CURSO DE BIOLOGÍA CELULAR 2021

Señalización celular II

FACULTAD DE CIENCIAS
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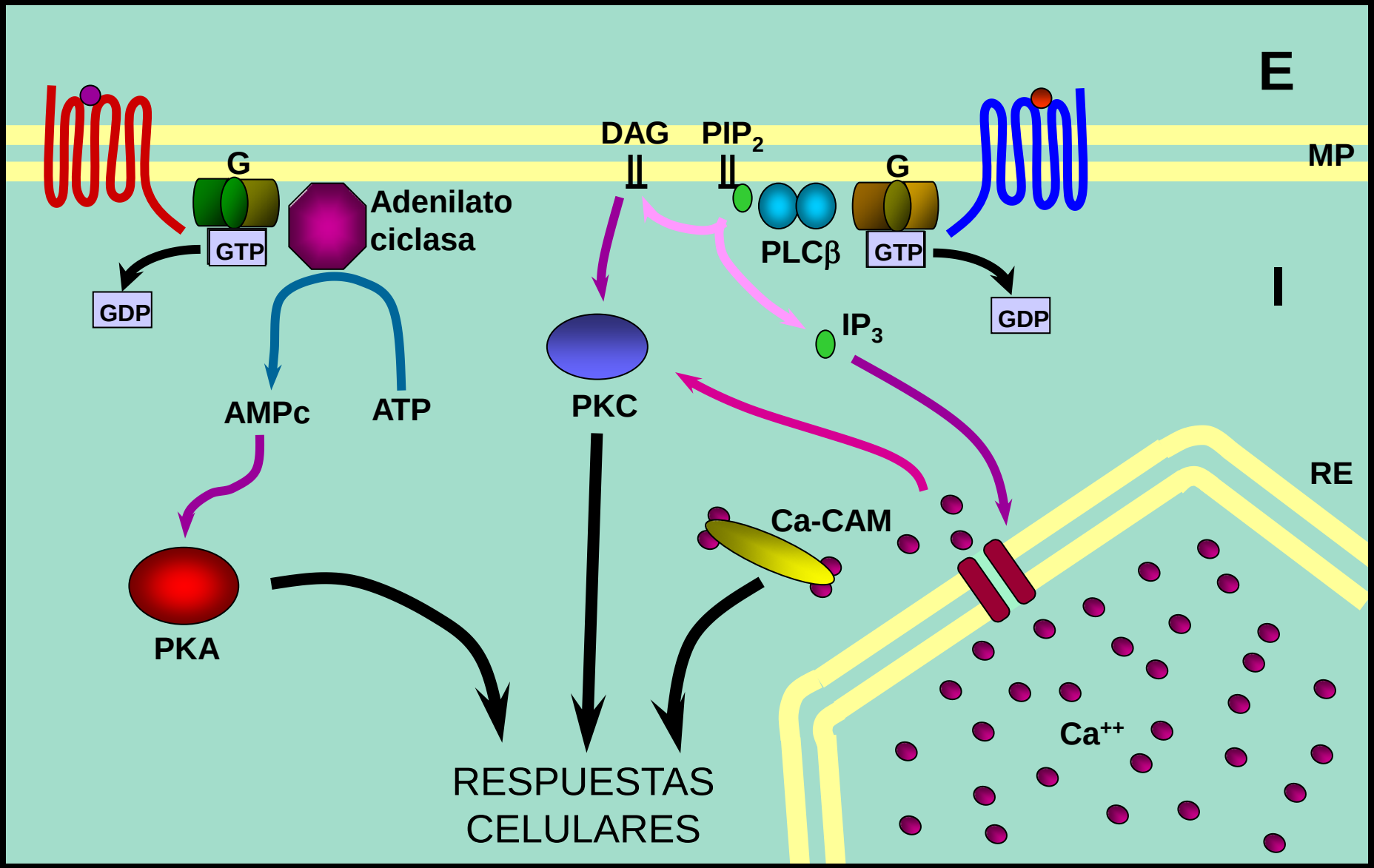
UNIVERSIDAD DE LA REPÚBLICA
URUGUAY

A - Activación de proteínas G

B - Interacciones moleculares

C - Segundos mensajeros

D - Fosforilación de proteínas



Propiedades de los segundos mensajeros:

- Son moléculas pequeñas, difunden rápido

- Son producidos rápidamente (precursores o stock abundantes)

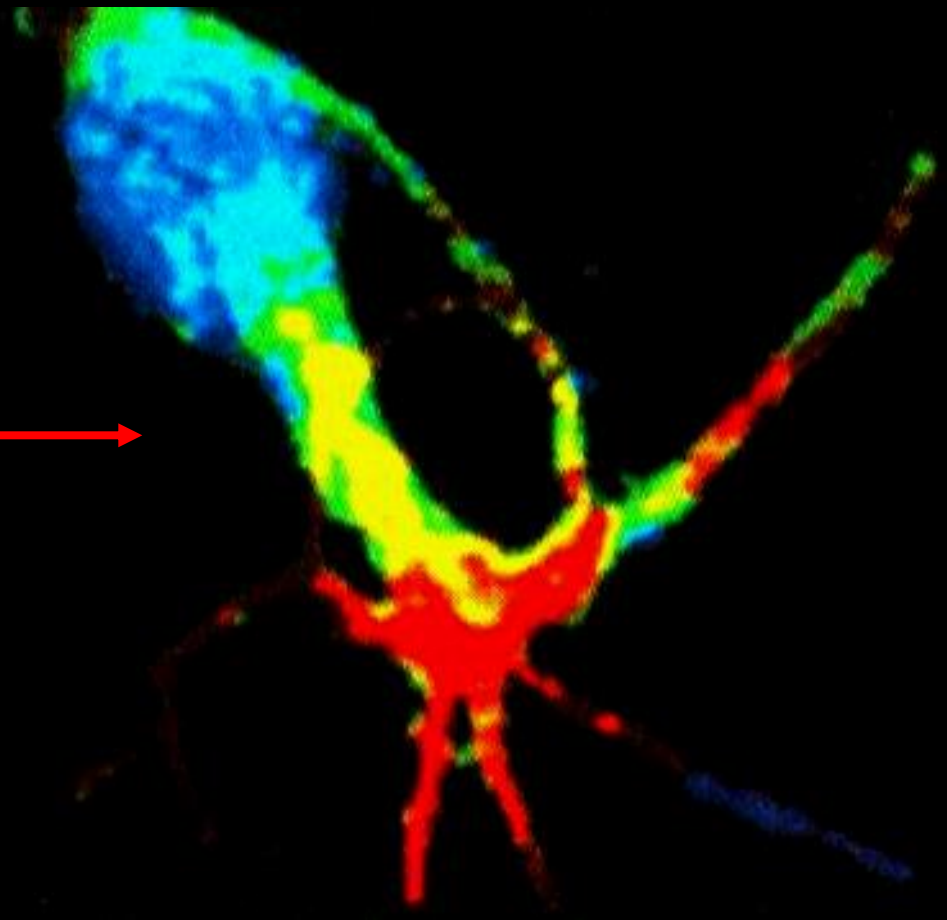
- Son eliminados rápidamente (degradación o remoción)

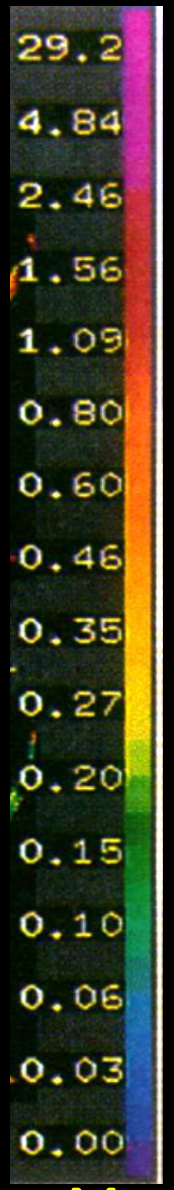
- Interactúan con proteínas efectoras

Segundos mensajeros: concentración de AMPc

FICRhR

Serotonina ⟶

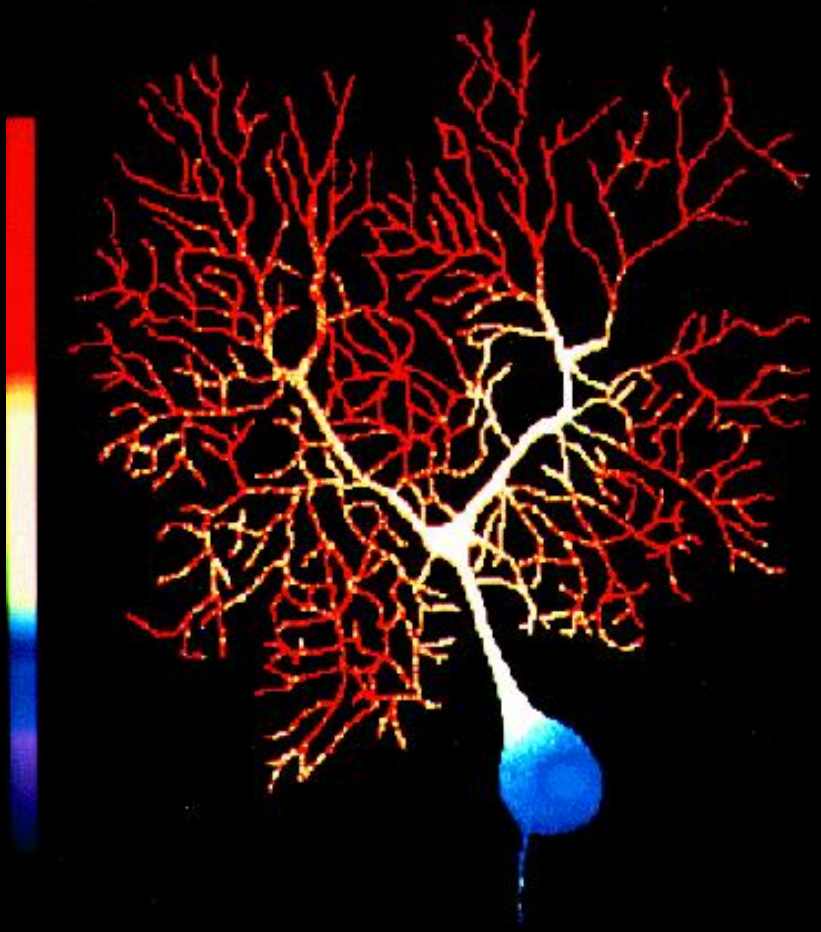




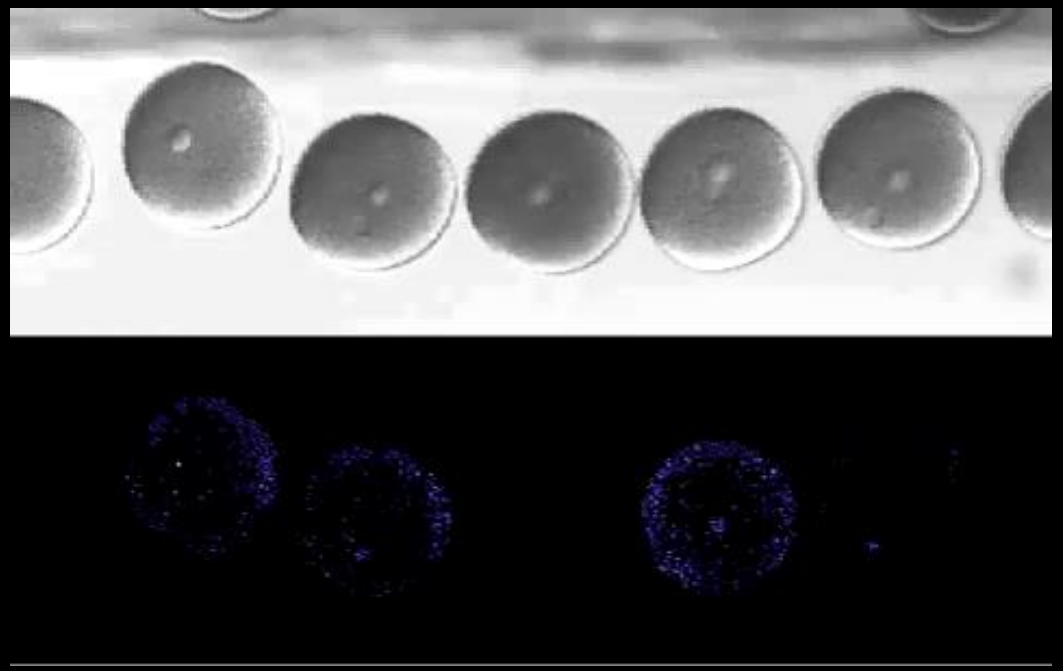
20-50 seg

$> 10^{-6}$ M

Segundos mensajeros: Detección fluorescente de calcio



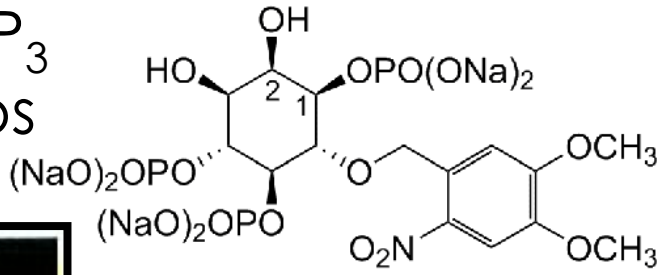
Neurona de Purkinje



Ovocitos de erizo de mar

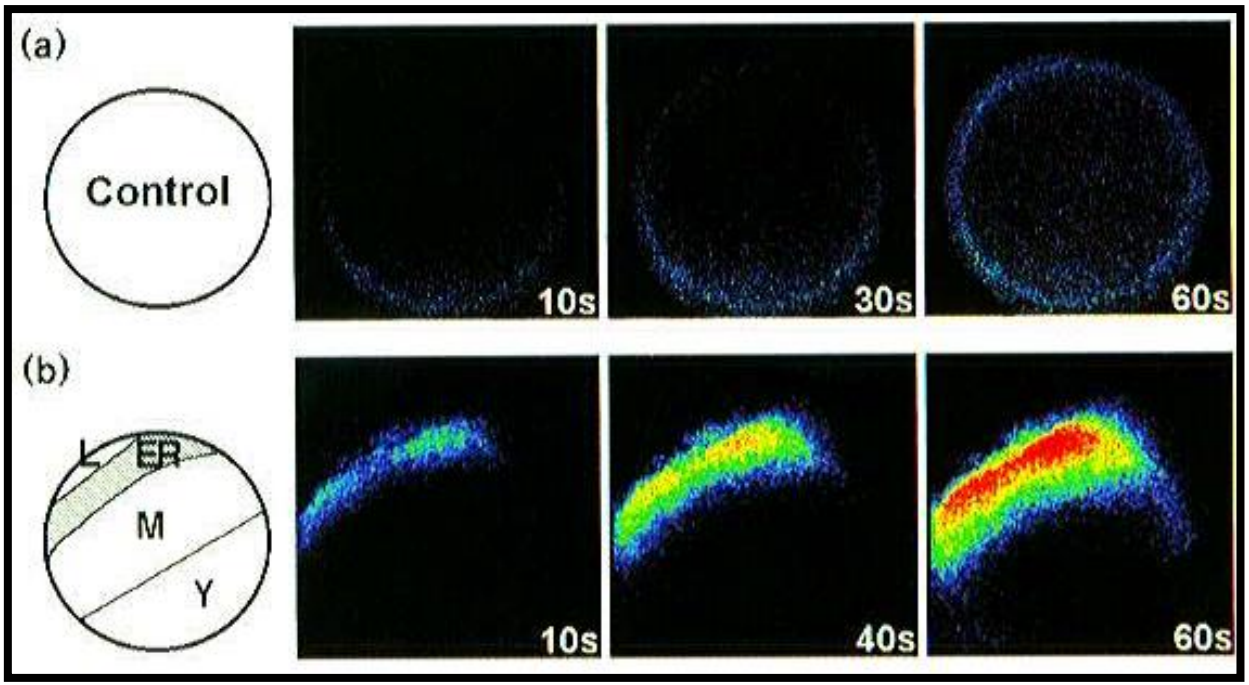
https://youtu.be/BH06WgFua_4

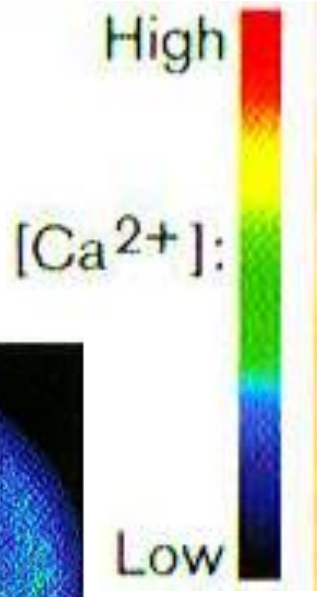
Liberación de Ca++ provocada por IP_3 en ovocitos de *Xenopus* estratificados

