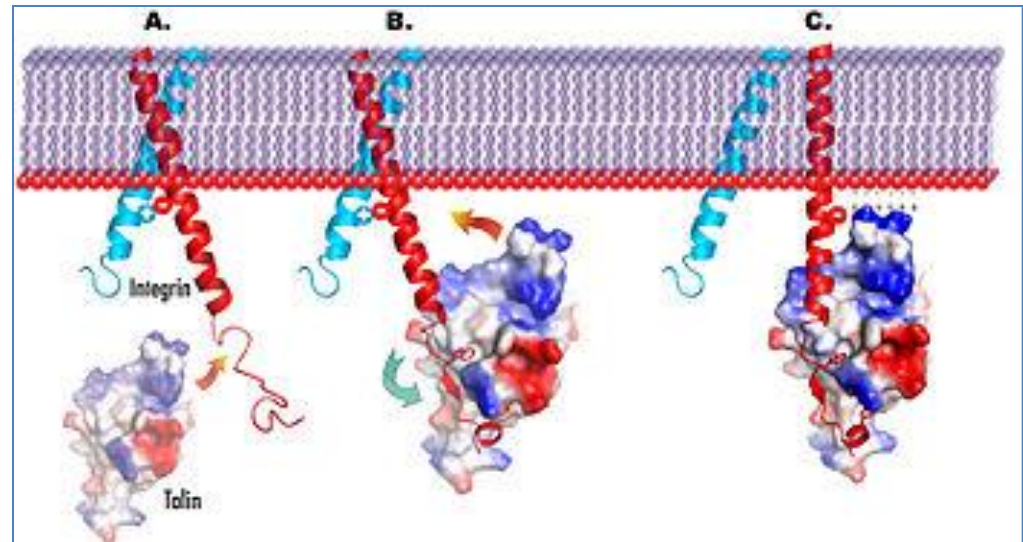
Οι θέσεις προσκόλλησης των ινιδίων απόκρισης στο κυτταρικό στρες (stress fibers) ονομάζονται εστιακές προσφύσεις (focal adhesions)



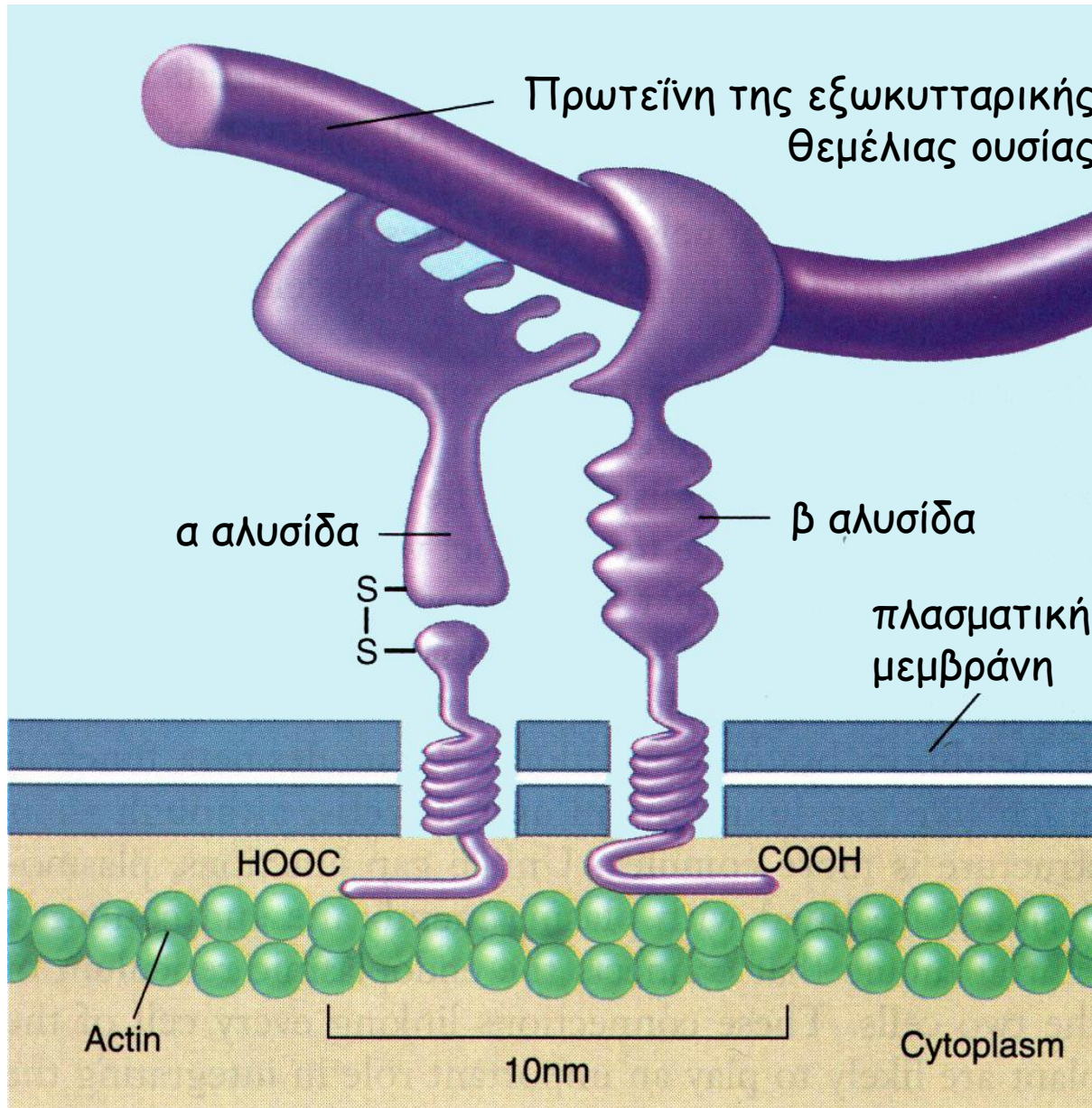
Αλληλεπίδραση ιντεγκρινών – κυτταροσκελετού: Focal adhesion



Στις εστιακές προσφύσεις η β υπομονάδα των ιντεγκρινών προσδένεται στον κυτταροσκελετό ακτίνης μέσω της α-ακτινίνης, της ταλίνης και της βινκουλίνης.



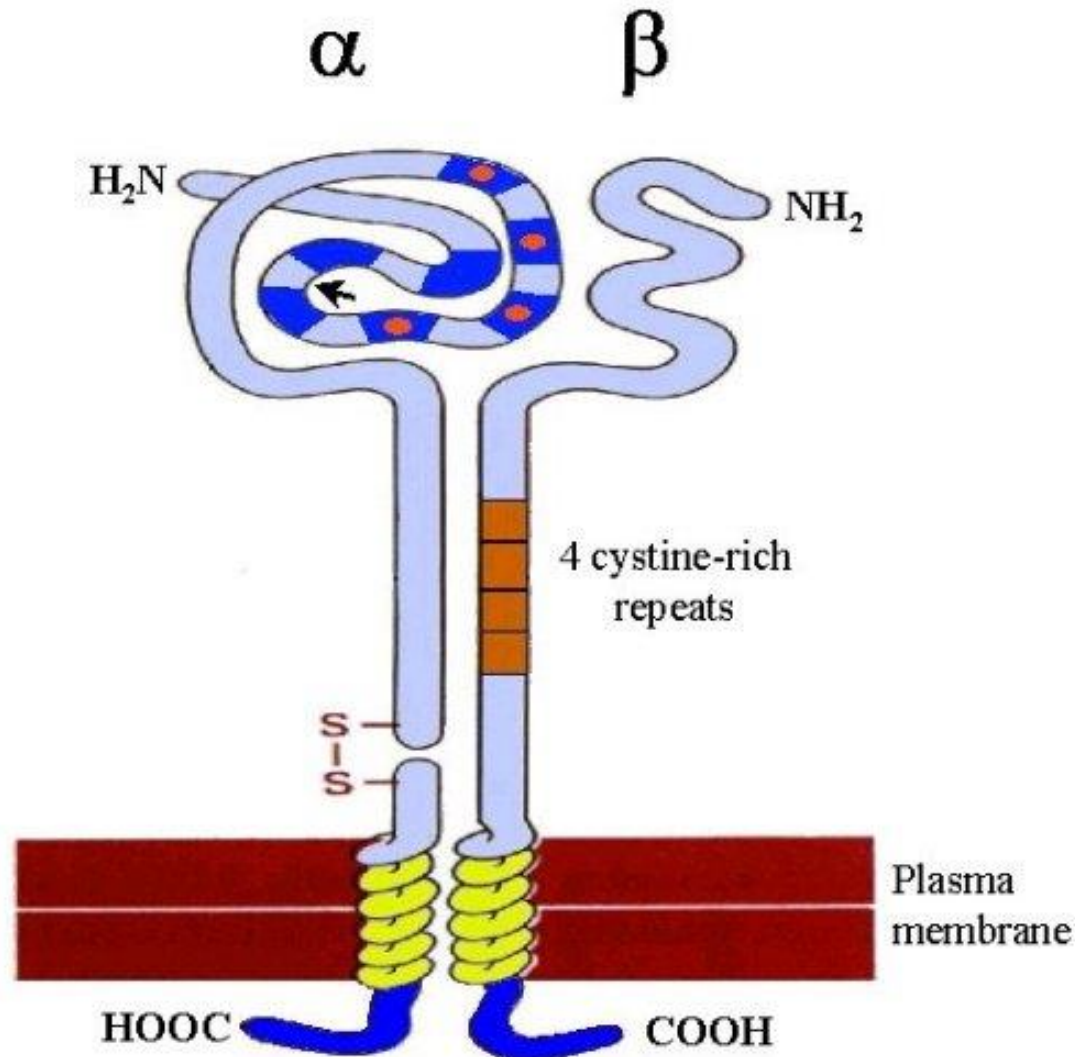
Ιντεγκρίνη



Schematic drawing of a typical integrin dimer

Arrow shows the region where an I domain is inserted in some α subunits. Not all α subunits are posttranslationally cleaved. Internal disulphide bonds within subunits are not shown. Dark blue regions in the head segment of the α subunit represent homologous repeats.

