



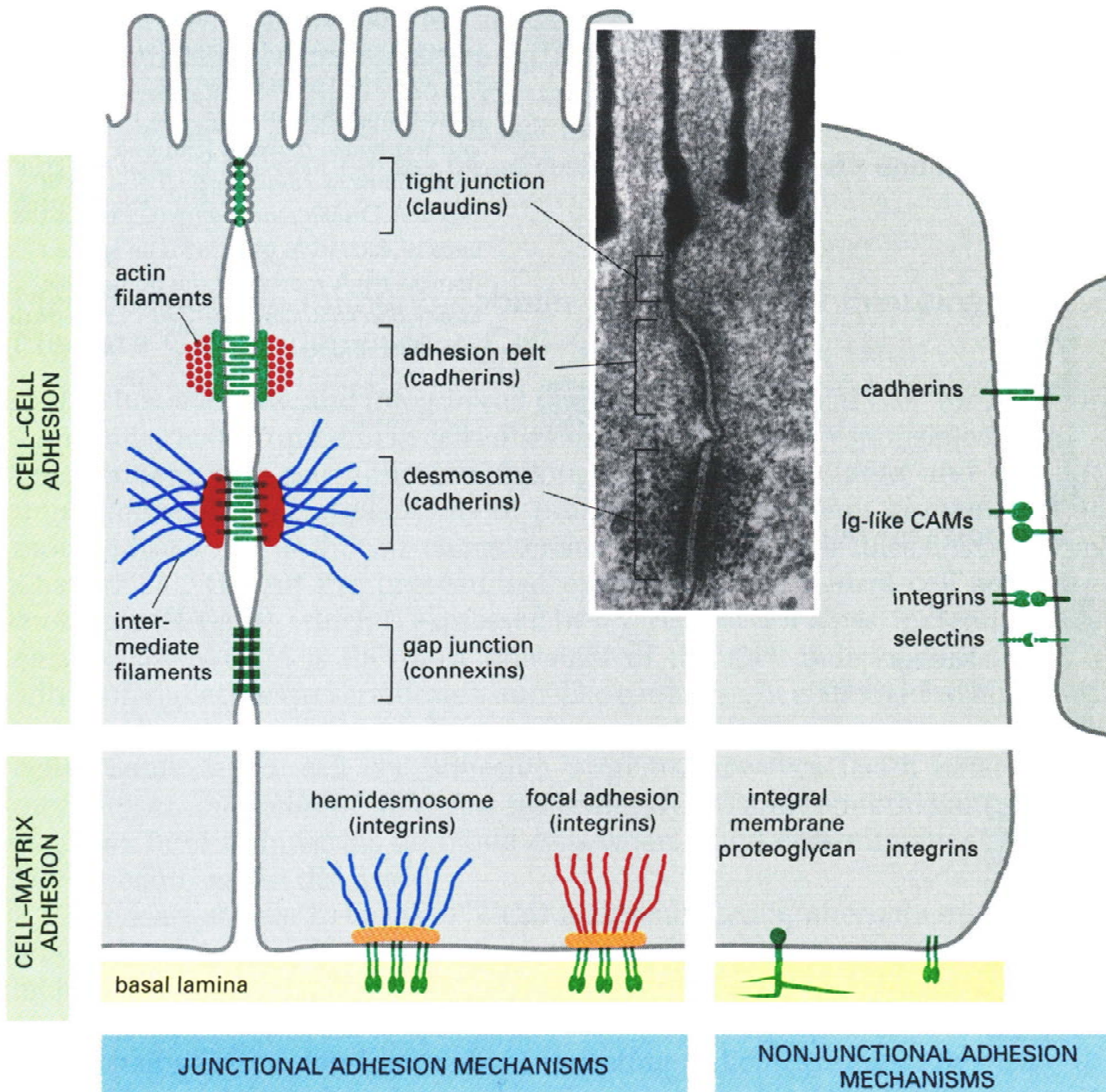
**Escuela de Verano 2006  
Curso Células Cancerosas  
Facultad de Medicina**



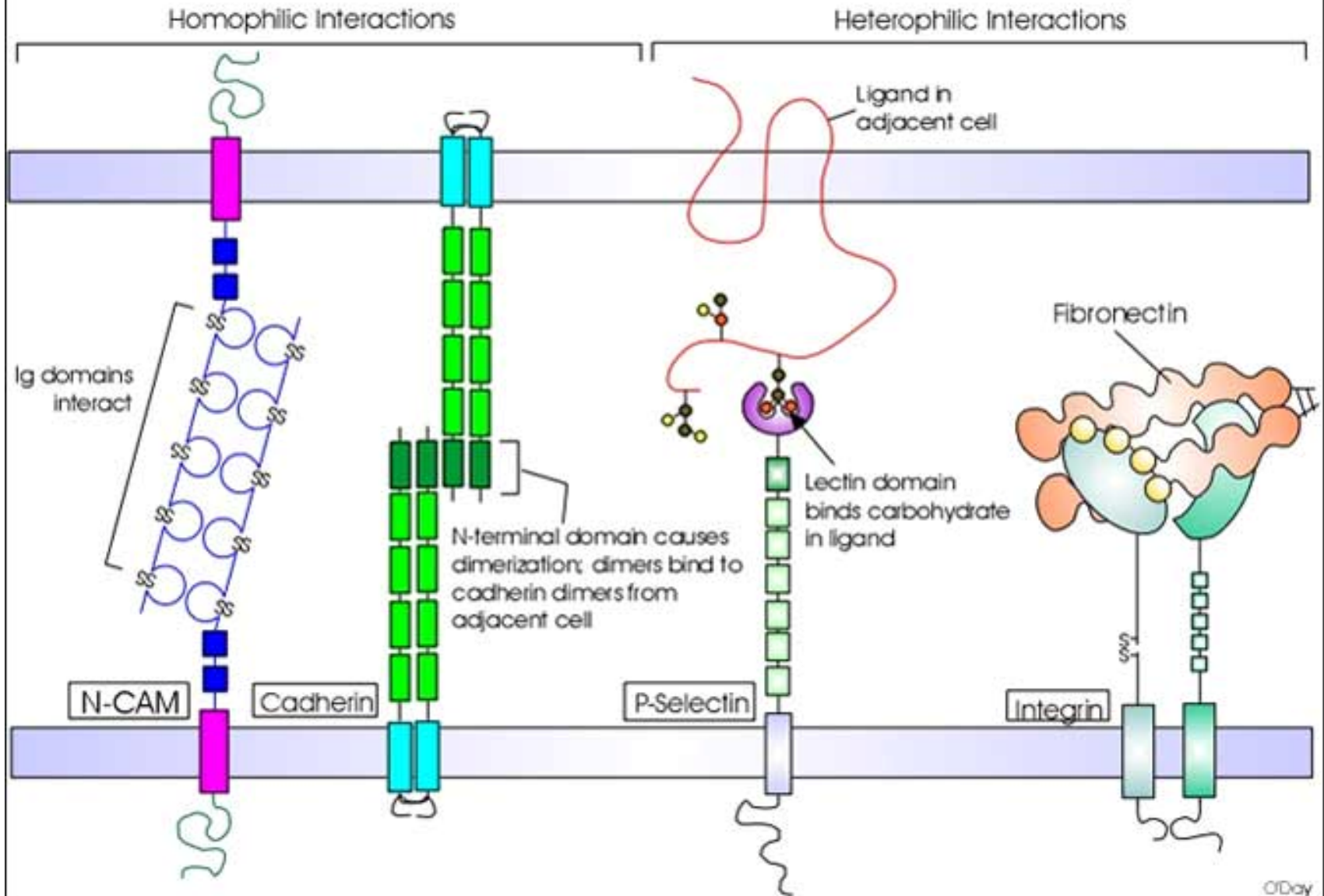
# Moléculas de adhesión celular

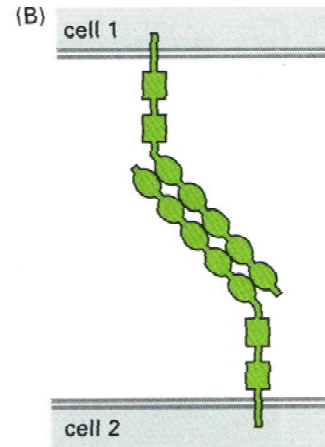
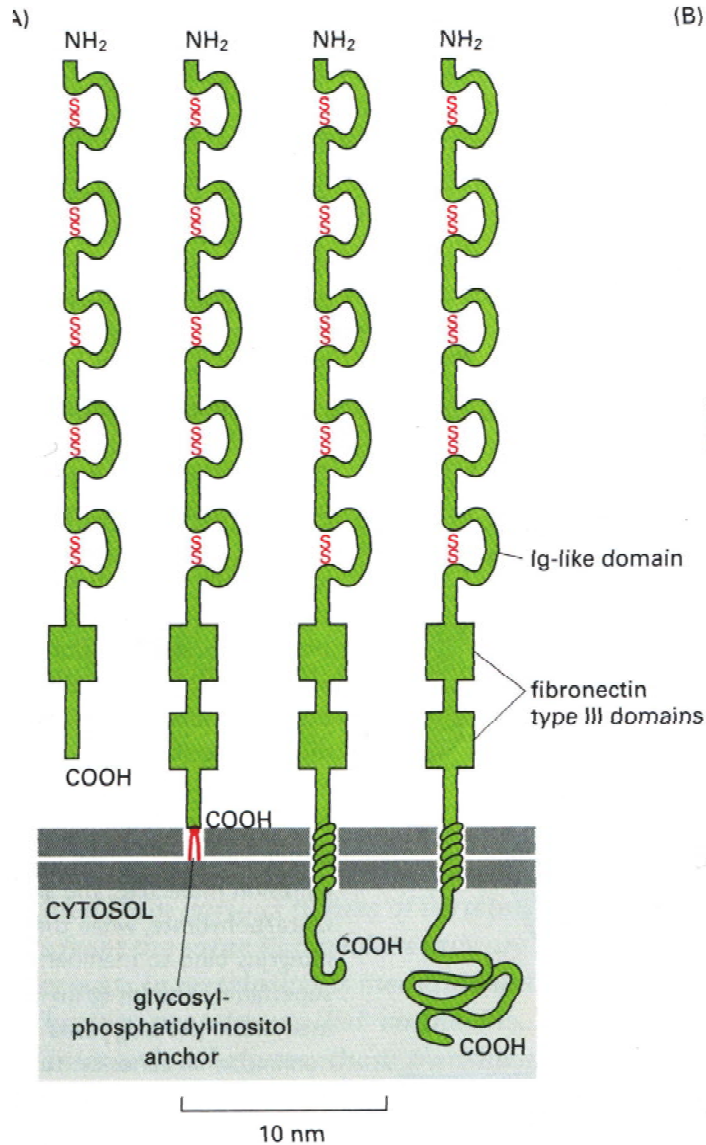
**Héctor R. Contreras M.**

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Instituto de Ciencias Biomédicas  
Facultad de Medicina. Universidad de Chile*