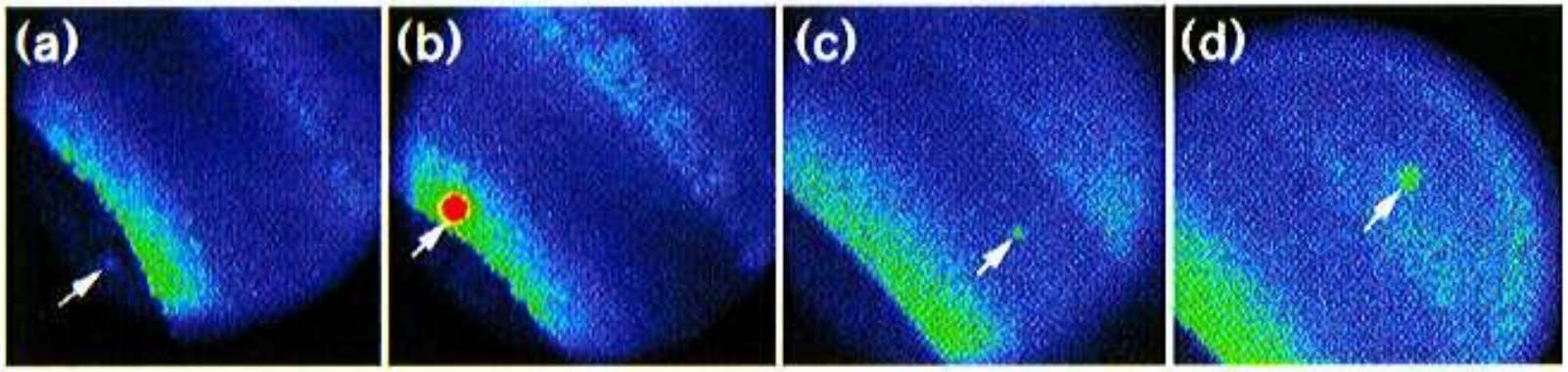


"Caged IP3"

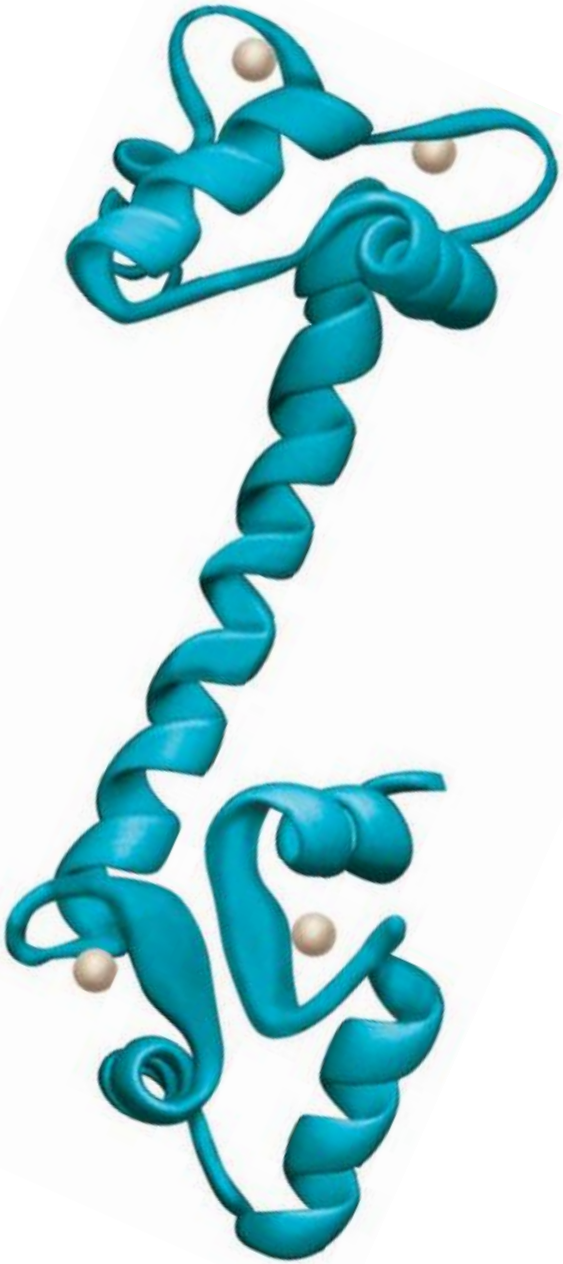
6-O-(2-Nitro-45-Dimethoxy)benzyl)-myo-Inositol 145 Trisphosphate



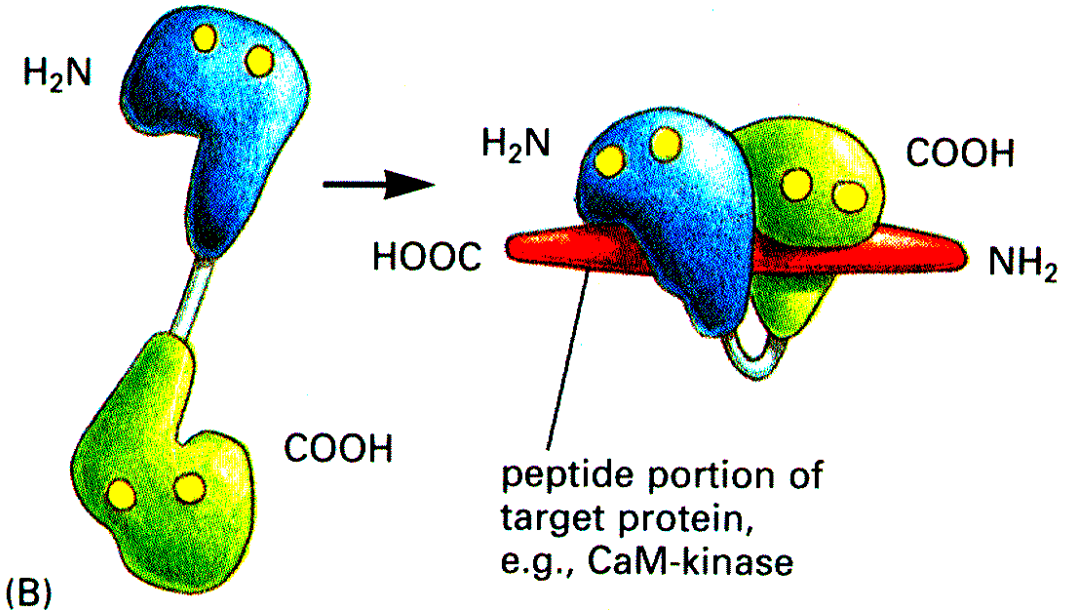




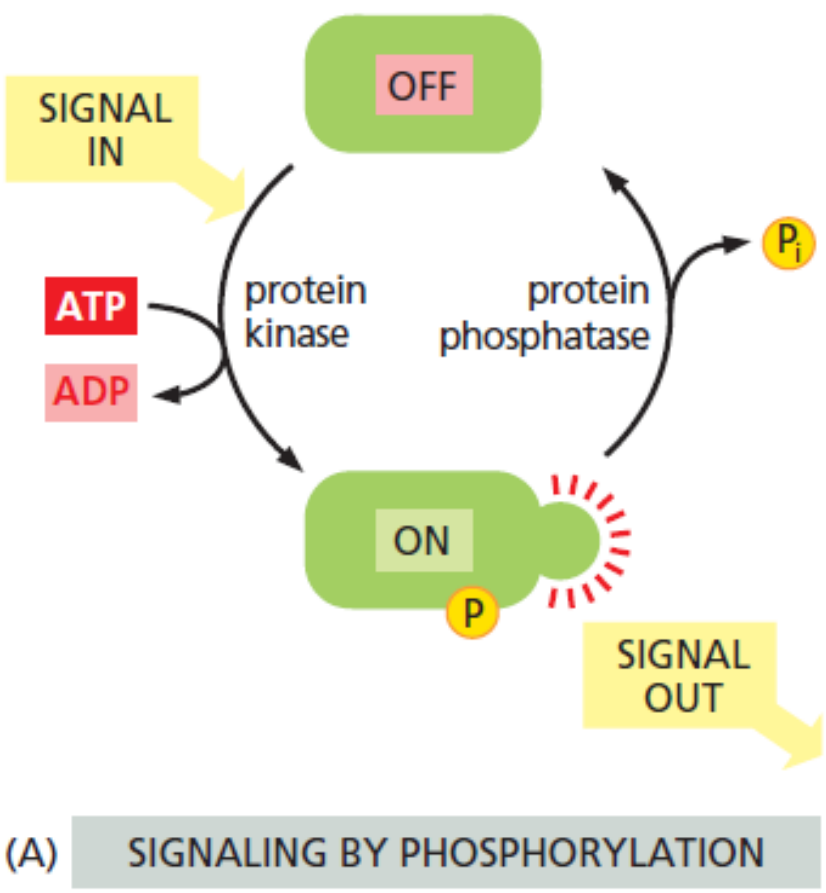
Segundos mensajeros: El calcio y la calmodulina