Those with the EF-hand consensus sequence are marked with red circles to denote binding sites for divalent metal ion.



adherent cells:

interactions between the cells and the extracellular matrix

leukocytes:

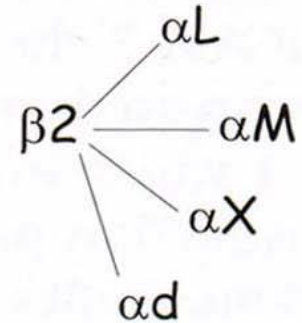
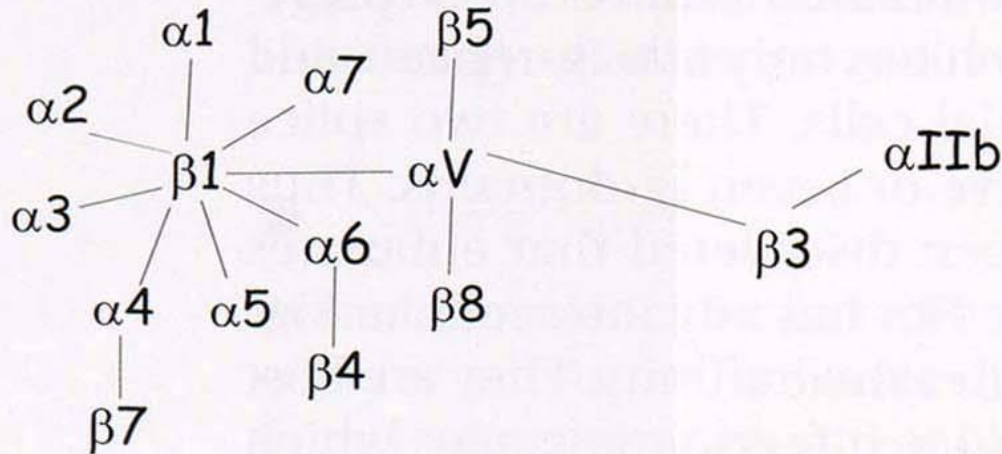
interactions with adherent cells

platelets:

binding to fibrinogen, fibronectin, thrombospondin and von Willebrand's factor

leukocytes:

interactions with adherent cells and fibrinogen



examples:

cell-to-extracellular matrix

$\alpha7\beta1$ -- laminin

$\alphaV\beta3$ -- vitronectin/fibronectin

$\alpha5\beta1$ -- fibronectin

$\alpha6\beta4$ -- laminin

$\alpha1\beta1$ -- collagen, laminin

leukocytes-to-adherent cells

$\alpha4\beta1$ -- VCAM-1

$\alpha4\beta7$ -- MadCAM

examples

cell-to-cell

$\alphaL\beta2$ -- ICAM1, ICAM2, ICAM3

$\alphaM\beta2$ -- ICAM1

$\alphaL\beta2$ -- ICAM1, ICAM2, ICAM3

$\alphaD\beta2$ -- ICAM-3, VCAM-1

cells-to-extracellular matrix

$\alphaM\beta2$ -- C3bi, fibrinogen, ICAM1

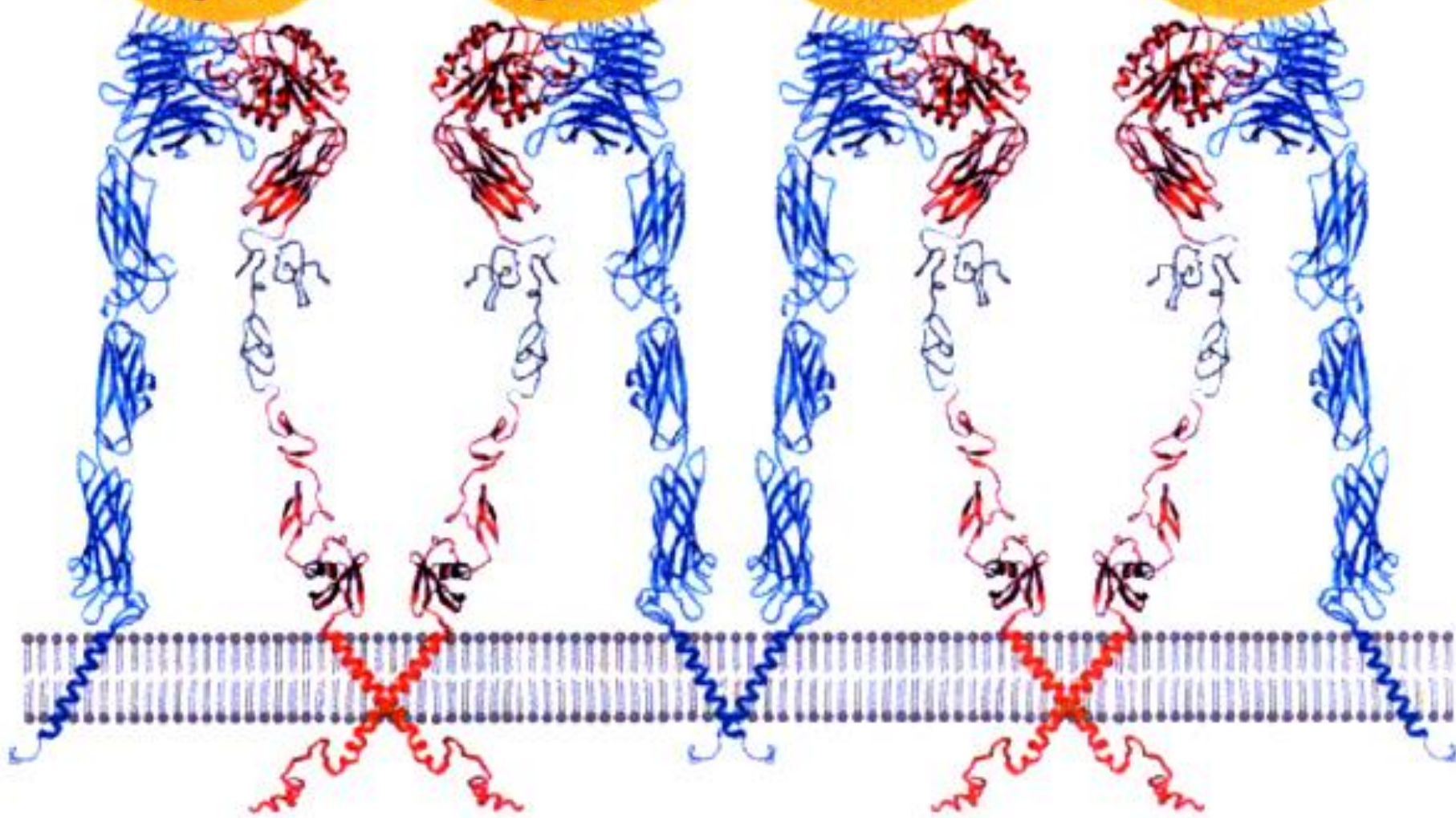
$\alphaX\beta2$ -- fibrinogen

Ligand

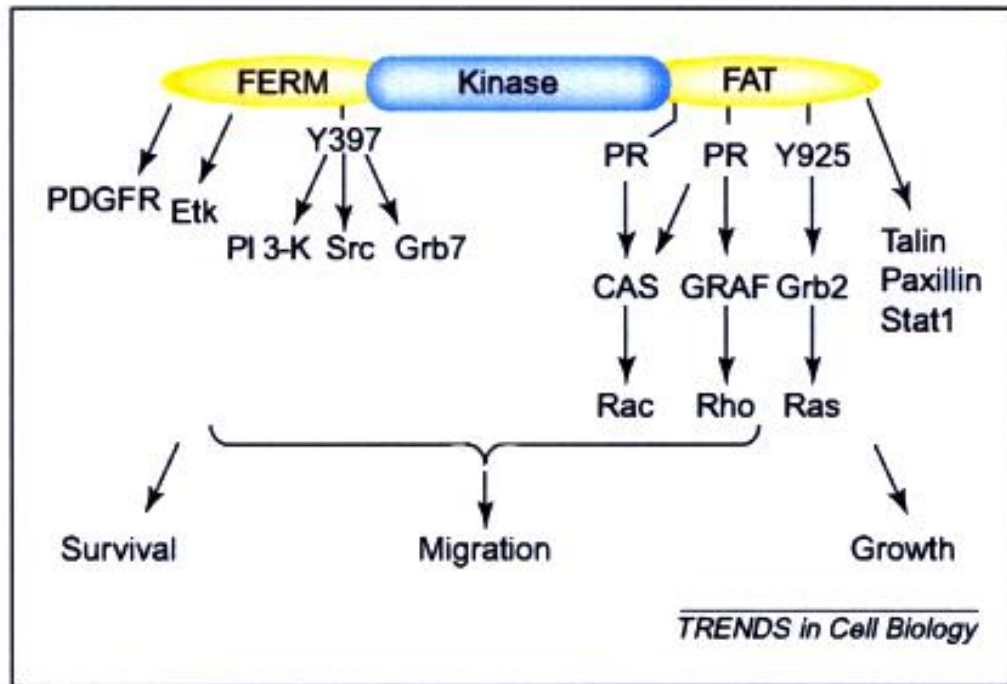
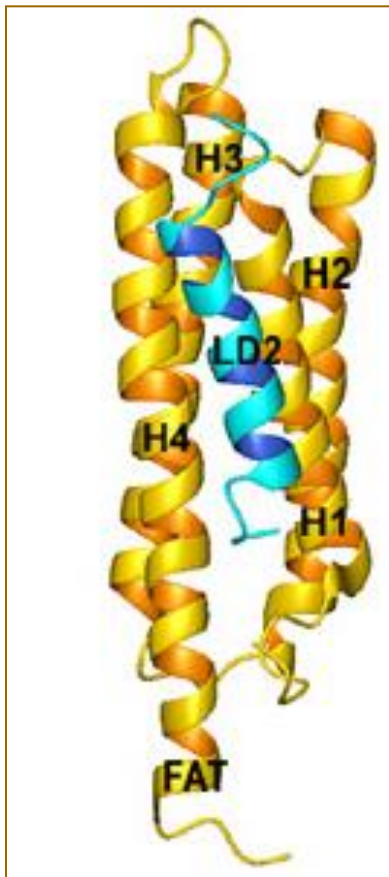
Ligand

Ligand

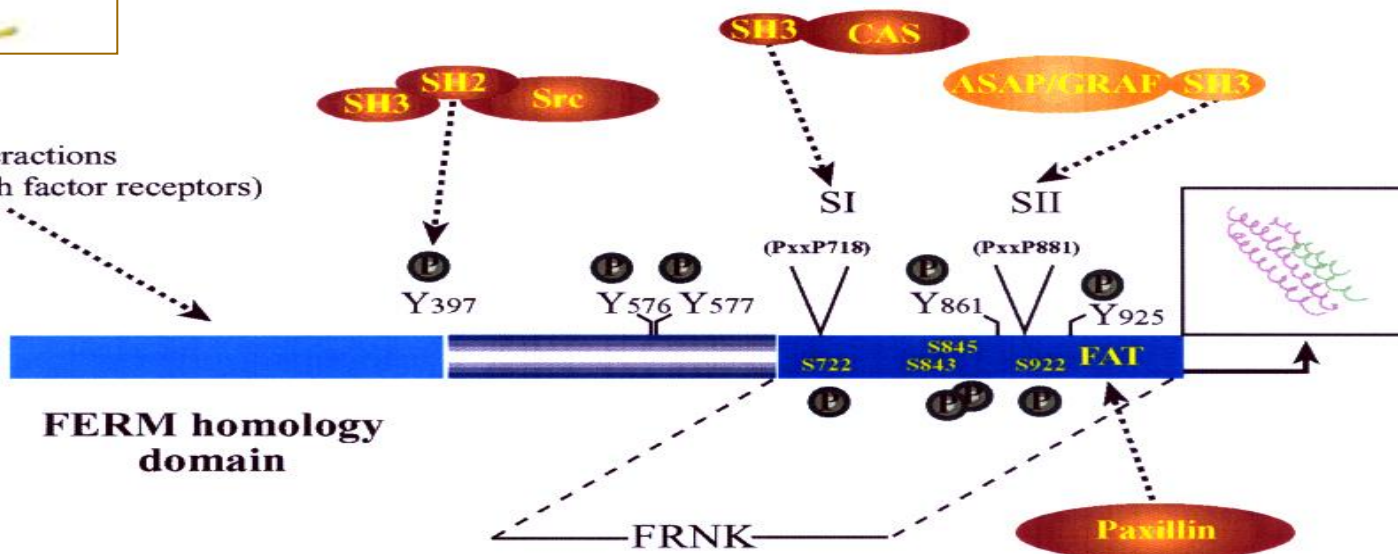
Ligand



Kiváron FAK (focal adhesion kinase)