## Homophilic & Heterophilic Interactions of Cell Adhesion Molecules





Ig superfamily CAMs  
N-CAM

**ICAM:** intracellular adhesion molecules

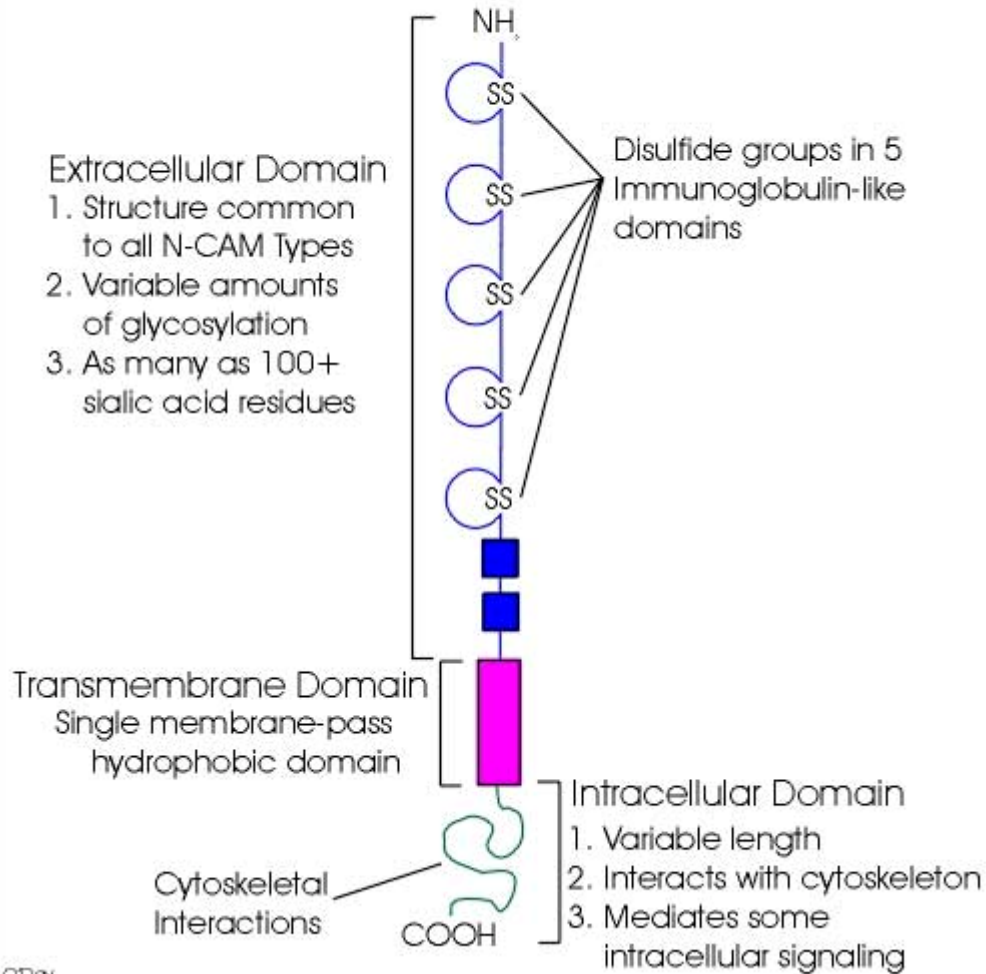
**VCAM:** vascular cell adhesion molecules

**PECAM:** platelet endothelial cell adhesion molecules

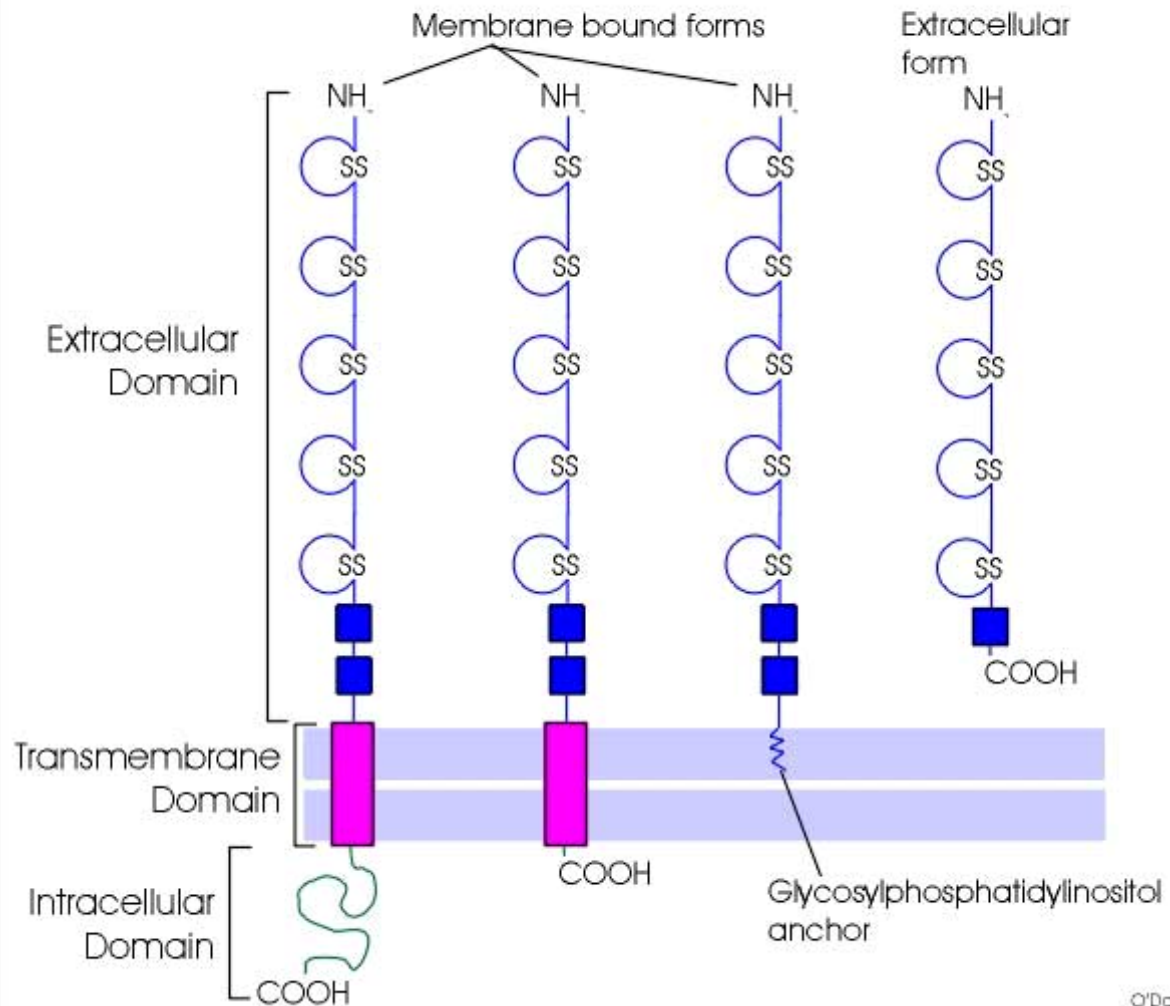
**NCAM:** neural cell adhesion molecules