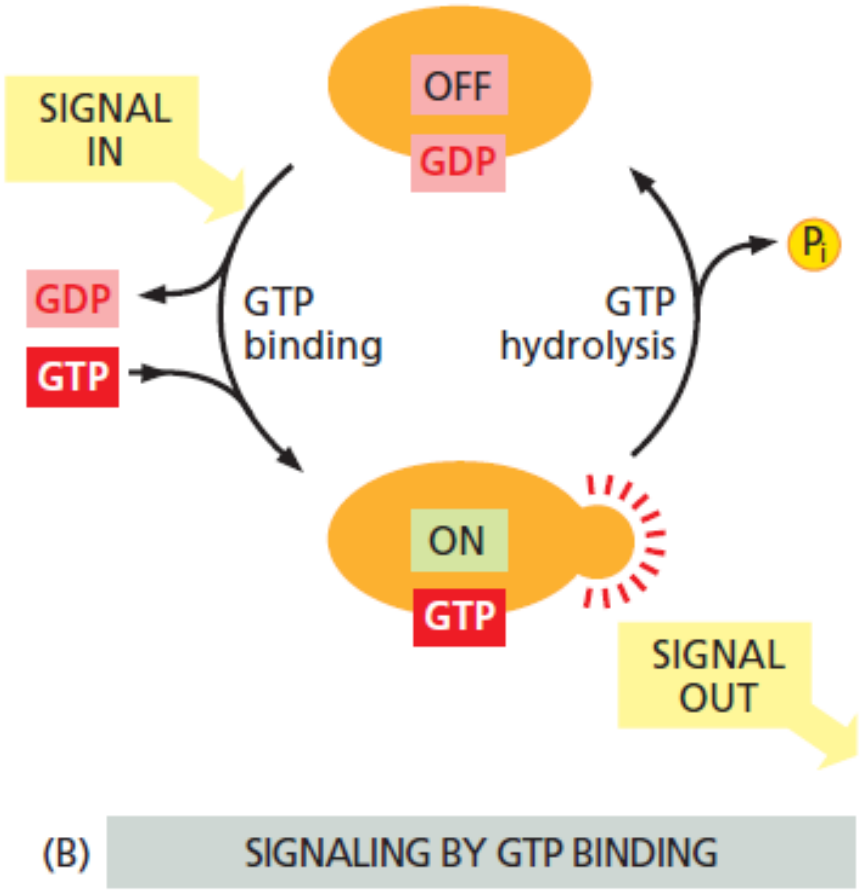
Ca^{2+}-CaM



Switches moleculares: fosforilación y proteínas G

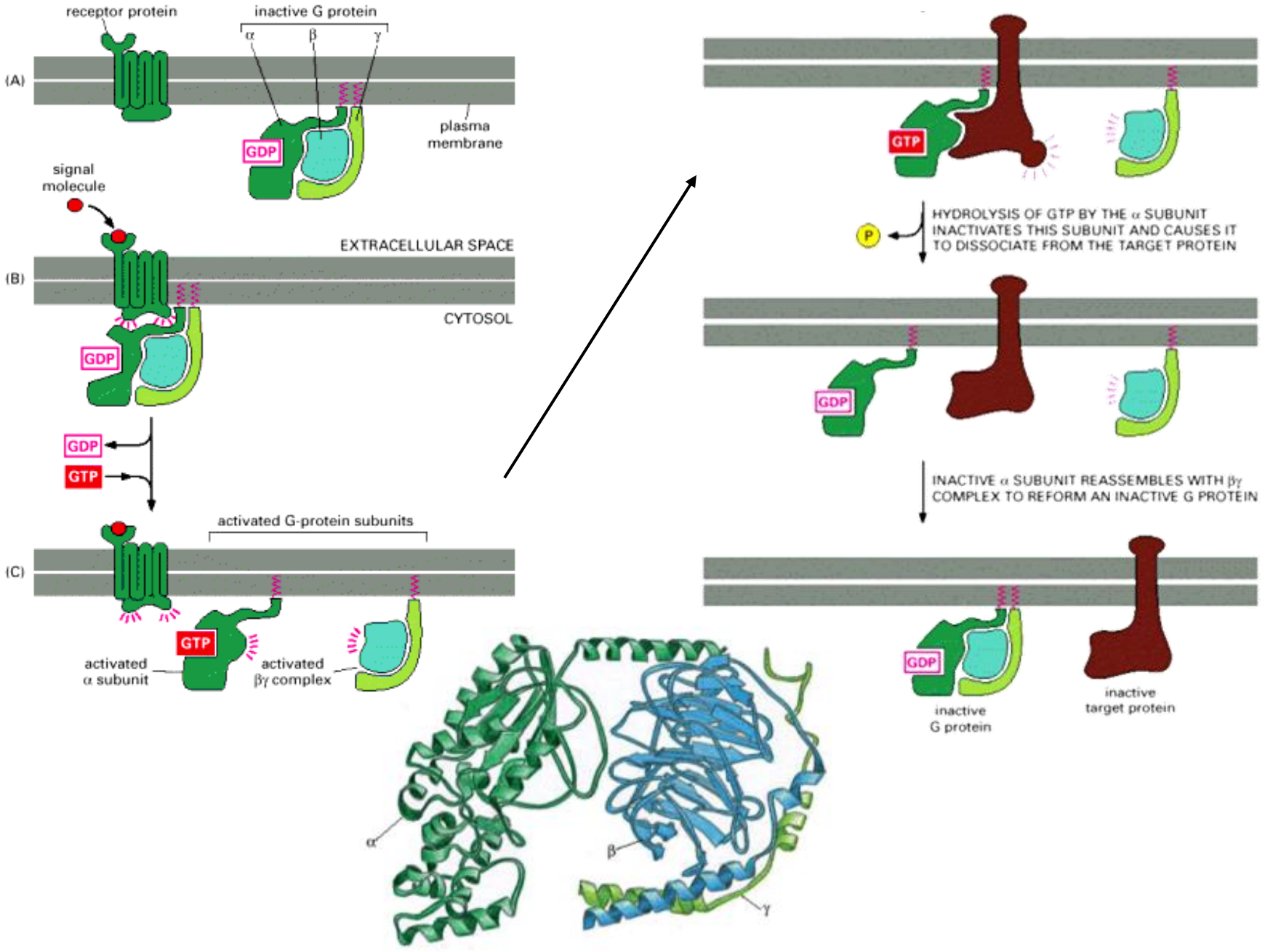


(A) SIGNALING BY PHOSPHORYLATION

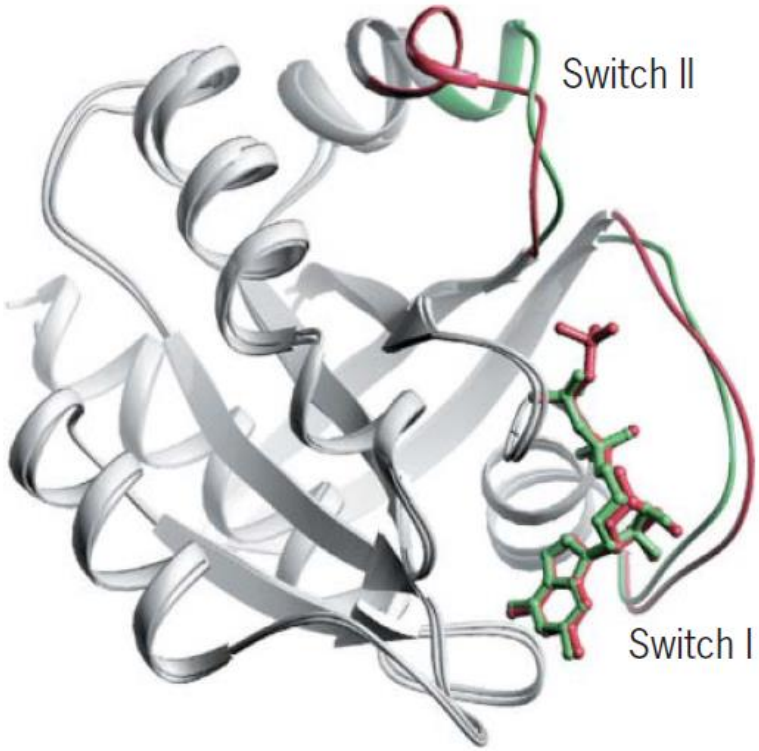


(B) SIGNALING BY GTP BINDING

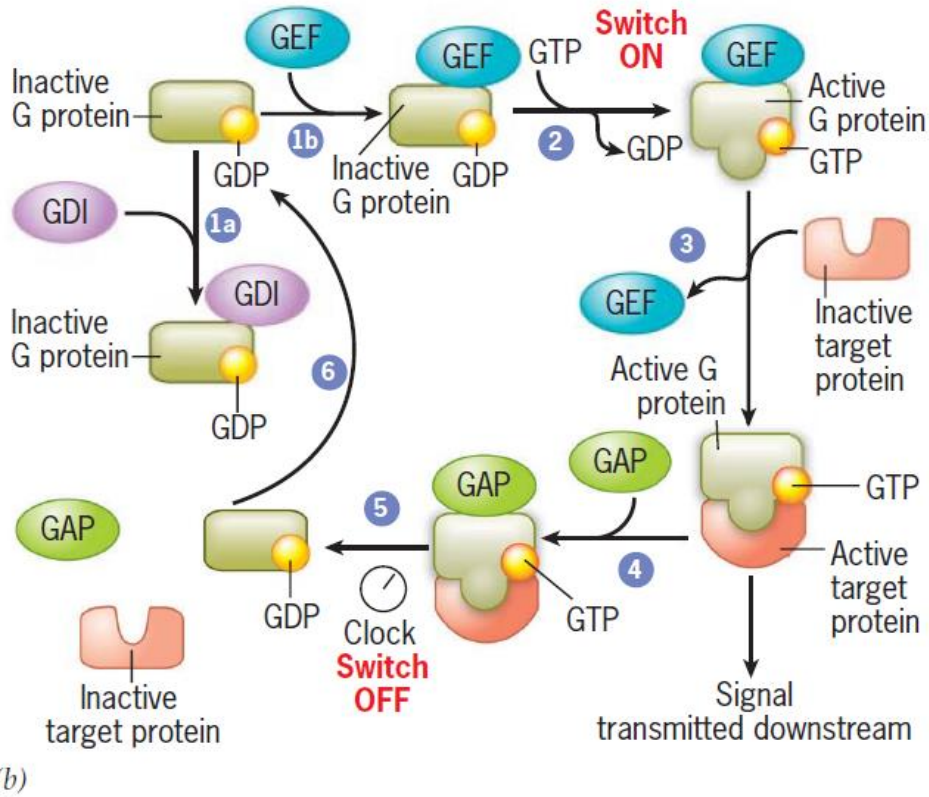
Proteínas G heterotriméricas



Proteínas G monoméricas



Ras

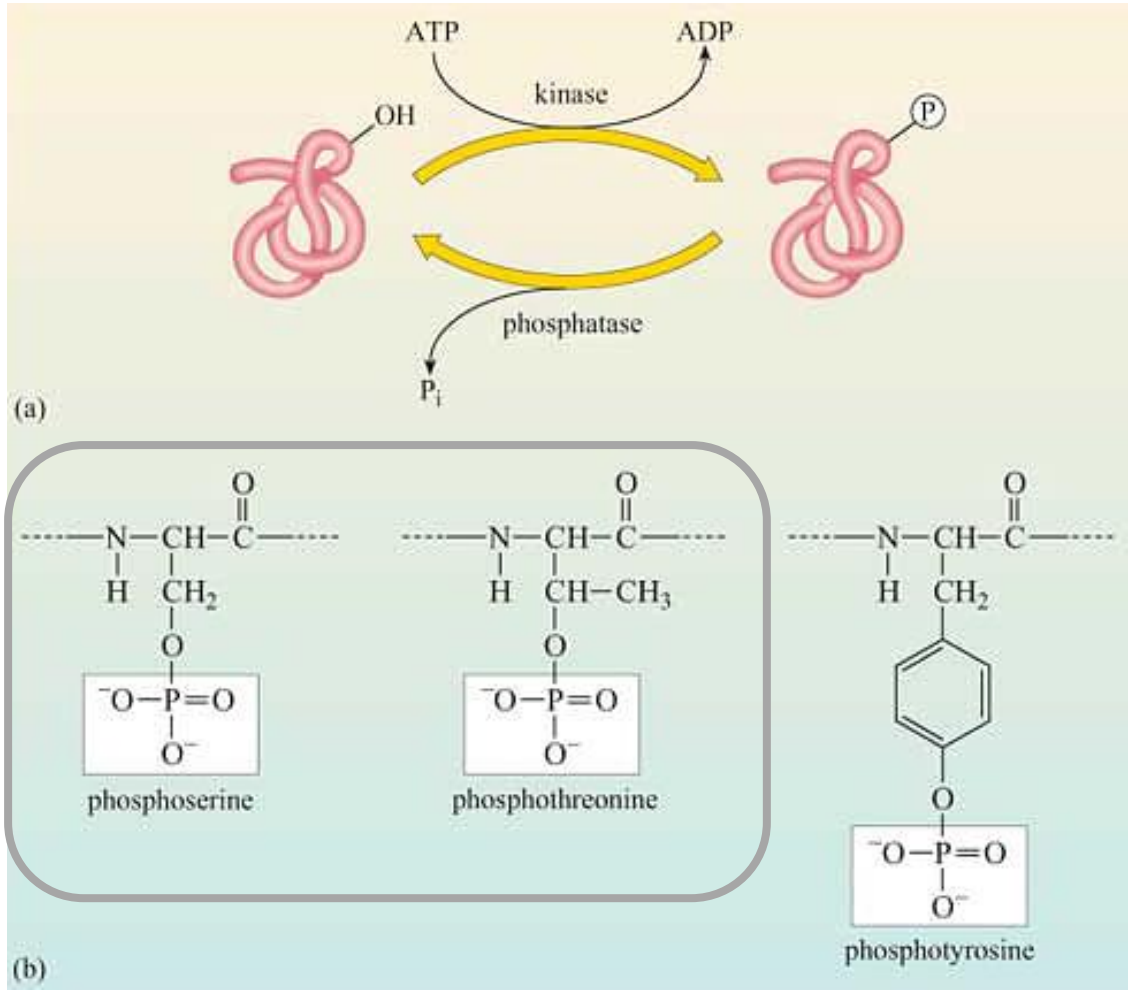


GEF: factor de intercambio de GTP

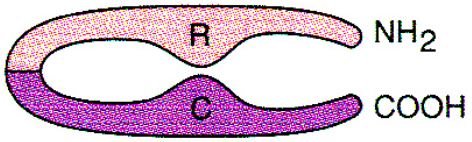
GAP: proteína activadora de GTPasa

GDI: inhibidor de la disociación de GDP

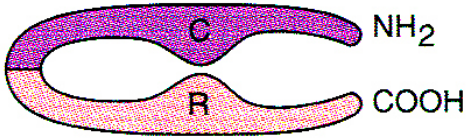
Fosforilación de proteínas



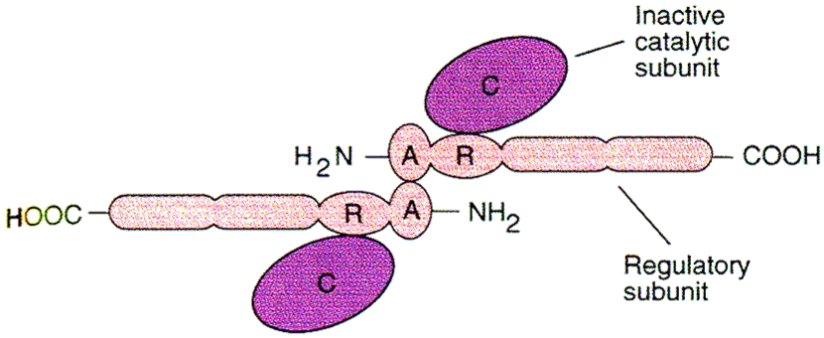
Protein kinase C

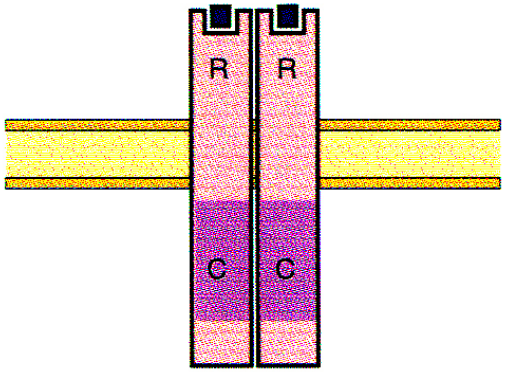


Ca^{2+}/Calmodulin-dependent protein kinase

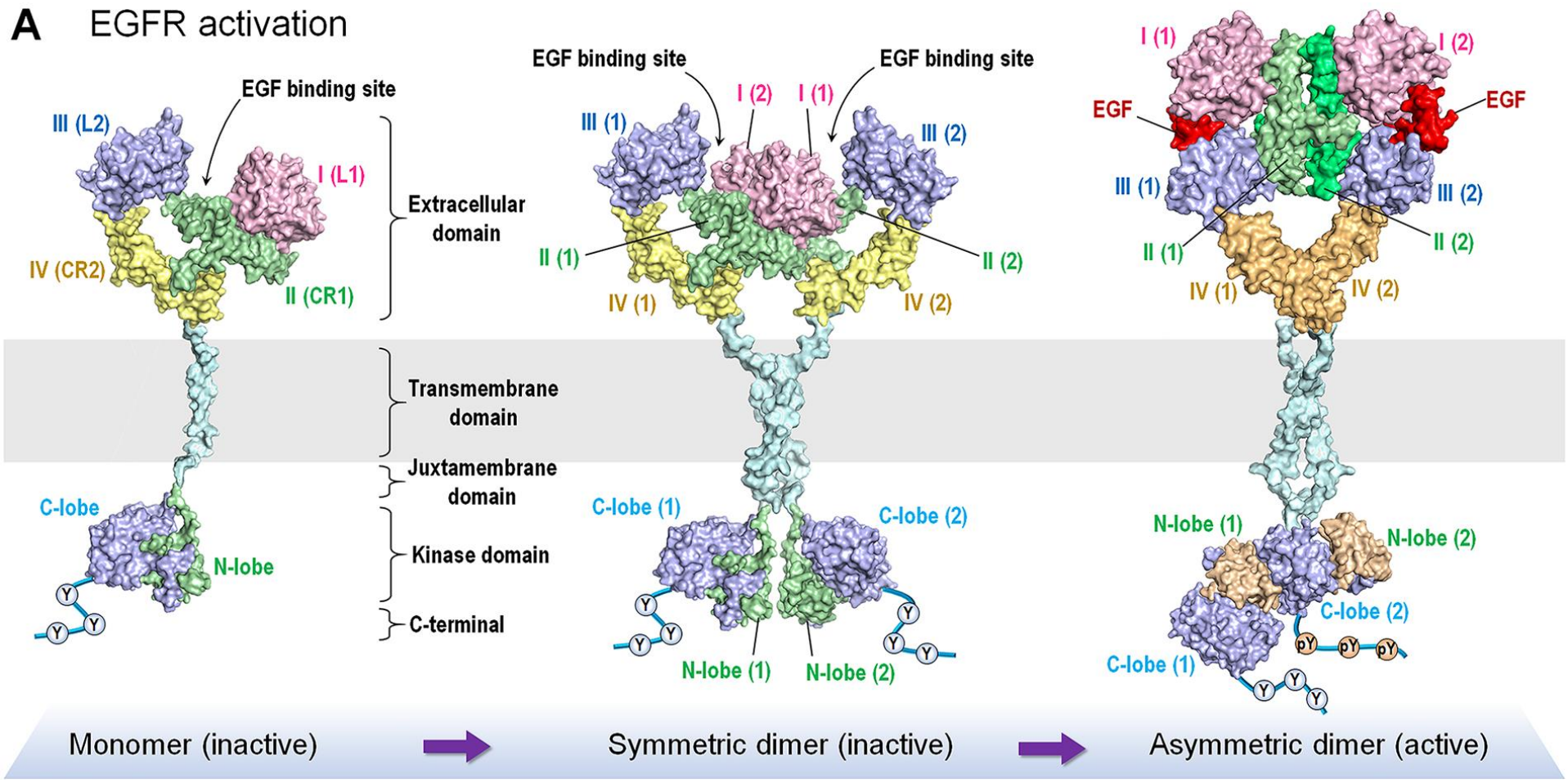


Tyrosine protein kinase





Activación de receptores tirosina-kinasa: EGFR

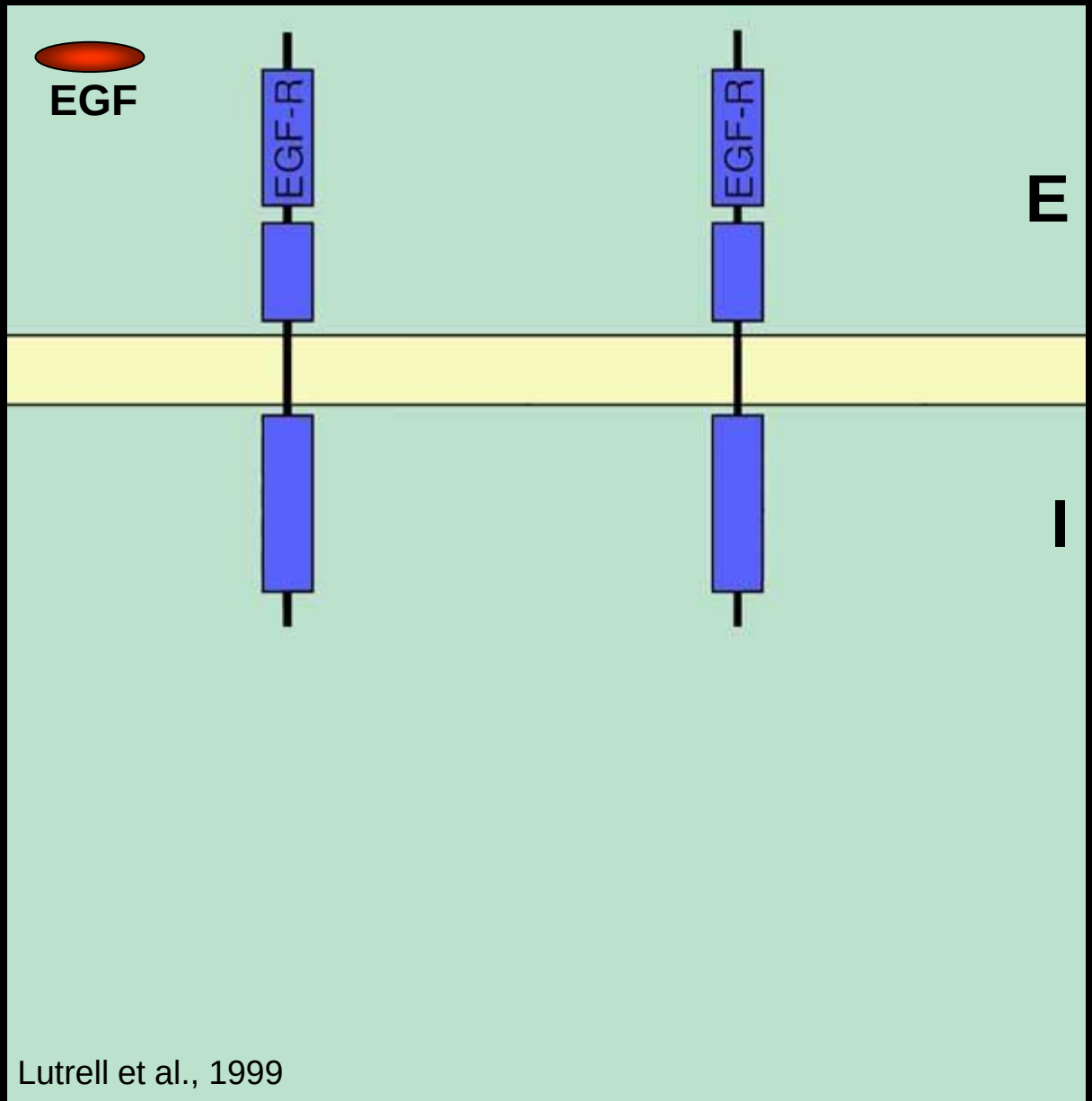


Nussinov et al., 2019; https://doi.org/10.1371/journal.pcbi.1006658

Activación de receptores tirosina-quinasa

