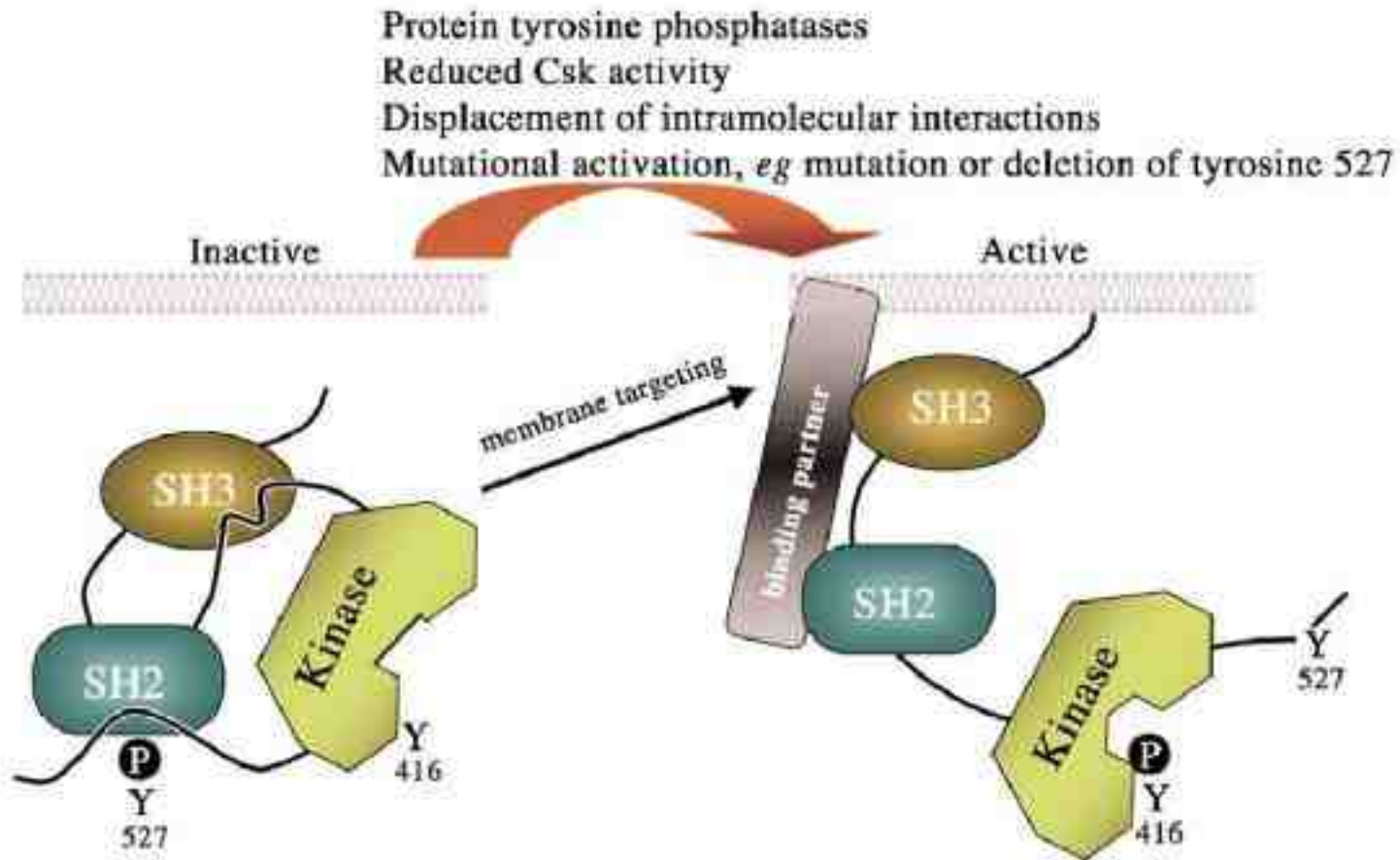
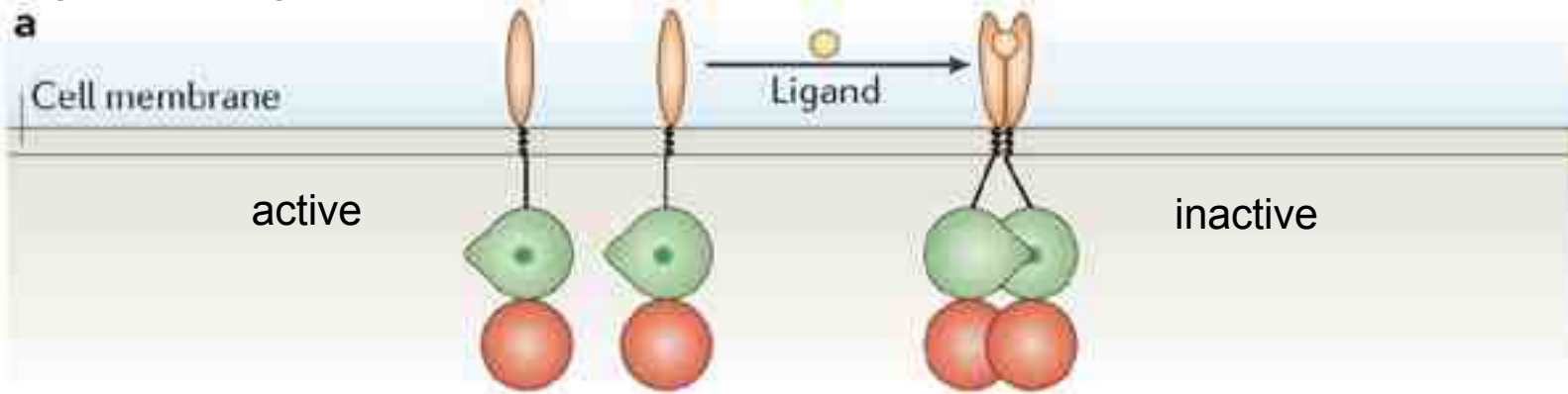


Src family of tyrosine kinase

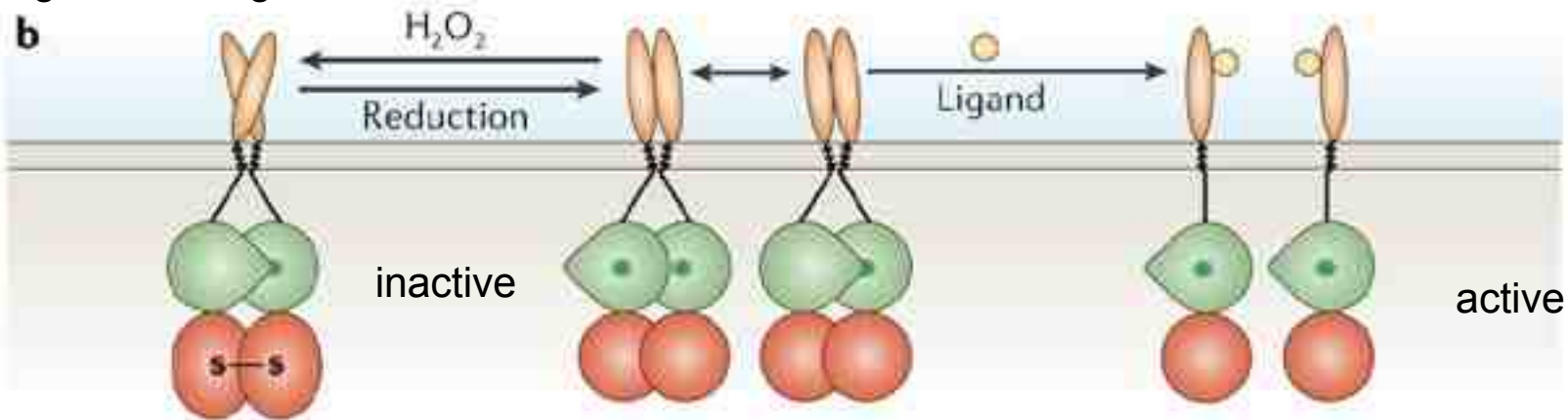


RPTP: Receptor tyrosine phosphatase:

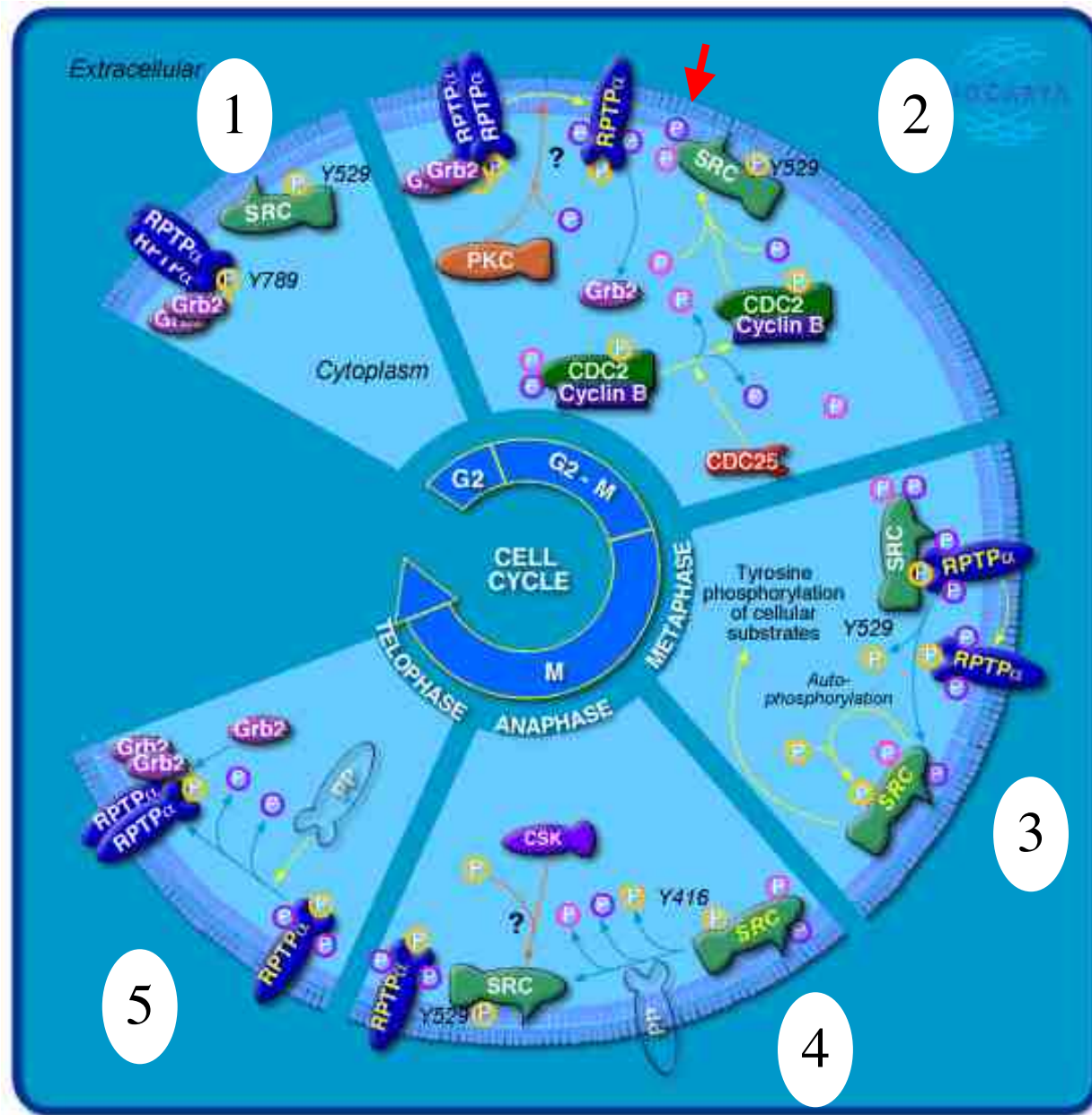
Ligand binding = inhibition

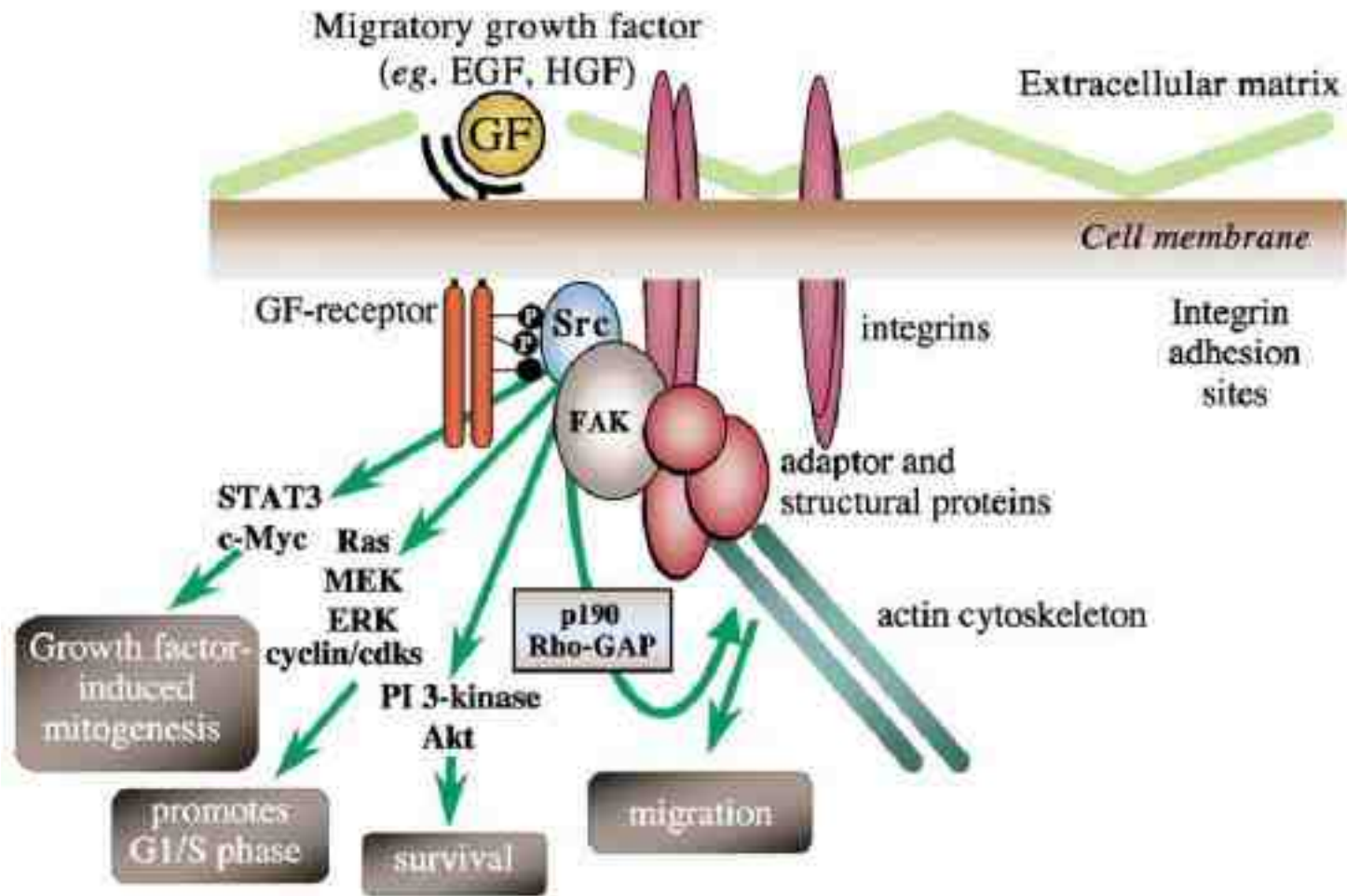


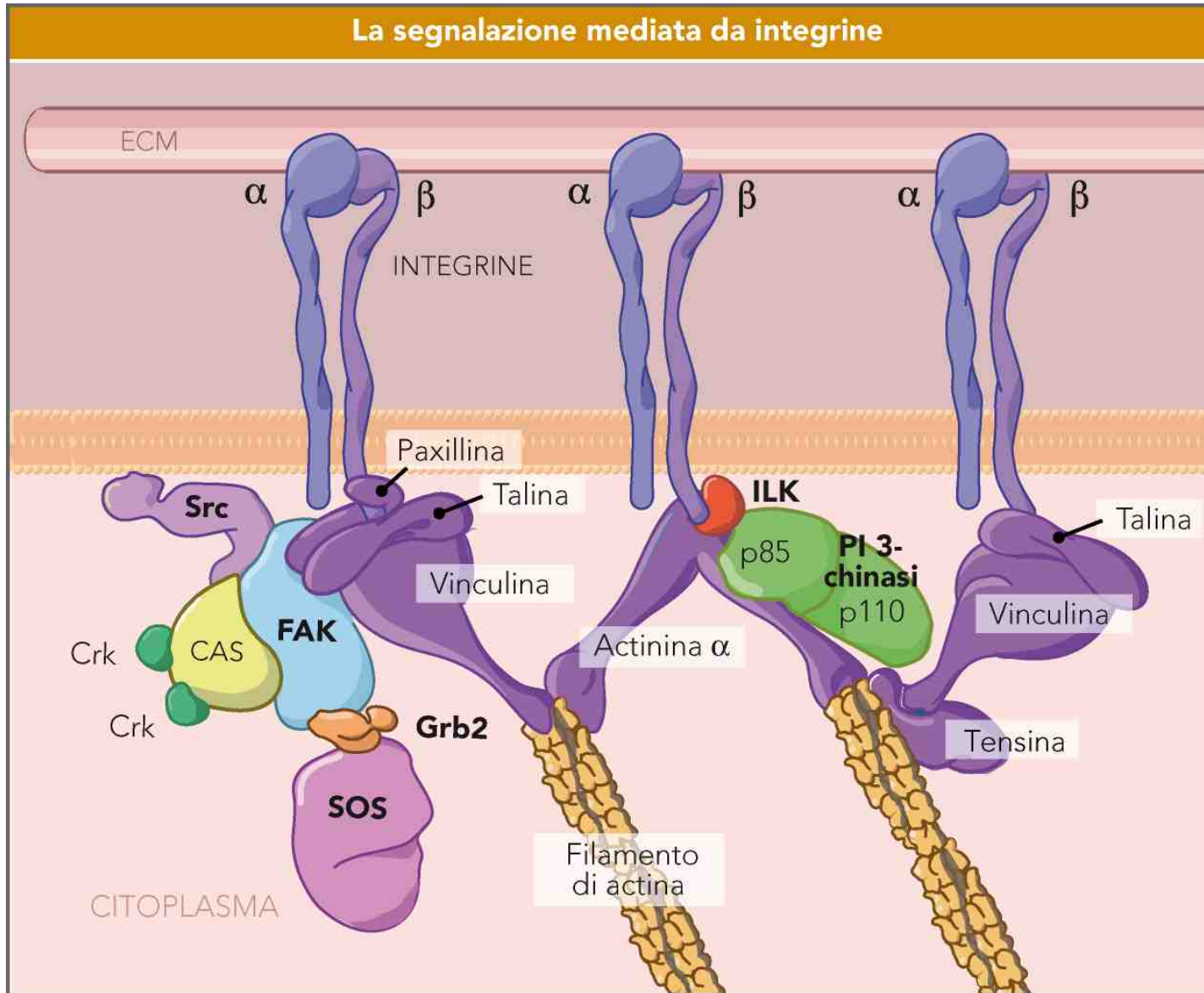
Ligand binding = activation

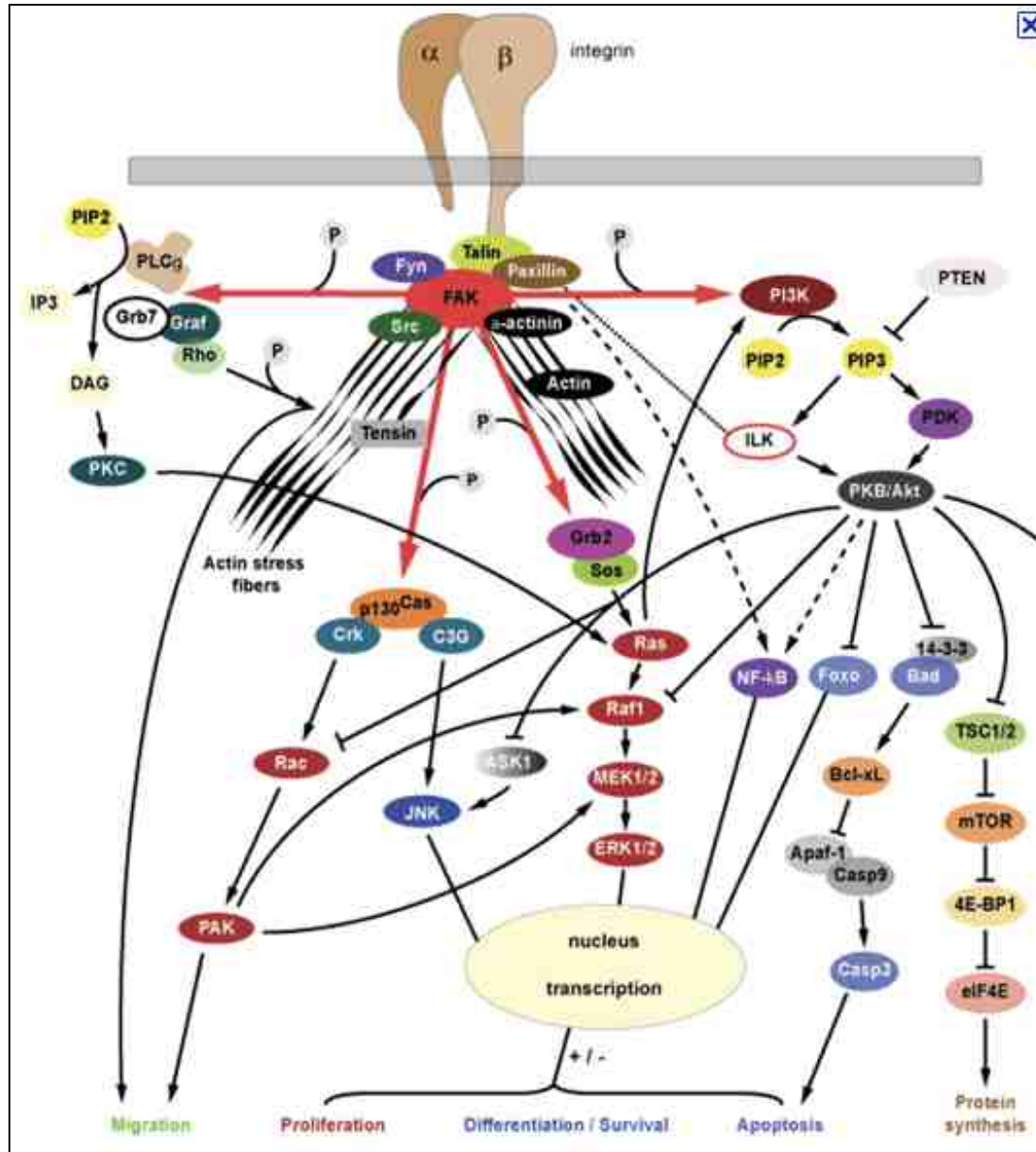


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NOTCH

* La segnalazione dovuta all'attivazione di Notch è fondamentale durante lo sviluppo embrionale.

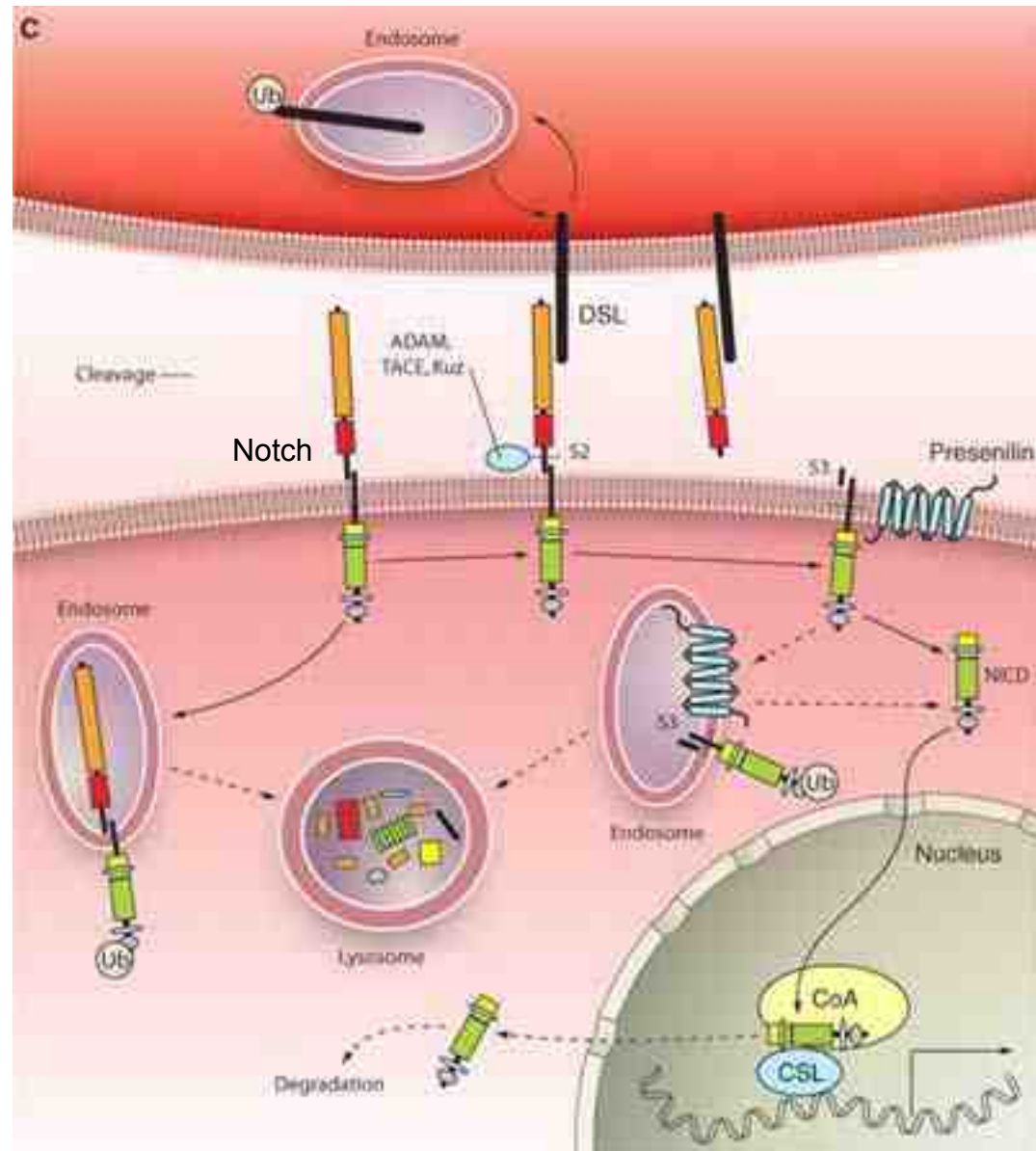
* Il precursore del recettore Notch è una proteina di 300kD che subisce già un taglio proteolitico (S1) durante la sua maturazione nel Golgi. Le due subunità rimangono associate e trasportate in membrana.

* Notch è attivato da Delta (DSL) mediante comunicazione juxtacrina (interazione cellula-cellula).

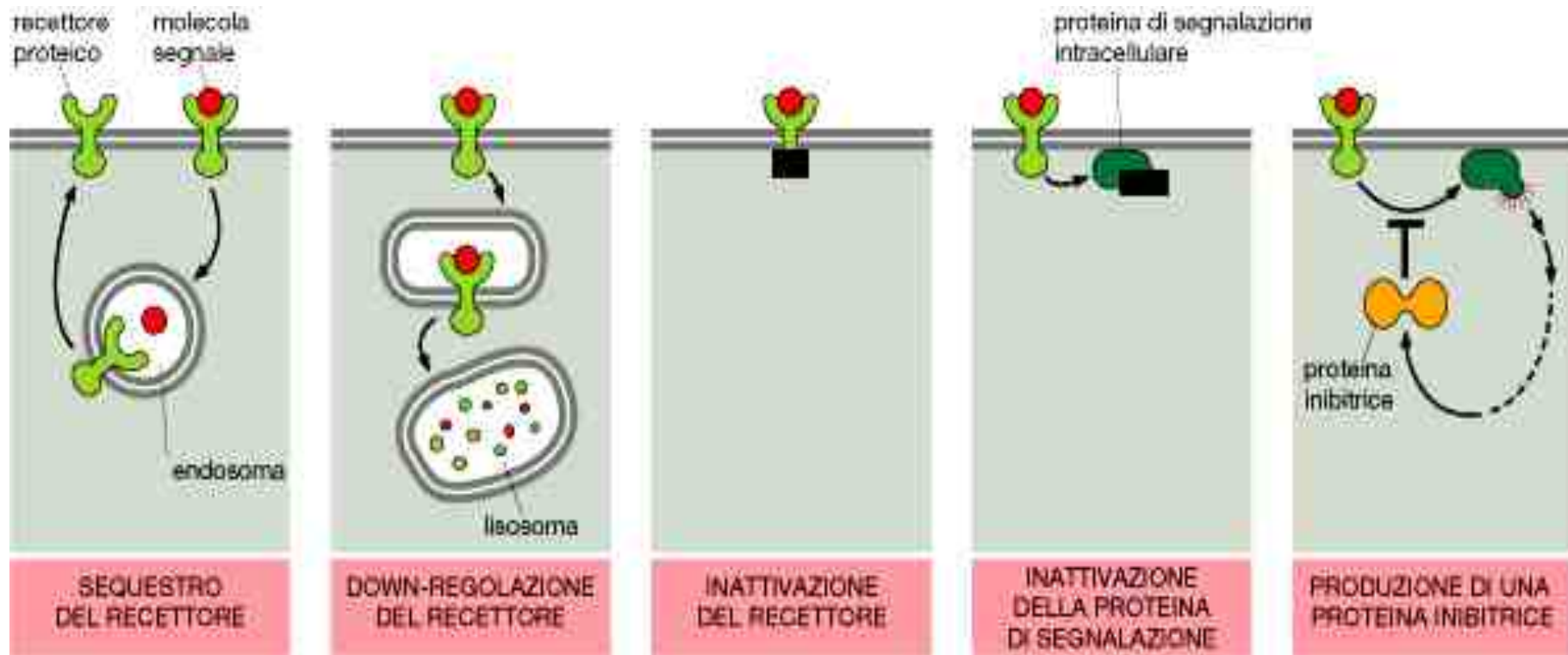
* Il legame di Delta induce il taglio proteolitico di Notch nella regione extracellulare (S2) da parte della metalloprotease ADAM/TACE. Il dominio extracellulare rimane associato a Delta e viene endocitato e degradato dalla cellula che esprime Delta.