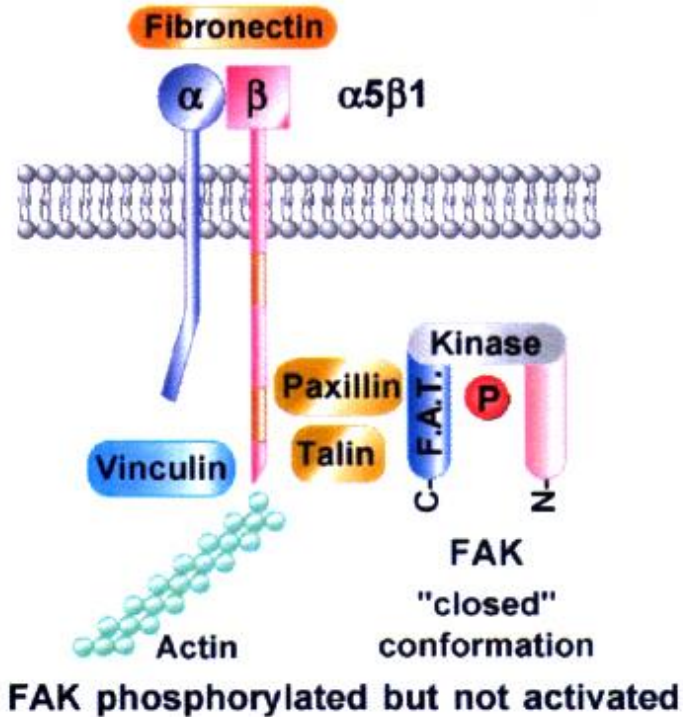


Cytoplasmic interactions
(integrins, growth factor receptors)

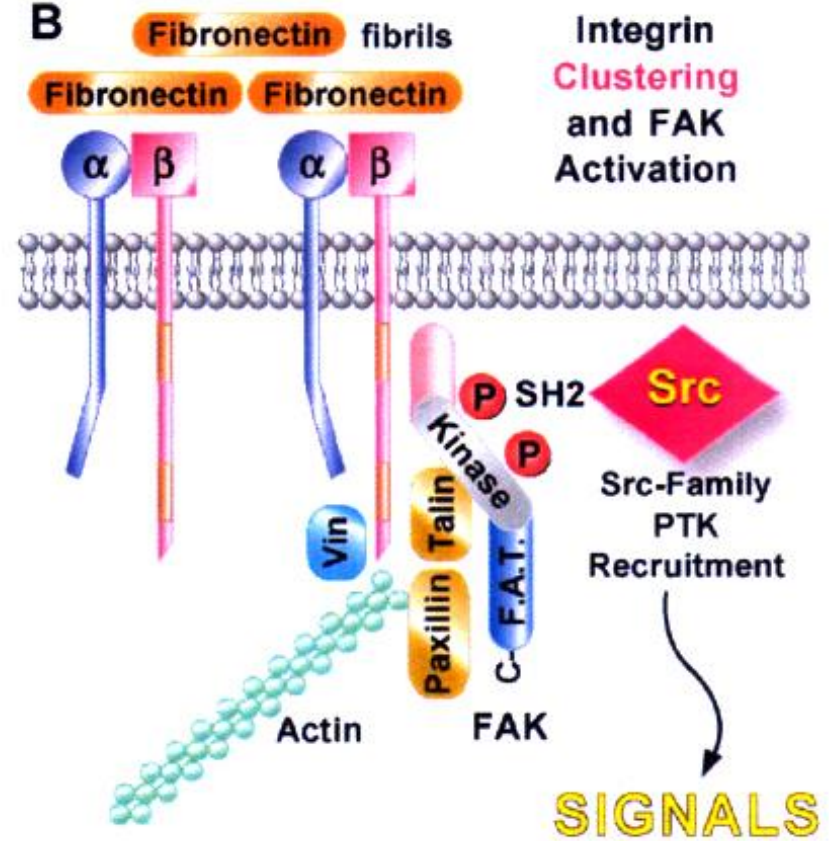


Model of β -integrin-mediated FAK Activation

A

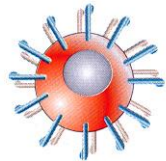
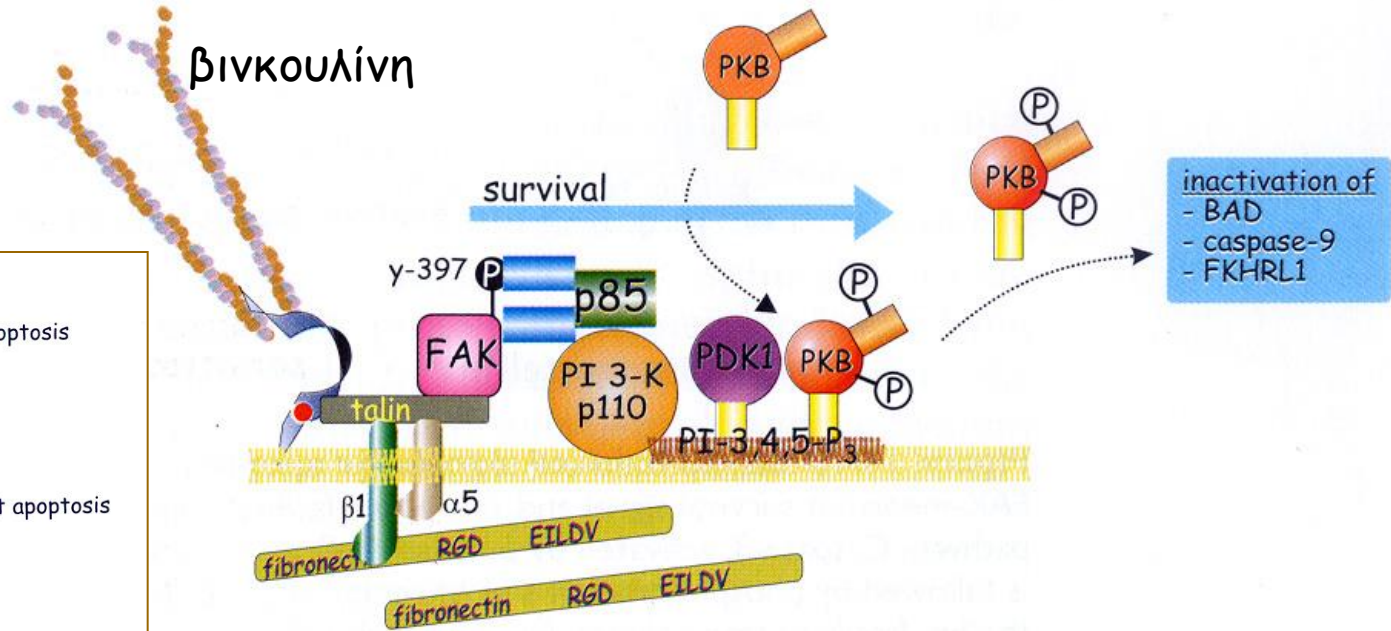


B



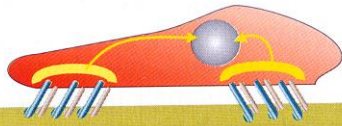
1. Επιβίωση και πολλαπλασιασμός

(a)



unattached cell
susceptible to apoptosis

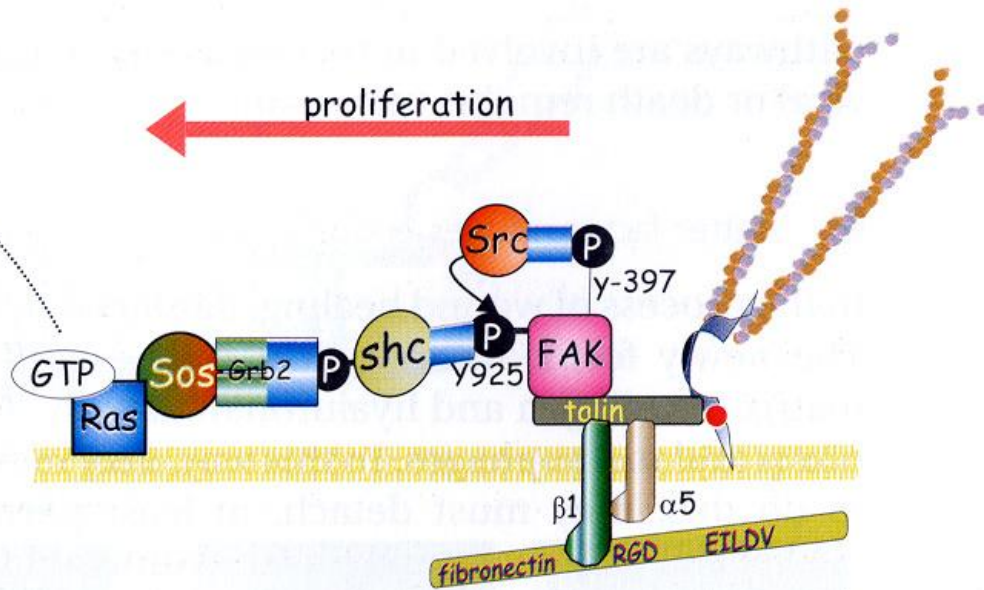
attached cell
protected against apoptosis