Señal

Receptor

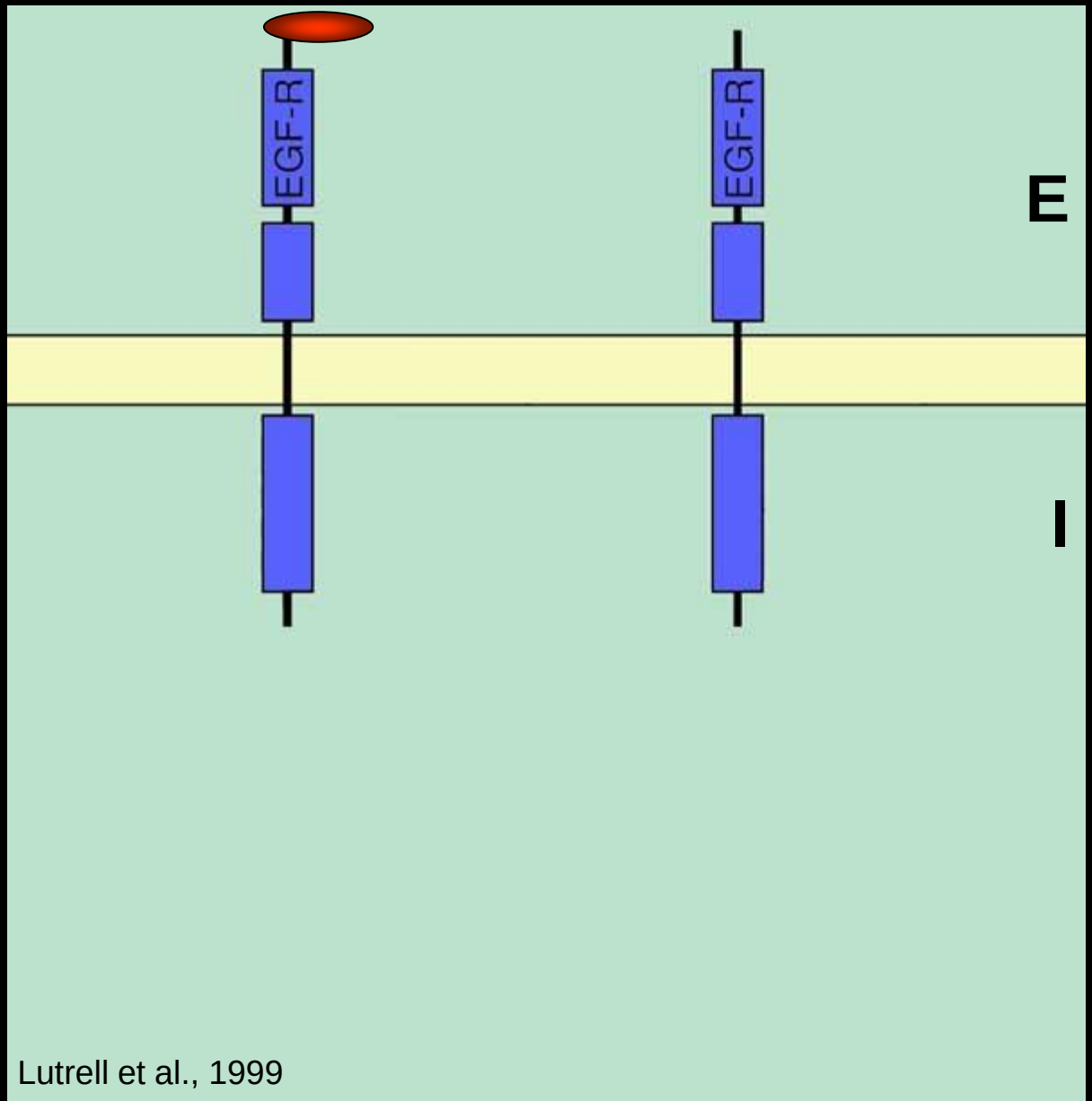


Lutrell et al., 1999

Activación de receptores tirosina-quinasa

Señal

Receptor



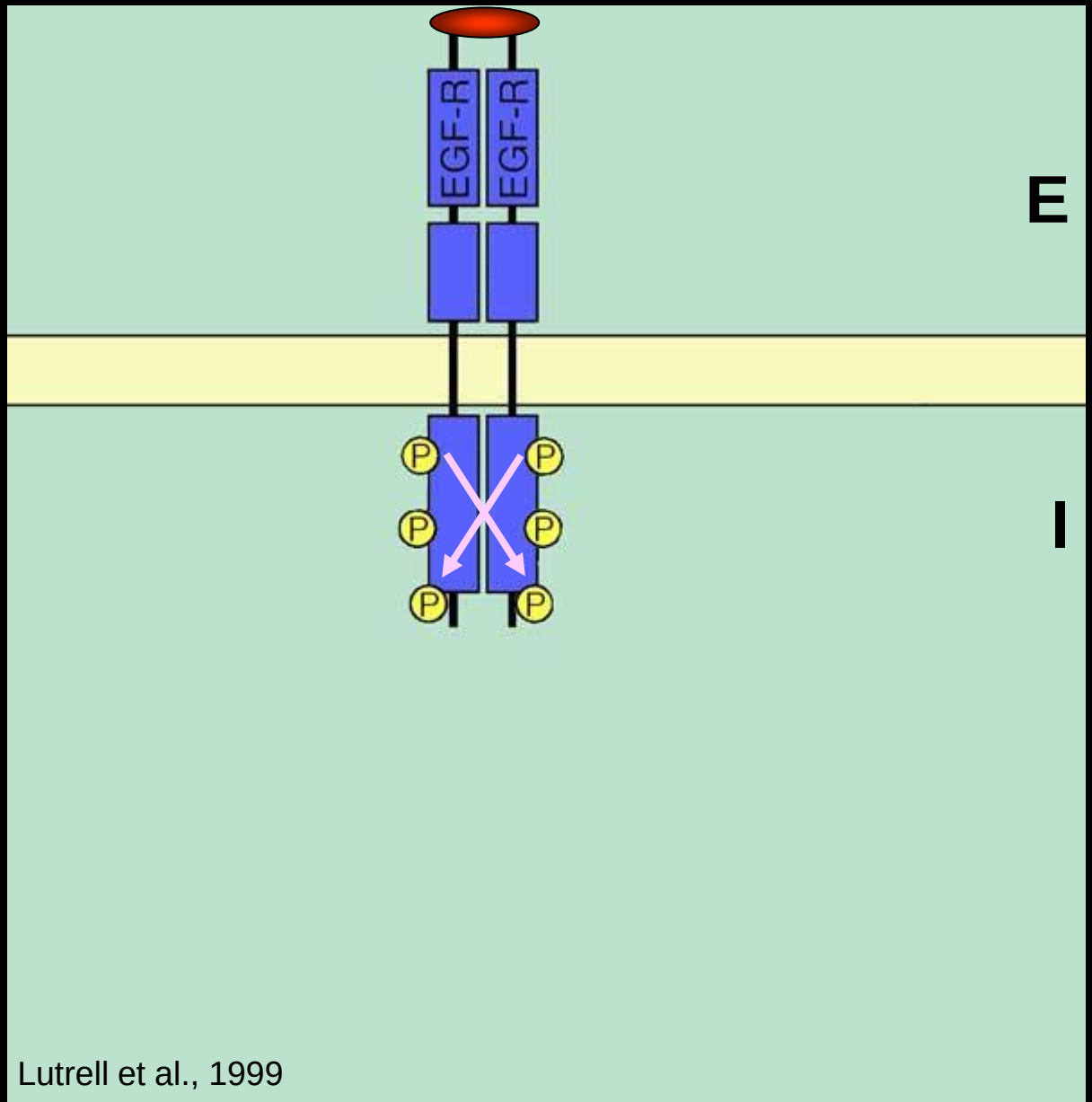
Lutrell et al., 1999

Activación de receptores tirosina-quinasa

Señal

Receptor

Auto-fosforilación



Lutrell et al., 1999

Activación de receptores tirosina-quinasa

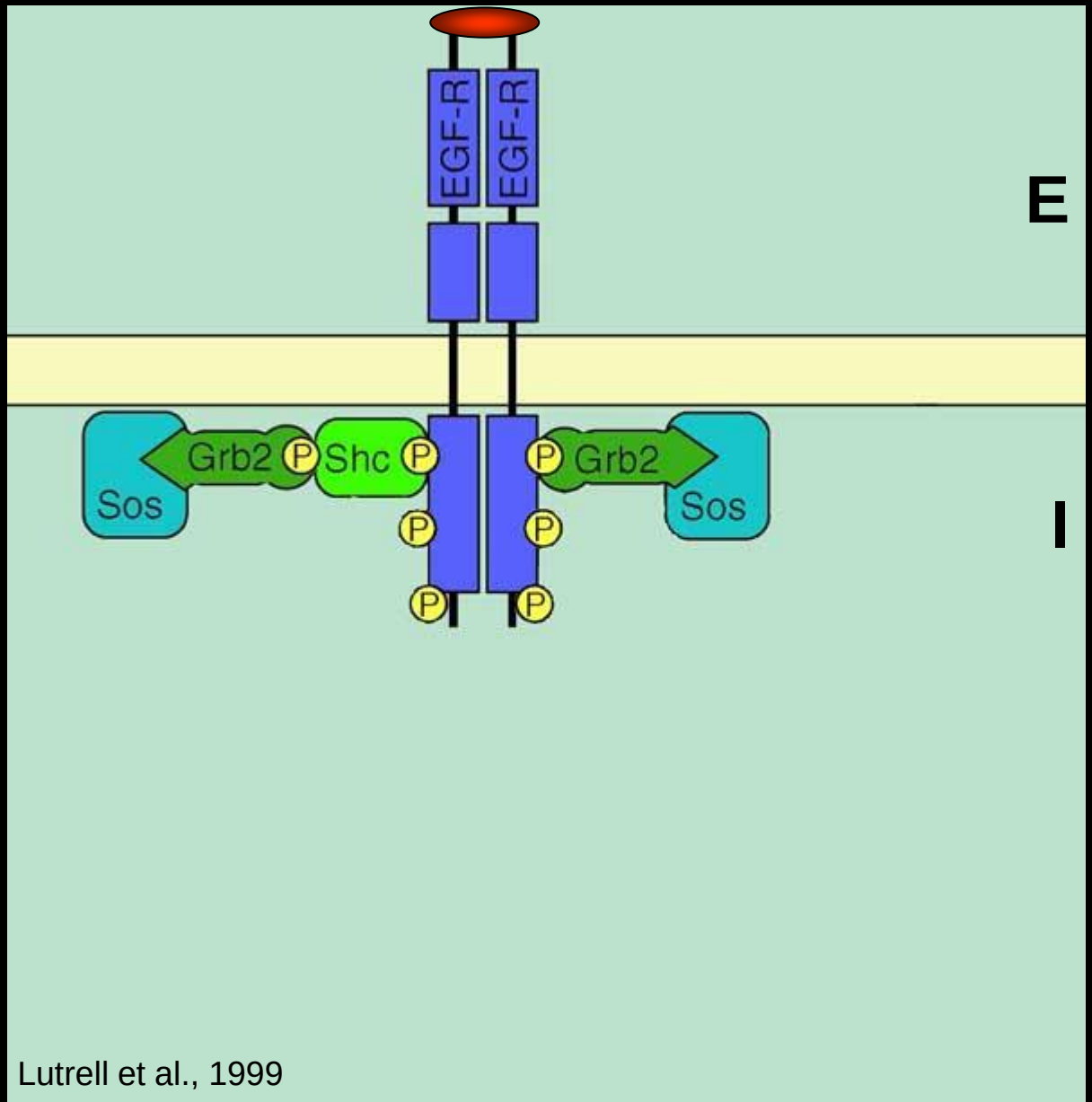
Señal

Receptor

Auto-fosforilación

Adaptadores

GEF



Lutrell et al., 1999

Activación de receptores tirosina-quinasa

Señal

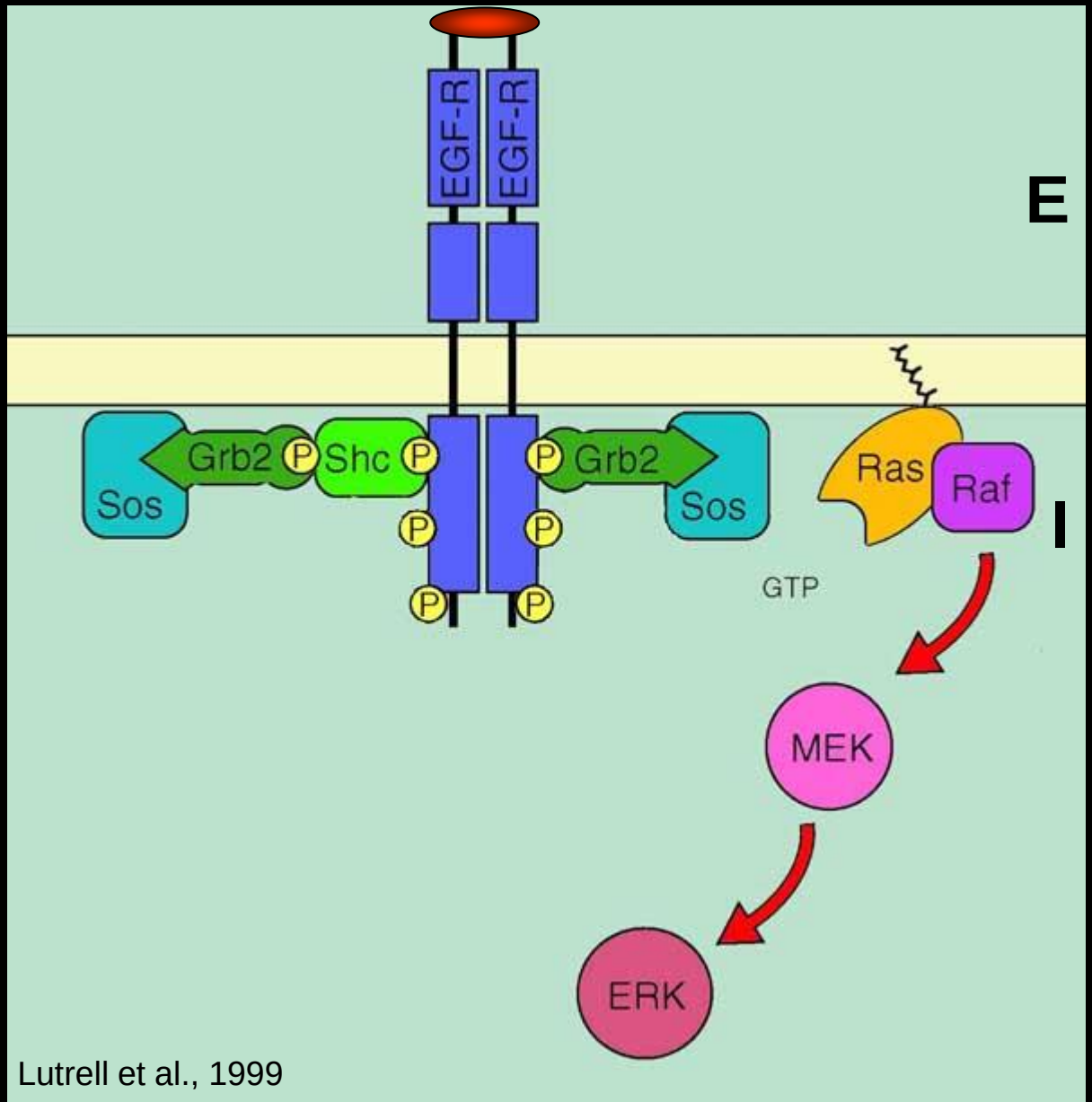
Receptor

Auto-fosforilación

Adaptadores

GEF

Cascada de fosforilación



Lutrell et al., 1999

Activación de receptores tirosina-quinasa

Señal

Receptor

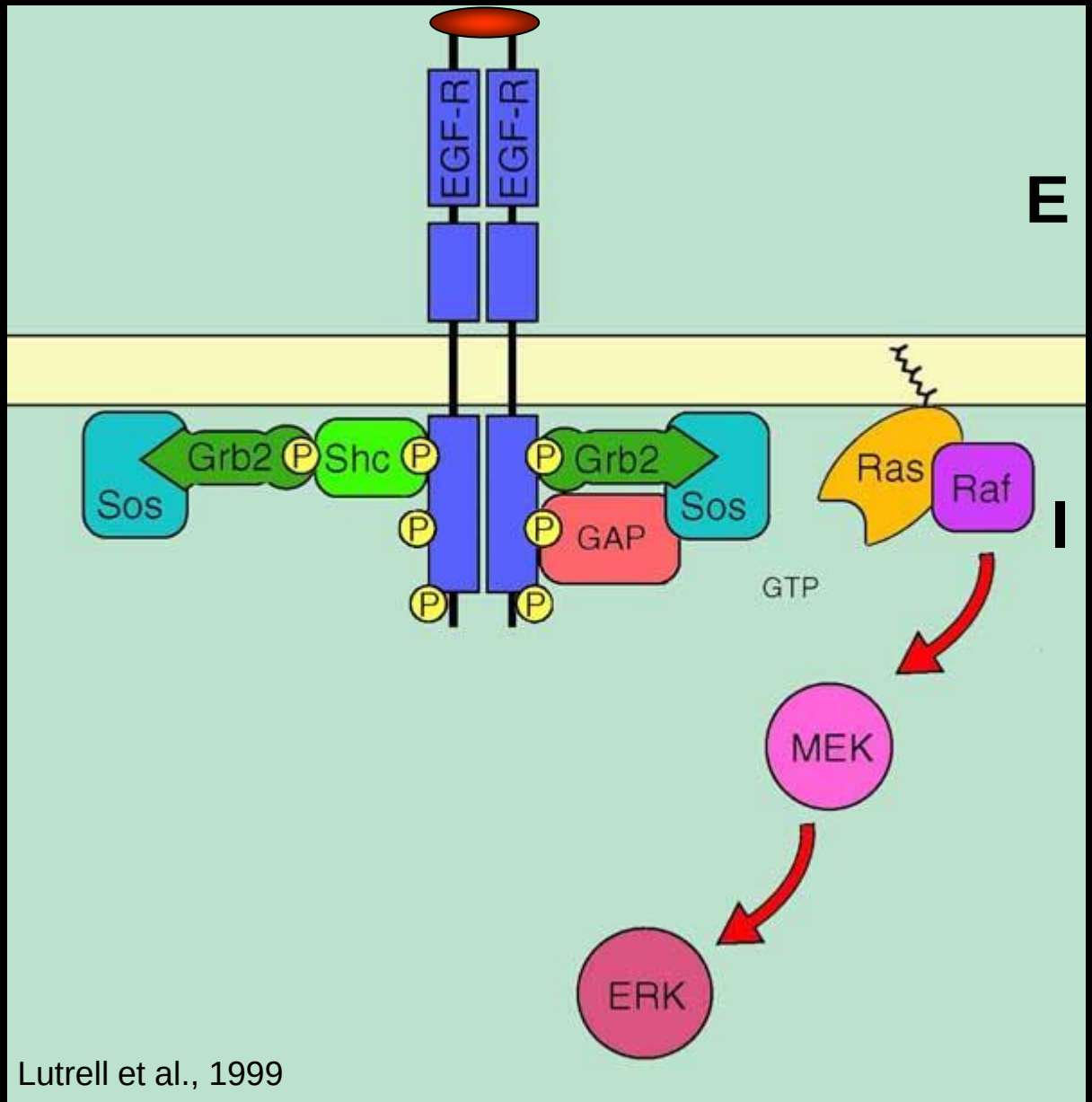
Auto-fosforilación

Adaptadores

GEF

GAP

Cascada de fosforilación



Lutrell et al., 1999

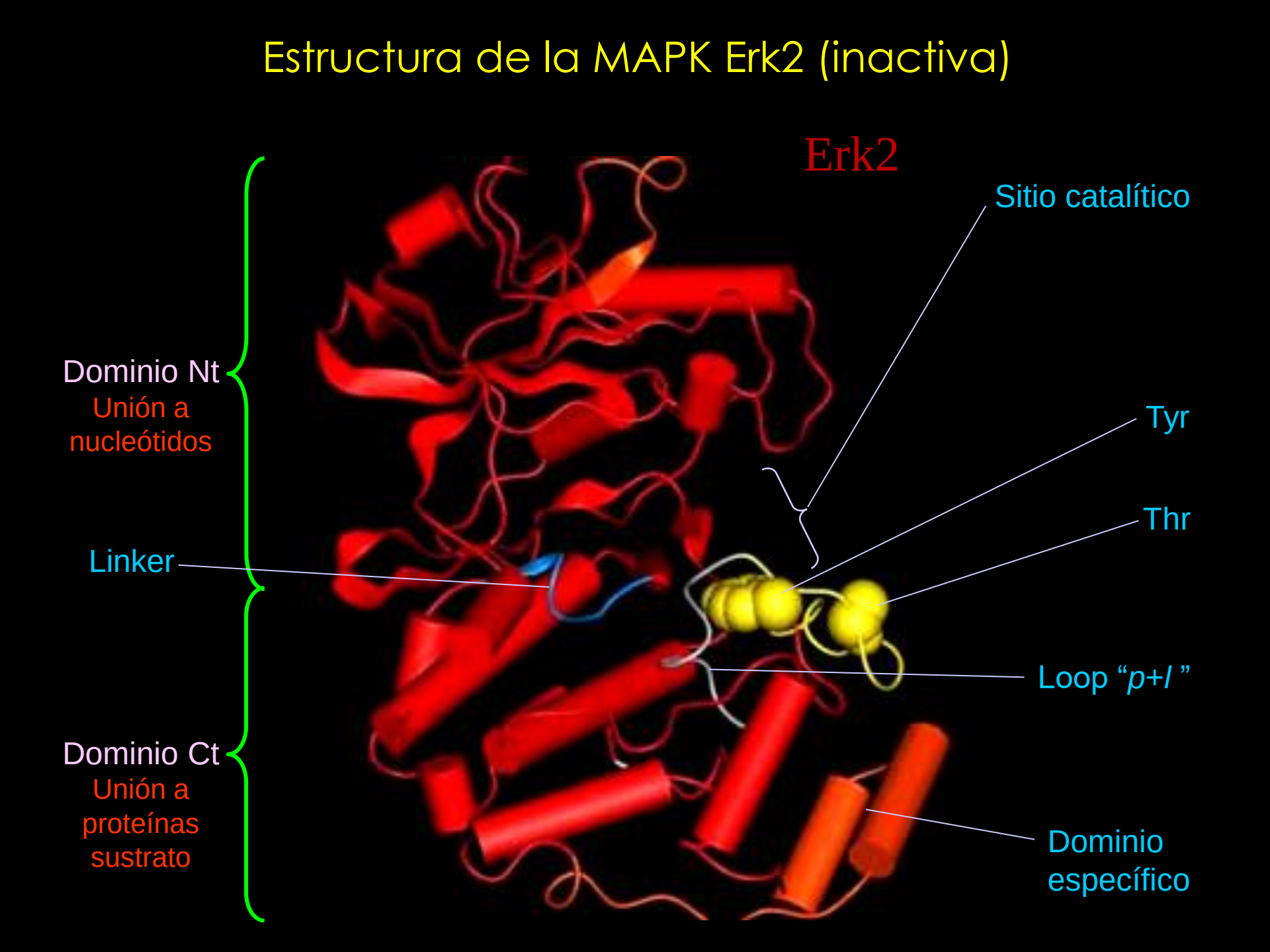
Prot. G monomérica

MAPKKK

MAPKK

MAPK

Estructura de la MAPK Erk2 (inactiva)



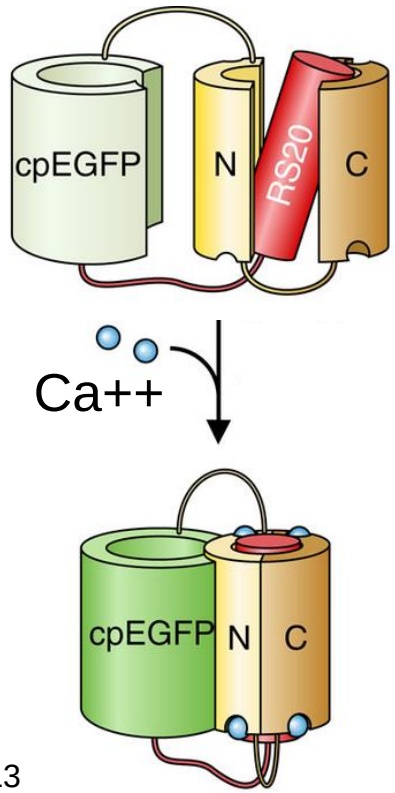
