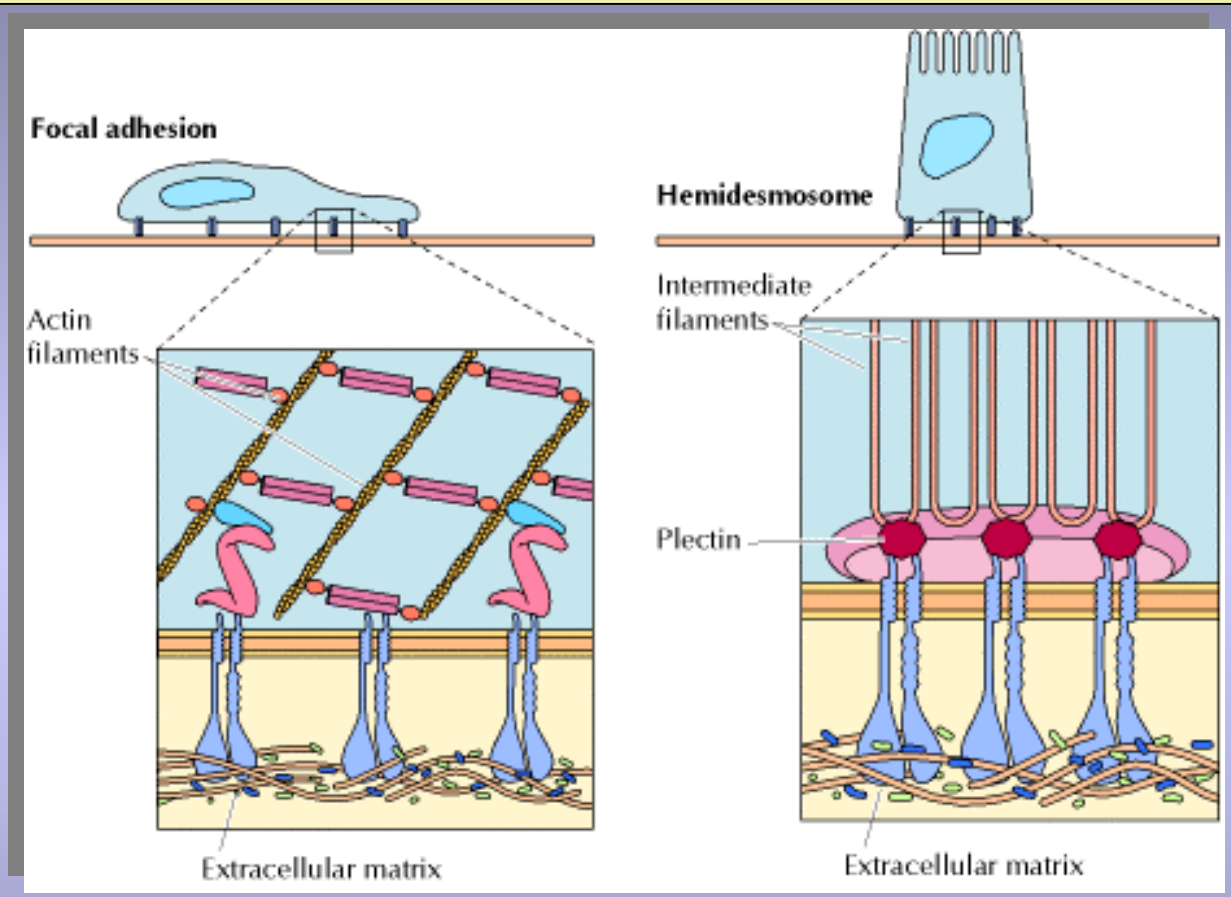