* Il dominio transmembrana di Notch interagisce con la beta-secretase (protease) chiamata presenilina e viene tagliato (S3) e/o internalizzato assieme alla presenilina.

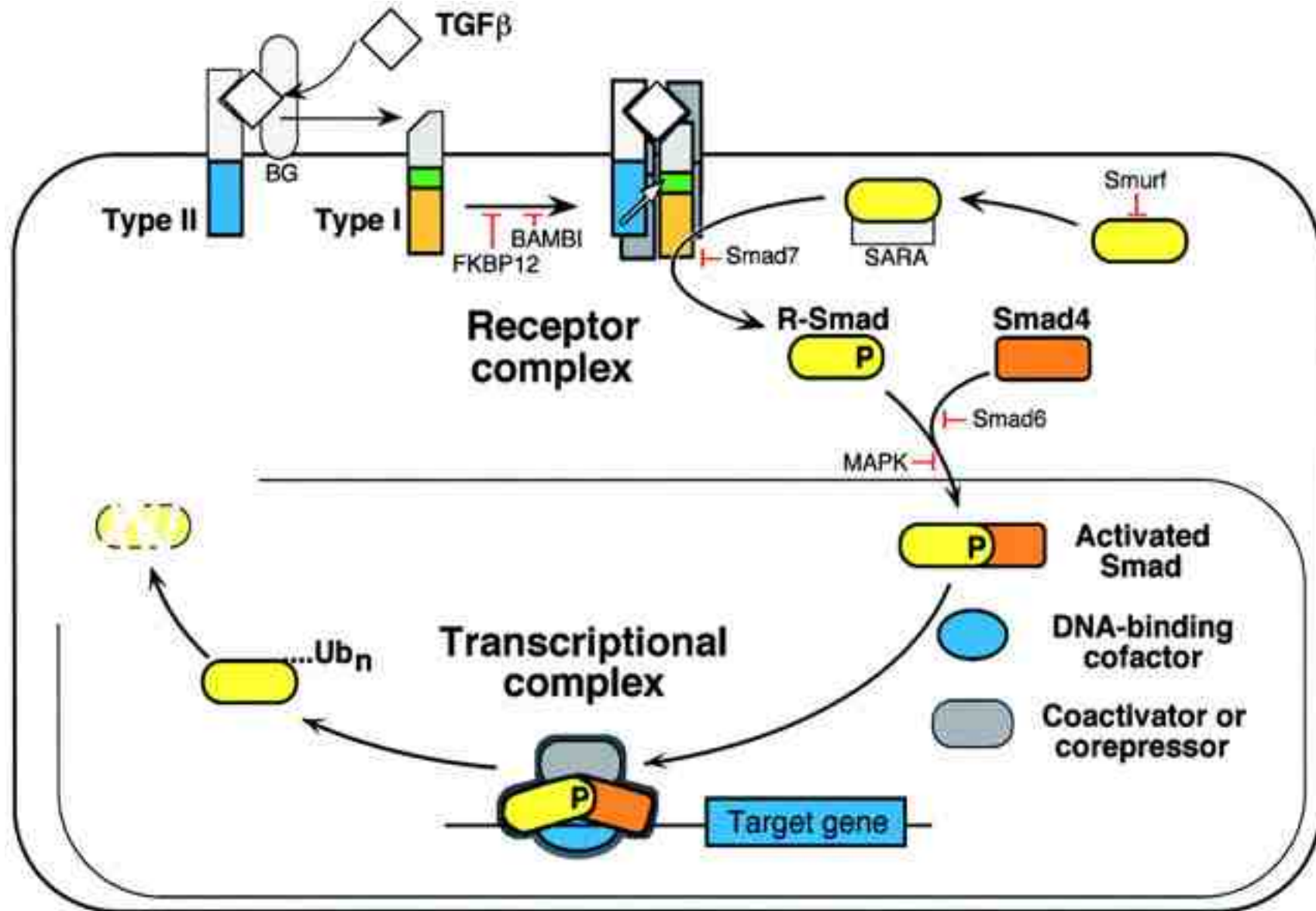
* Il risultato del taglio S3 libera il dominio citoplasmatico (NICD) che è trasportato nel nucleo dove si associa e regola fattori trascrizionali.

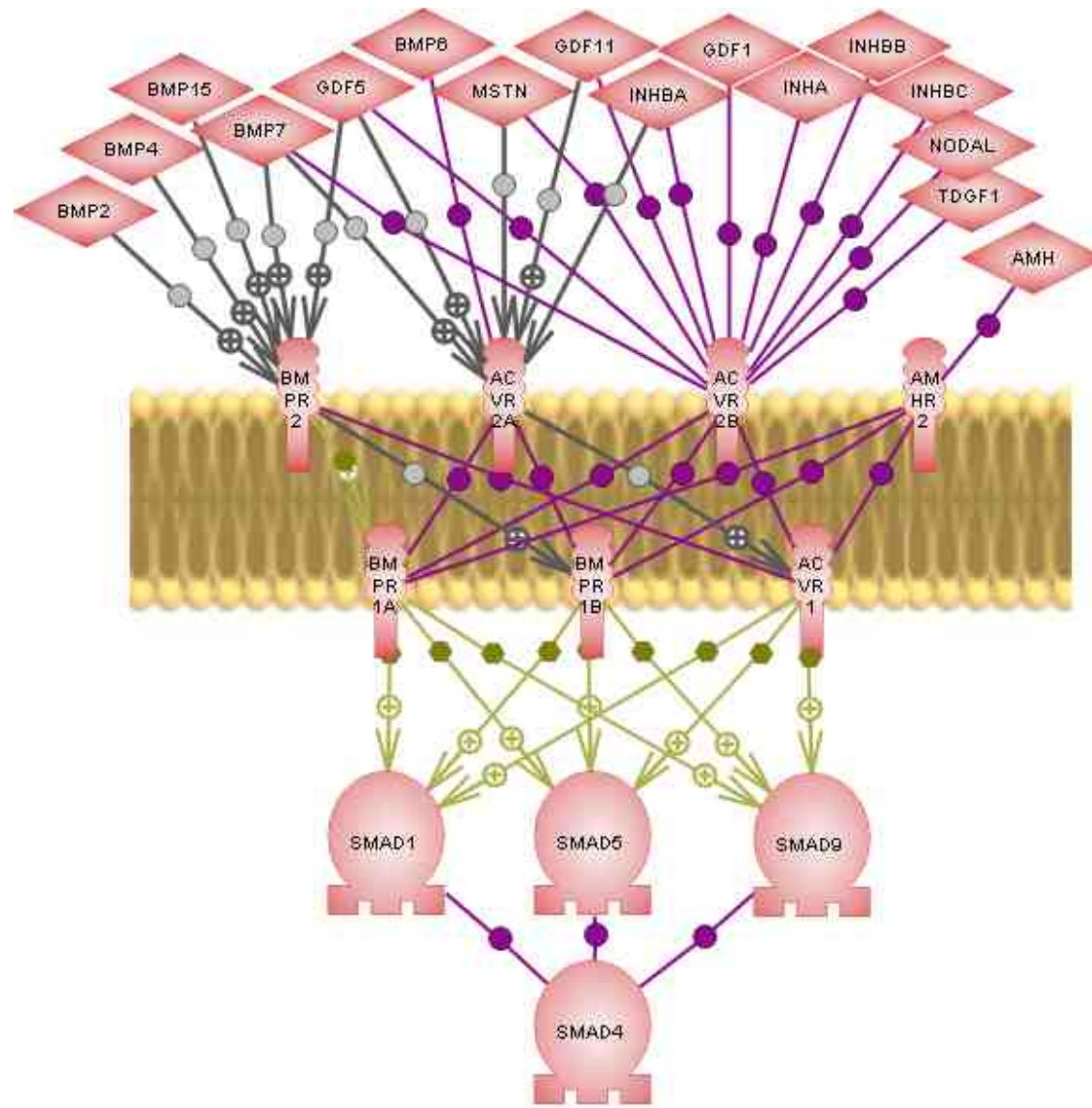


diversi modi di desensibilizzazione ad una molecola segnale

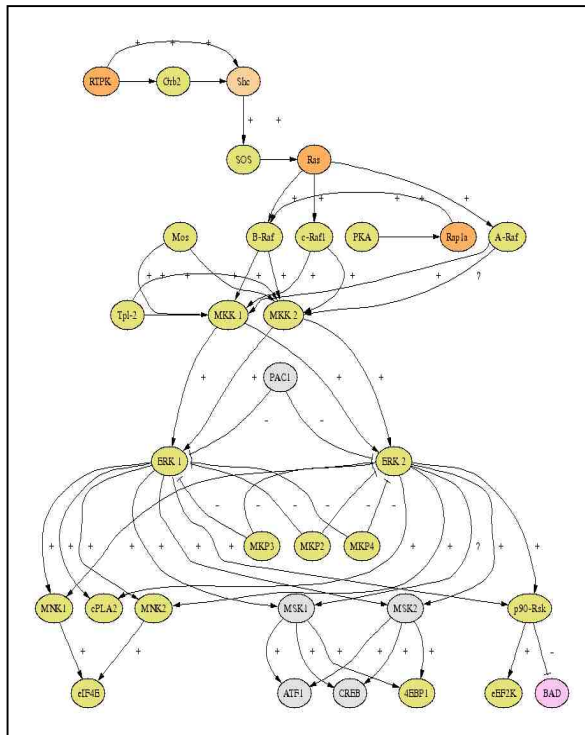


Serine-threonine receptors

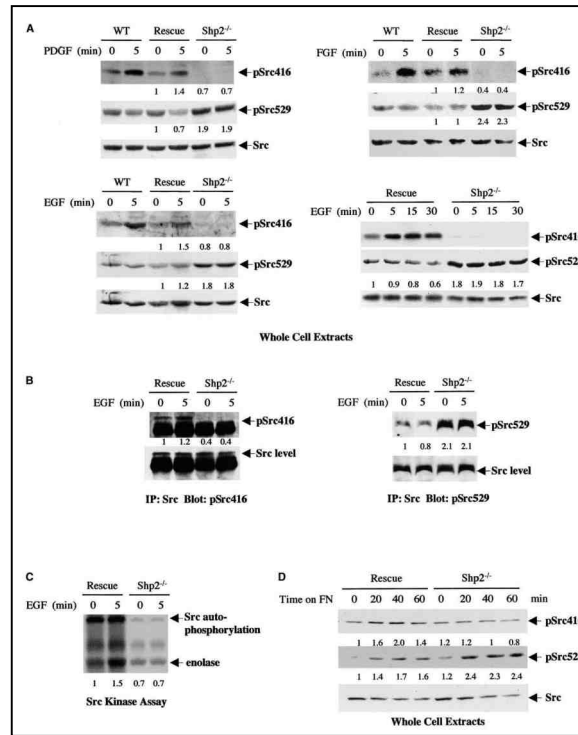




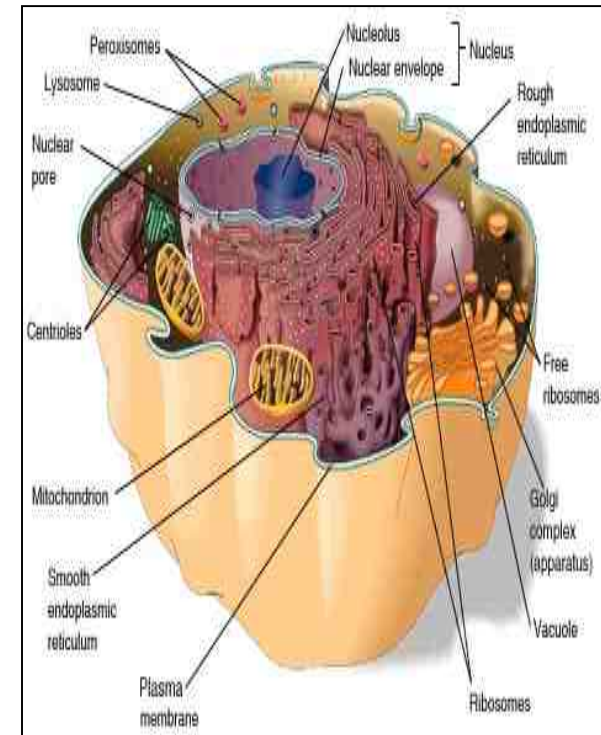
Signal Transduction



What?

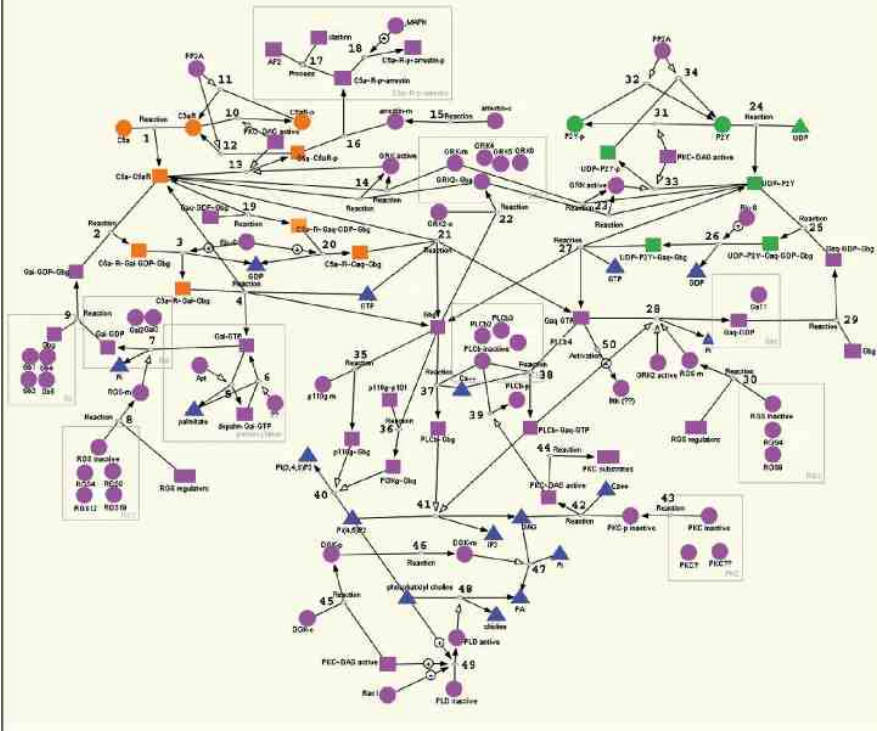
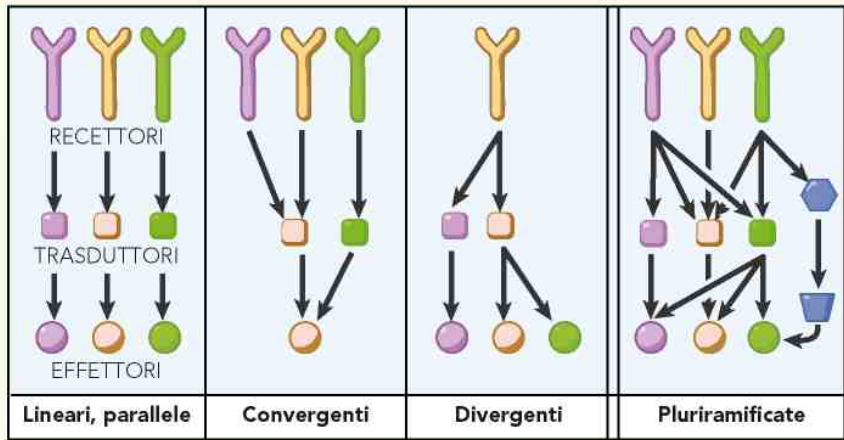