Current Biology 23, 307–311, February 18, 2013 ©2013 Elsevier Ltd All rights reserved http://dx.doi.org/10.1016/j.cub.2012.12.040

https://www.sciencedirect.com/science/article/pii/S096098221300002X

Real-Time Visualization of Neuronal Activity during Perception

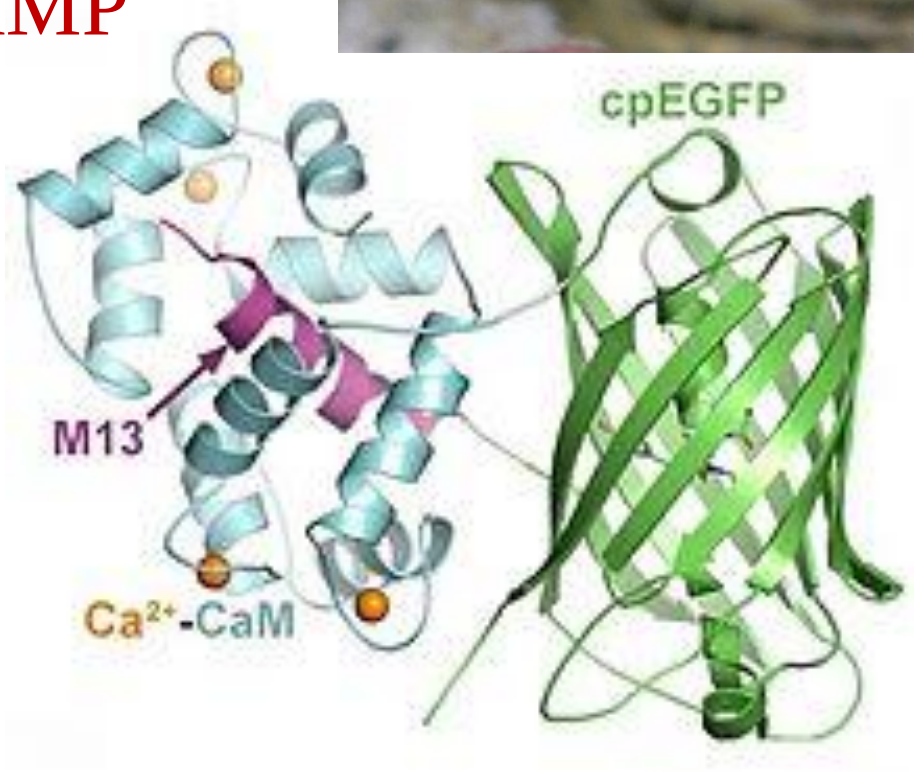
Akira Muto,[1,2,4] Masamichi Ohkura,[3,4] Gembu Abe,[1] Junichi Nakai,[3,*] and Koichi Kawakami[1,2,*]

"cyclically permuted enhanced GFP"



Sun et al., 2013

GCaMP



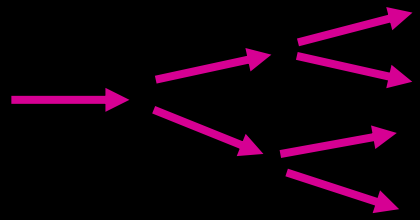
Video de larva de pez y paramecia: https://youtu.be/AyiAT3gIBBc

Música: Dave Brubeck (1959) Take Five

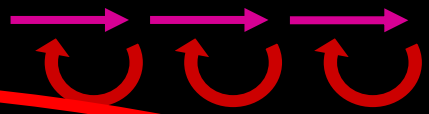
Propiedades básicas de los sistemas de transducción intracelular de señales

A - Reacciones encadenadas

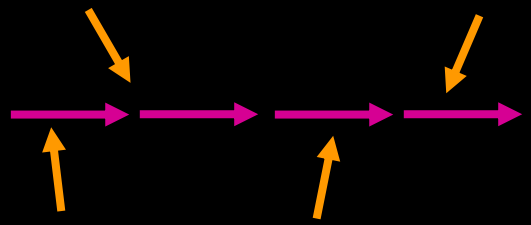
B - Amplificación de la señal



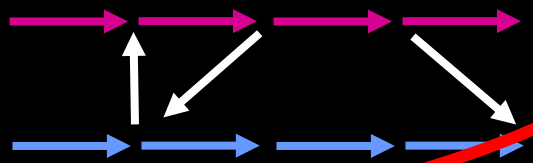
C - Reversibilidad de cada reacción



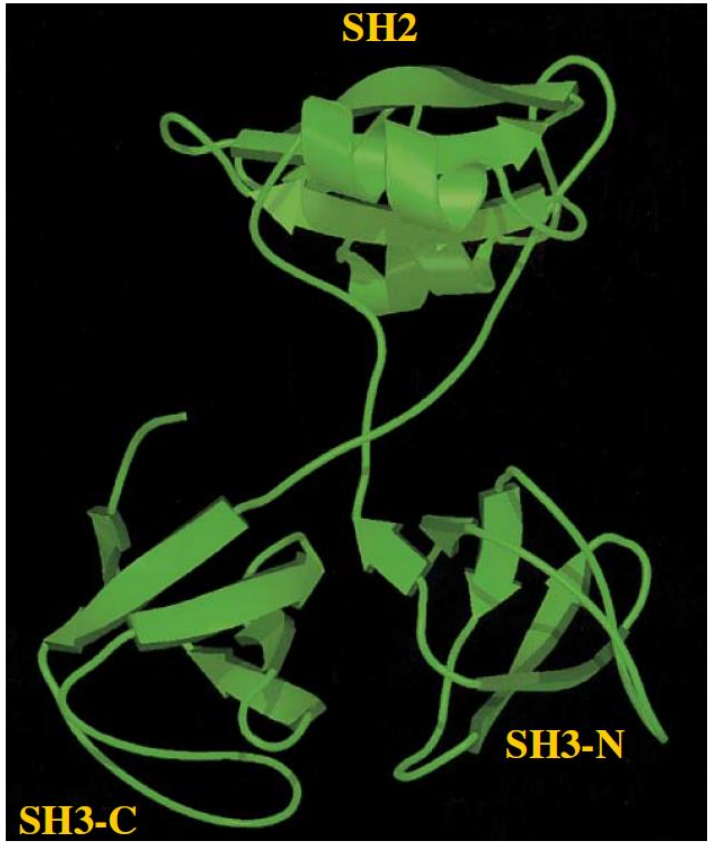
D - Regulación



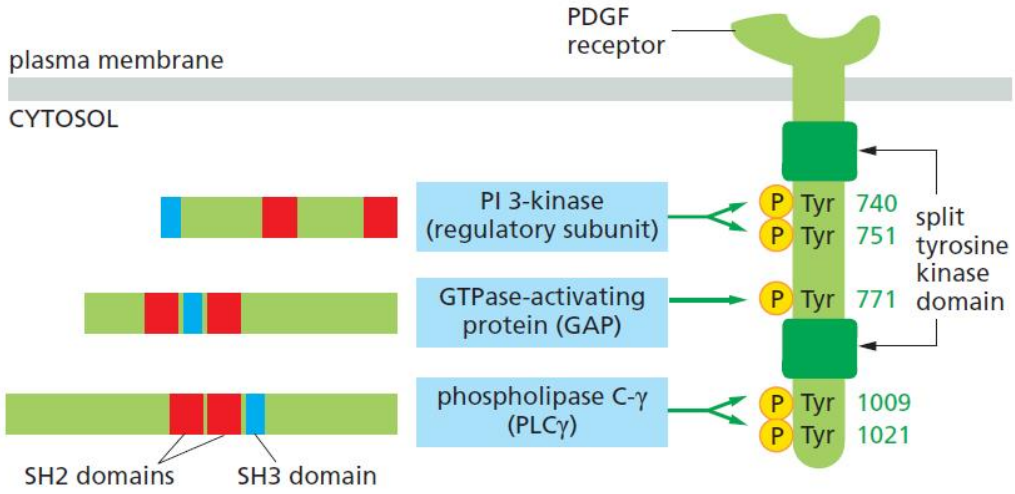
E - Intercomunicación entre vías
("crosstalk")