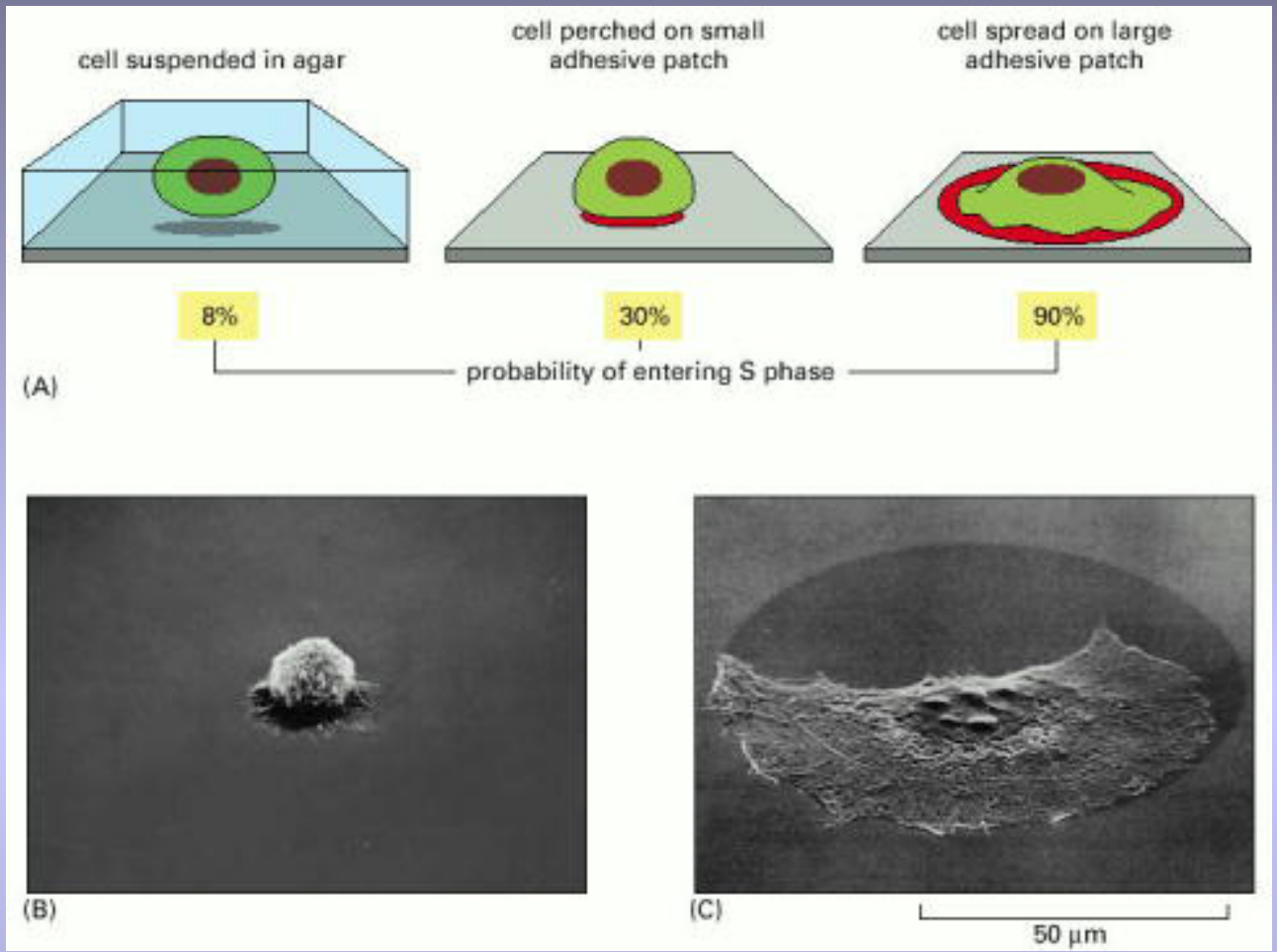
TIPOS DE ANCLAJE CÉLULA-MATRIZ