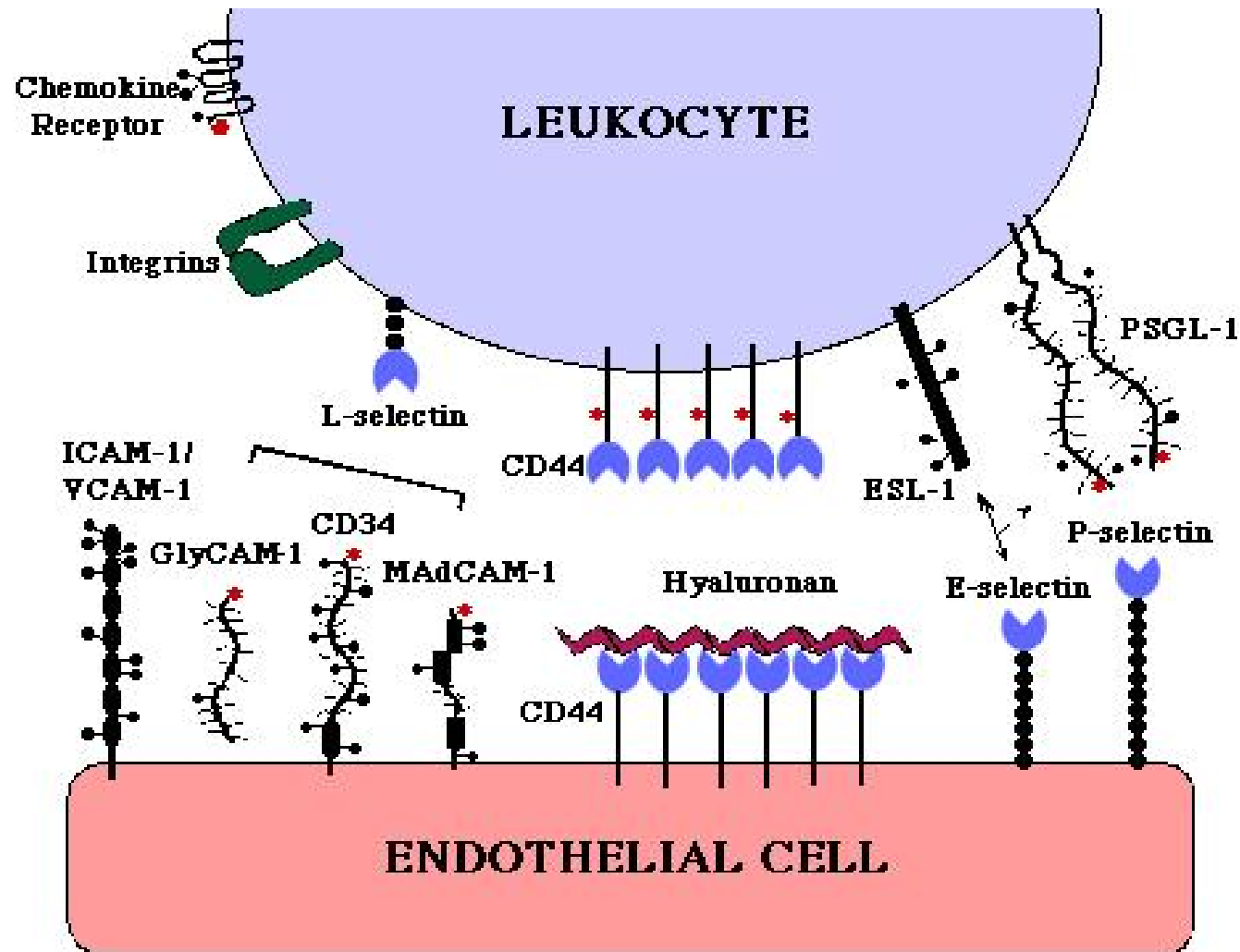


## N-CAM: An Ig-Like Cell Adhesion Molecule

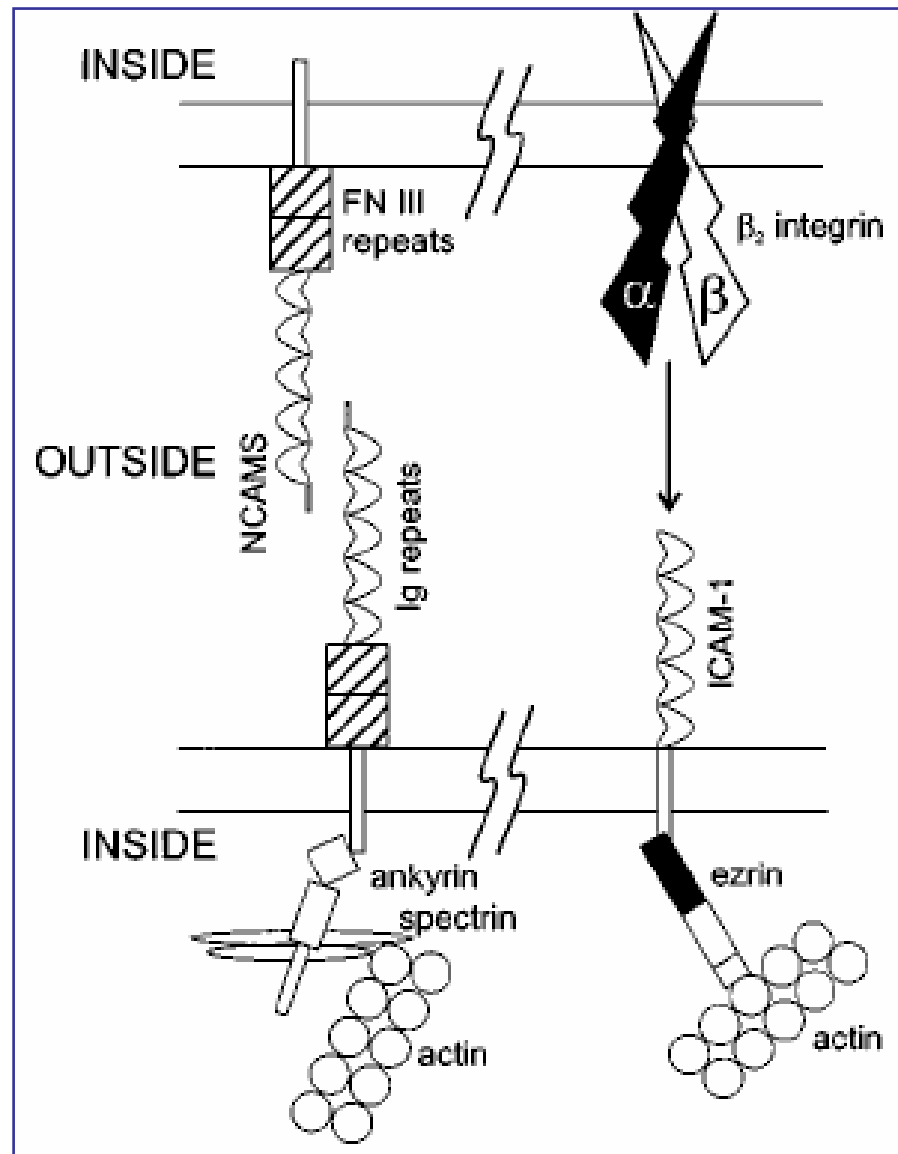


# Four Forms of N-CAM



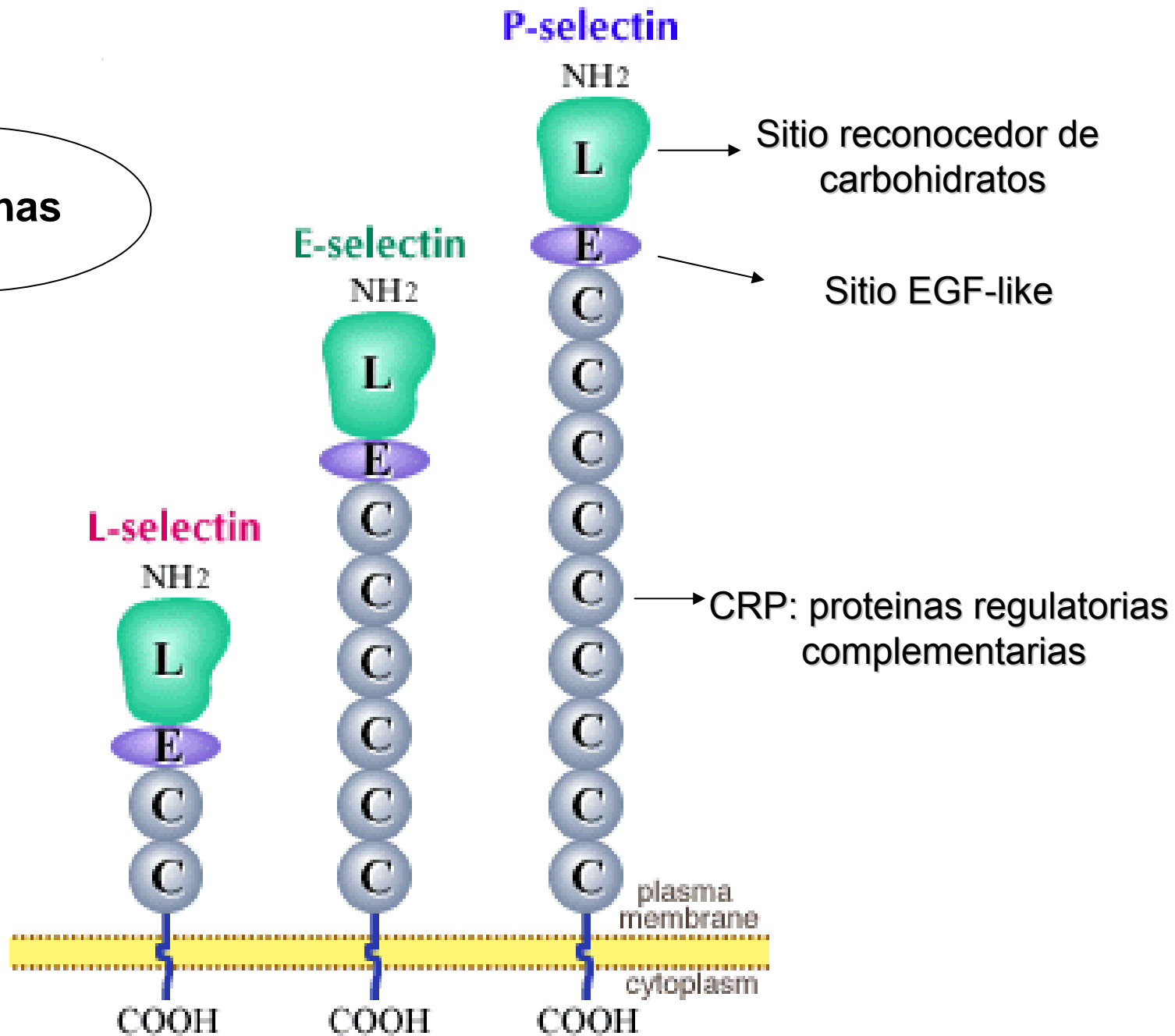


# Immunoglobulin superfamily

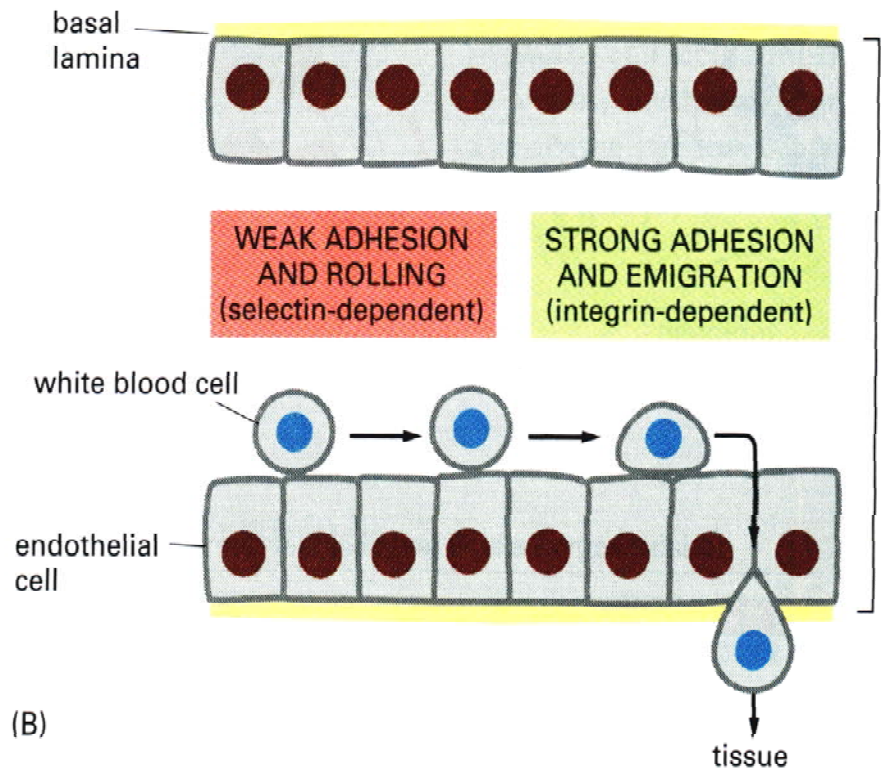
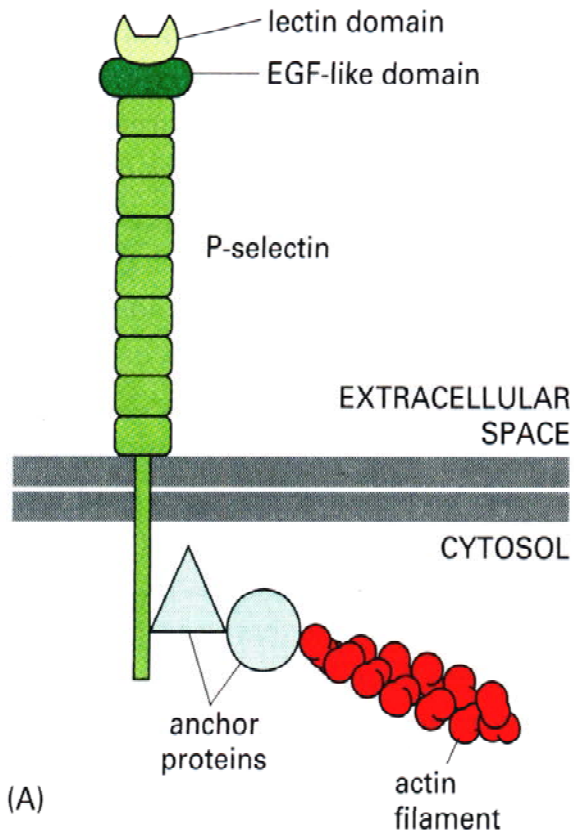