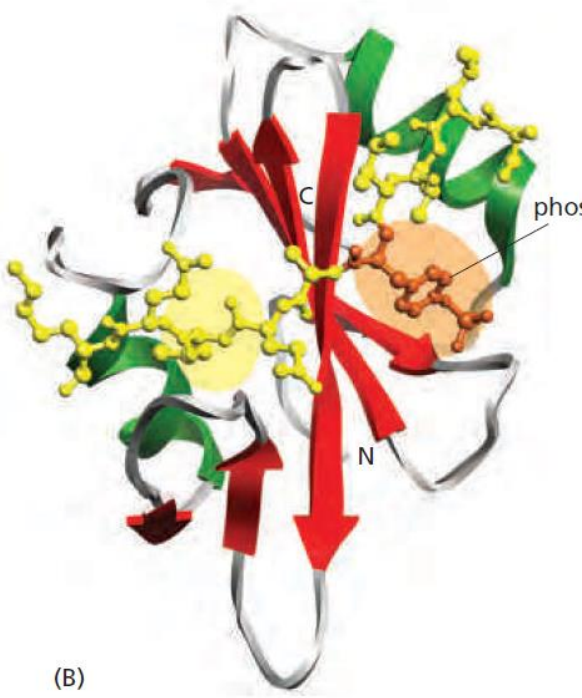
Proteínas adaptadoras "modulares": dominio SH2



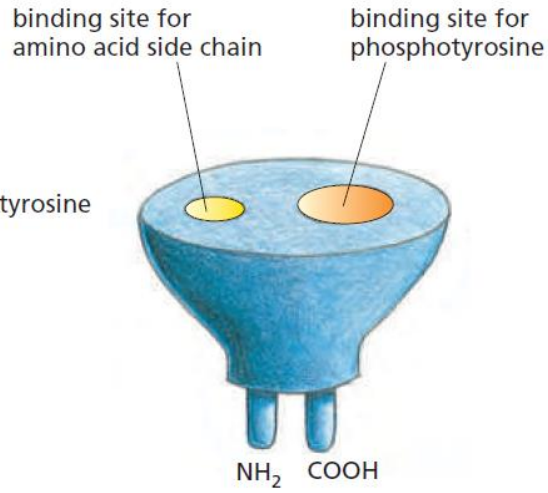
Grb2



(A)

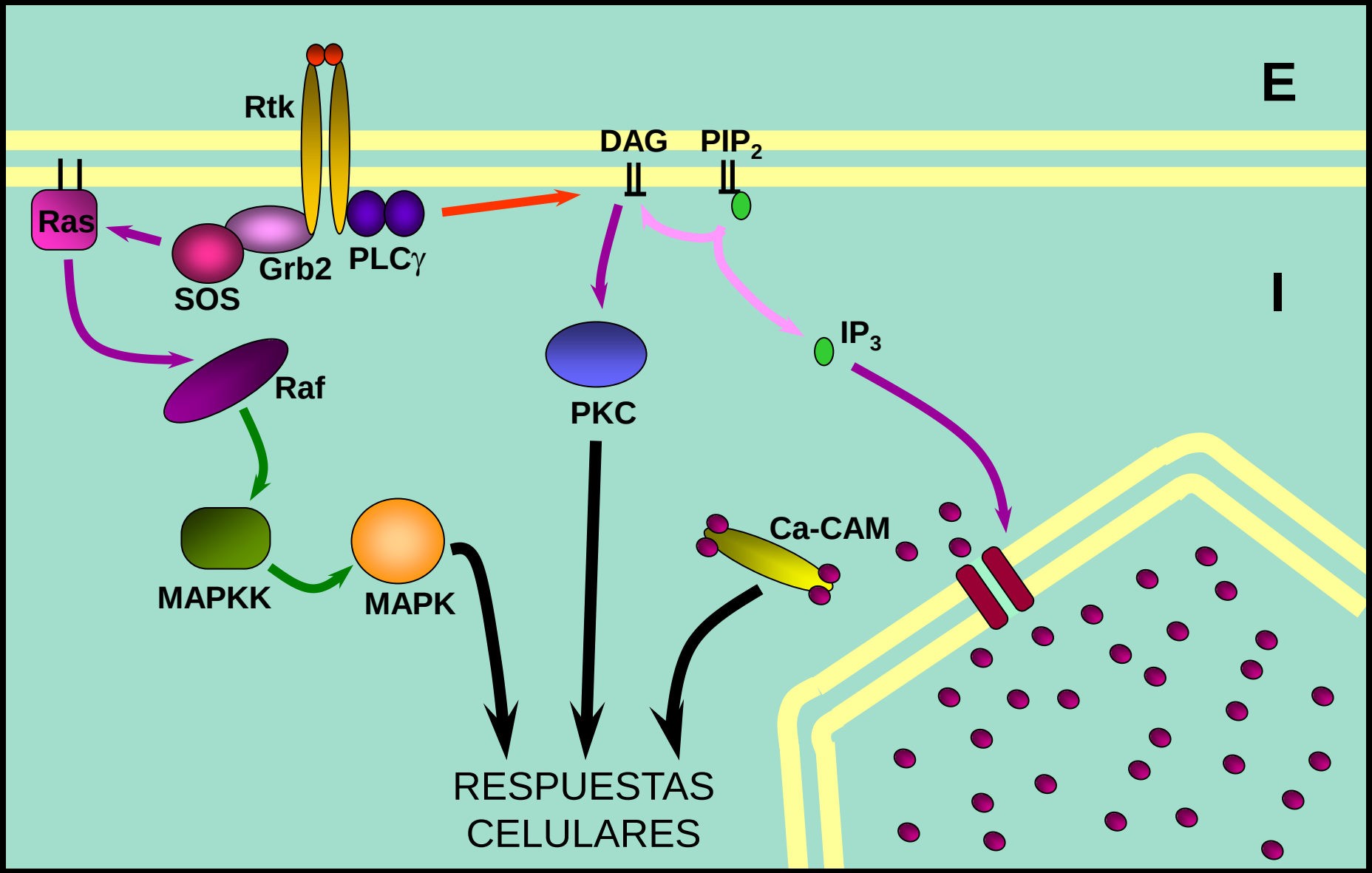


(B)

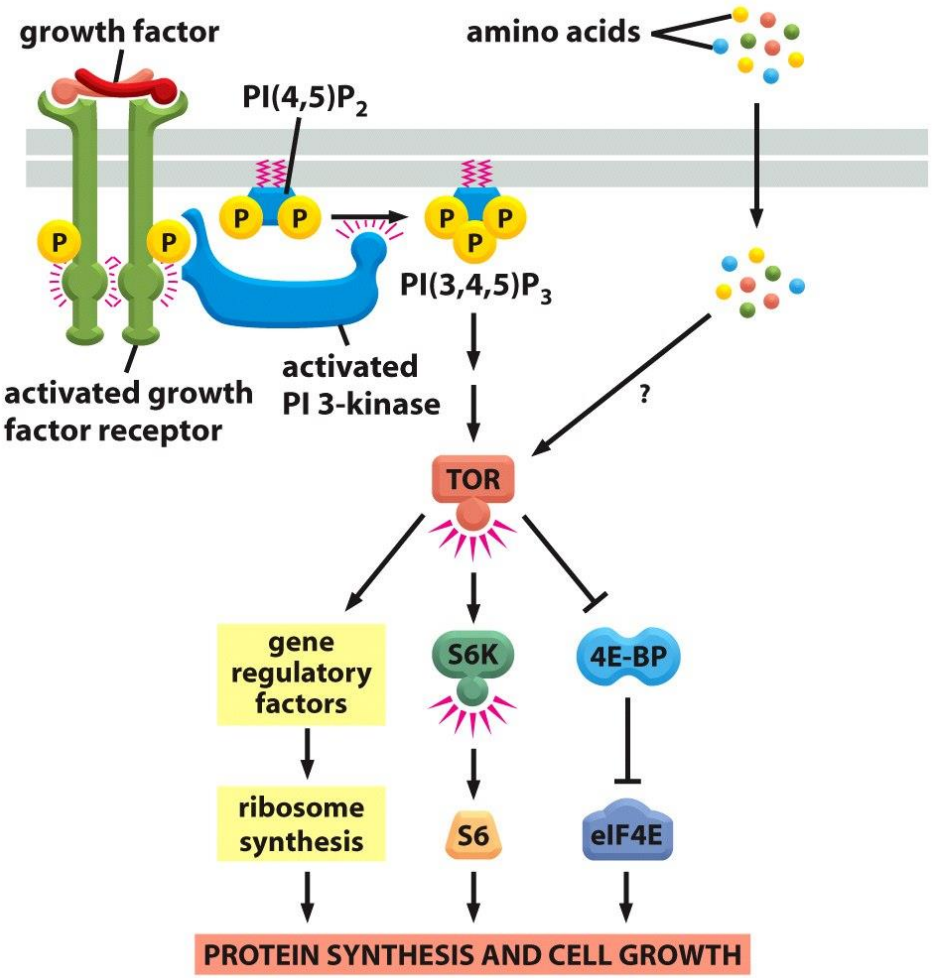


(C)

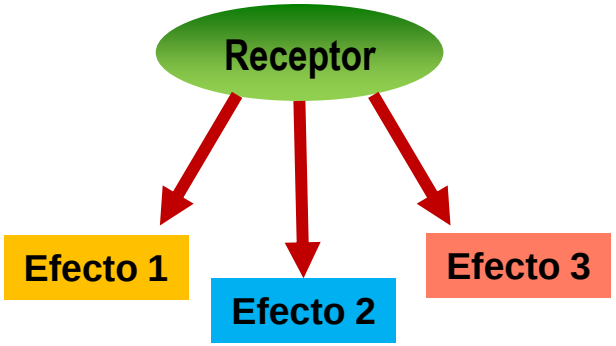
Intercomunicación entre vías de señalización



Intercomunicación entre vías de señalización



Divergencia:



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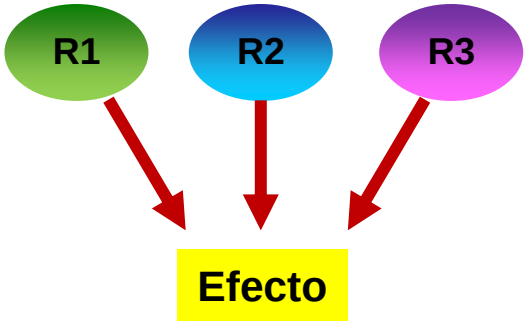
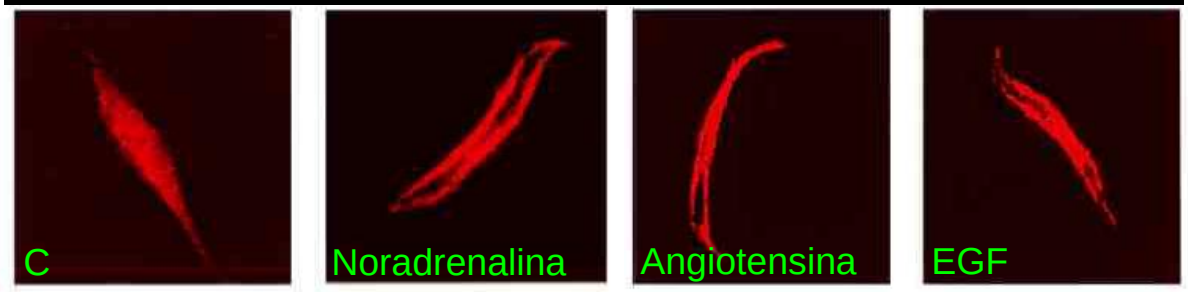
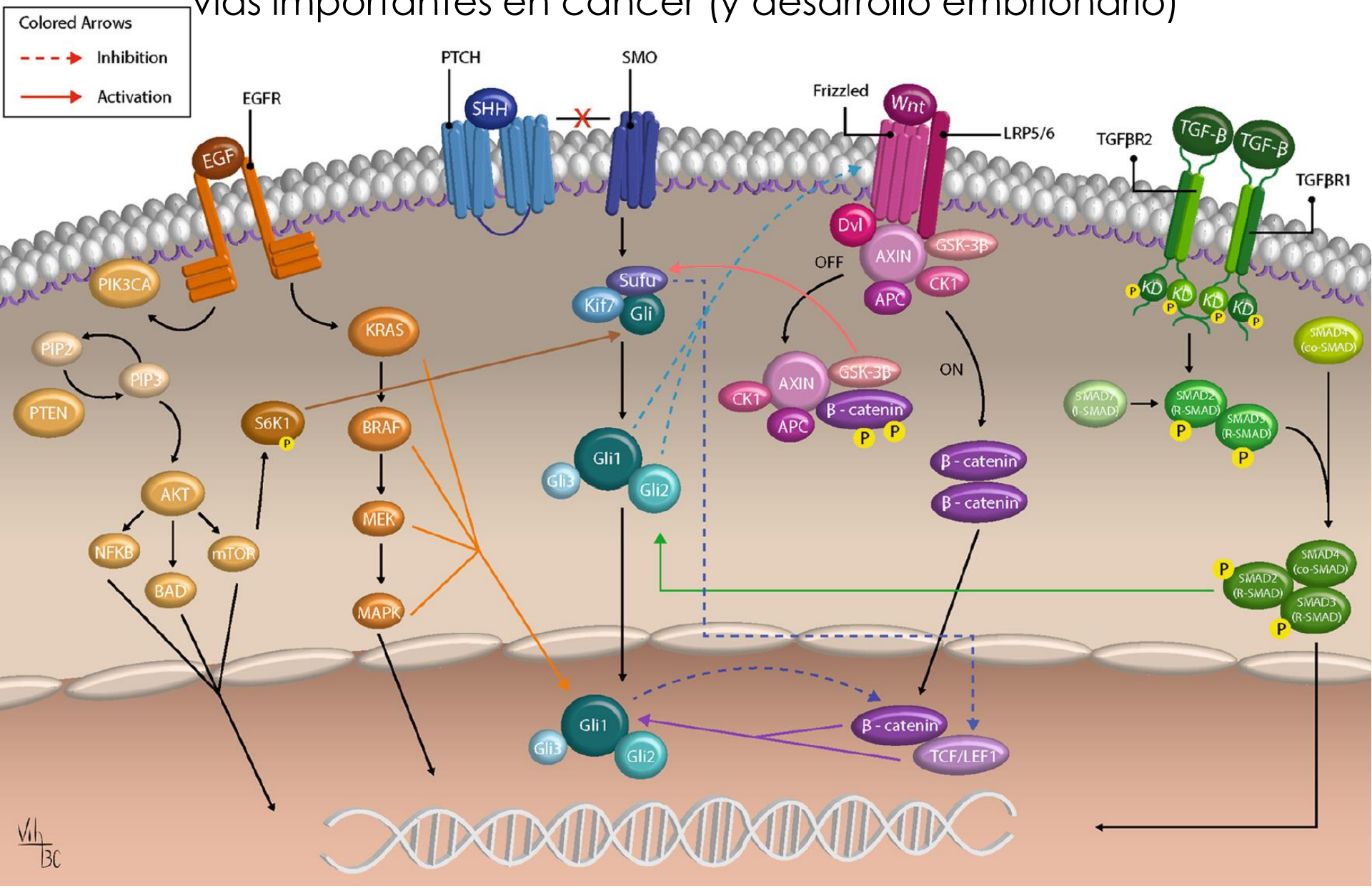