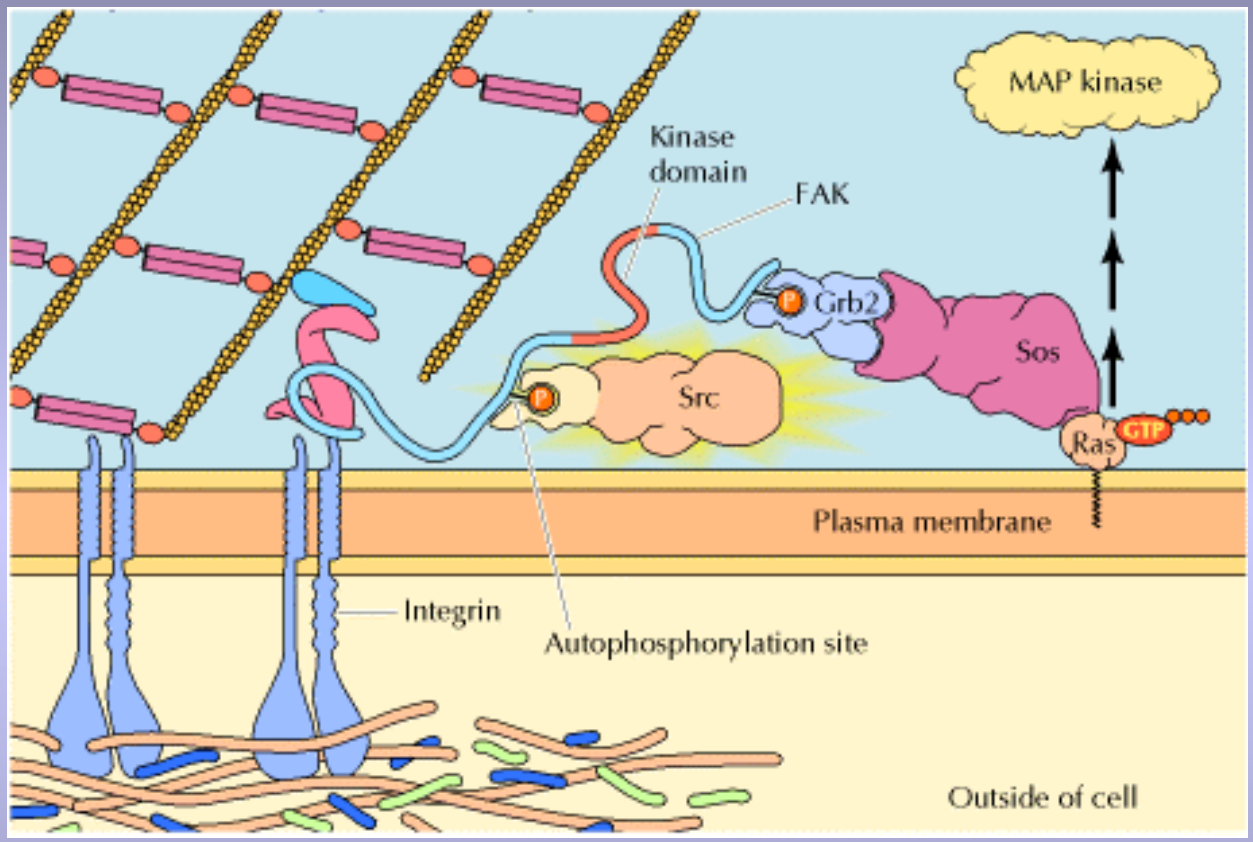
Junctions between cells and the extracellular matrix. Integrins mediate two types of stable junctions in which the cytoskeleton is linked to the extracellular matrix. In focal adhesions, bundles of actin filaments are anchored to the b subunits of most integrins via associations with a number of other proteins, including a-actinin, talin, and vinculin. In hemidesmosomes, $\alpha 6\beta 4$ integrin links the basal lamina to intermediate filaments via plectin. Fuente: Cooper, 2000.