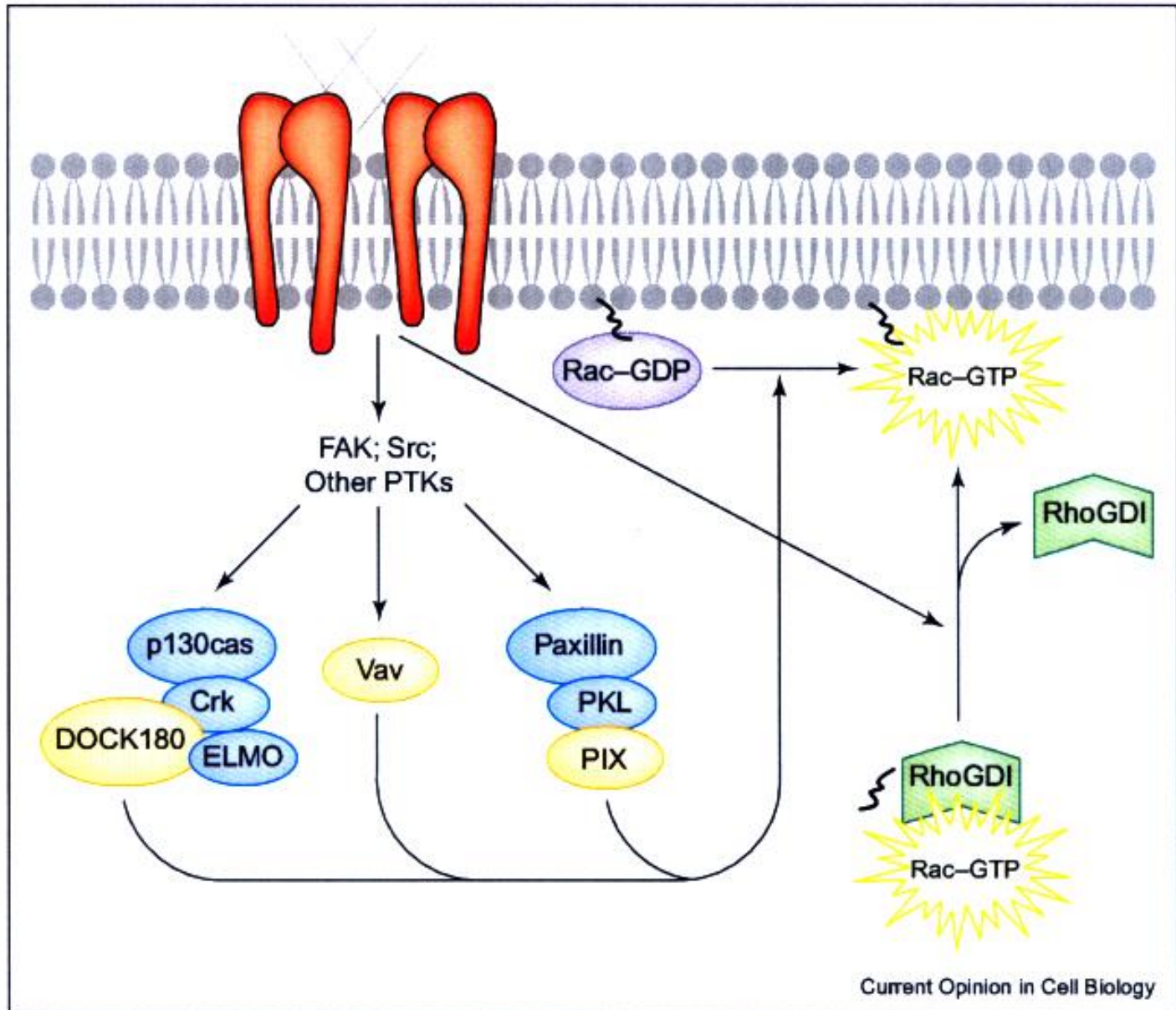
(b)