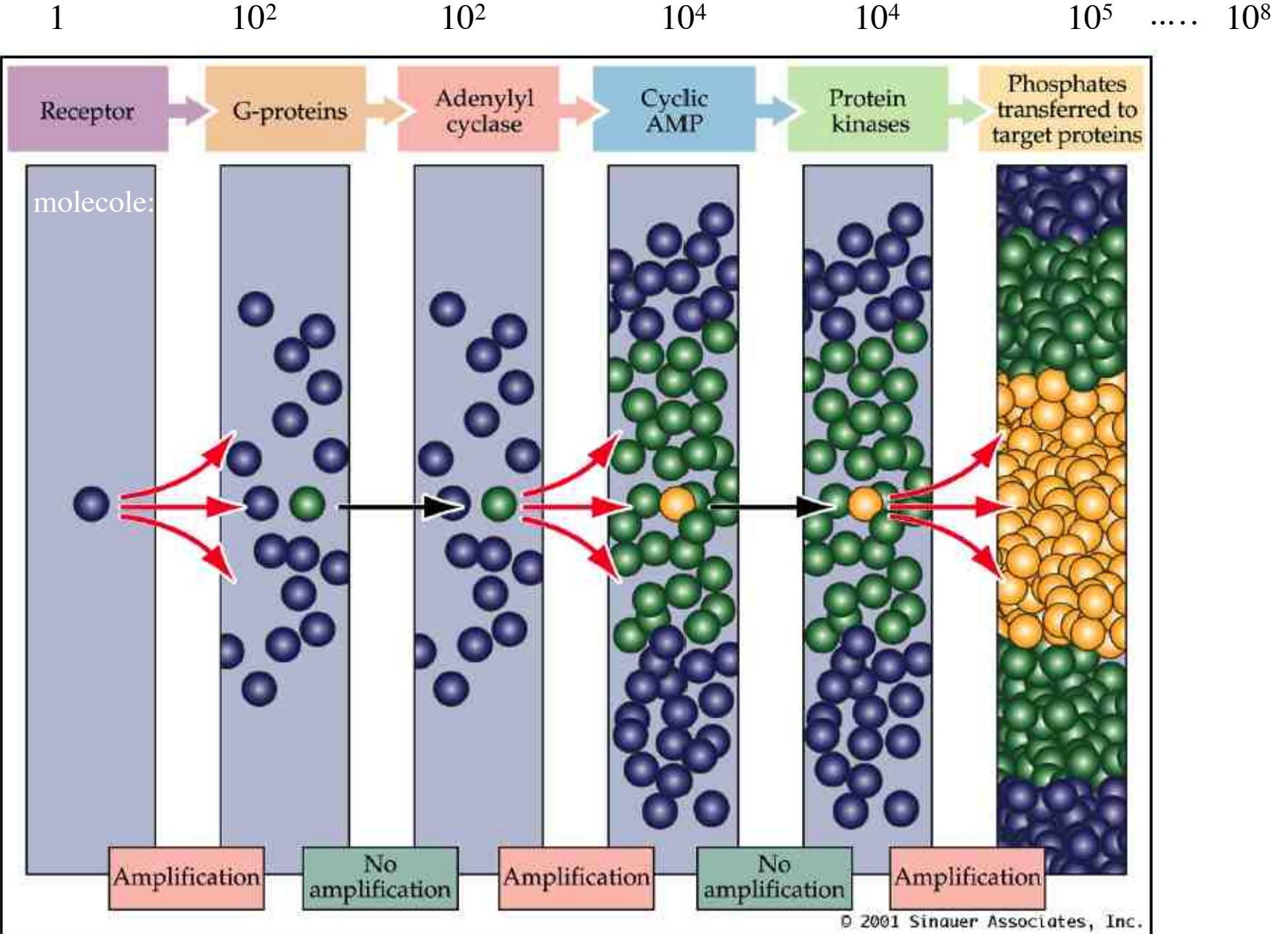
When?

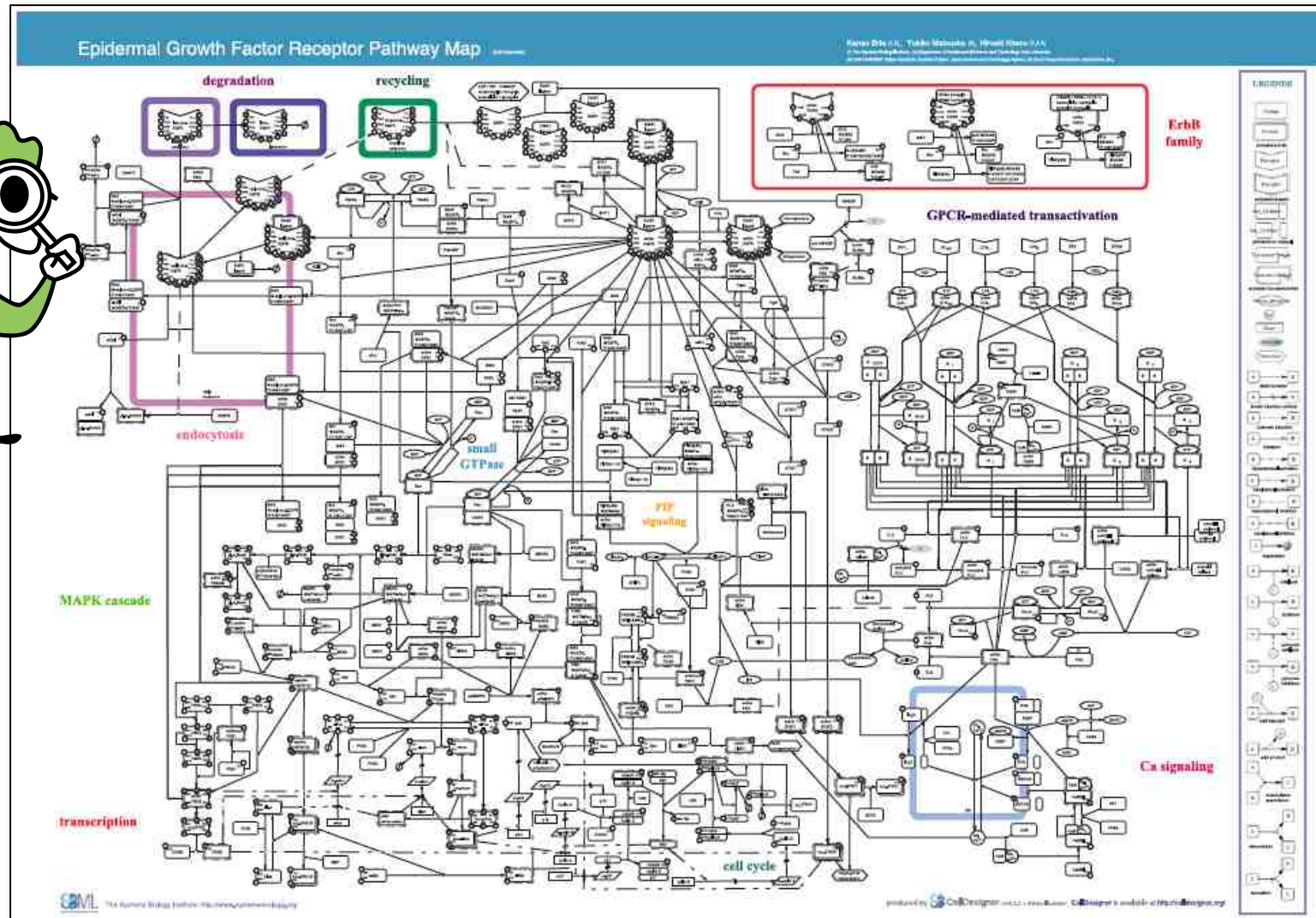
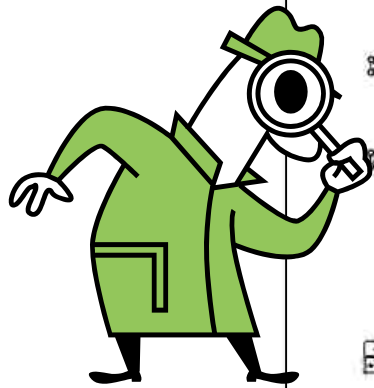


Where?

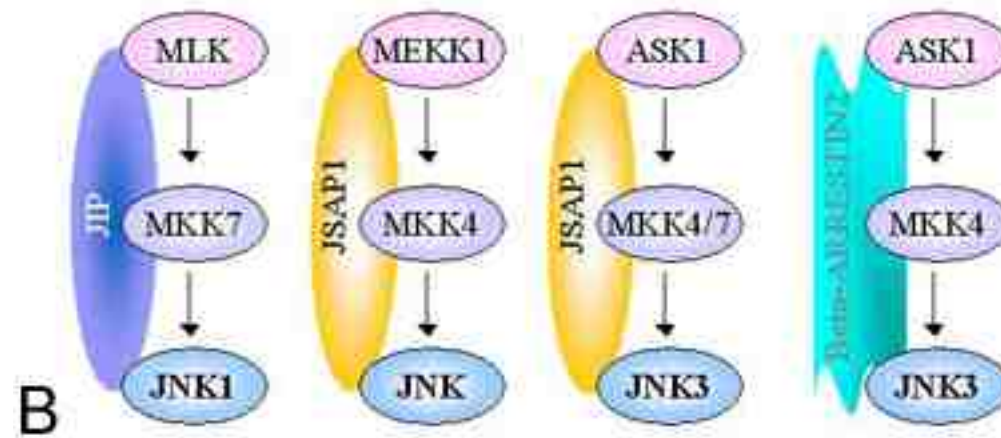
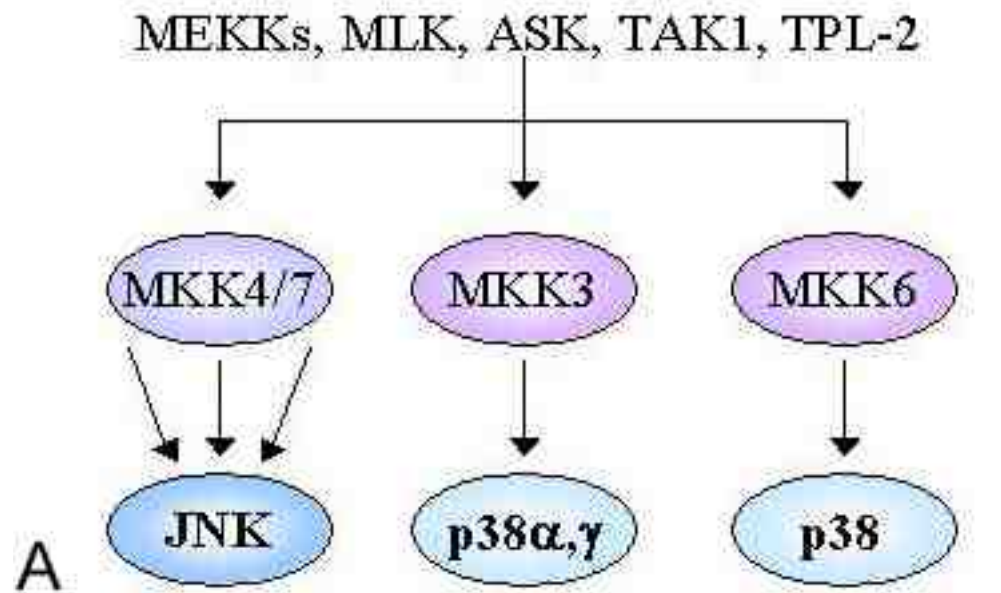
Vie di segnalazione convergenti e divergenti







protein-protein interaction:
Experimental approach

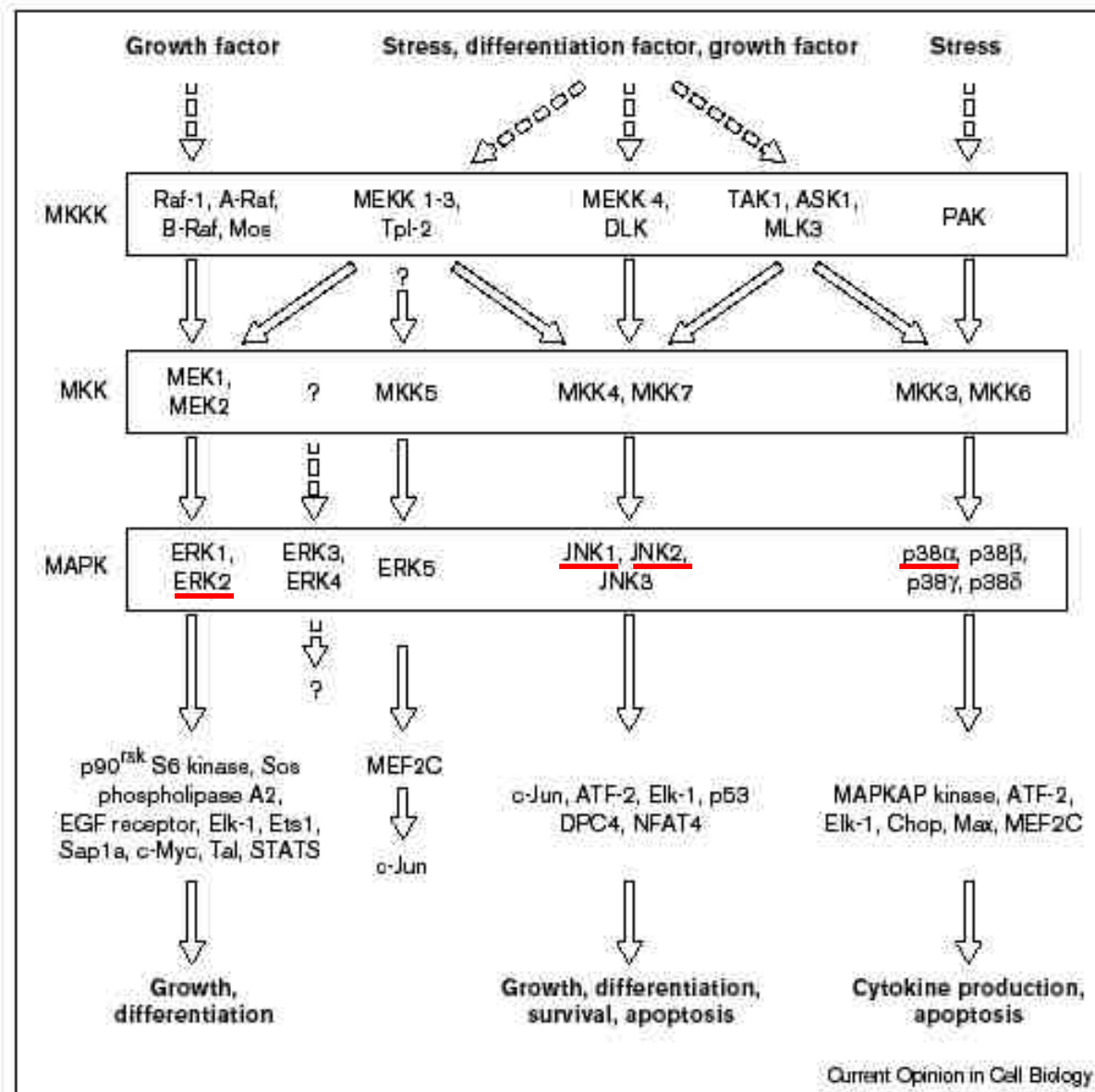


A Mammalian Scaffold Complex That Selectively Mediates MAP Kinase Activation

**Alan J. Whitmarsh, Julie Cavanagh, Cathy Tournier, Jun Yasuda,
Roger J. Davis***

The c-Jun NH₂-terminal kinase (JNK) group of mitogen-activated protein (MAP) kinases is activated by the exposure of cells to multiple forms of stress. A putative scaffold protein was identified that interacts with multiple components of the JNK signaling pathway, including the mixed-lineage group of MAP kinase kinase kinases (MLK), the MAP kinase kinase MKK7, and the MAP kinase JNK. This scaffold protein selectively enhanced JNK activation by the MLK signaling pathway. These data establish that a mammalian scaffold protein can mediate activation of a MAP kinase signaling pathway.