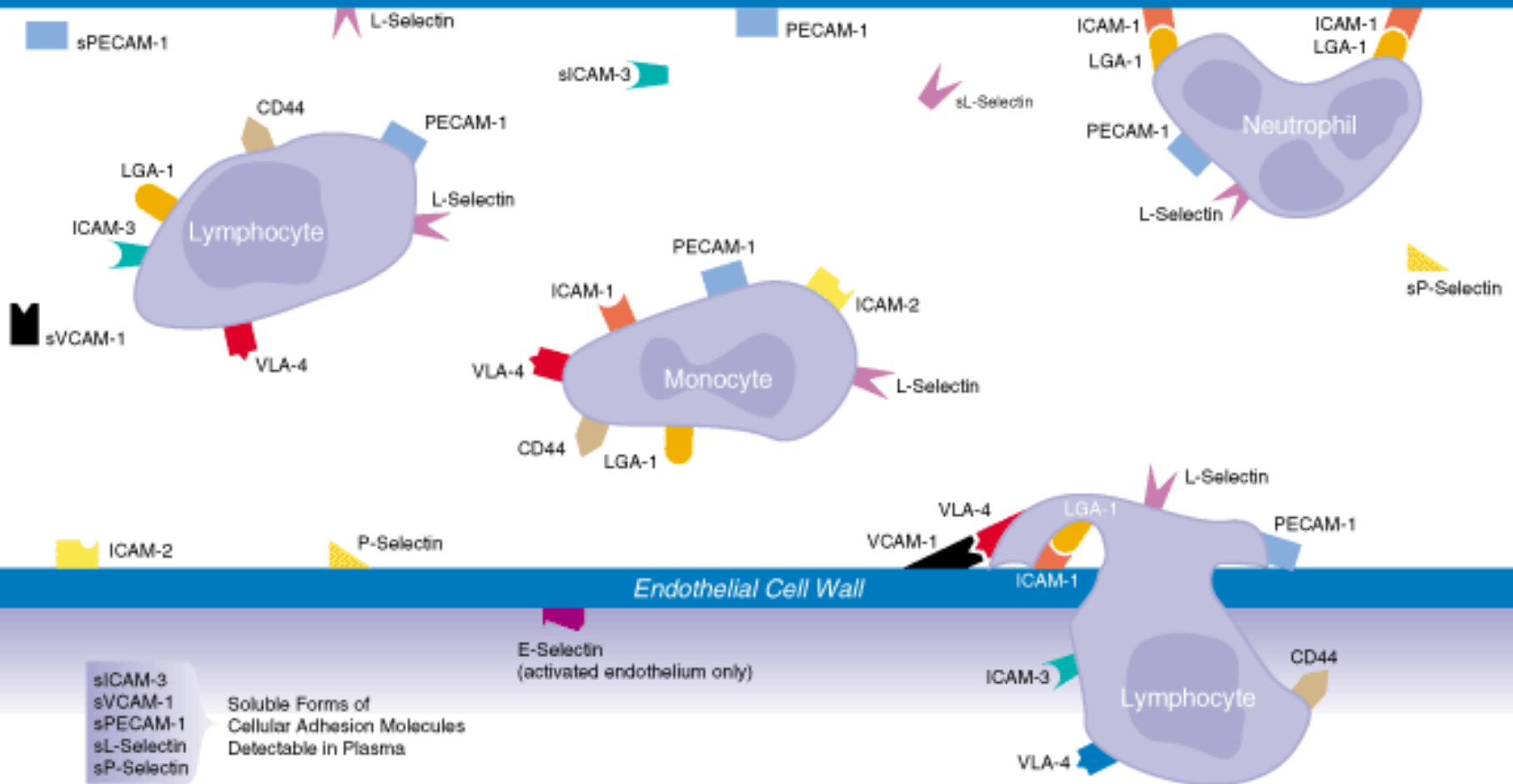
# Selectinas



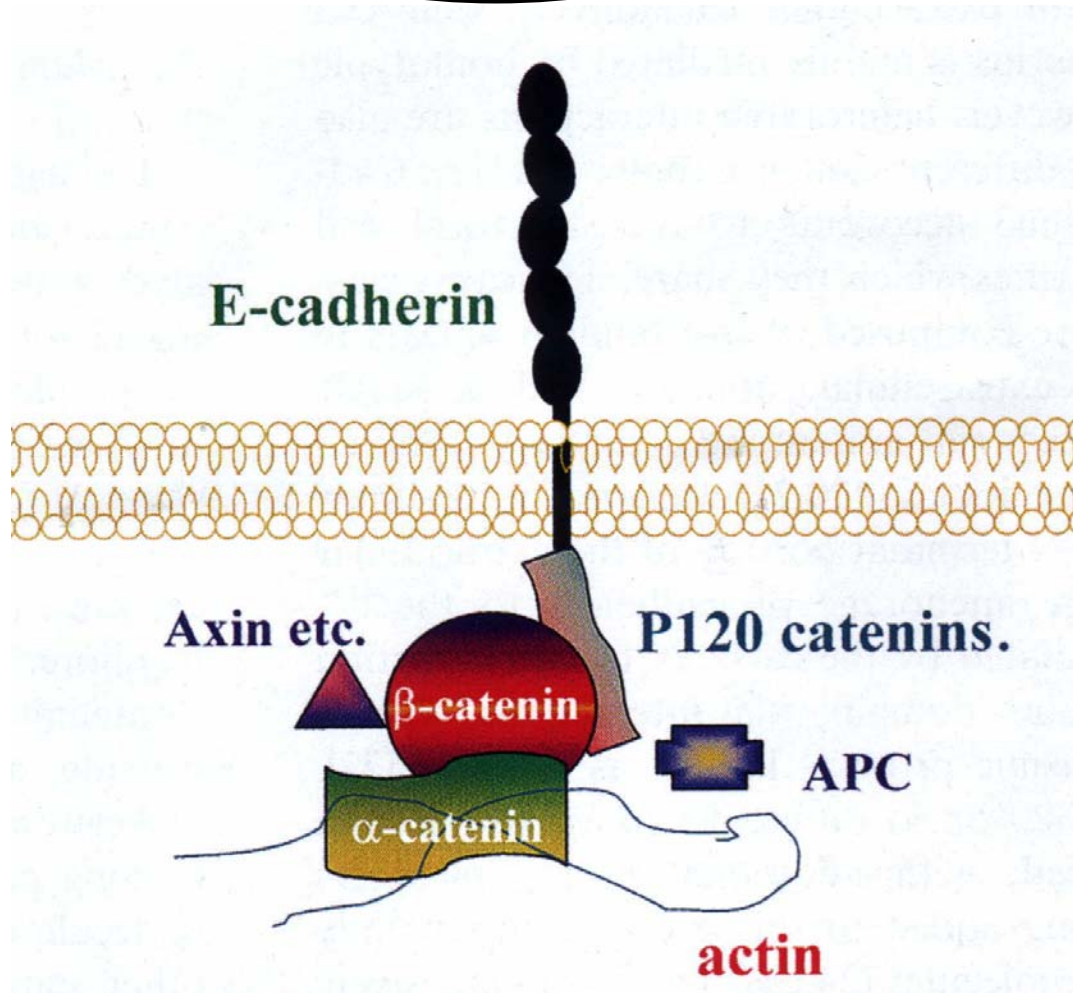
# Selectinas

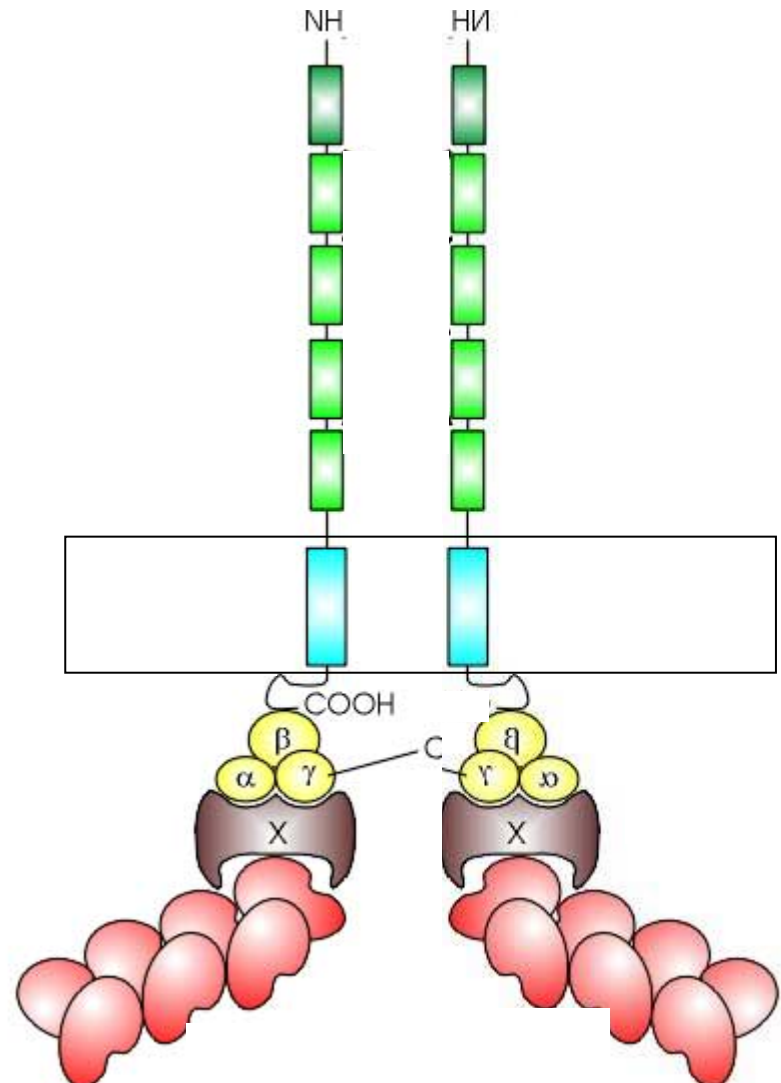
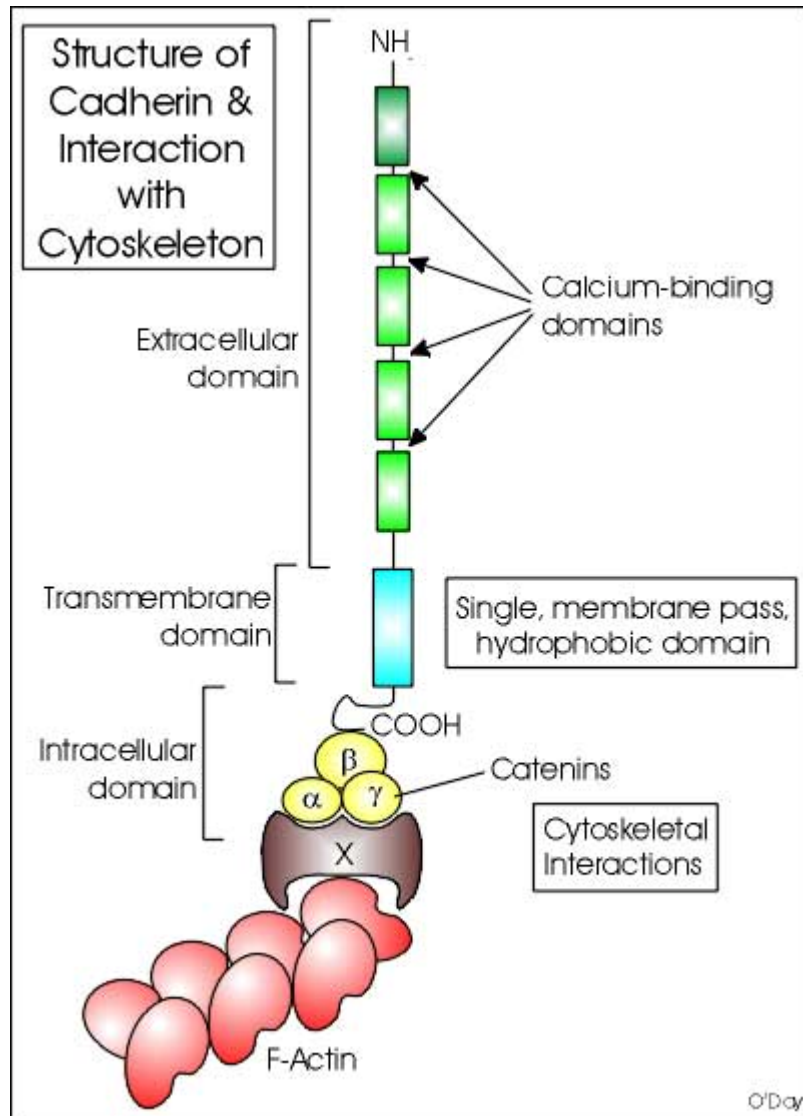