Inmunodetección de Ras en células musculares lisas en cultivo

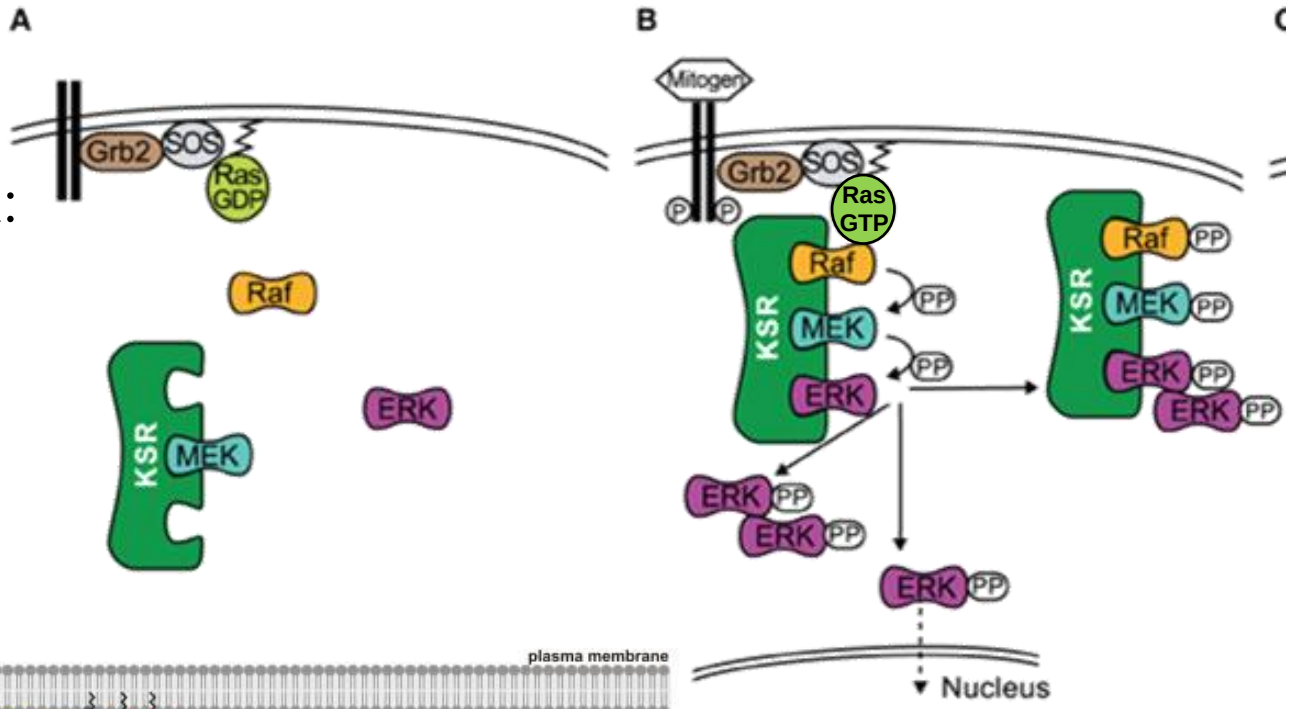


Intercomunicación entre vías de señalización:
vías importantes en cáncer (y desarrollo embrionario)

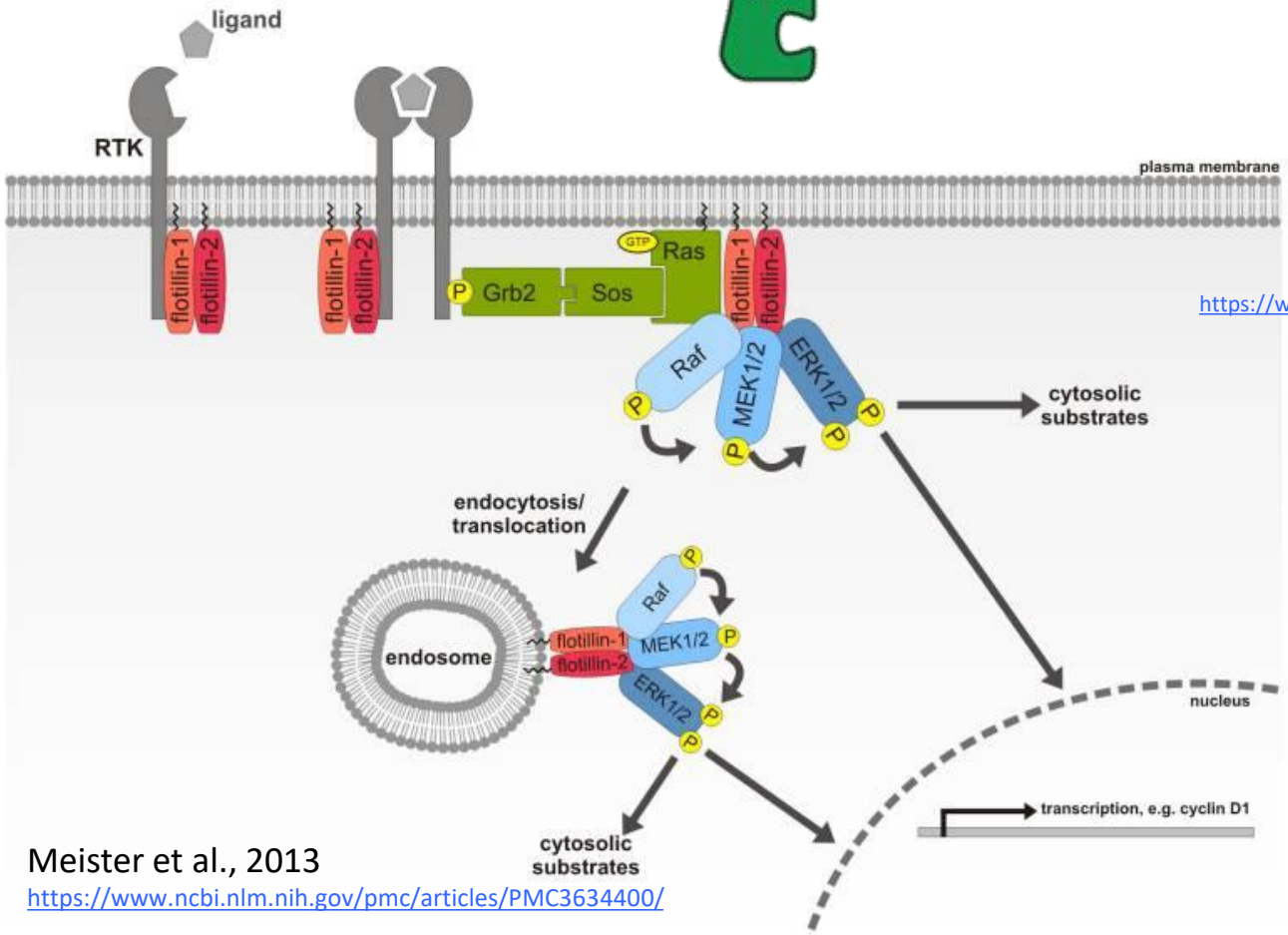


Basile et al., 2018 https://biosignaling.biomedcentral.com/articles/10.1186/s12964-018-0220-7

Módulos MAPKKK/MAPKK/MAPK: Proteínas "scaffold" y adaptadores locales



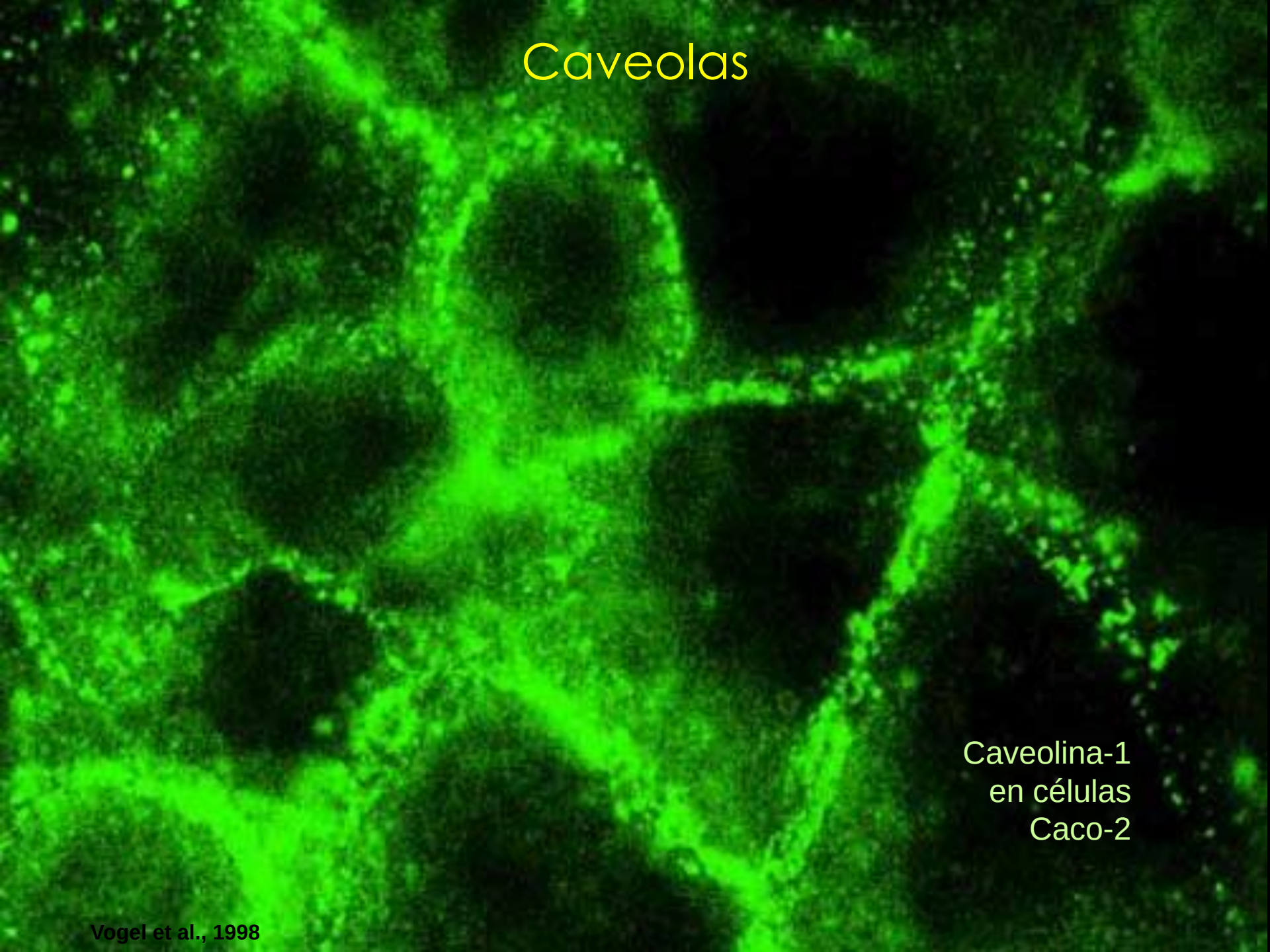
Witzel et al., 2012
https://www.frontiersin.org/articles/10.3389/fphys.2012.00475/full



Meister et al., 2013
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3634400/