Science. 1998 Sep 11;281(5383):1671-4.



Which MAPK interact with JIP-1?

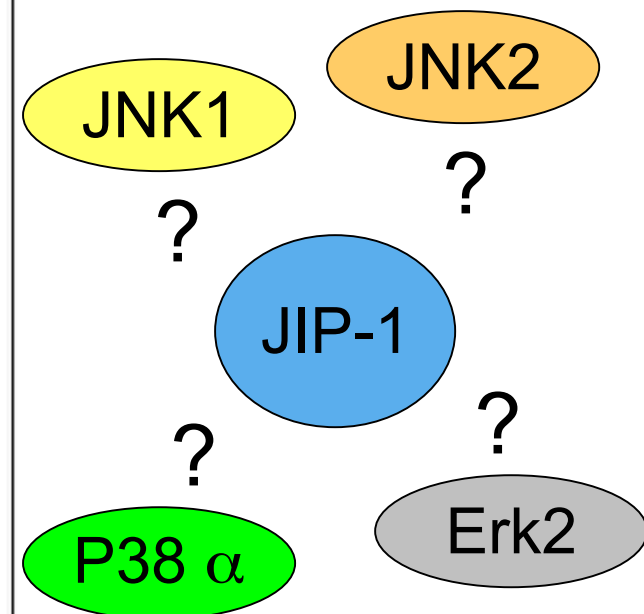
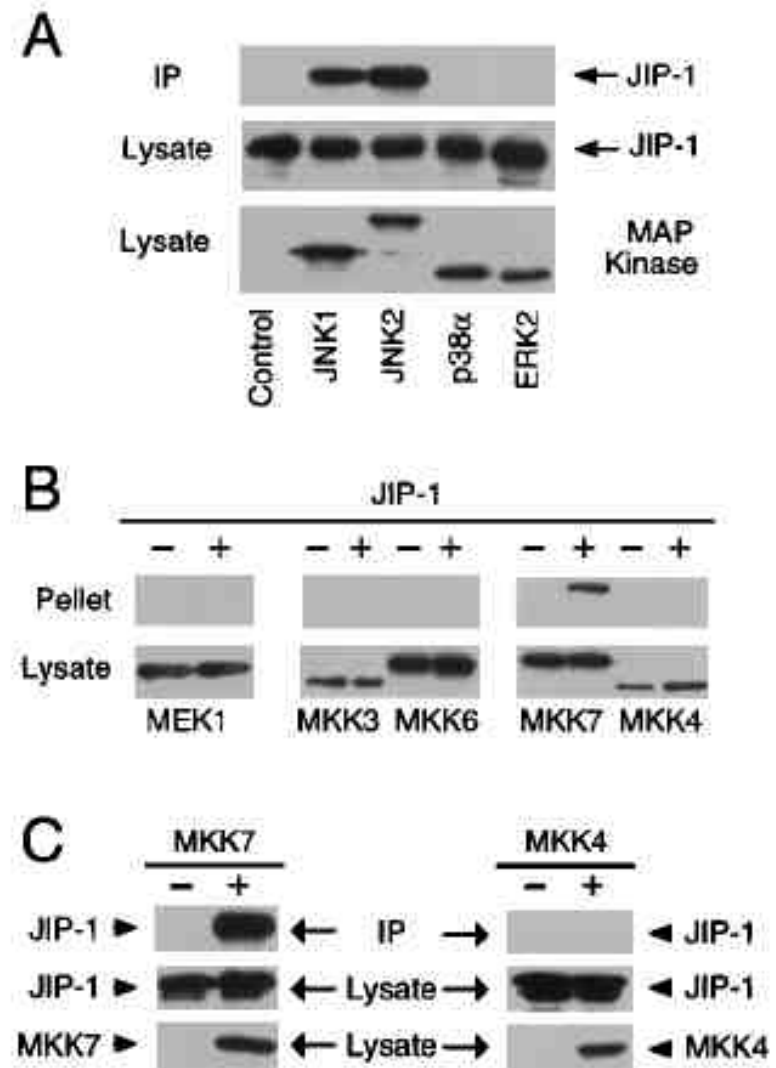


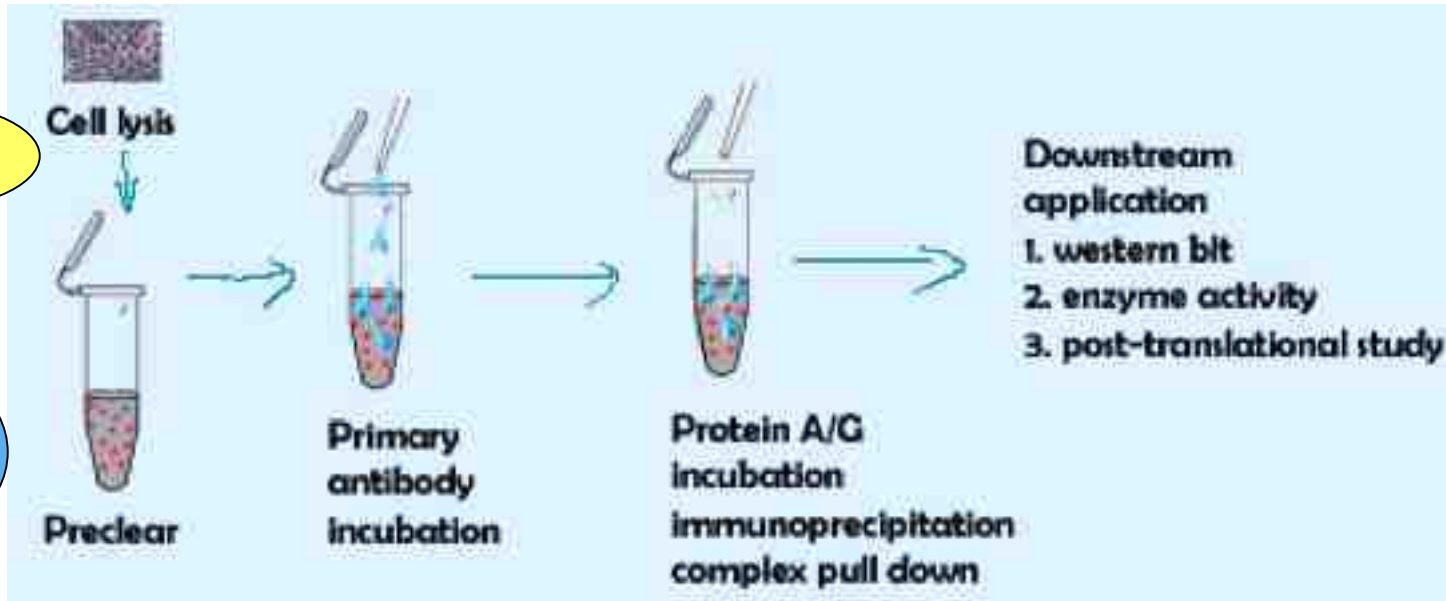
Fig. 1. Selective binding of JIP-1 to the MAP kinase JNK and the MAP kinase kinase MKK7. **(A)** Epitope-tagged JIP-1 (T7-Tag) was expressed in cells with the HA-tagged MAP kinases ERK2, p38 α , JNK1, and JNK2 (15, 16). The MAP kinases were immunoprecipitated with an antibody to HA. The presence of JIP-1 in the immunoprecipitates (IP) was detected on immunoblots probed with an antibody to T7-Tag. The amount of JIP-1 and MAP kinases in the cell lysates was examined by protein immunoblot analysis. **(B)** JIP-1 was expressed in cells as a GST fusion protein together with epitope-tagged MEK1, MKK3, MKK4, MKK6, or MKK7 (15, 16). JIP-1 was precipitated from cell lysates with glutathione-agarose, and the MAPKKs present in the pellet were detected by protein immunoblot analysis. The amount of the MAPKKs in the cell lysates was examined by protein immunoblot analysis. **(C)** Epitope-tagged JIP-1 (T7-Tag) was expressed in cells with Flag-tagged MKK4 or MKK7 (15, 16). The presence of JIP-1 in Flag IP was detected by protein immunoblot analysis with an antibody to T7-Tag. The amount of the MAPKKs in the cell lysates was examined by protein immunoblot analysis.



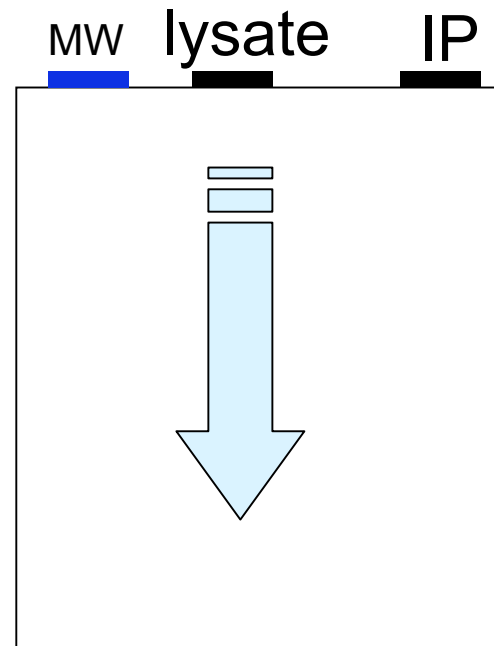
JNK1

?

JIP-1



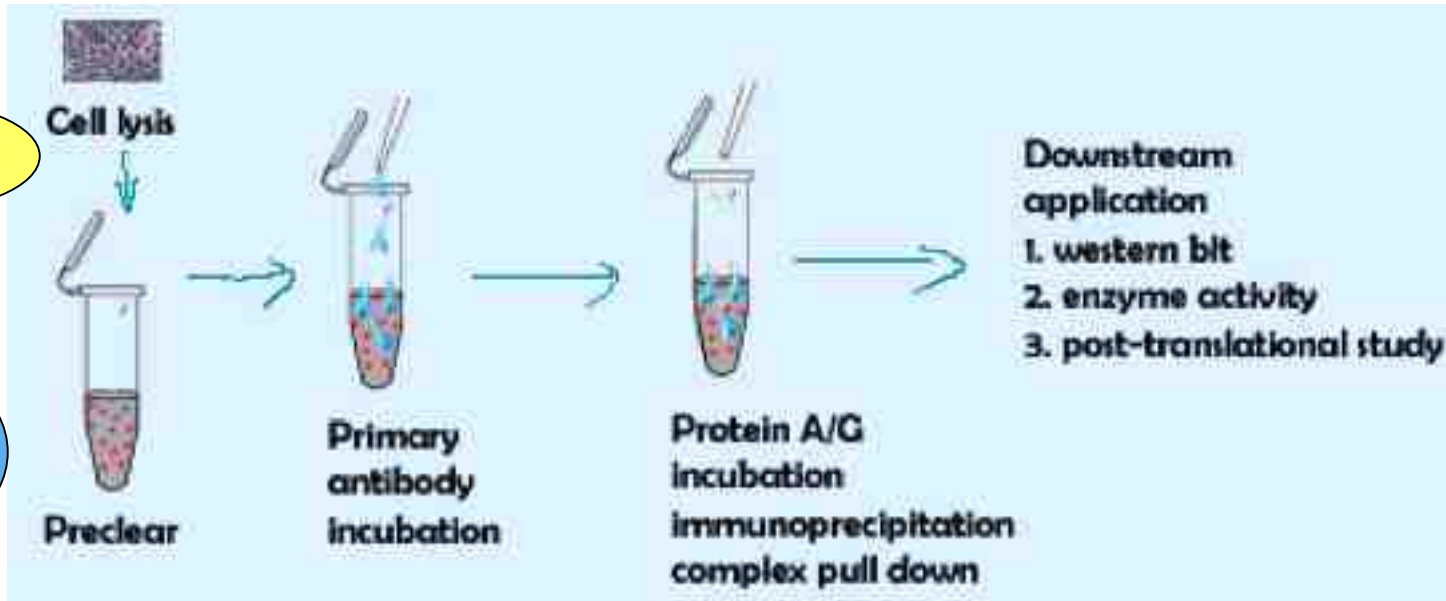
IP anti JNK1



JNK1

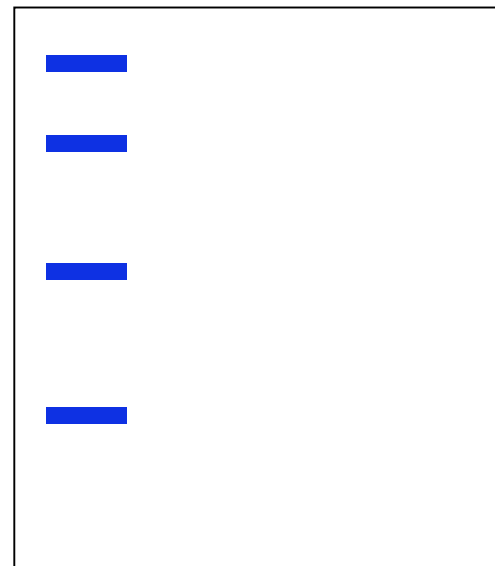
?