MAP kinase pathway

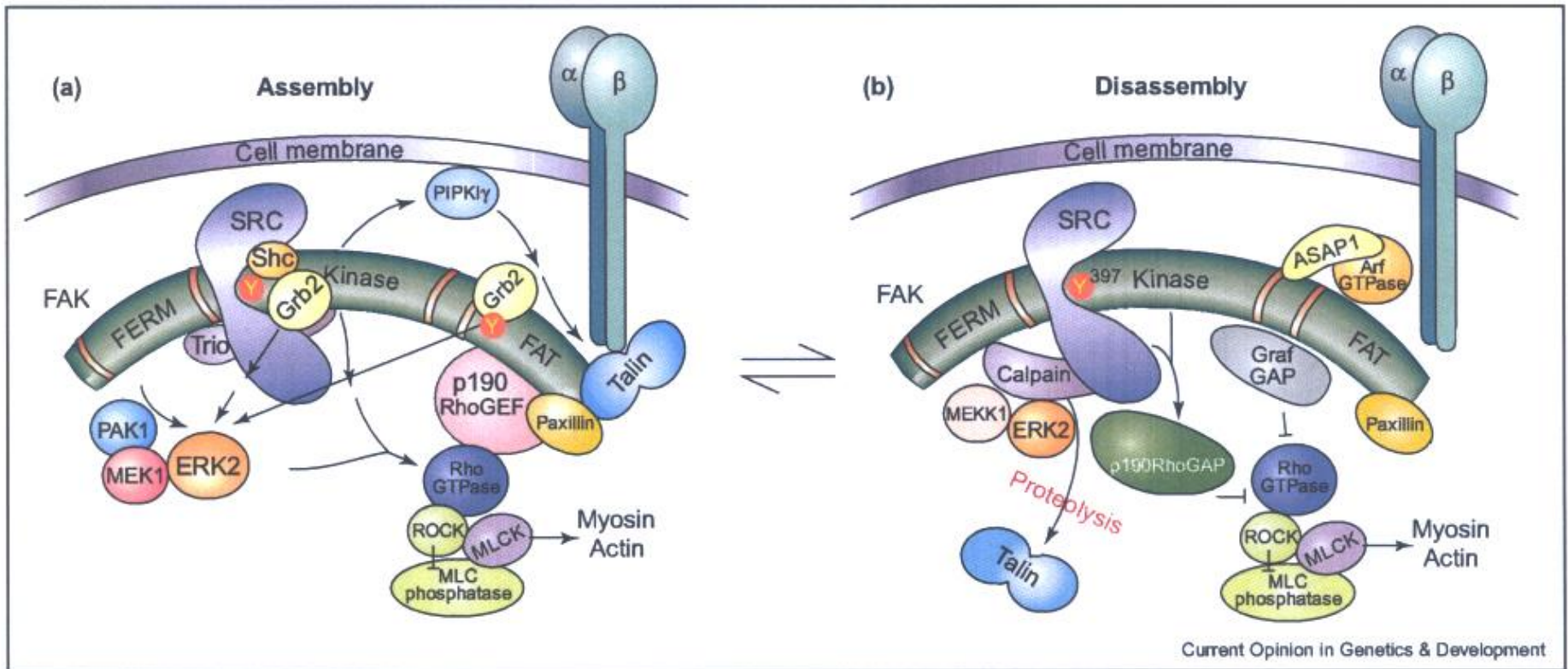
proliferation

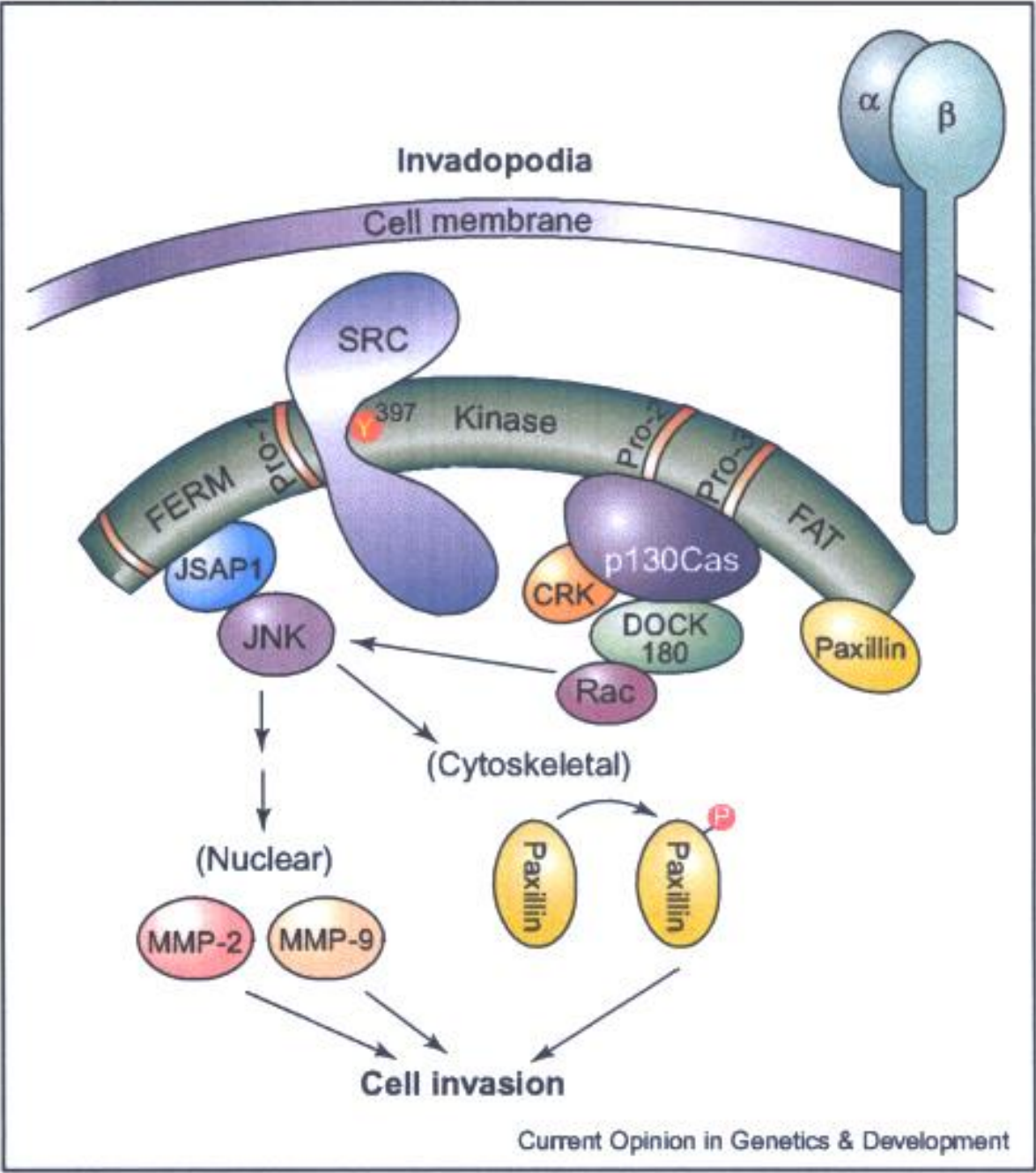


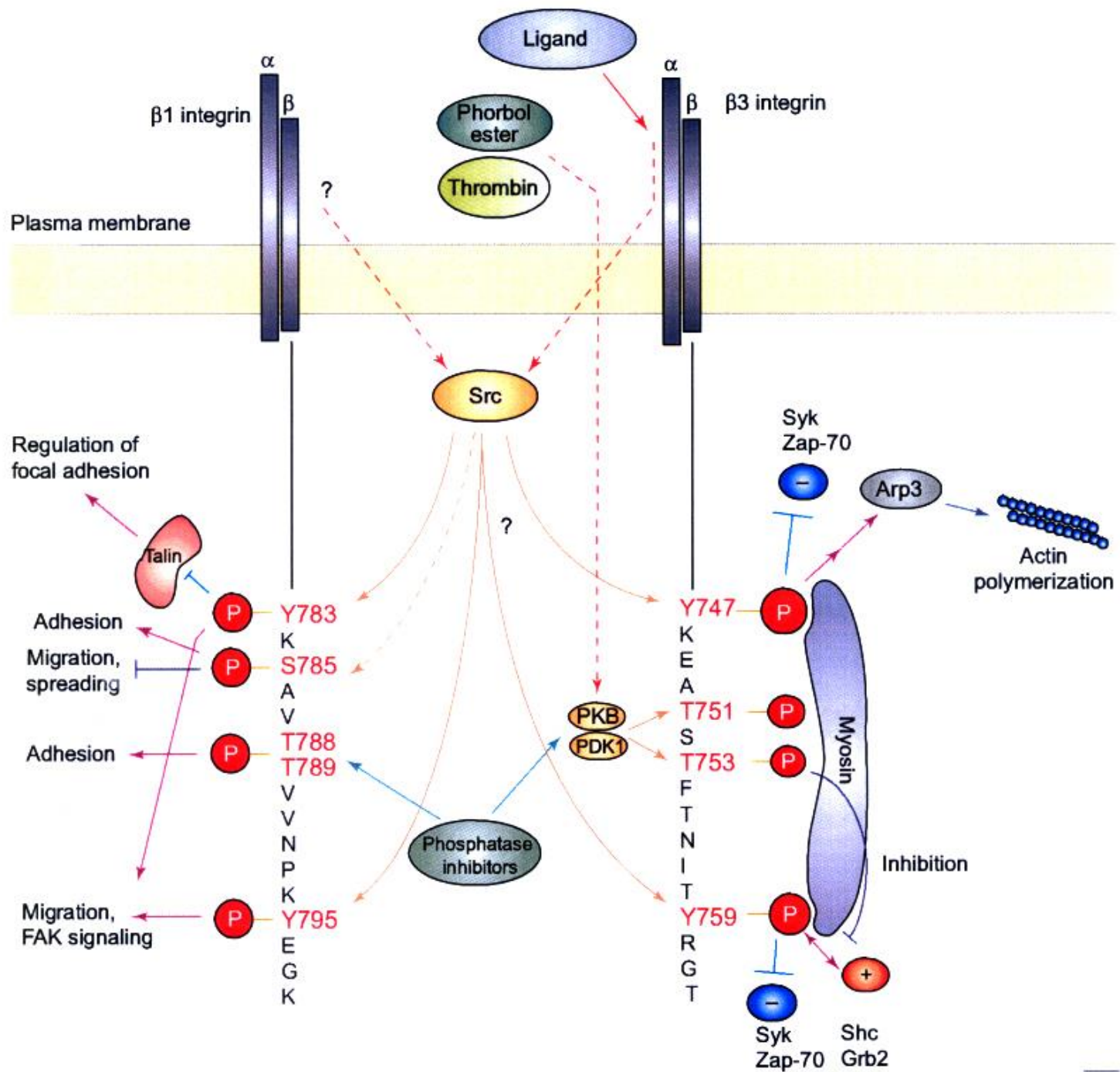
Οι ιντεγκρίνες μέσω της FAK κινάσης μπορούν να προωθήσουν τη δημιουργία ή την αποσυναρμολόγηση των θέσεων εστιακής προσκόλλησης στοχεύοντας τις πρωτεΐνες Rho



Οι ιντεγκρίνες μέσω της FAK κινάσης μπορούν να προωθήσουν τη δημιουργία ή την αποσυναρμολόγηση των θέσεων εστιακής προσκόλλησης στοχεύοντας τις πρωτεΐνες Rho.



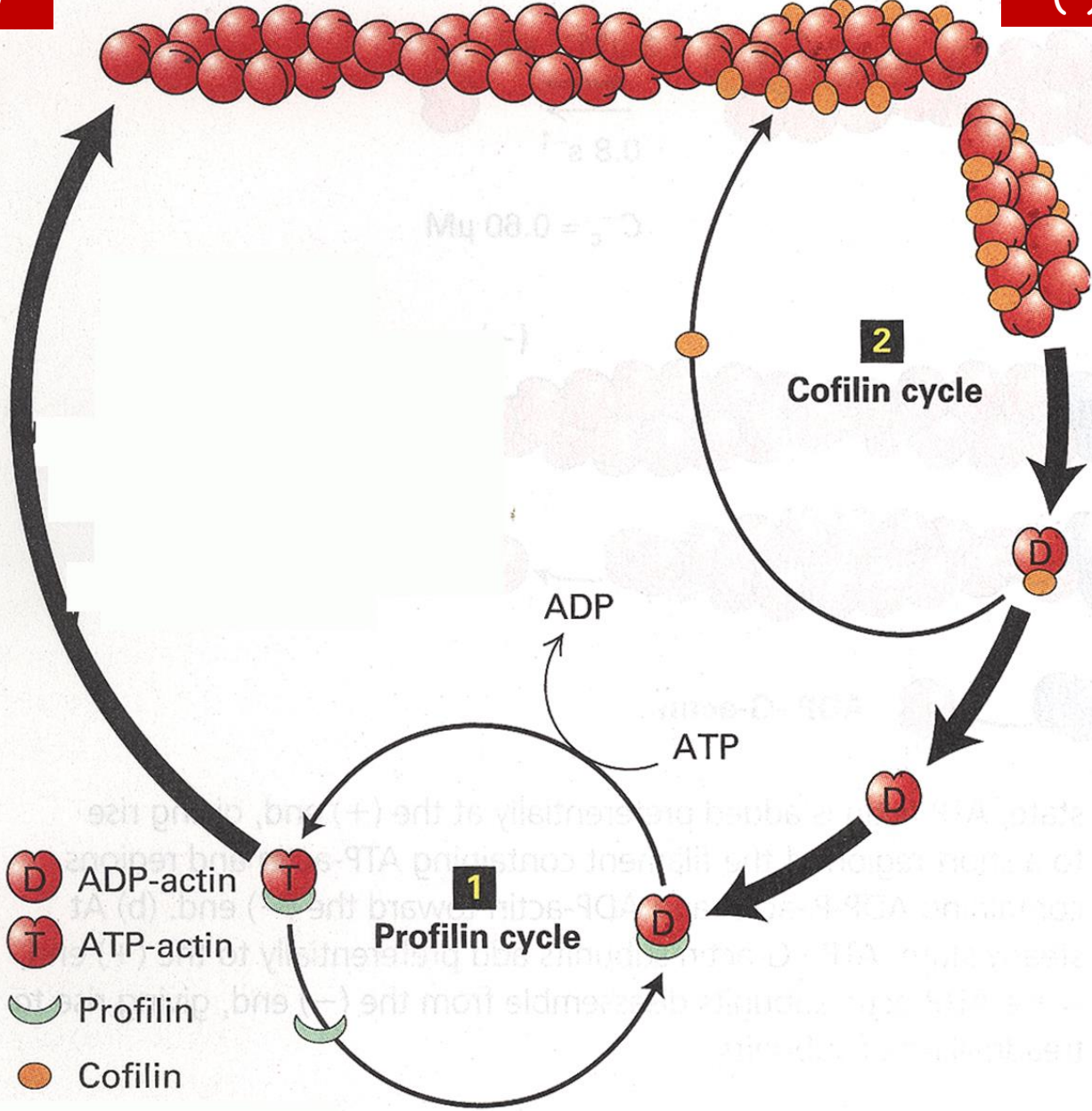




(+) άκρο

Actin-ATP Actin-ADP-P_i Actin-ADP

(-) άκρο

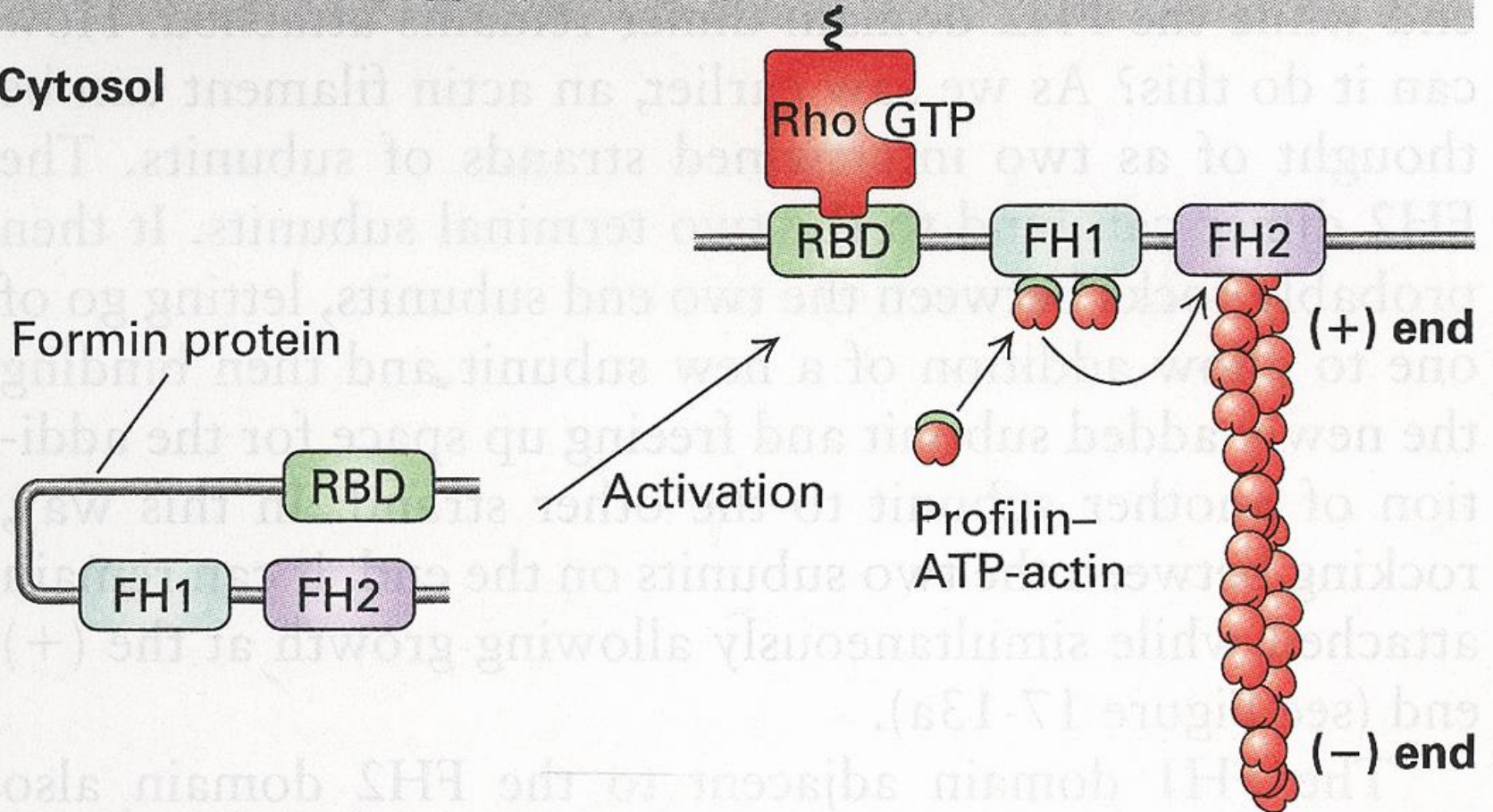


- D ADP-actin
- T ATP-actin
- Profilin
- Cofilin

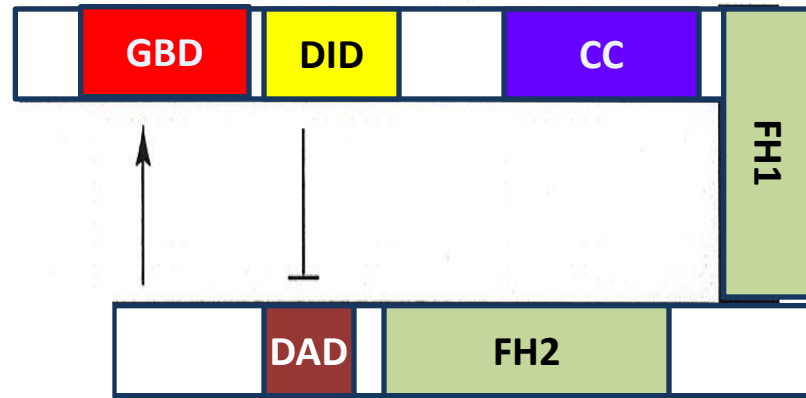
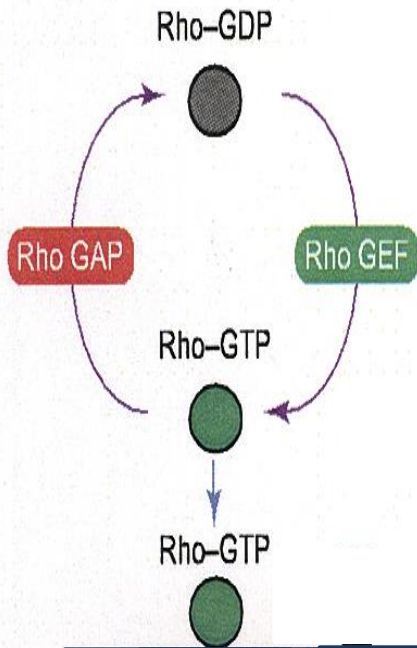
Exterior