The dependence of cell division on cell shape and anchorage. In this experiment, cells are either held in suspension or allowed to settle on patches of an adhesive material (palladium) on a nonadhesive substratum. The patch diameter, which is variable, determines the extent to which an individual cell spreads and the probability that it will progress into S phase. 3H-thymidine is added to the culture medium, and after 1 or 2 days, the culture is fixed and autoradiographed to determine the percentage of cells that have entered S phase. (A) Few cells of the 3T3 cell line enter S phase when held rounded up in suspension, but adherence even to a very tiny patch one that is too small to allow spreading enables many of them to enter S phase. (B and C) These scanning electron micrographs show a cell perched on a small patch compared with a cell spread on a large patch. In contrast to fibroblasts and epithelial cells, some cell types in the body (including lymphocytes and blood cell precursors) can divide readily in suspension.

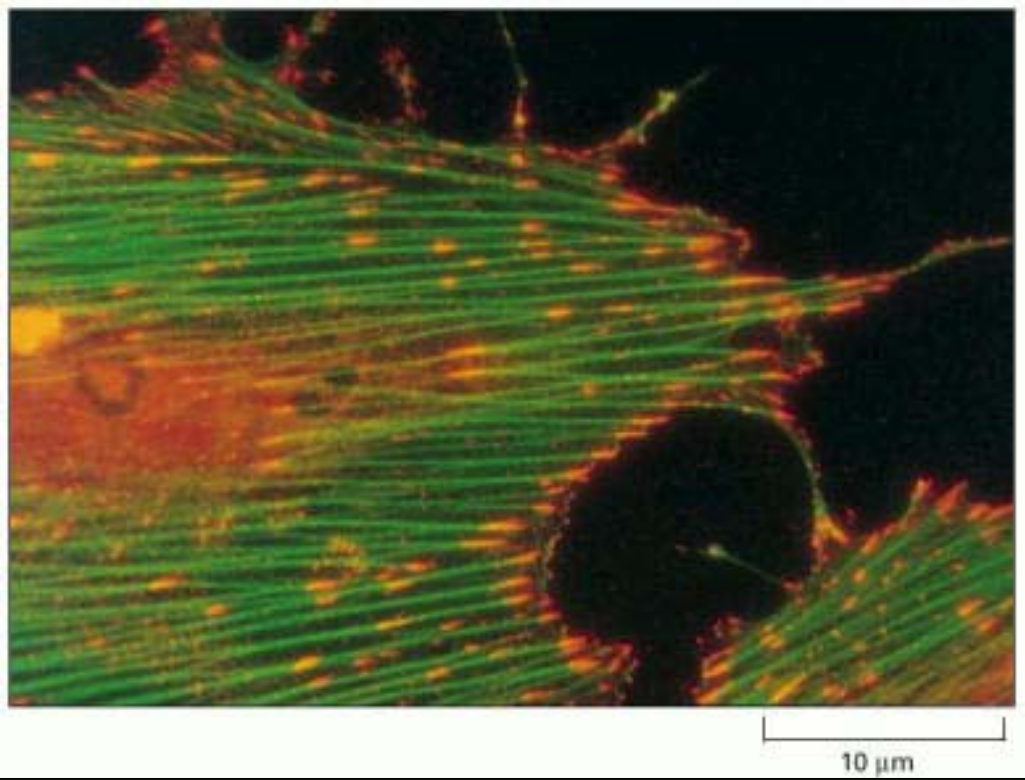
Fuente: Alberts et al., 2002.