# Endothelial Cell Wall



# Cadherinas



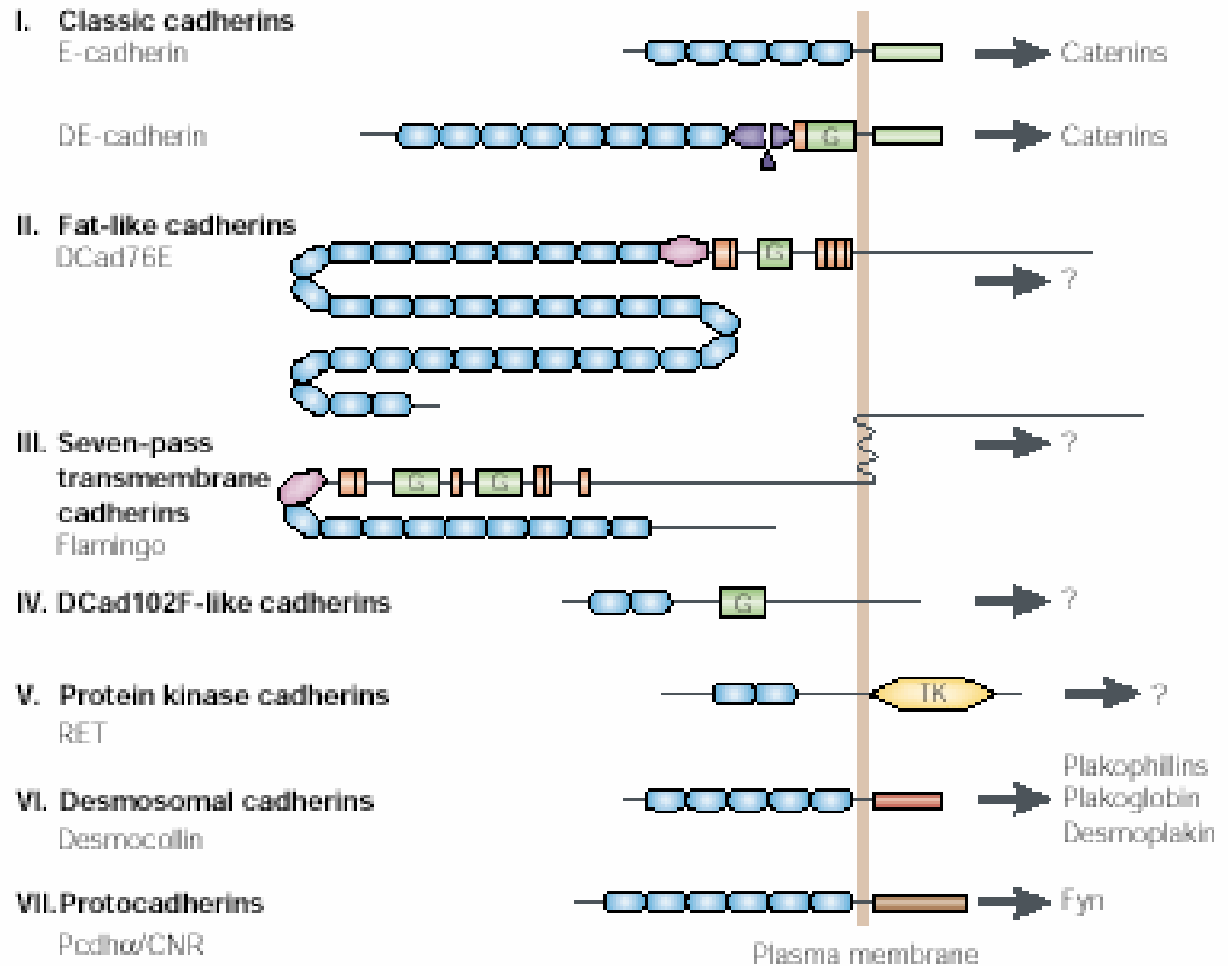


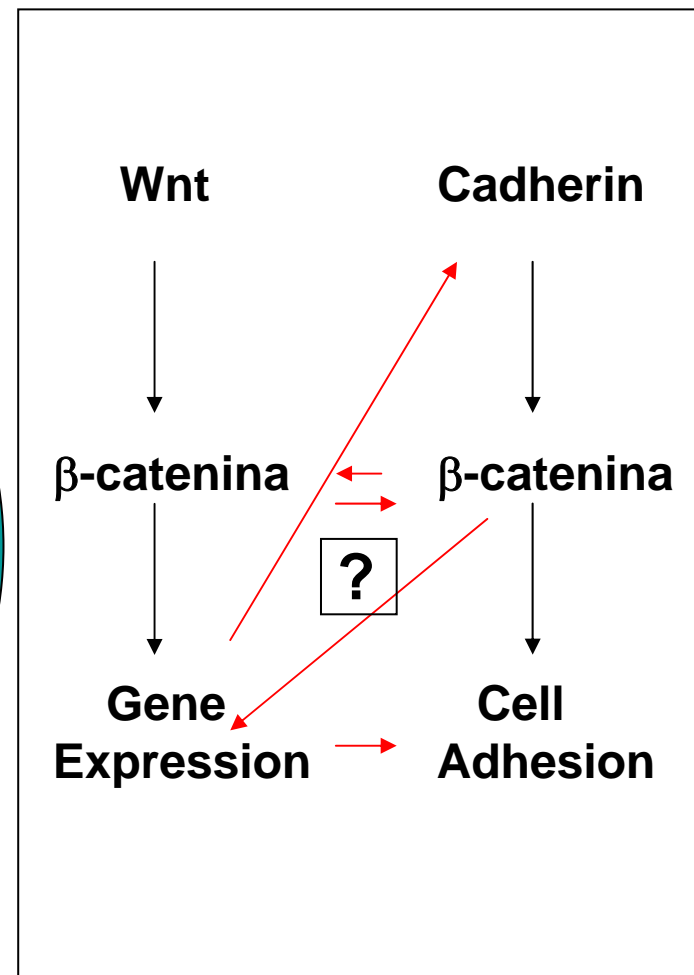
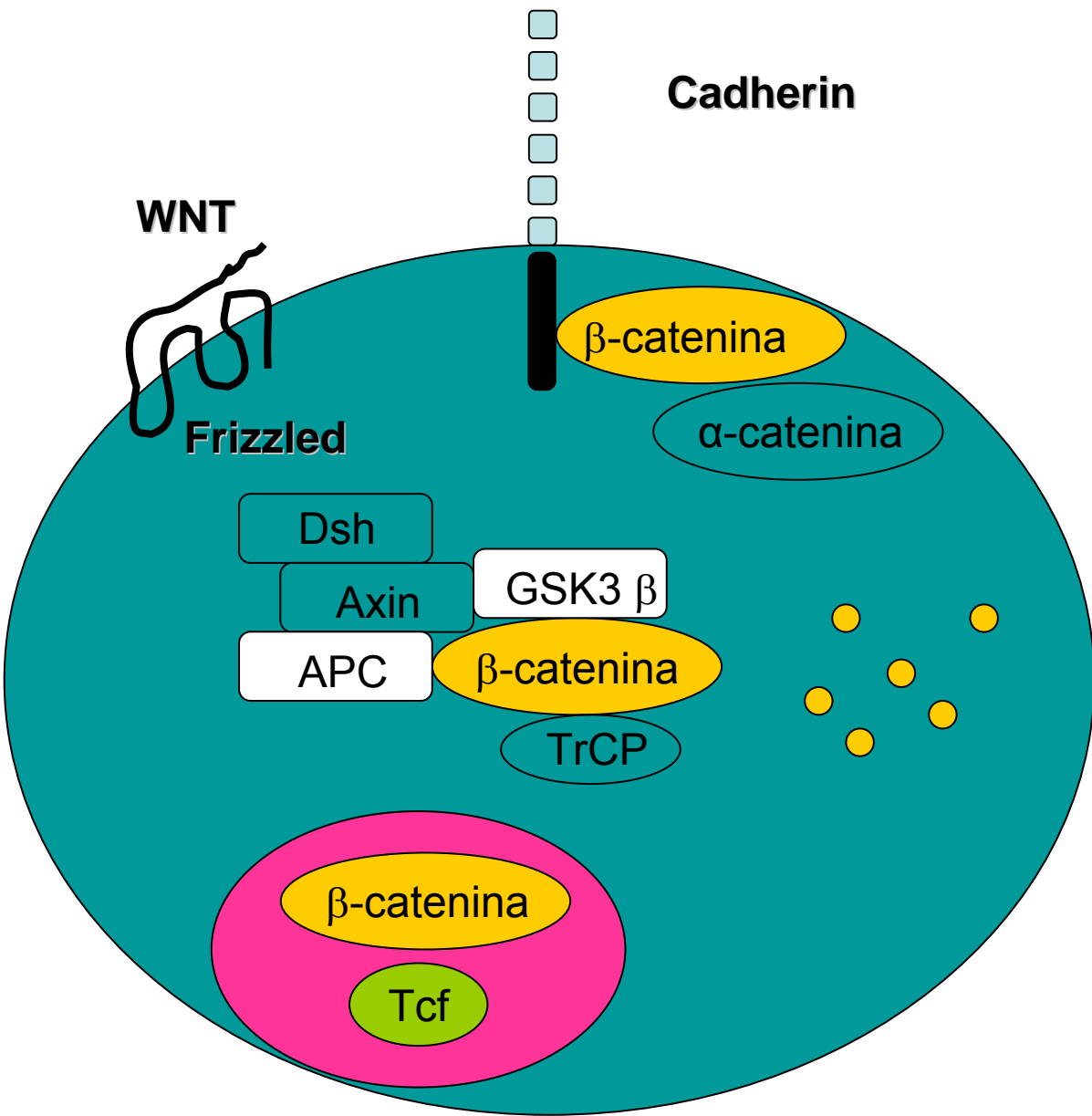
**TABLE 19-3 Some Members of the Cadherin Superfamily**