Plasma membrane

Cytosol



mDia auto-inhibited state



mDia



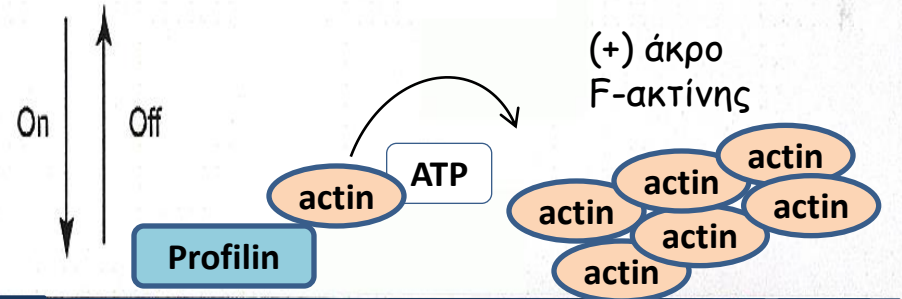
GTPase binding domain

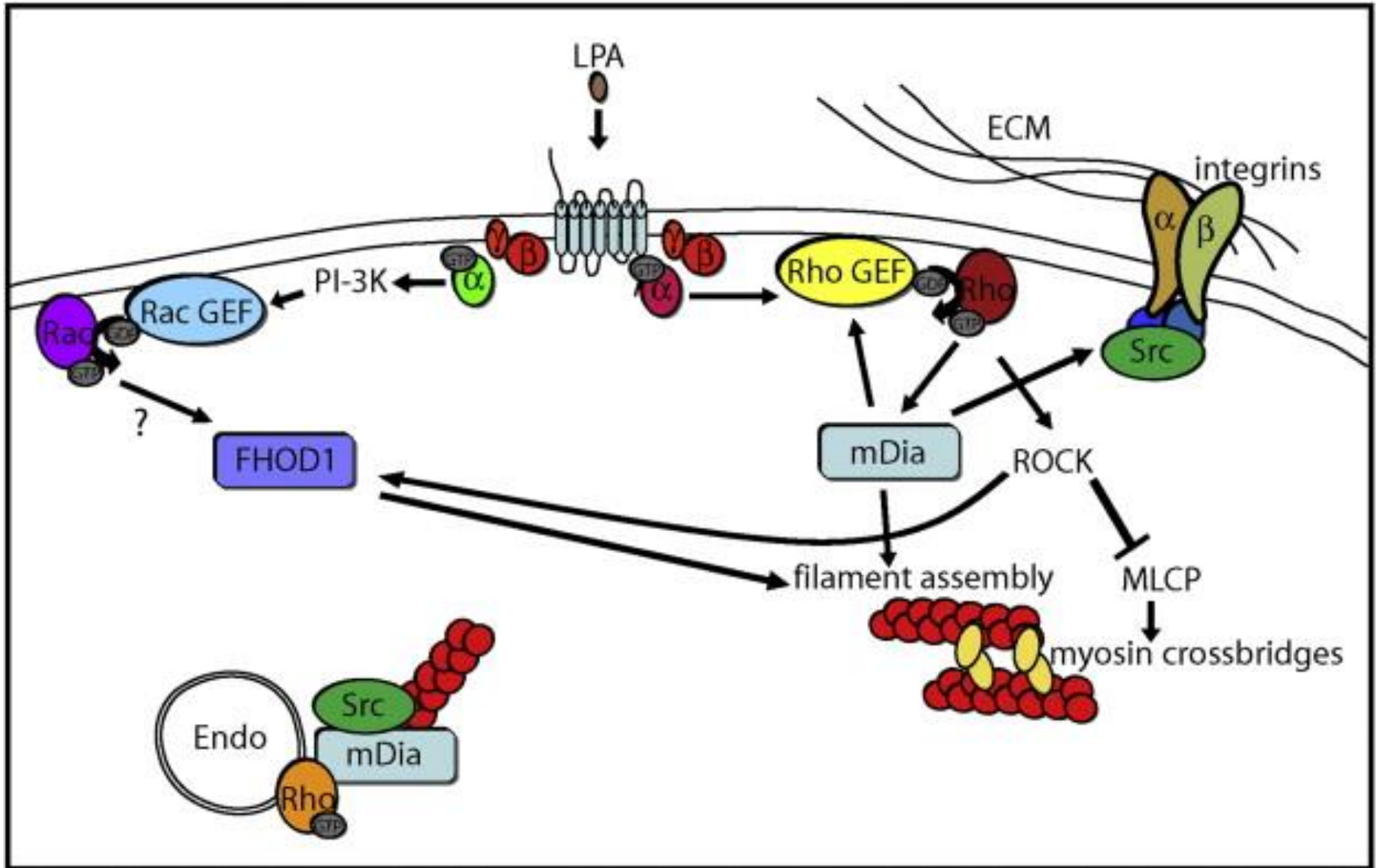
Diaphanous inhibitory domain

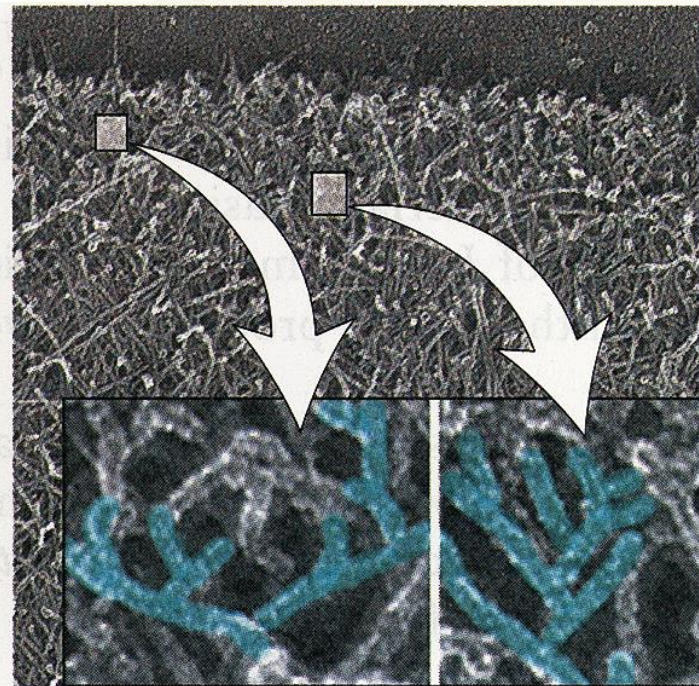
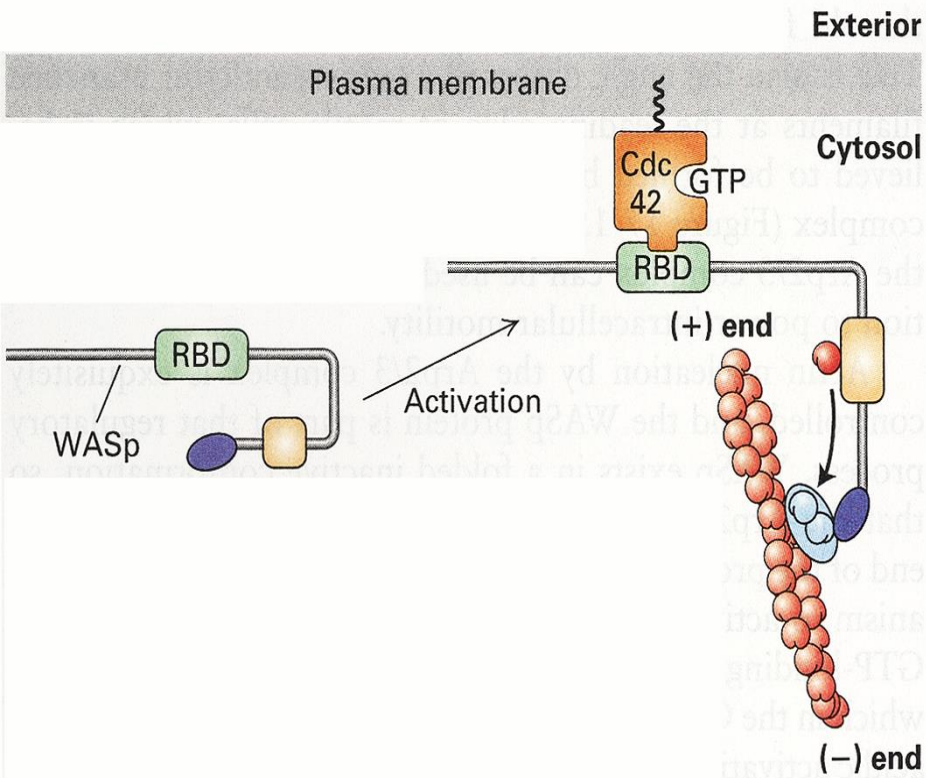
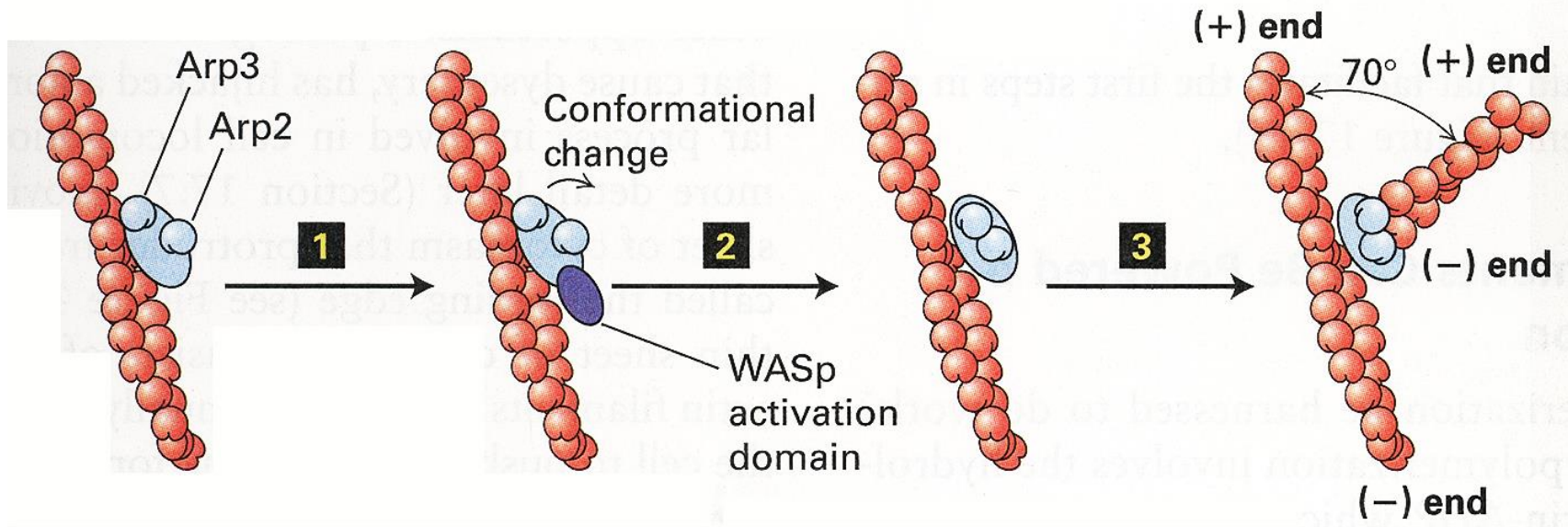
coiled coil domain