SEÑALIZACIÓN MEDIADA POR FAK



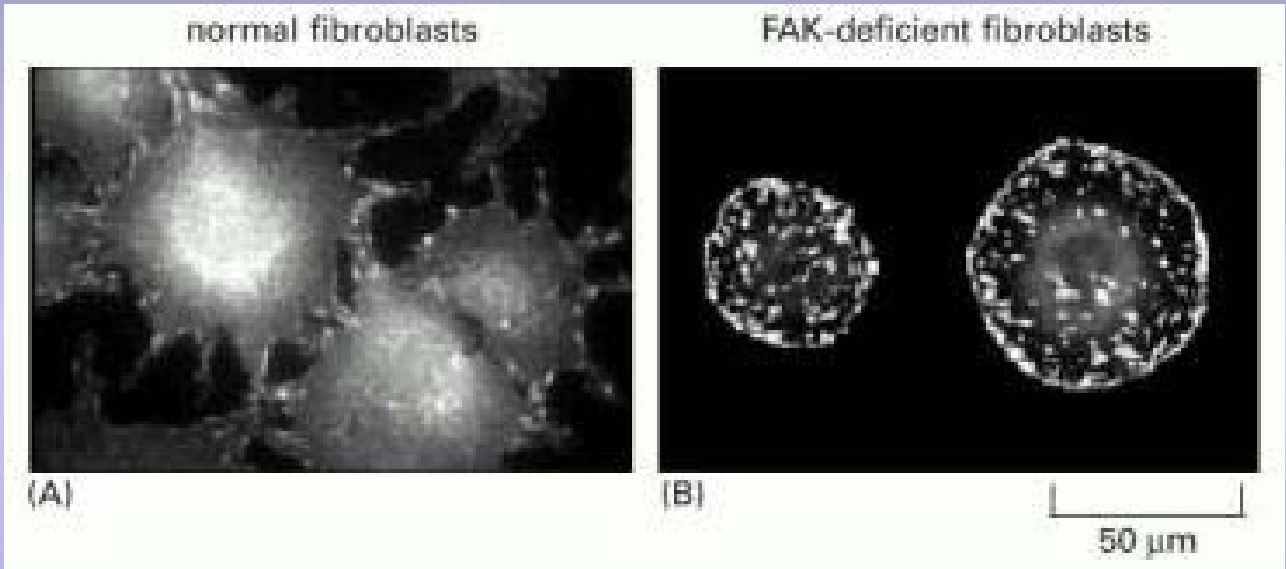
Model for signaling from the FAK protein-tyrosine kinase. Binding of integrins to the extracellular matrix stimulates FAK activity, leading to its autophosphorylation. Src then binds to the FAK autophosphorylation site and phosphorylates FAK on additional tyrosine residues. These phosphotyrosines serve as binding sites for the Grb2-Sos complex, leading to activation of Ras and the MAP kinase cascade, as well as for additional downstream signaling molecules, including PI 3-kinase. Fuente: Cooper, 2000.