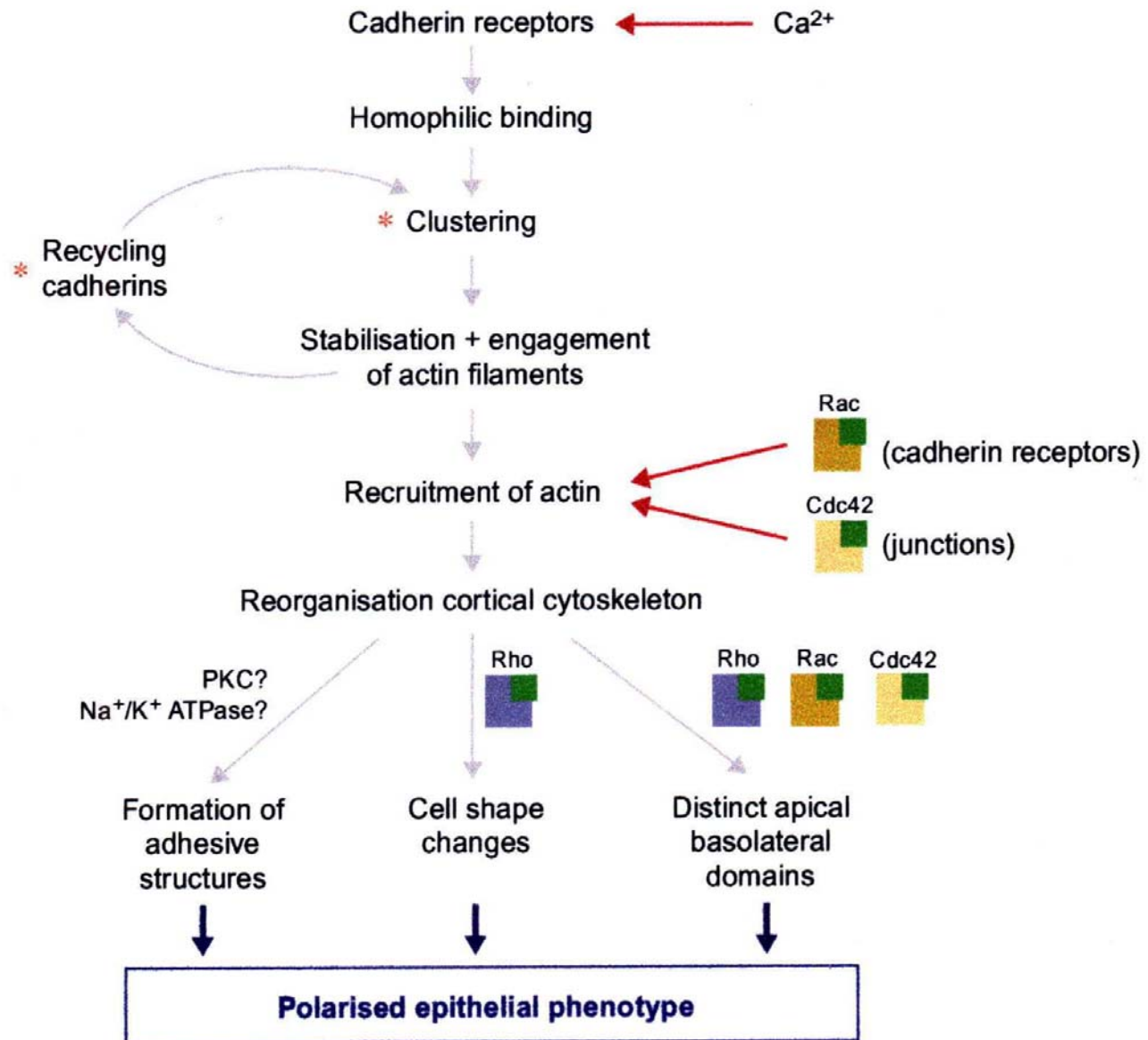
| NAME                          | MAIN LOCATION  | JUNCTION ASSOCIATION                     | PHENOTYPE WHEN INACTIVATED IN MICE                                     |
|-------------------------------|--|--|--|
| <i>Classical cadherins</i>    |  |  |  |
| E-cadherin                    | epithelia  | adherens junctions                       | die at blastocyst stage; embryos fail to undergo compaction            |
| N-cadherin                    | neurons, heart, skeletal muscle, lens, and fibroblasts | adherens junctions and chemical synapses | embryos die from heart defects   |
| P-cadherin                    | placenta, epidermis, breast epithelium                 | adherens junctions                       | abnormal mammary gland development                                     |
| VE-cadherin                   | endothelial cells                                      | adherens junctions                       | abnormal vascular development (apoptosis of endothelial cells)         |
| <i>Nonclassical cadherins</i> |  |  |  |
| Desmocollin                   | skin   | desmosomes                               | unknown  |
| Desmoglein                    | skin   | desmosomes                               | blistering skin disease due to loss of keratinocyte cell–cell adhesion |
| T-cadherin                    | neurons, muscle  | none                                     | unknown  |
| Fat (in <i>Drosophila</i> )   | epithelia and CNS                                      | none                                     | enlarged imaginal discs and tumors                                     |
| Protocadherins                | neurons  | chemical synapses                        | unknown  |

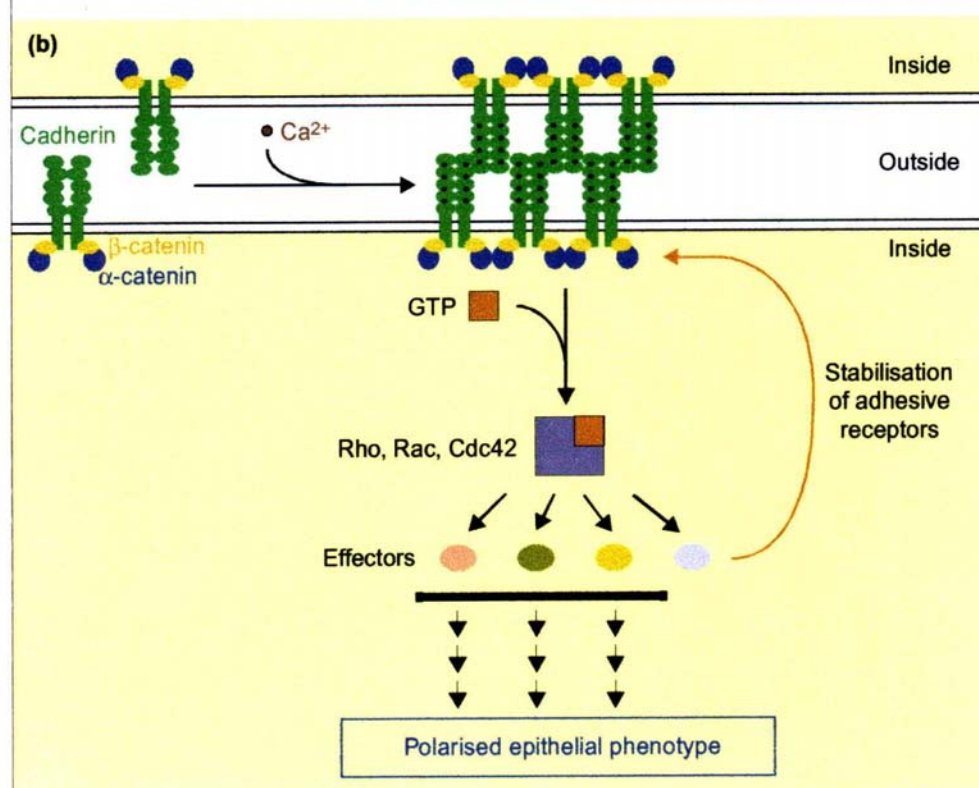


# Cadherin superfamily









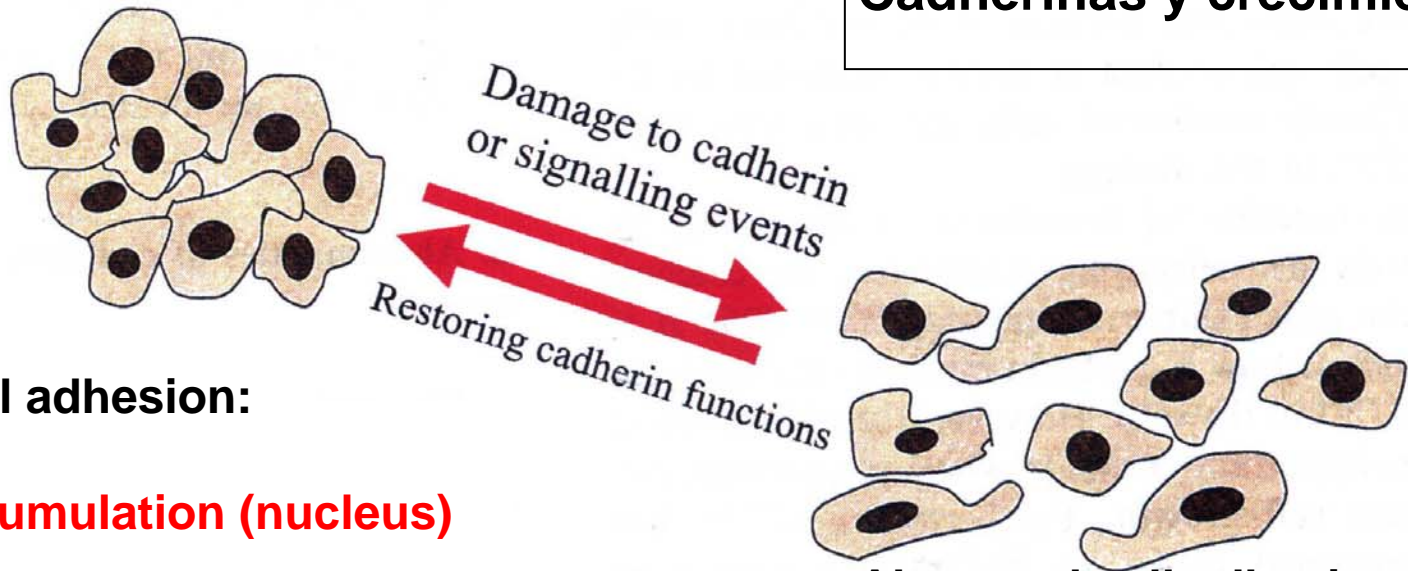
**Table 3**

**Effects of cadherin-dependent adhesion and the small GTPases Rho, Rac and Cdc42 on the different cytoskeletal networks.\***

| Protein / activity | Microfilaments  | Refs  | Microtubules   | Refs               | Intermediate filaments      | Refs    |
|--------------------|---|-------|--|--------------------|-----------------------------|---------|
| Cadherin receptors | Reorganisation, actin polymerisation and recruitment to junctions | [6]   | Reorganisation, stabilisation of microtubule ends, alteration of microtubule dynamics, localisation and orientation of mitotic spindle | [55 ,86–90]        | Reorganisation (desmosomes) | [49,50] |
| Rho                | Stress fibres, contraction  | [1,2] | Stabilisation, polymerisation orientation  | [61 ,91]           | Collapse (Rho kinase)       | [92]    |
| Rac                | Lamellae, ruffles, actin polymerisation                           | [1,2] | ?  |                    | Collapse                    | [93]    |
| Cdc42              | Filopodia, actin polymerisation                                   | [1,2] | Reorientation of MTOC and mitotic spindle  | [41,42,44, 94, 95] | Collapse                    | [93]    |

\*Please note that not all listed effects were observed in epithelial cells.