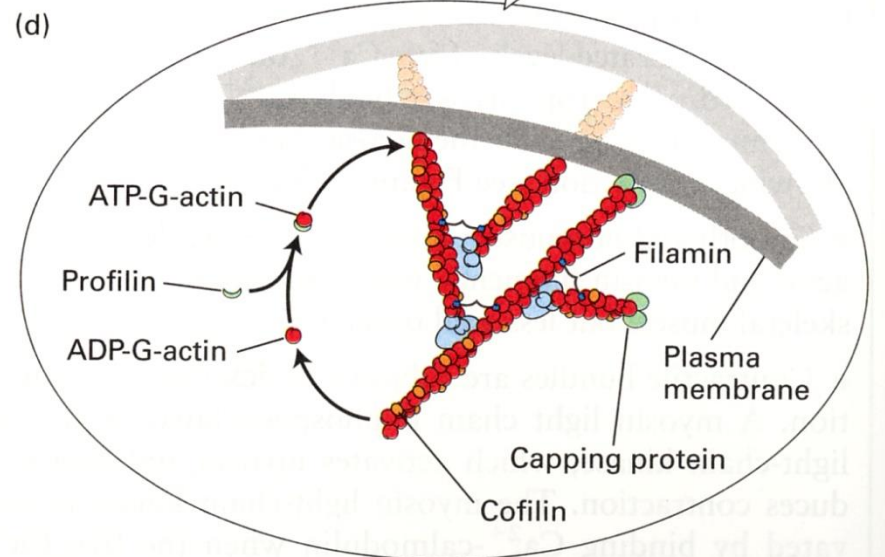
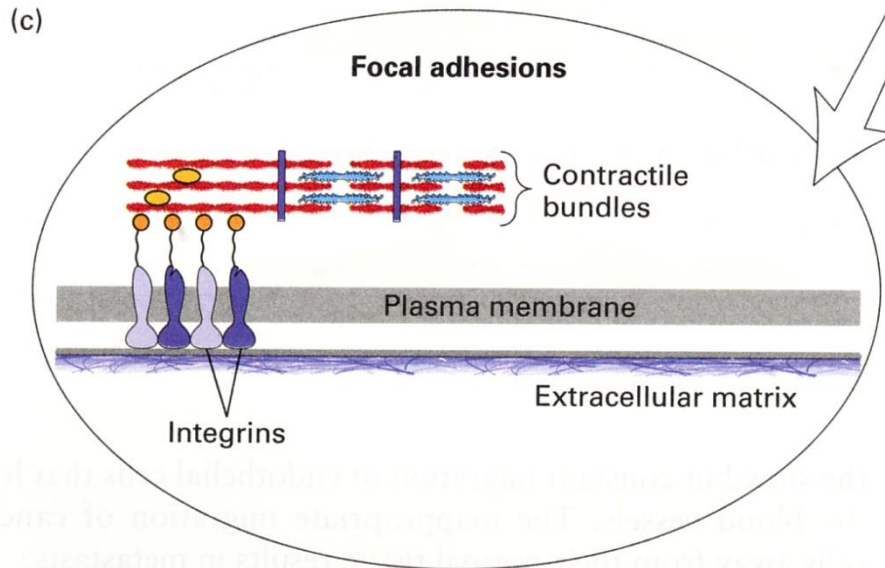
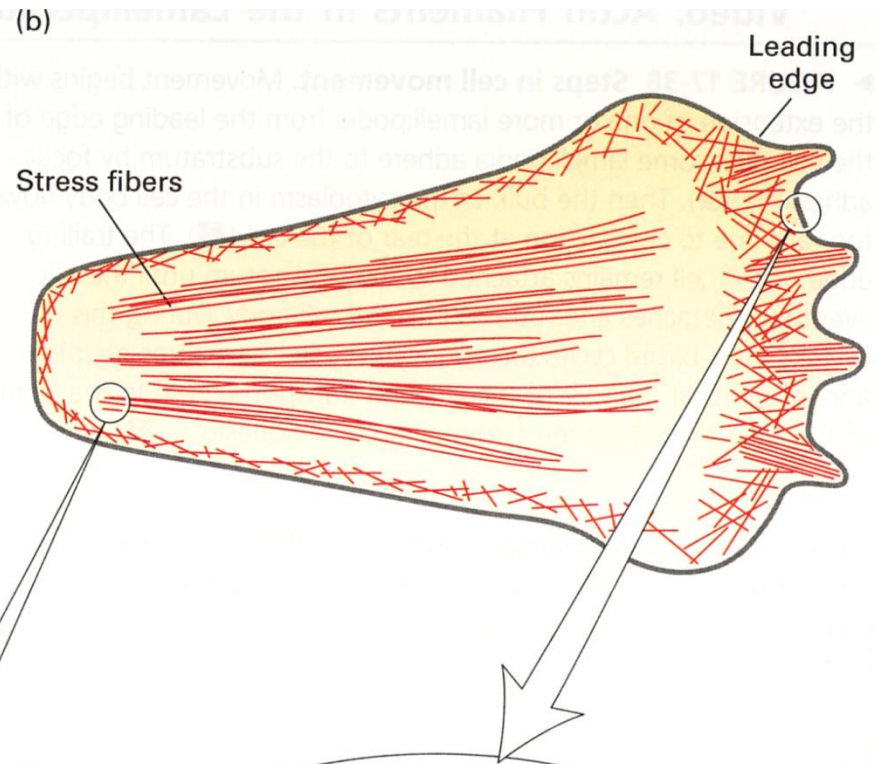
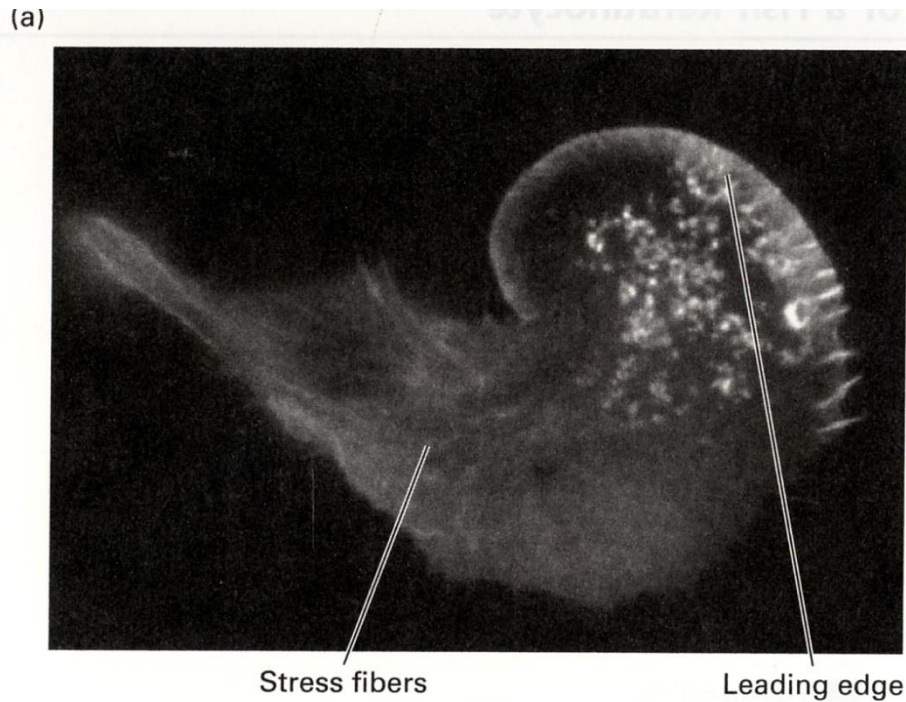
Formin homology domain 1 (Proline rich)