Fosfotirosinas en los contactos focales



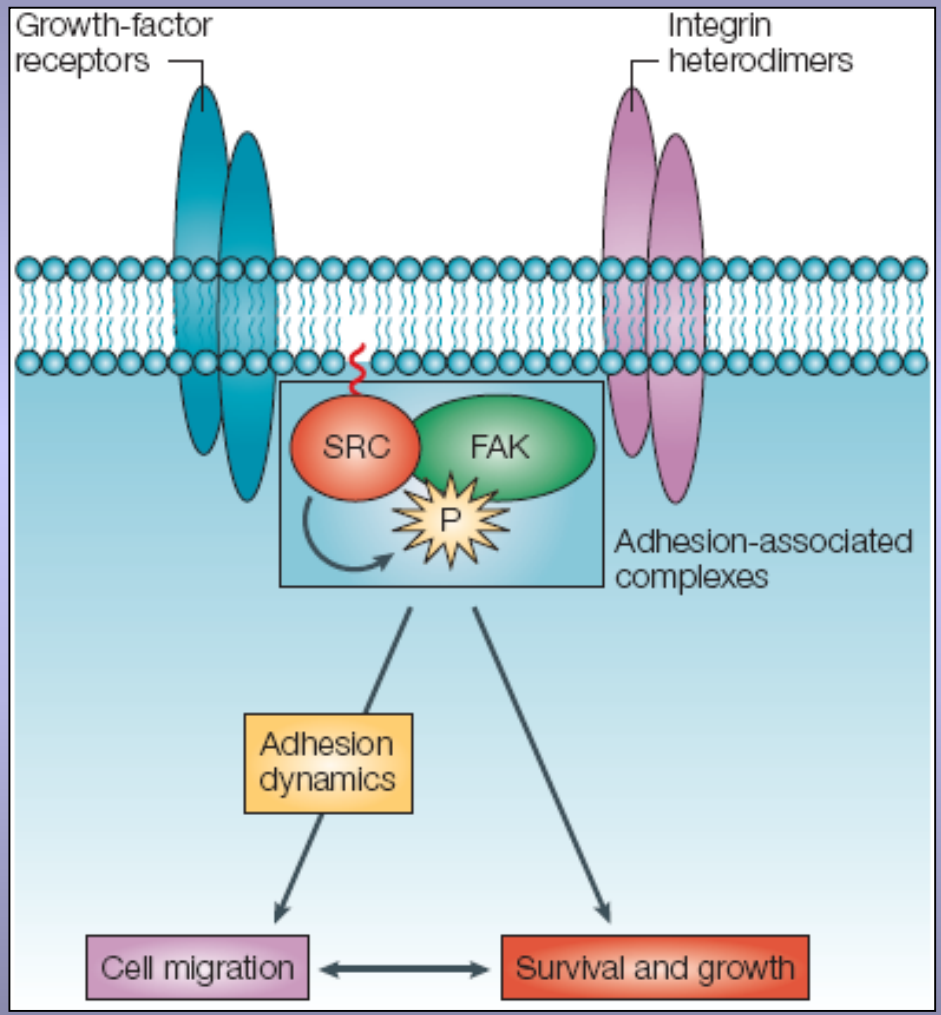
Focal adhesions as production sites of intracellular signals. This fluorescence micrograph shows a fibroblast cultured on a substratum coated with the extracellular matrix molecule fibronectin. Actin filaments have been labeled to fluoresce green, while activated proteins that contain phosphotyrosine have been labeled with an antibody that is tagged to fluoresce red. Where the two components overlap, the resulting color is orange. The actin filaments terminate at focal adhesions, where the cell attaches to the substratum. Proteins containing phosphotyrosine are also concentrated at these sites. This is thought to reflect the local activation of focal adhesion kinase (FAK) and other protein kinases stimulated by transmembrane integrin proteins that bind to fibronectin extracellularly and (indirectly) to actin filaments intracellularly. Signals generated at such adhesion sites help regulate cell division, growth, and survival, in both fibroblasts and epithelial cells. Fuente: Alberts et al., 2002.

CONTACTOS FOCALES EN CÉLULAS DEFICIENTES EN KINASAS DE ADHESIÓN FOCAL



Excessive numbers of focal adhesions in FAK-deficient fibroblasts. Normal and FAK-deficient fibroblasts were stained with antibodies against vinculin to reveal the location of focal adhesions. (A) The normal fibroblasts have fewer focal adhesions and have spread after 2 hours in culture. (B) At the same time point, the FAK-deficient fibroblasts have more focal adhesions and have not spread. Fuente: Alberts et al., 2002.