JIP-1



IP anti JNK1

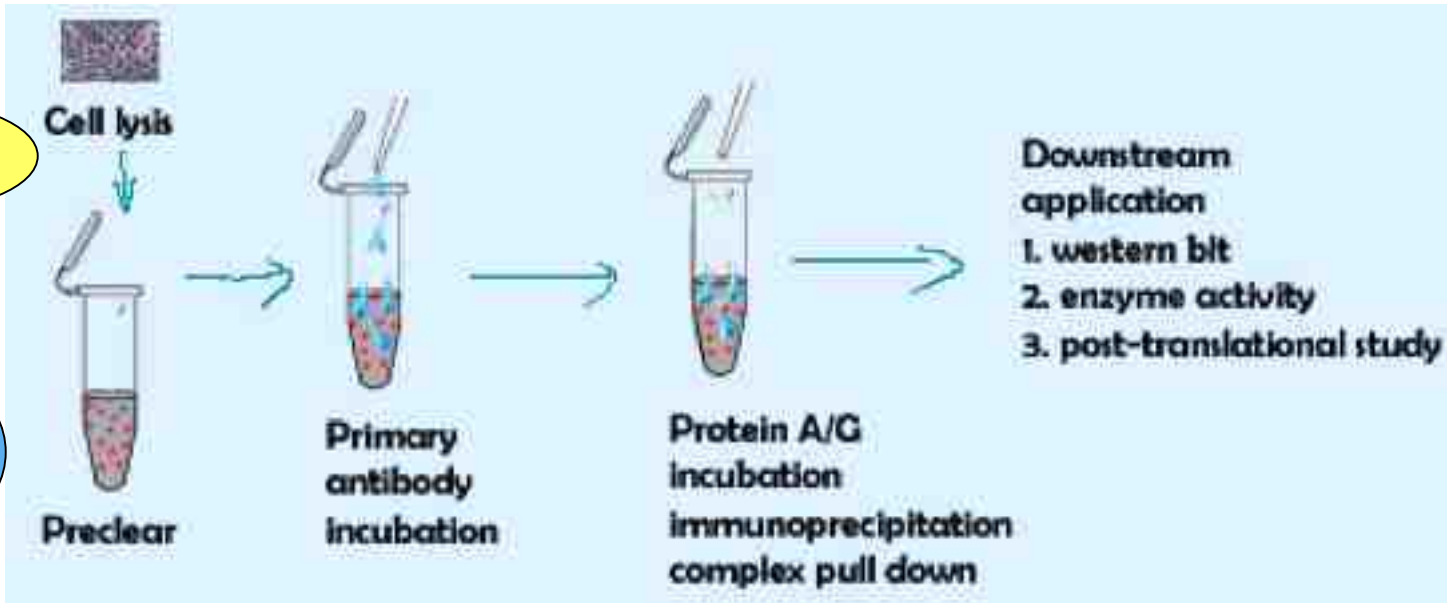
MW lysate IP



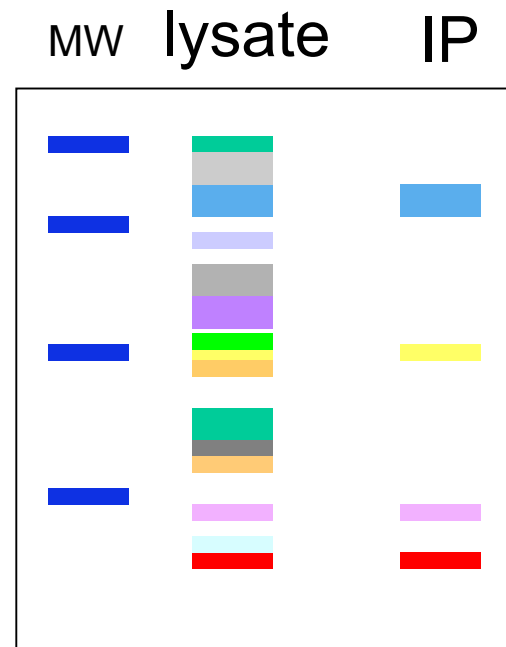
JNK1

?

JIP-1



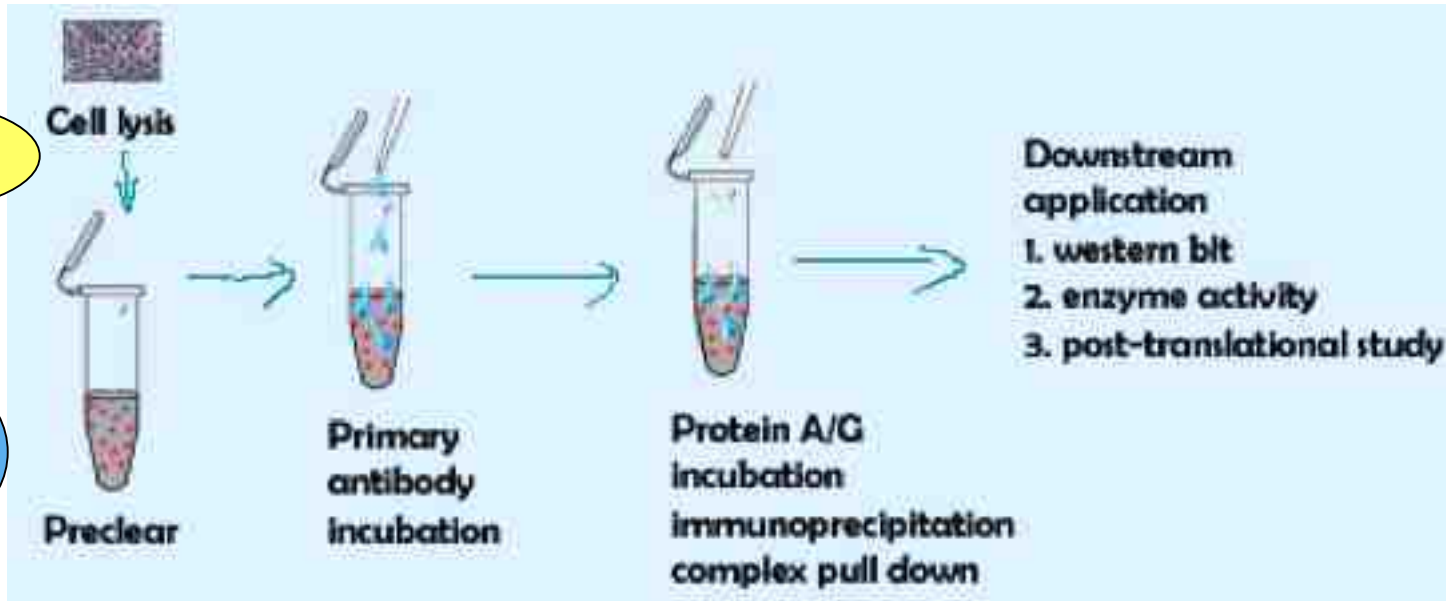
IP anti JNK1



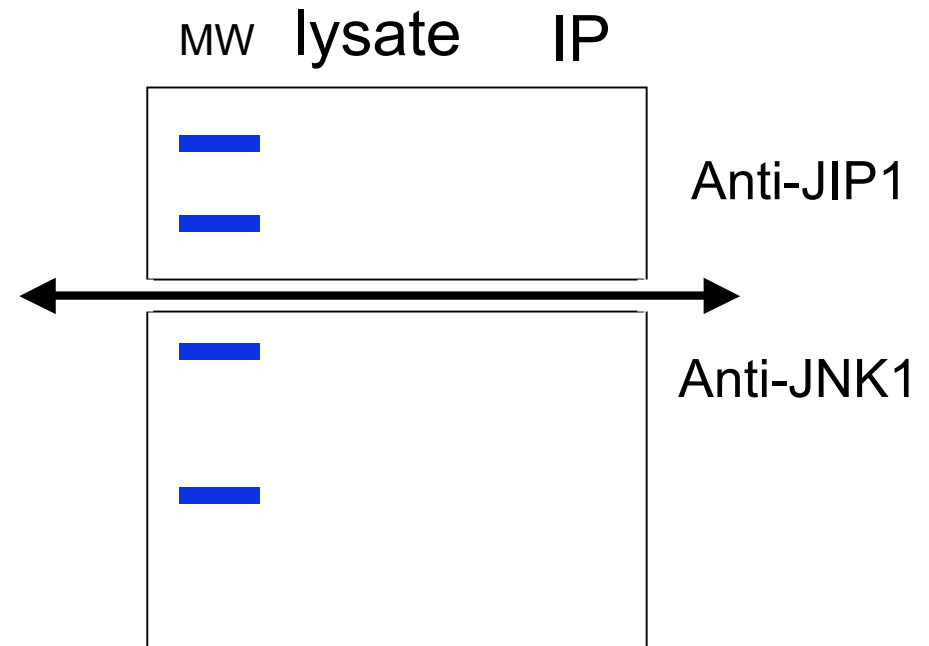
JNK1

?

JIP-1



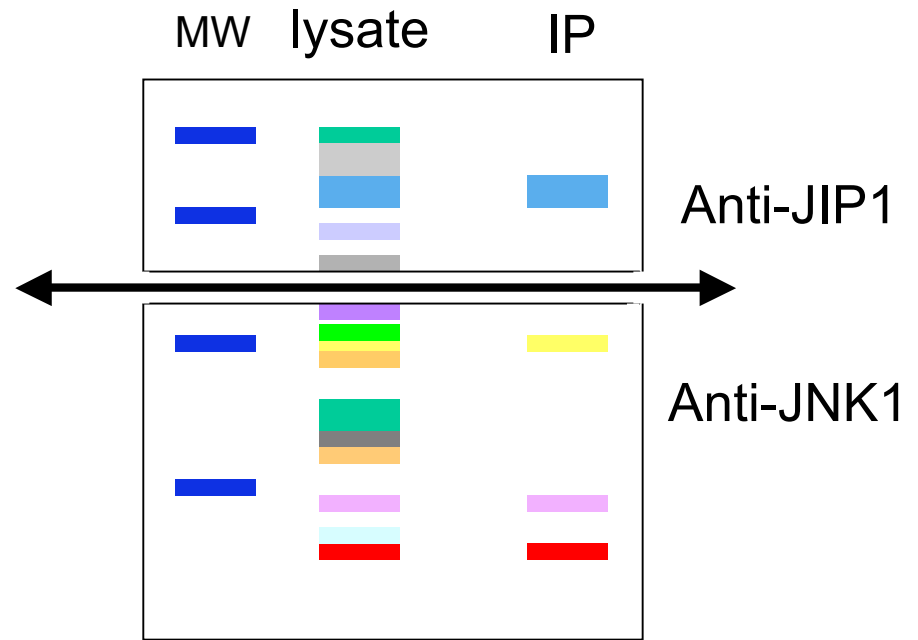
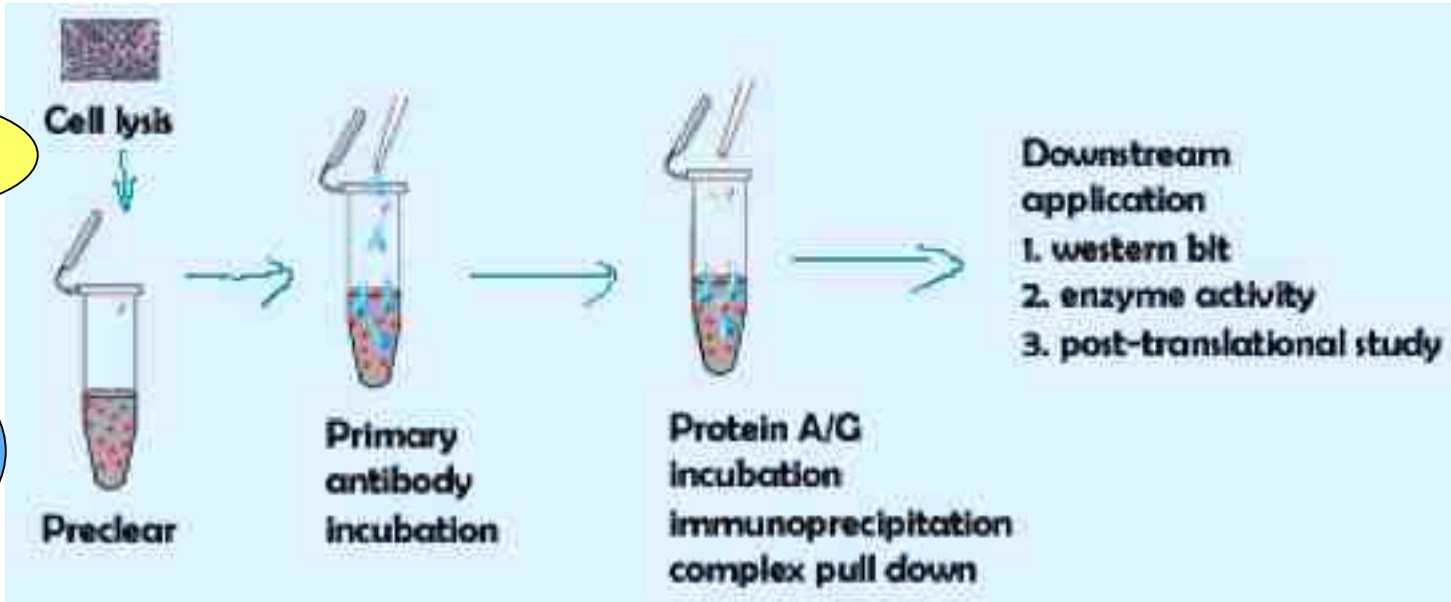
IP anti JNK1



JNK1

?

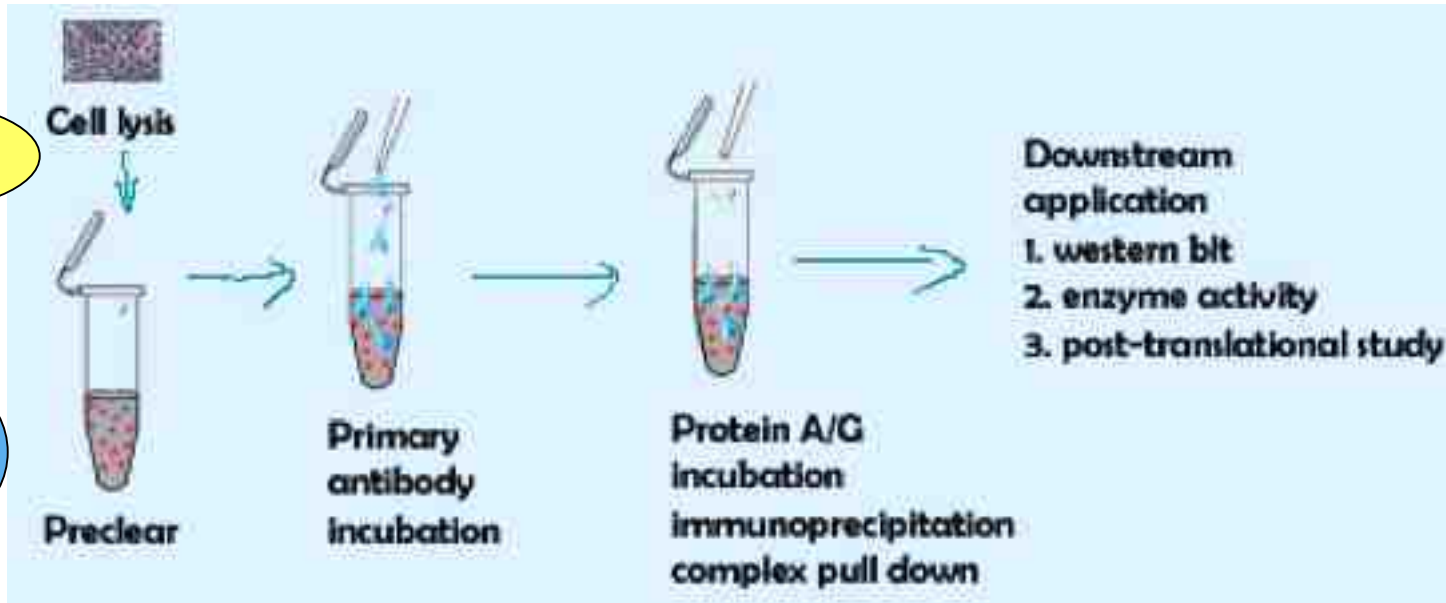
JIP-1



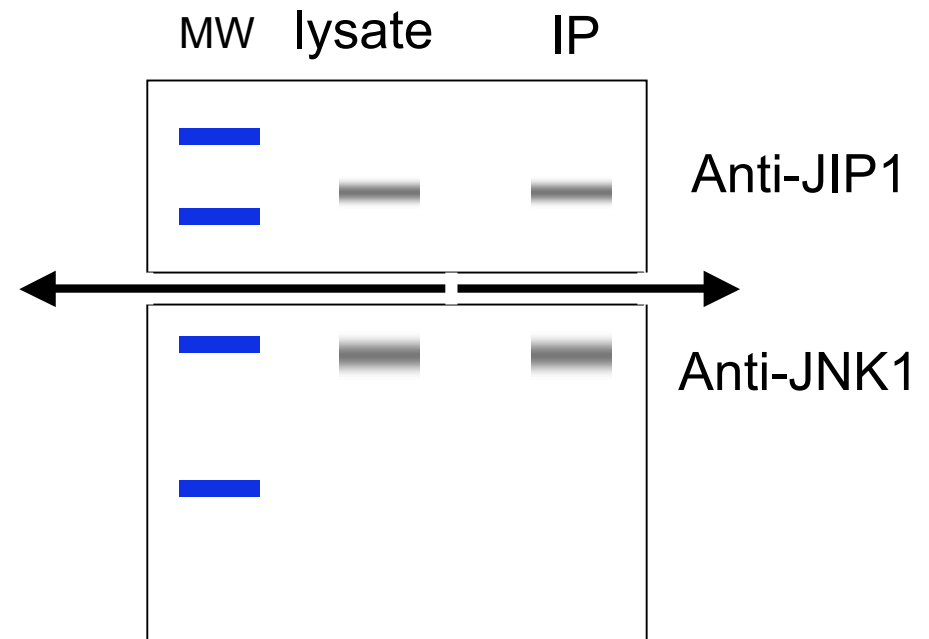
JNK1

?