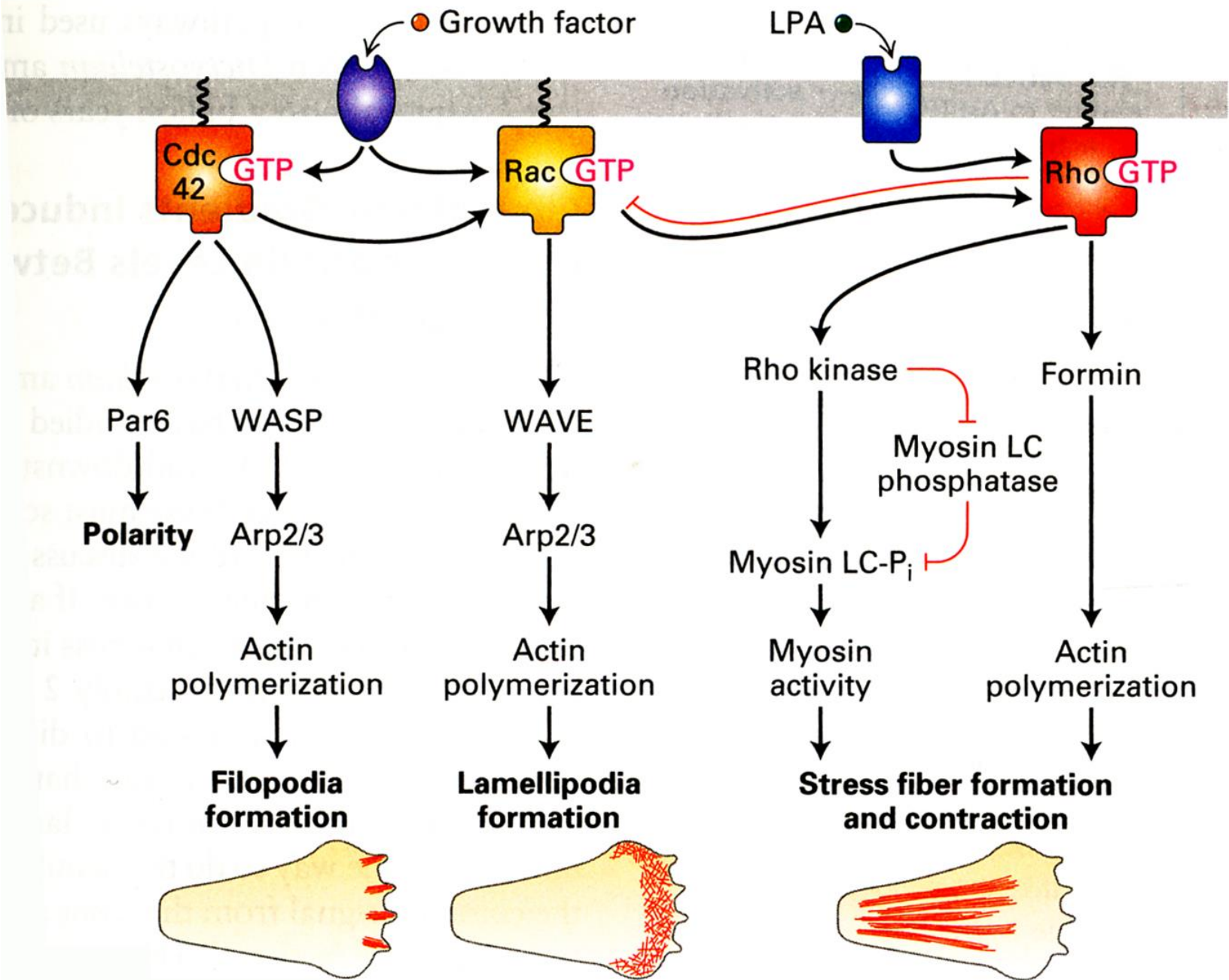
Diaphanous autoregulatory domain



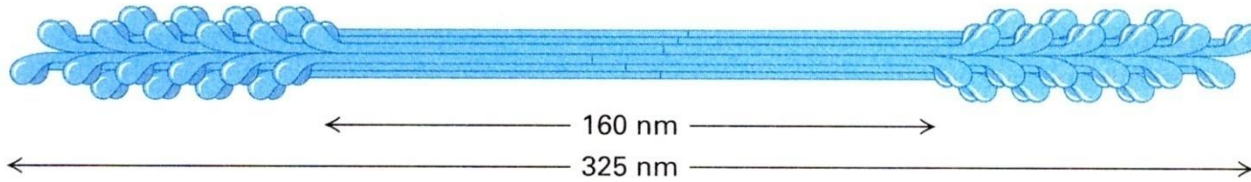




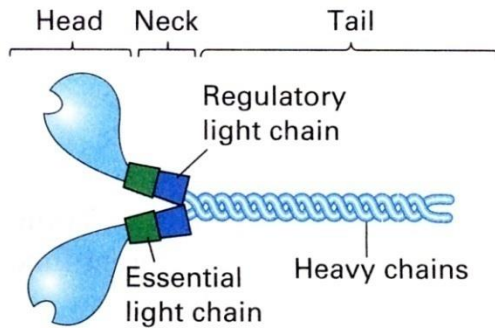




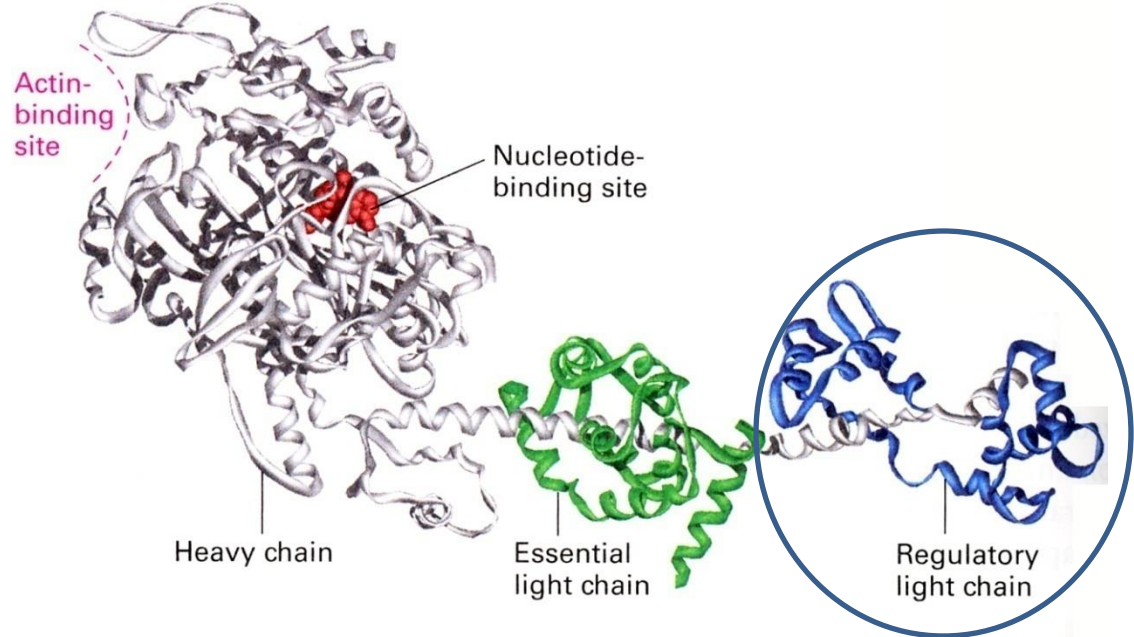
(a)



Μυοσίνη II

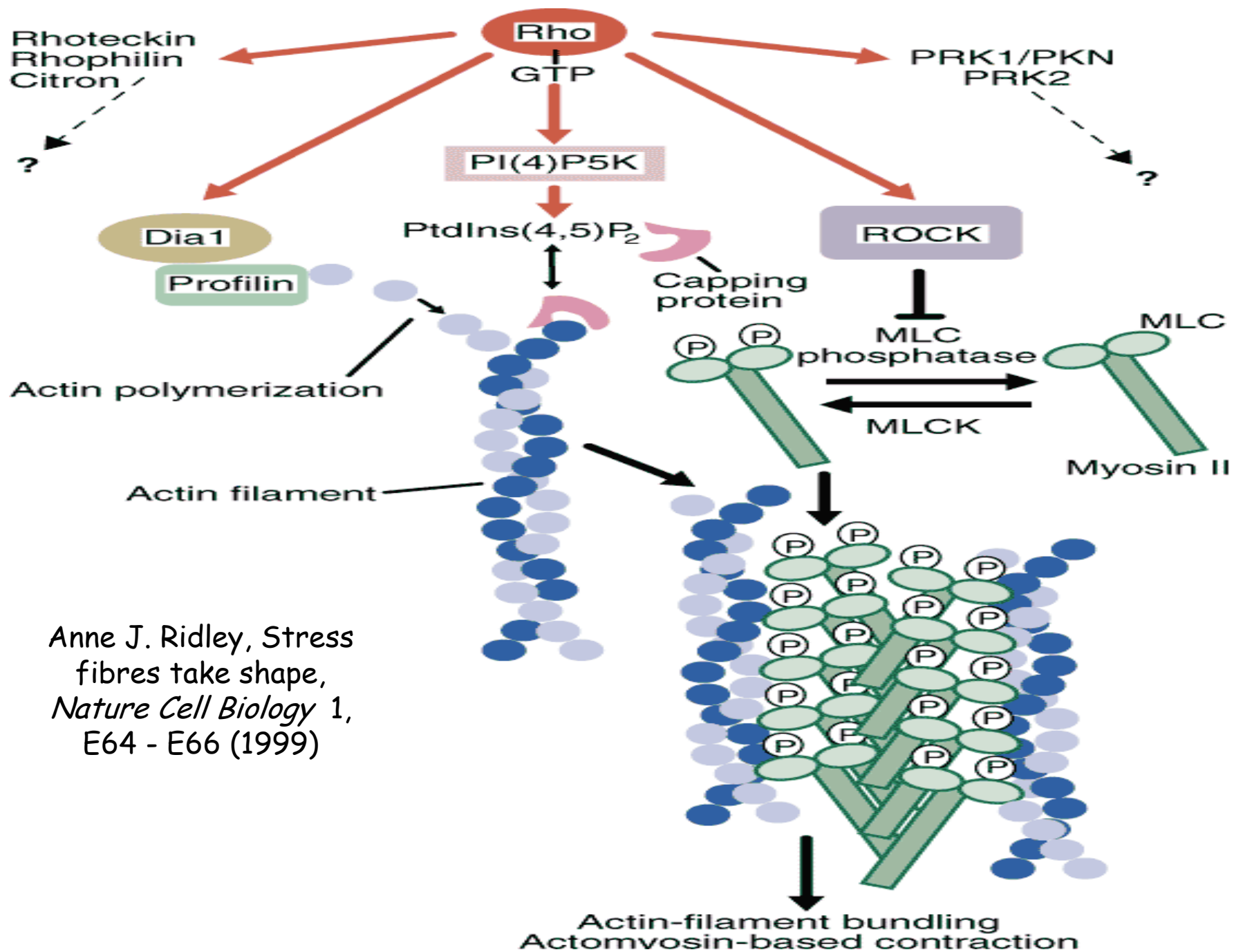


(c) Head and neck domain



Όταν η R-MLC δεν είναι φωσφορυλιωμένη, ο κύκλος της ΑΤΡάσης της μυοσίνης II είναι ανενεργός.

Τα λεία μυϊκά κύτταρα ή τα μη μυϊκά κύτταρα συσπώνονται όταν η R-MLC φωσφορυλιώνεται από την MLC κινάση, η οποία ενεργοποιείται από το Ca^{2+} από την ROCK/φωσφατάση της MLC

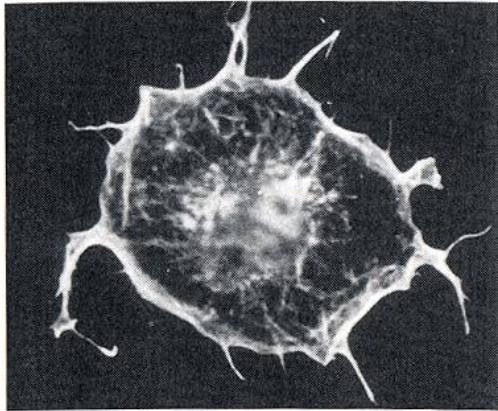


Anne J. Ridley, Stress
 fibres take shape,
Nature Cell Biology 1,
 E64 - E66 (1999)

Cdc42



Filopodia

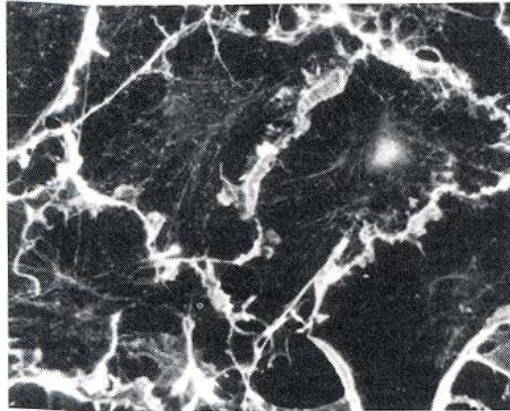


20 μm

Rac



Lamellipodia

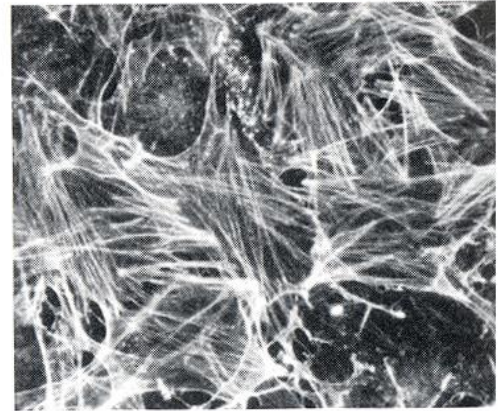


20 μm

Rho



Focal adhesions, stress fibers



20 μm