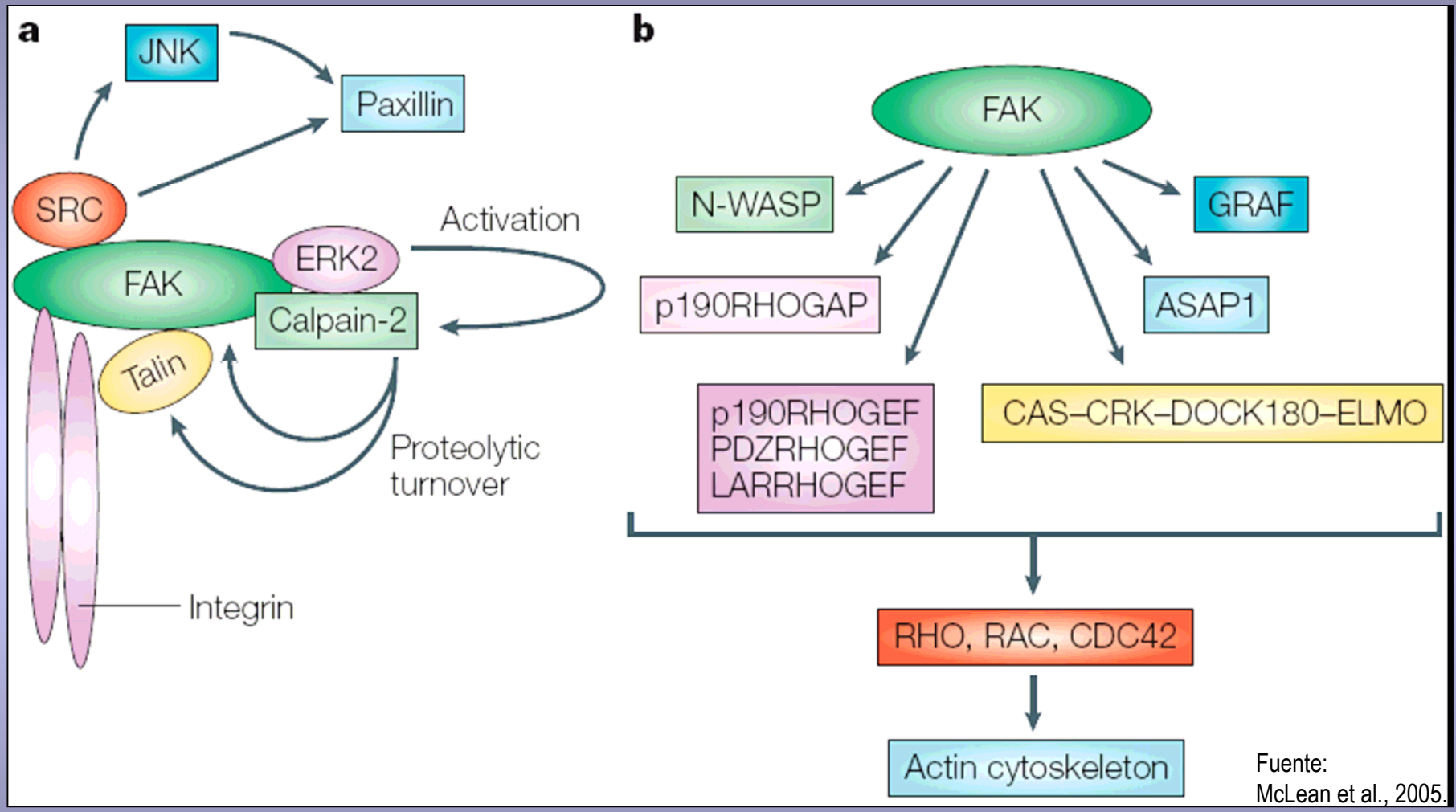
SINERGIA ENTRE LA SEÑALIZACIÓN MEDIADA POR FAK Y POR FACTORES DE CRECIMIENTO



Focal-adhesion kinase as a signal integrator.
Focal-adhesion kinase (FAK) acts to integrate signals from extracellular cues, such as growth-factor receptors and integrins, and from the upstream SRC-family kinases, to control and coordinate adhesion dynamics/cell migration with survival signalling. SRC binds to growth-factor receptors and FAK to integrins (although, this has not been shown in vivo), and they bind to each other. SRC binding to growth-factor receptors is widely believed to be important, as is FAK signalling from integrins, regardless of whether the interaction between FAK and these transmembrane receptors is direct.

Fuente: McLean et al., 2005.

FAK media la deadhesión de los contactos focales



Fuente:
McLean et al., 2005.

Así como regula las GTPasas Rho que a su vez regulan la organización del citoesqueleto de actina