JIP-1



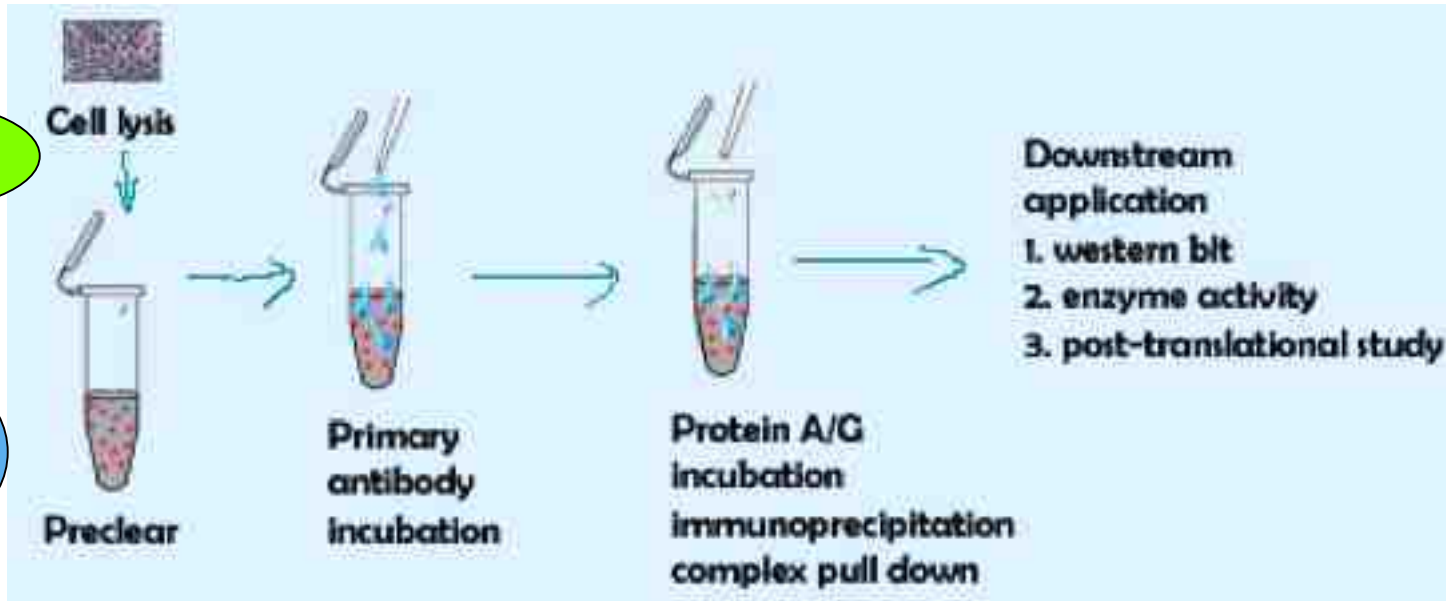
IP anti JNK1



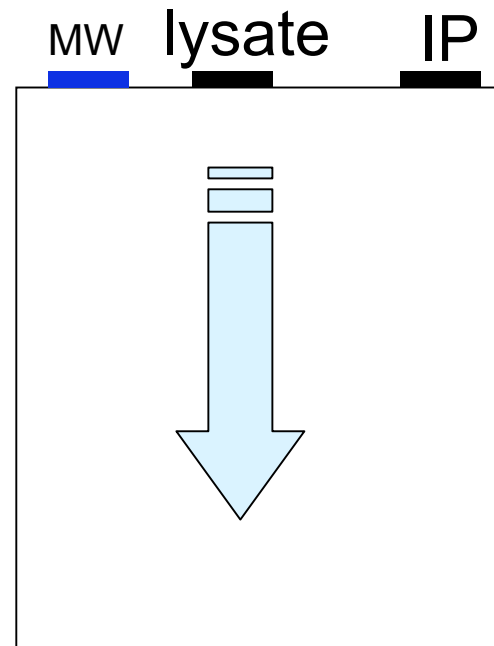
P38 α

?

JIP-1



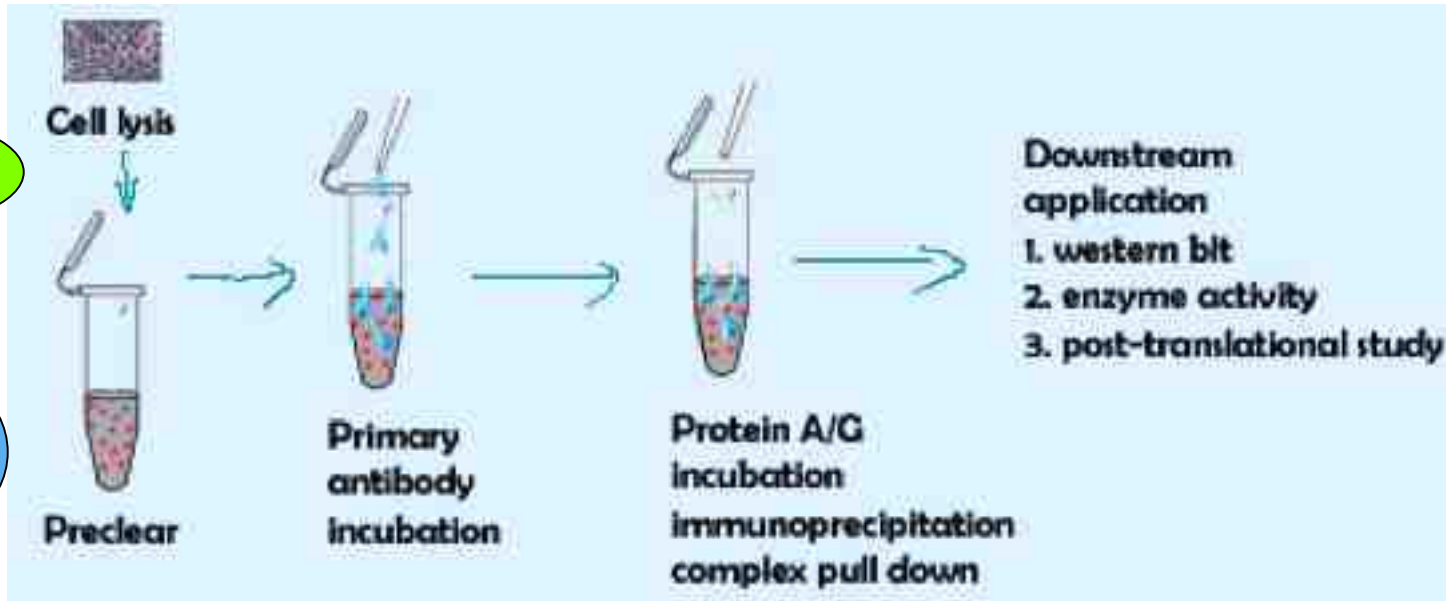
IP anti P38 α



P38 α

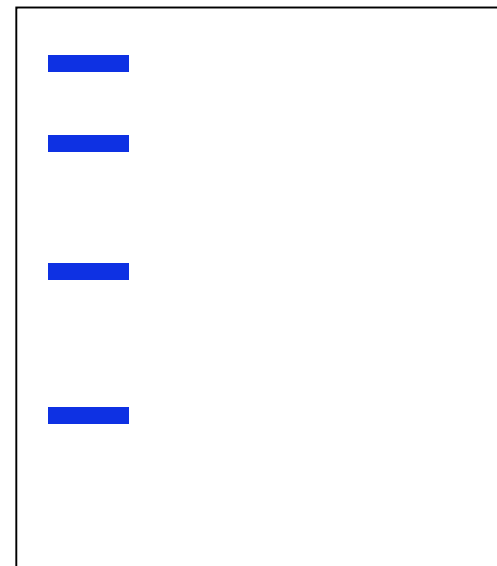
?

JIP-1



IP anti- P38 α

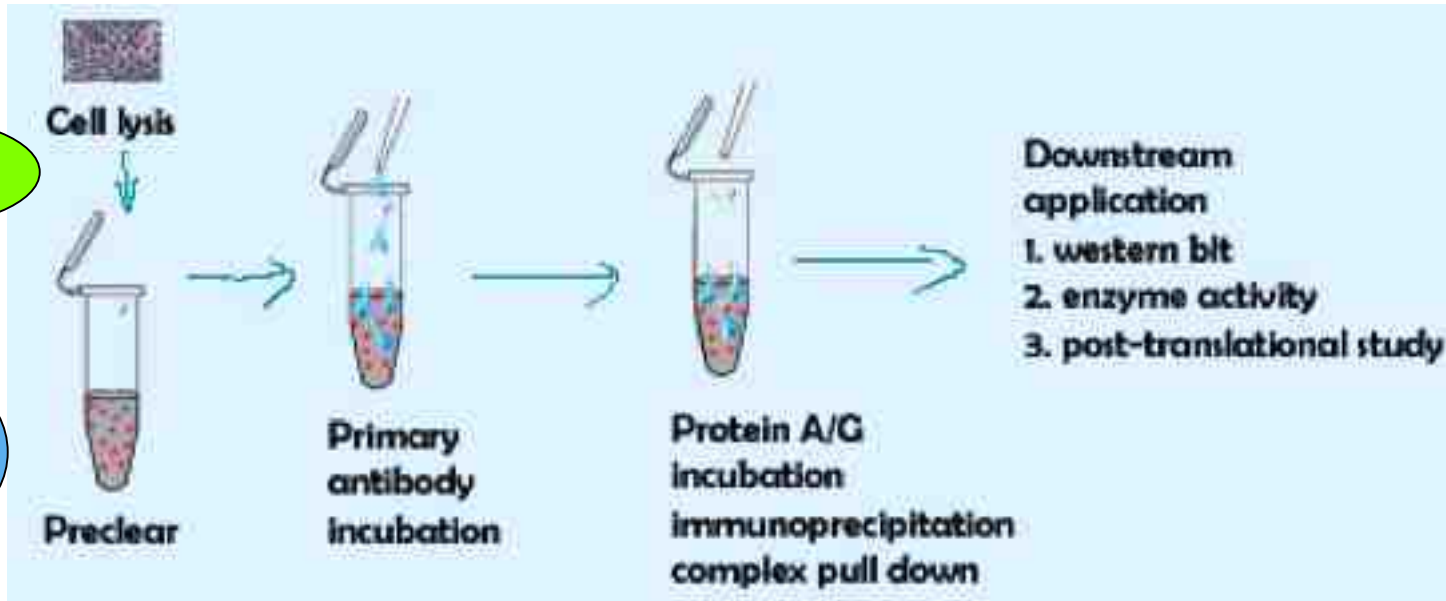
MW lysate IP



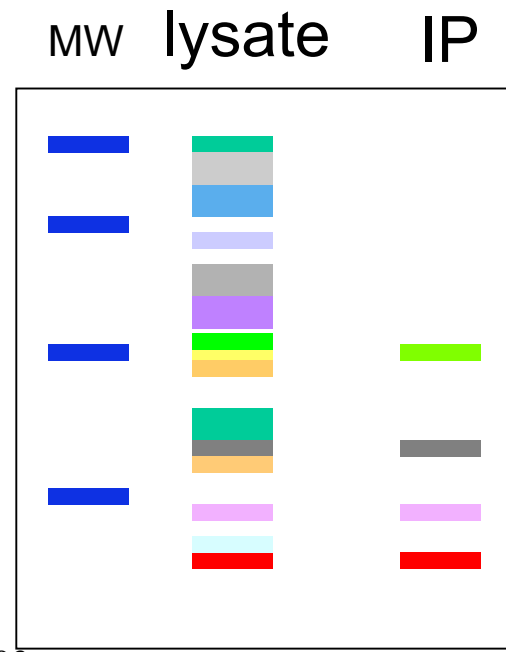
P38 α

?