## Cadherinas y crecimiento



**Normal cell adhesion:**

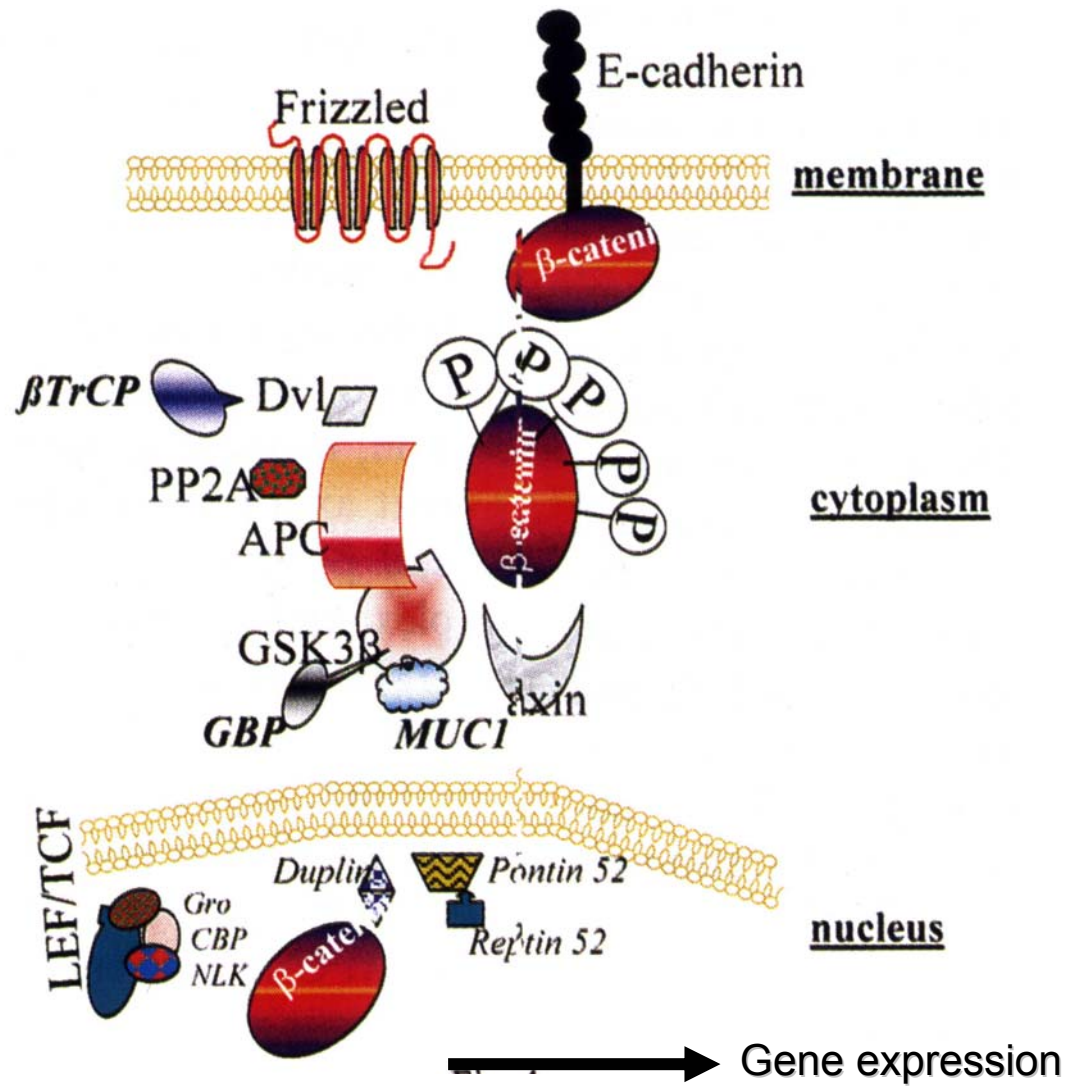
**P27<sup>kip1</sup> accumulation (nucleus)**

Normal cadherin function  
Slower cell growth  
Less motile/invasive

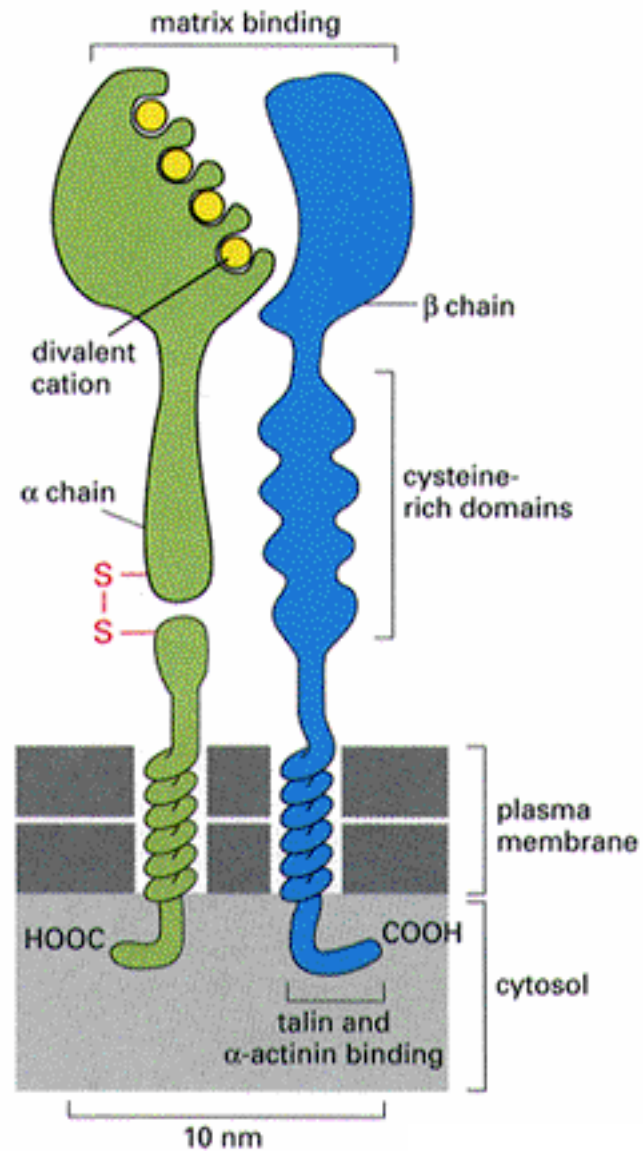
**Abnormal cell adhesion:**

**Reduction of P27<sup>kip1</sup> in nucleus**

Damaged cadherin function  
Cell growth accelerate  
Increased migration  
Gaining invasiveness