KSR:
Kinase Supressor of Ras

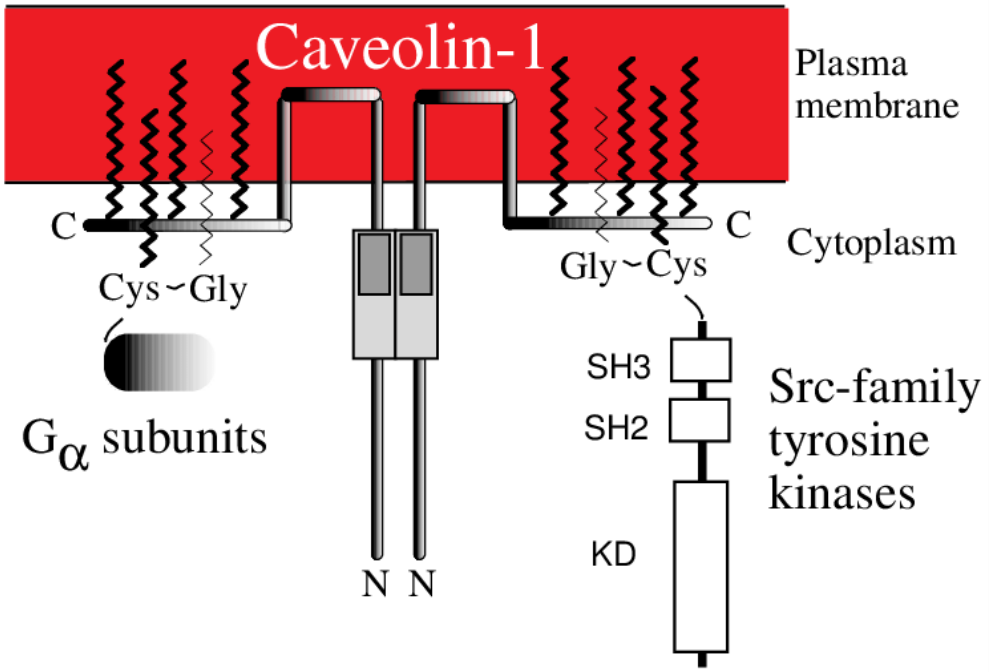
Caveolas

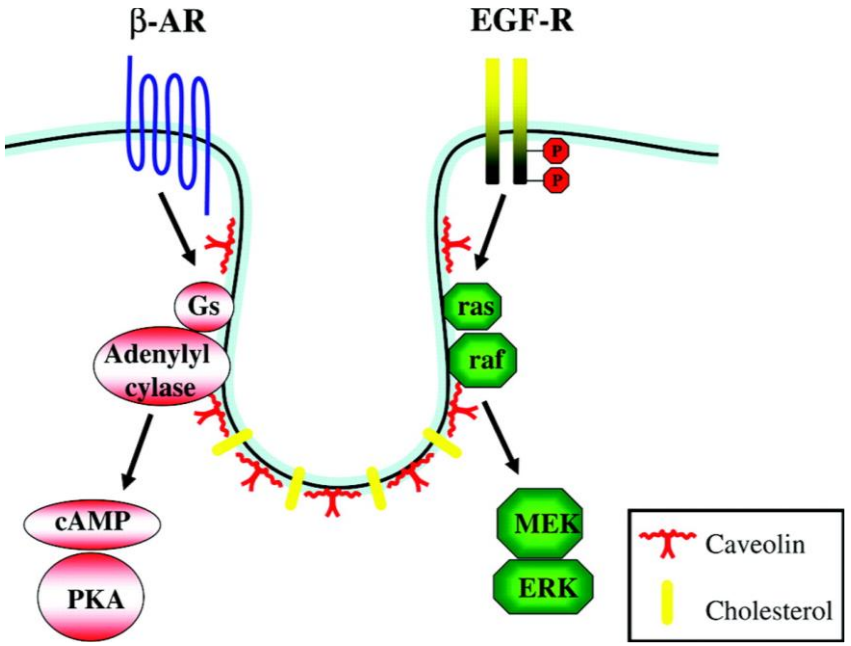


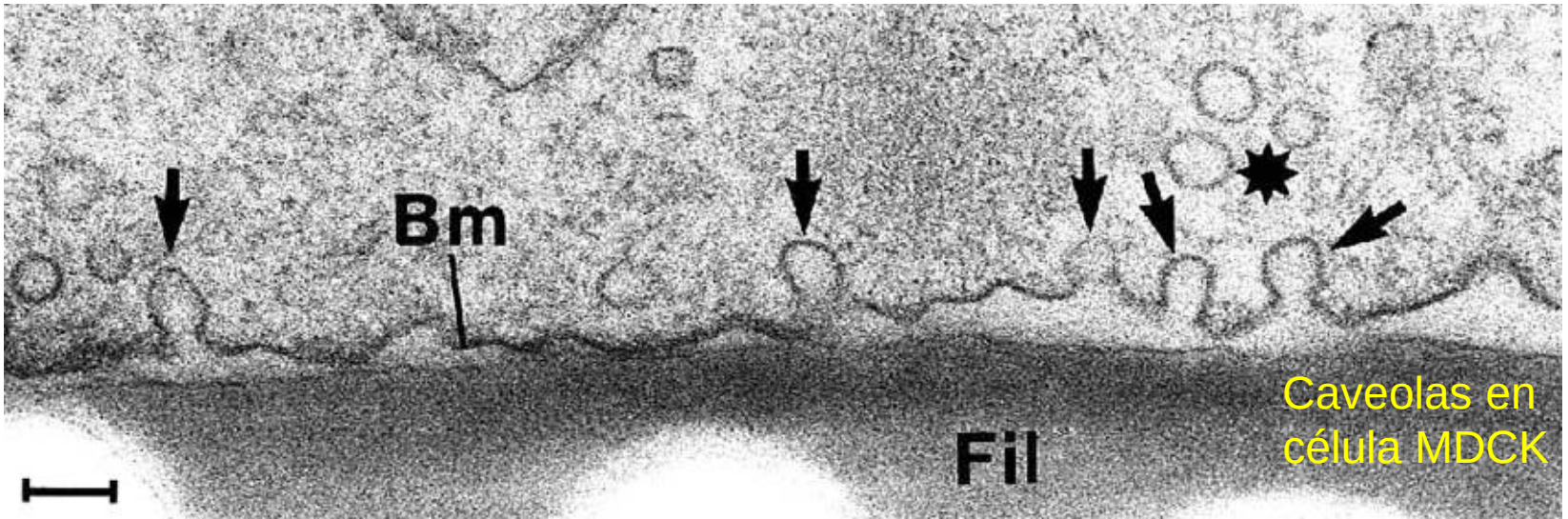
Caveolina-1
en células
Caco-2

Vogel et al., 1998

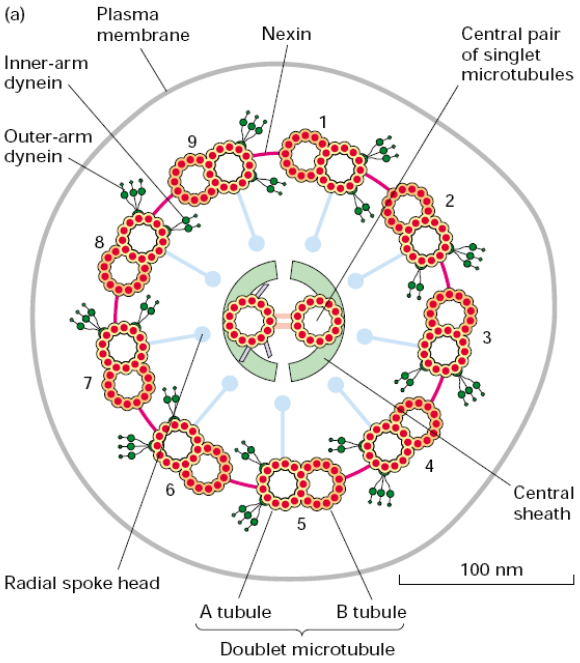
Caveolas

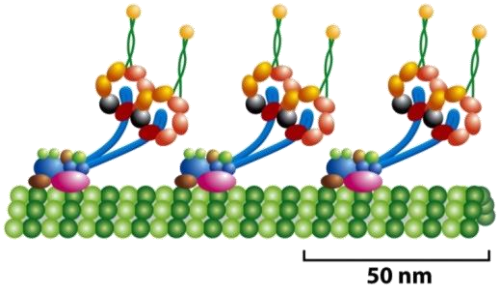

Caveolin-1
Plasma membrane
Cytoplasm
C
Cys~Gly
C
Gly~Cys
G_α subunits
N N
SH3
SH2
KD
Src-family tyrosine kinases

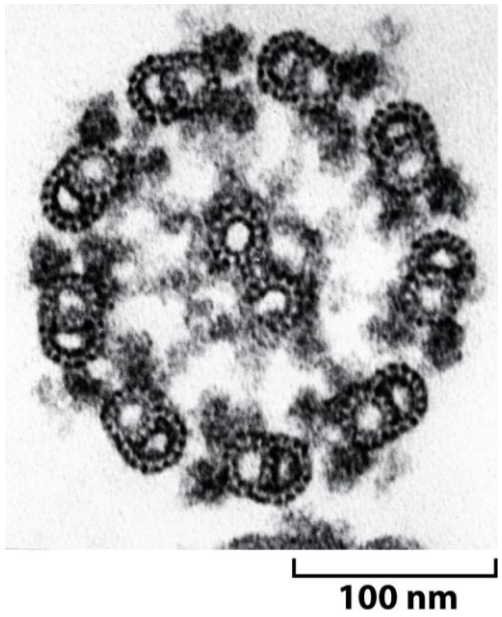

β-AR
EGF-R
Gs
Adenylyl cylase
cAMP
PKA
ras
raf
MEK
ERK
Caveolin
Cholesterol

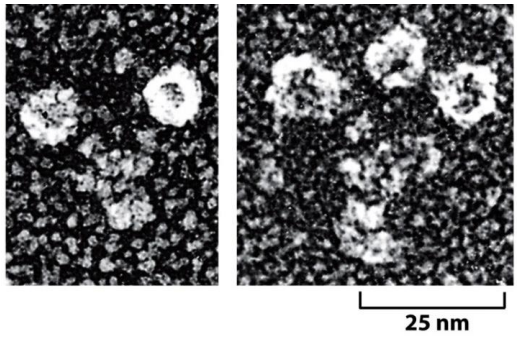

Bm
Fil
Caveolas en célula MDCK

Cilias móviles y cilias primarias



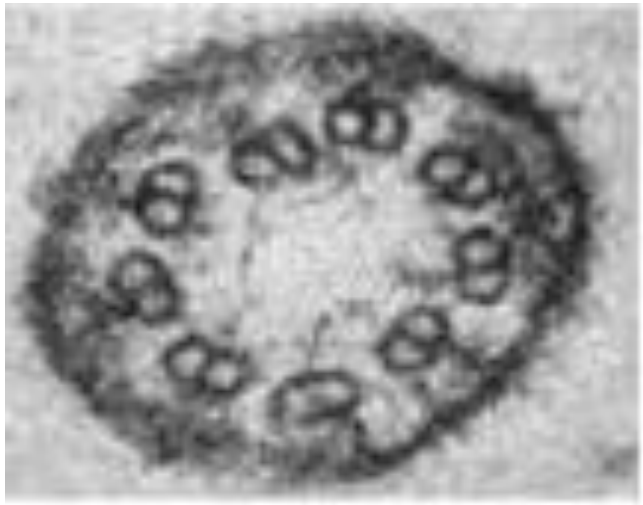






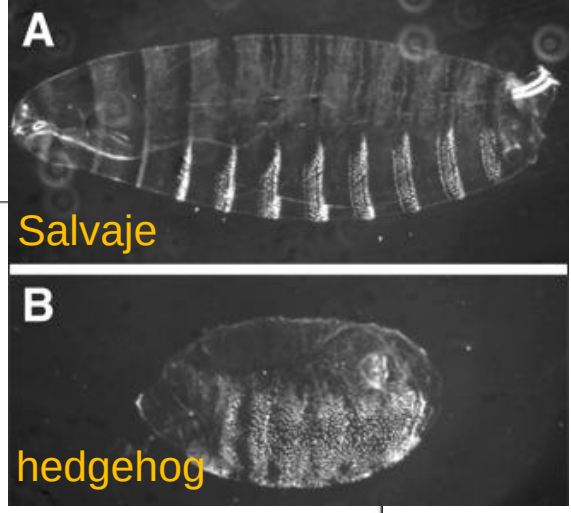
Cilia móvil: 9+2

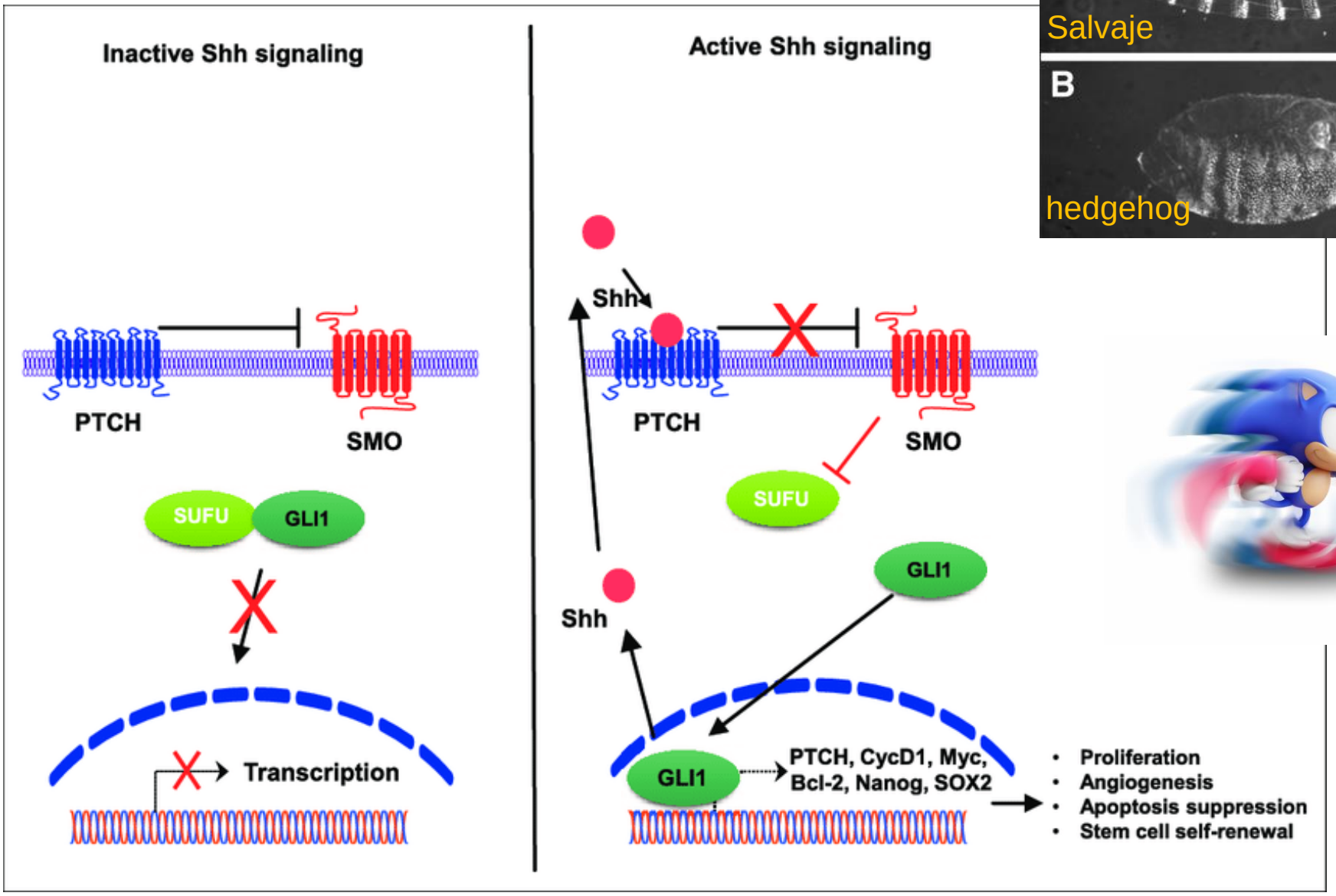
Cilia primaria: 9+0



¿FUNCIÓN?

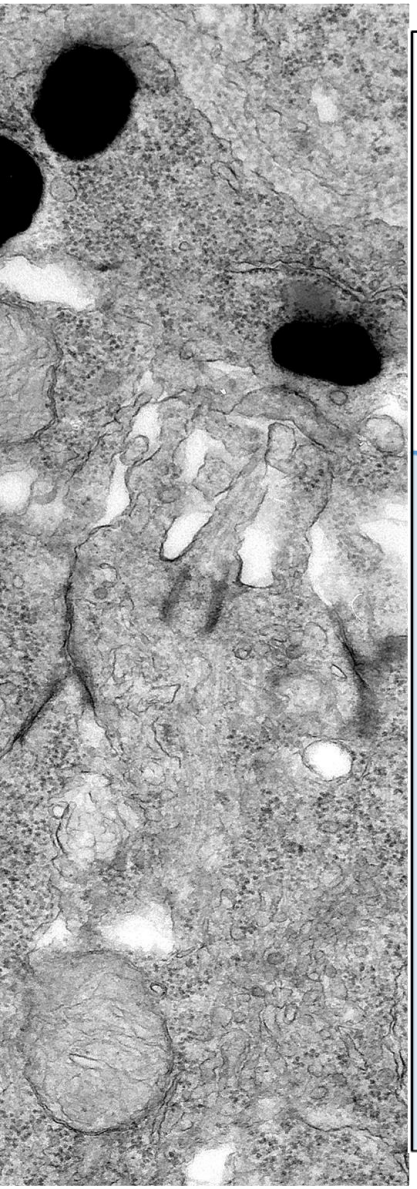
Vía de Sonic Hedgehog



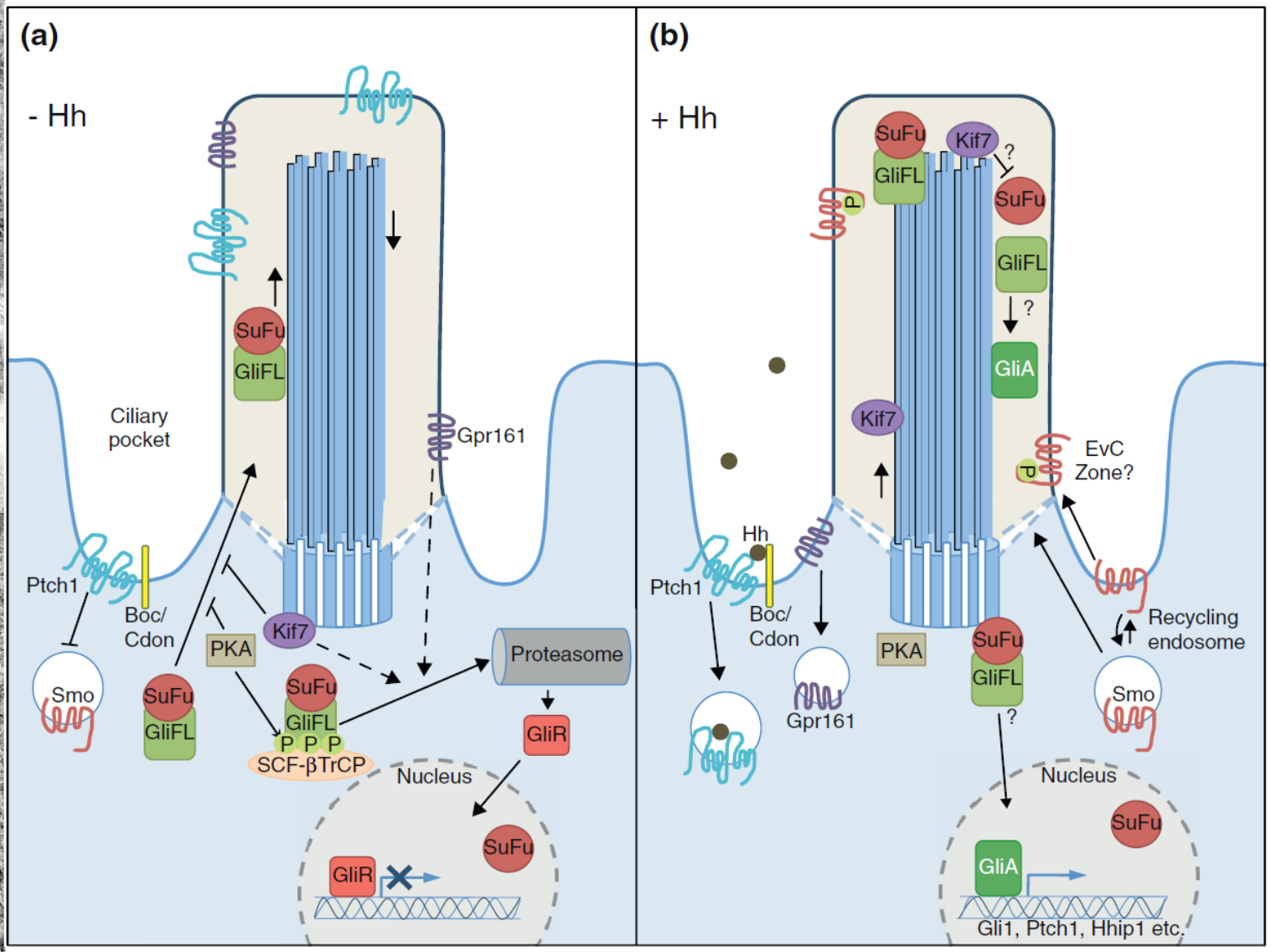


Lee et al., 2017

Las cilias como plataformas de señalización



Cilia primaria en una célula de retina en desarrollo



Nozawa et al., 2013

http://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC3913210&blobtype=pdf