JIP-1



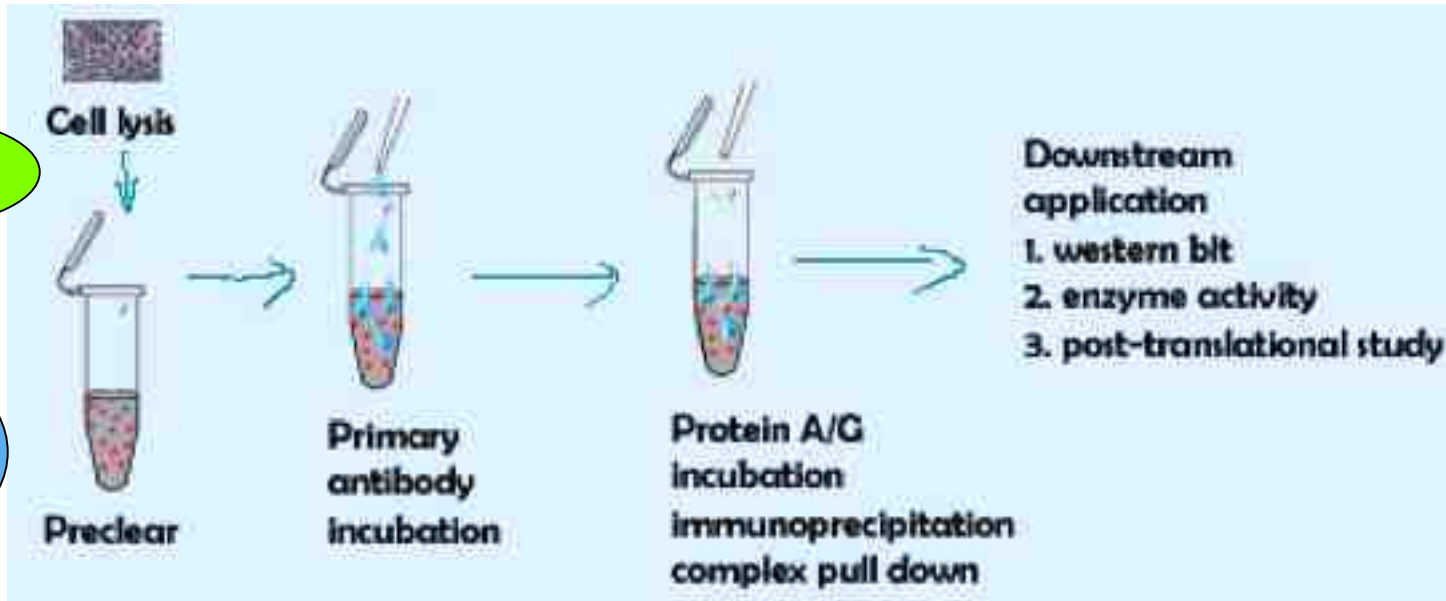
IP anti P38 α



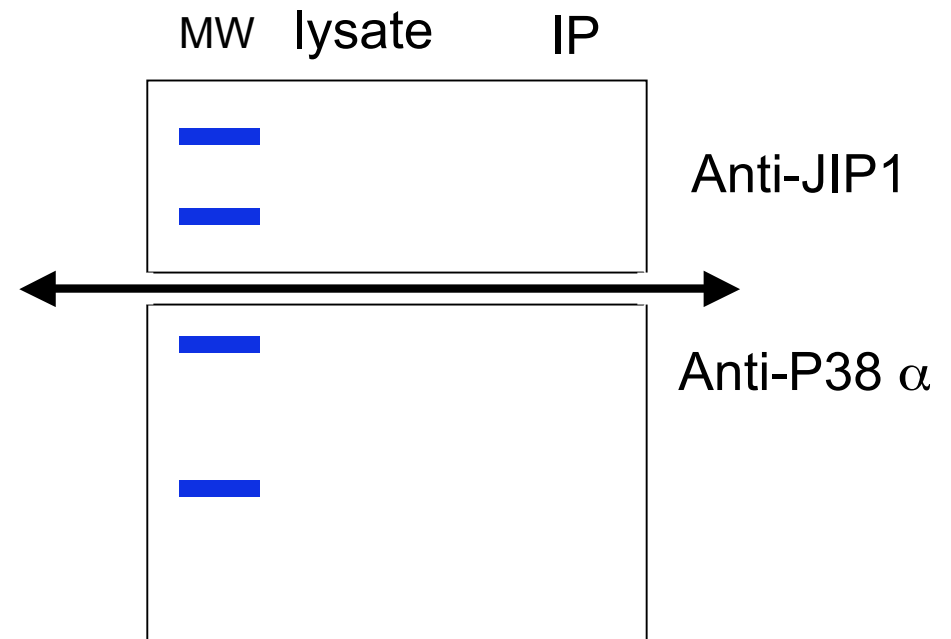
P38 α

?

JIP-1



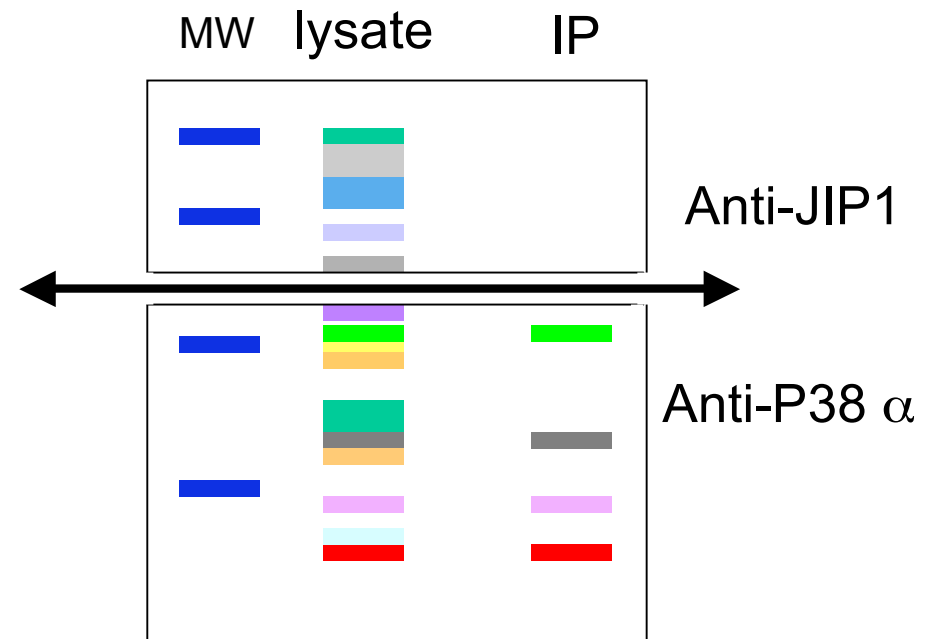
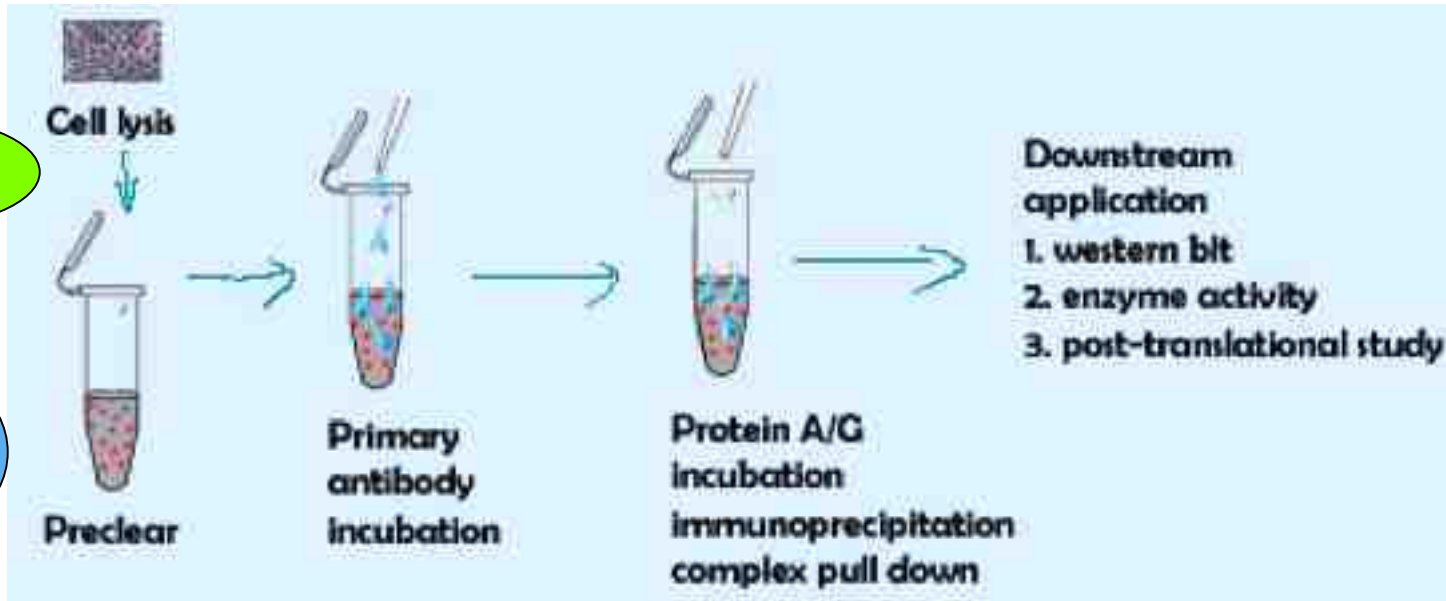
IP anti P38 α



P38 α

?

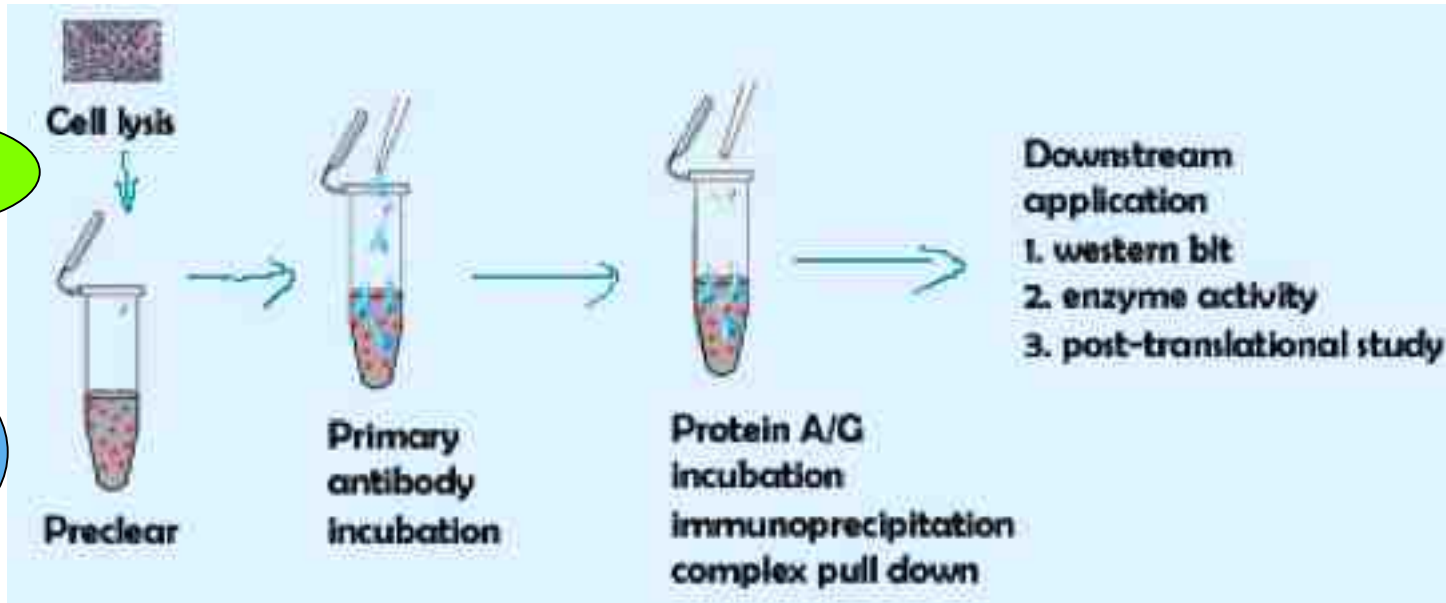
JIP-1



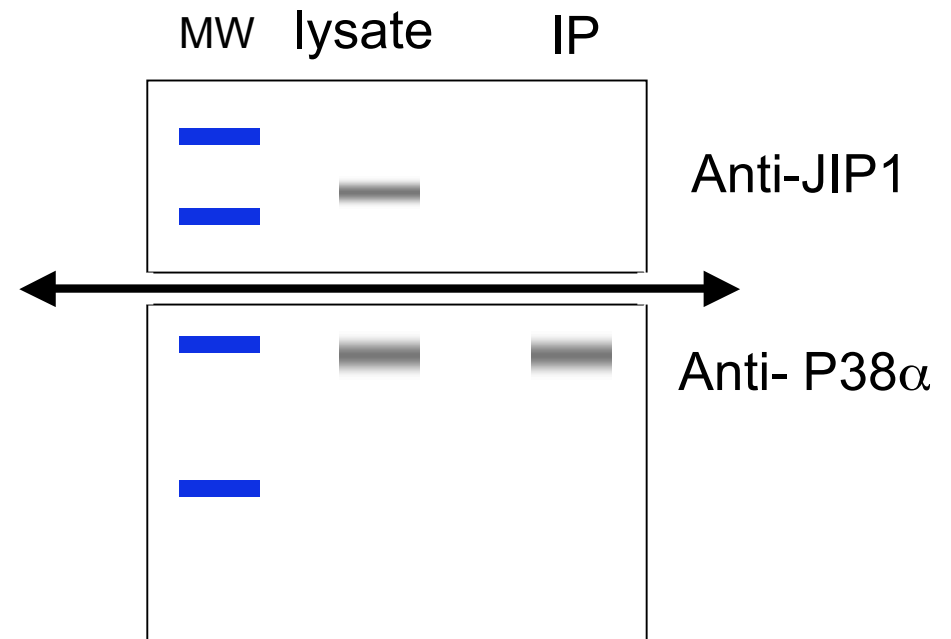
P38 α

?

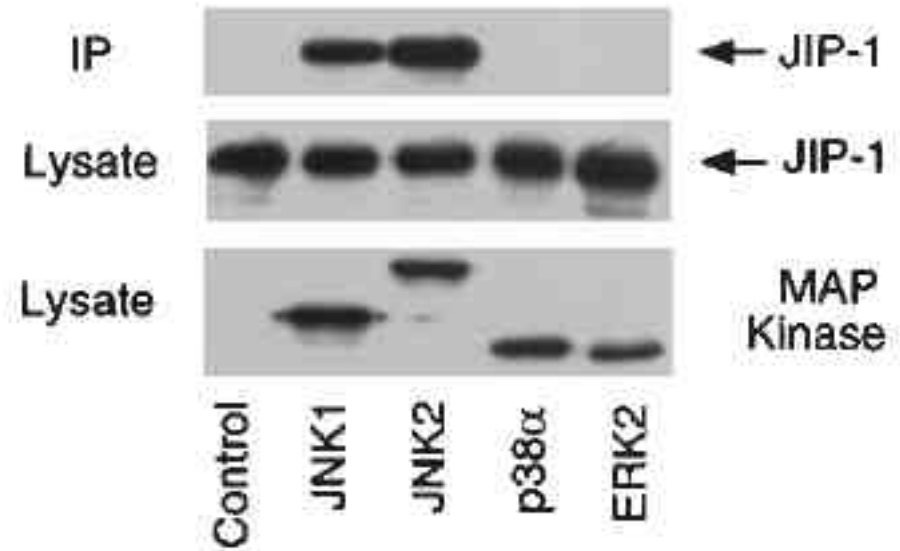
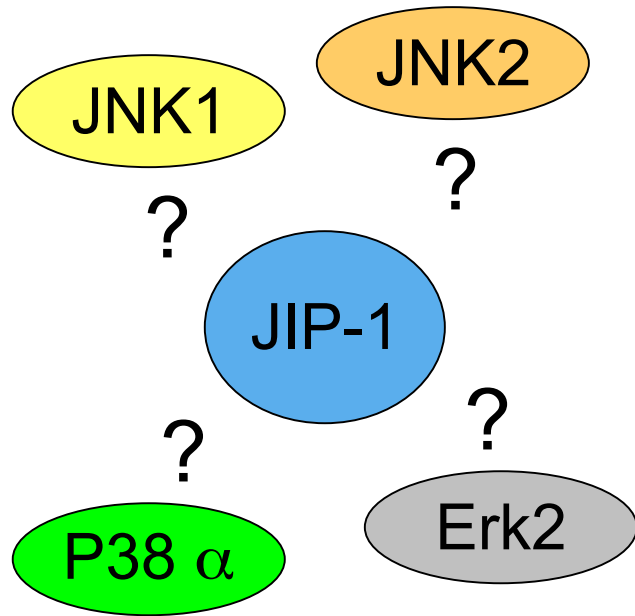
JIP-1



IP anti-P38 α



Selective binding of JIP-1 to the MAP kinase JNK



Selective binding of JIP-1 to the MAP kinase JNK