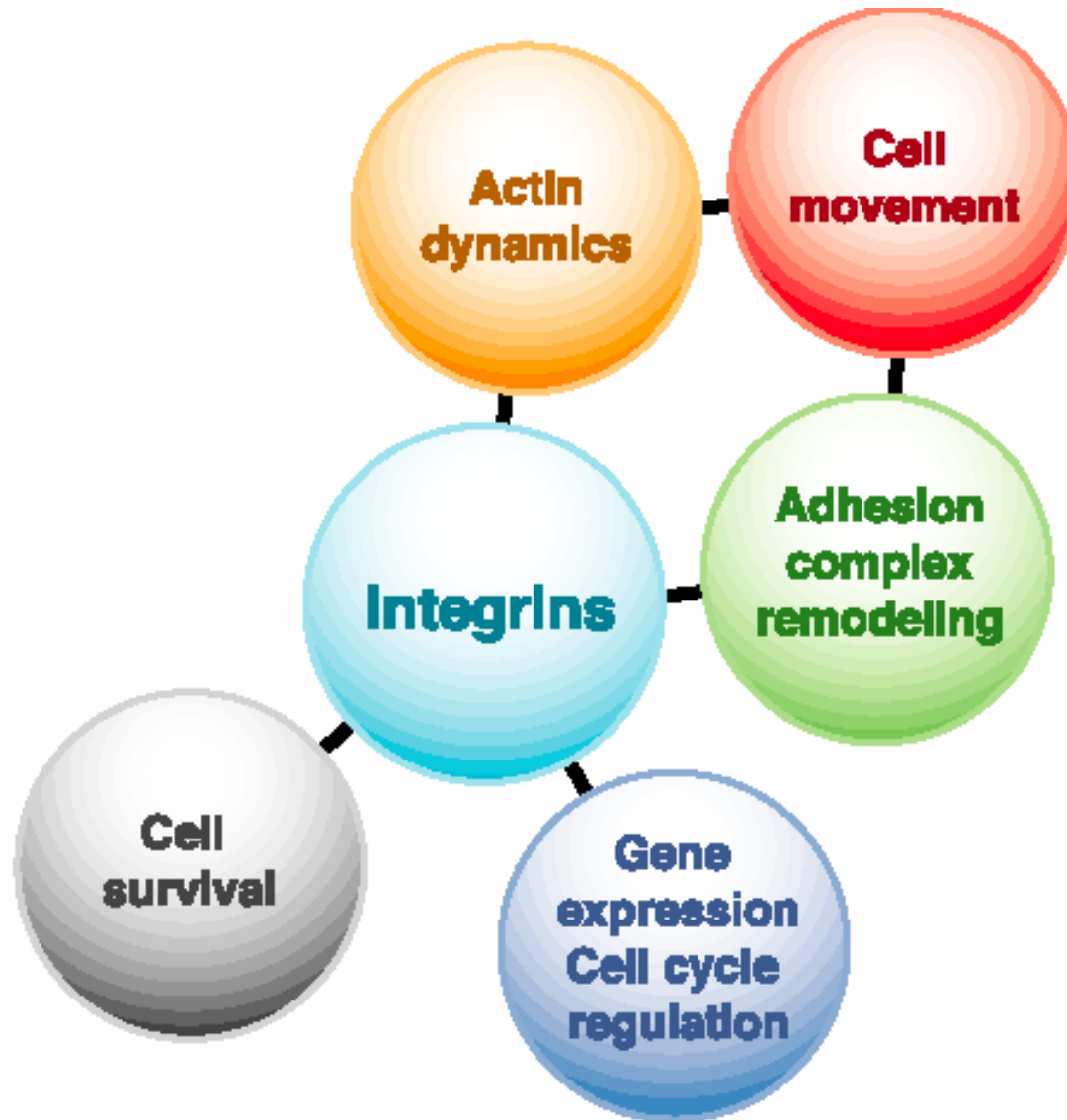






# Integrinas

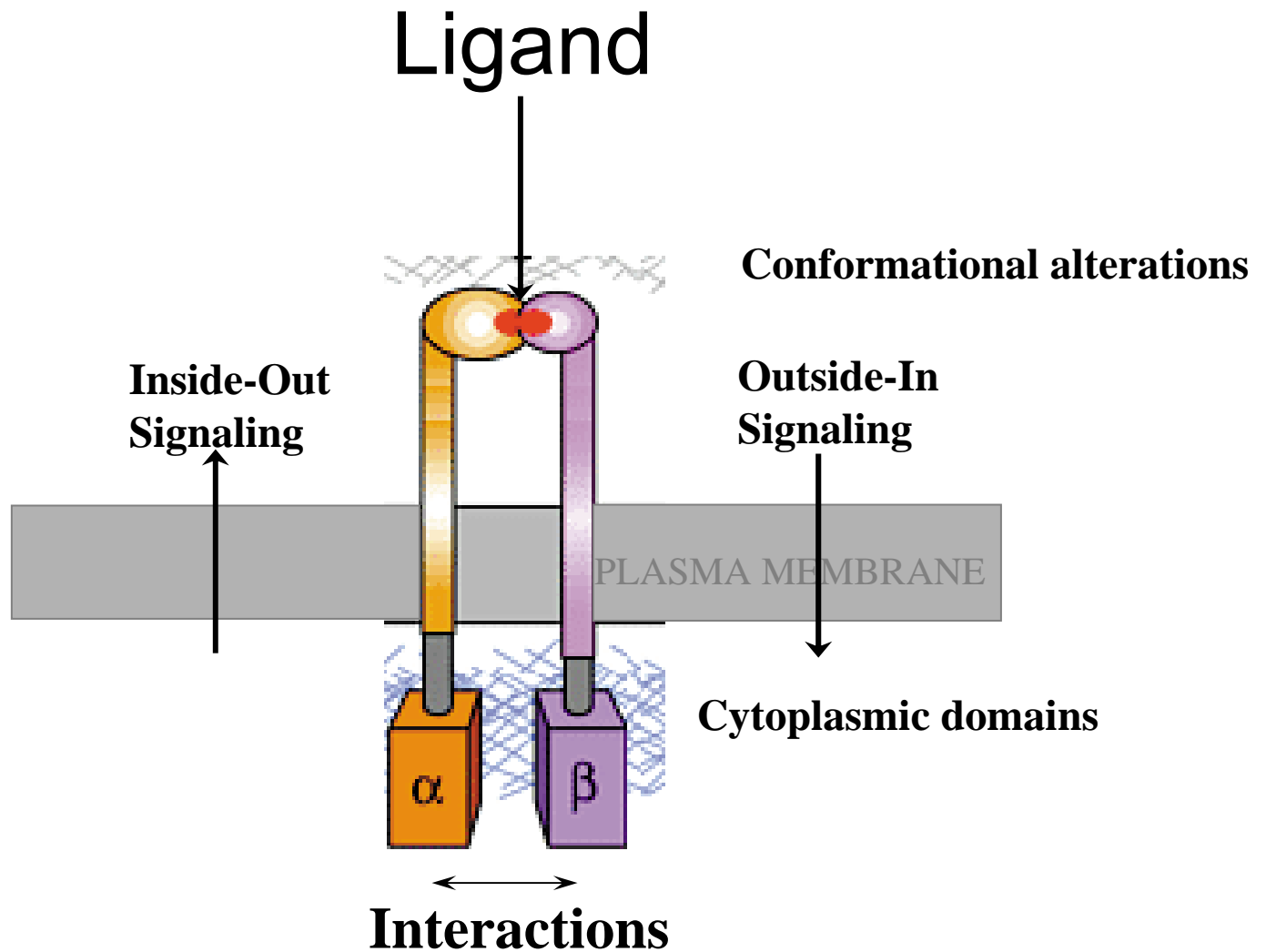
# Integrin functions

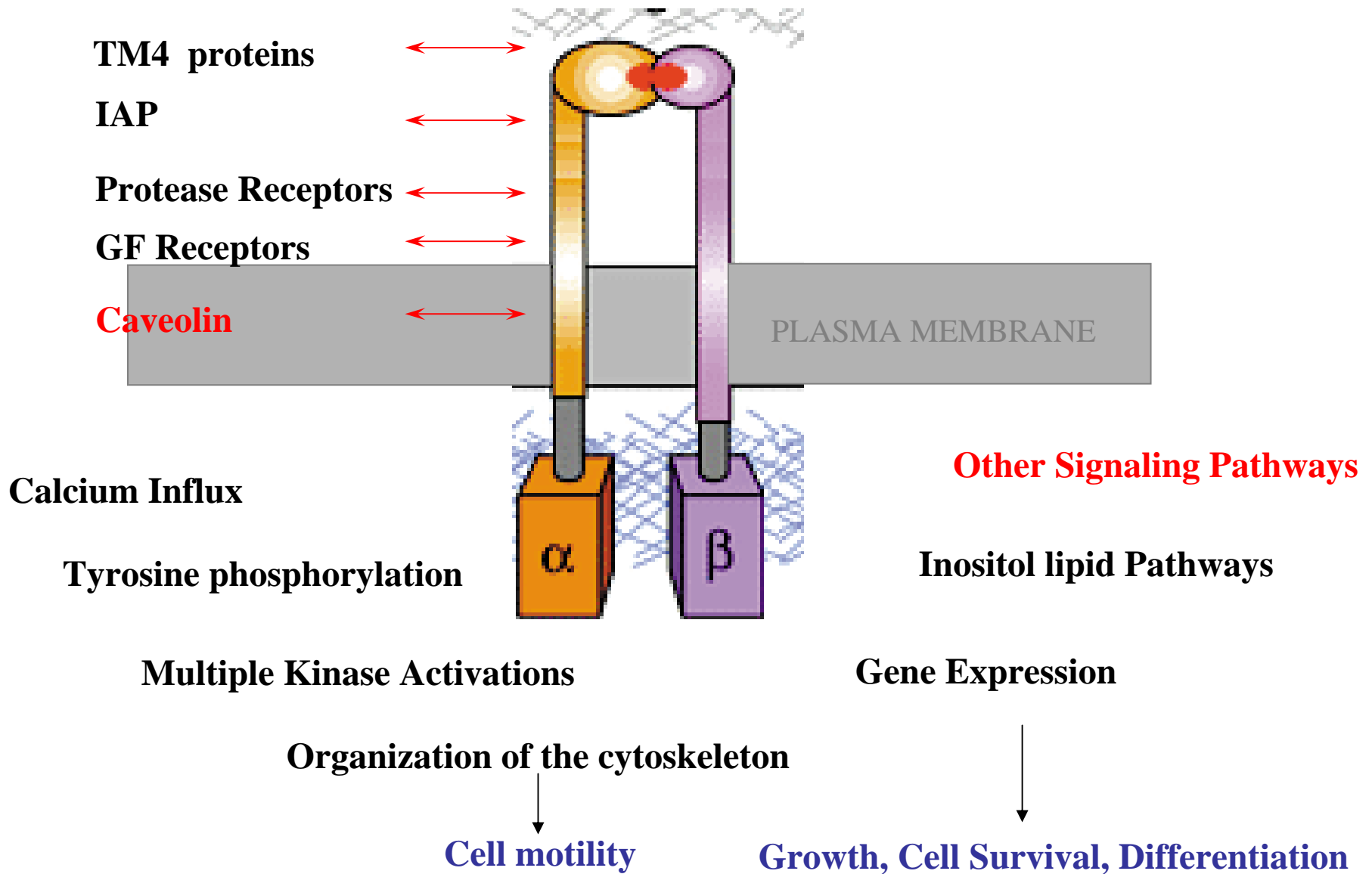


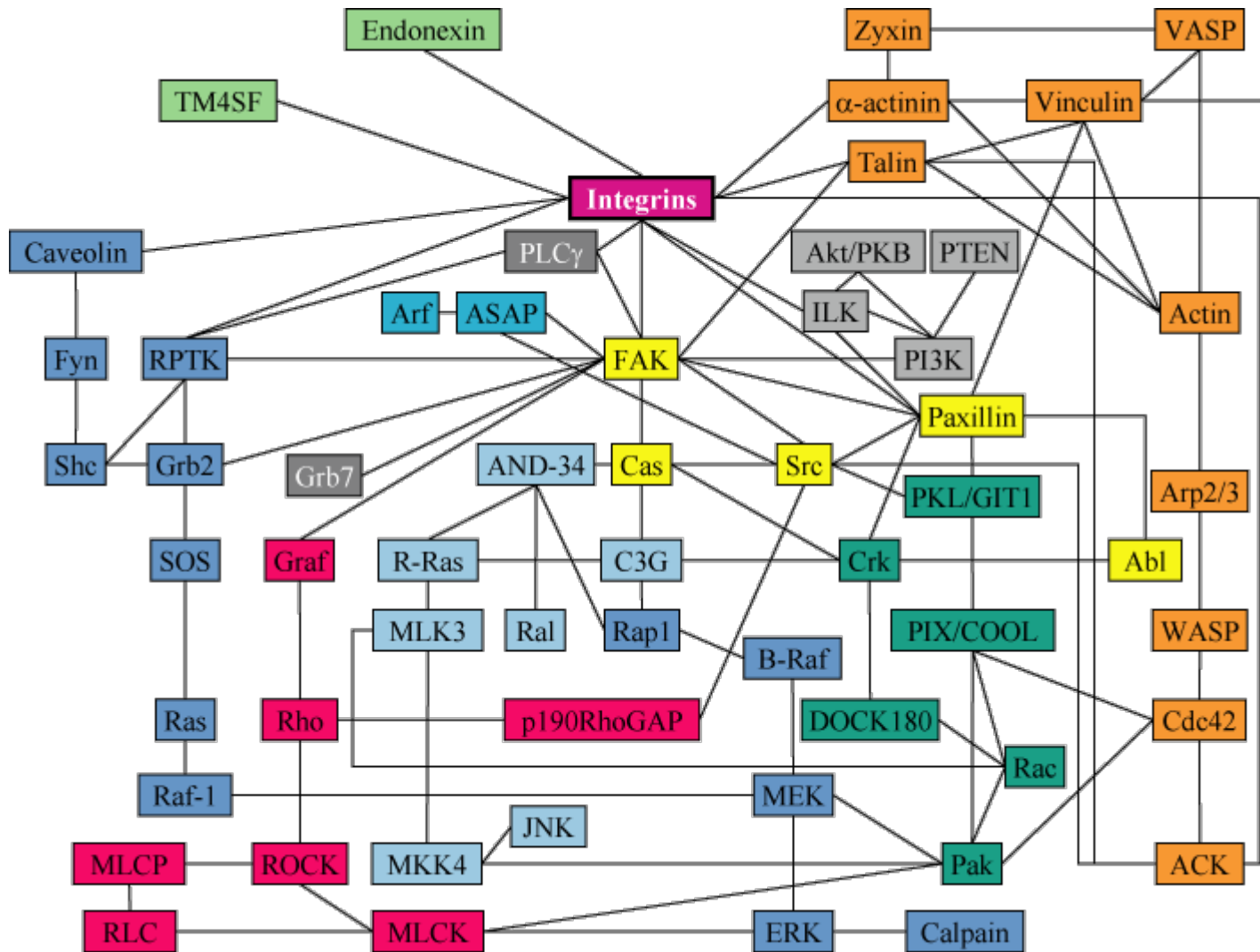
# Integrin ligands

|                      |
|----------------------|
| 15 $\alpha$ subunits |
| 8 $\beta$ subunits   |

| LIGAND                | INTEGRIN   |
|-----------------------|--|
| Bone Sialoprotein     | $\alpha v\beta 3, \alpha v\beta 5$   |
| Collagens             | $\alpha 1\beta 1, \alpha 2\beta 1, \alpha 11\beta 1, \alpha Ib\beta 3$   |
| Denatured collagen    | $\alpha v\beta 3, \alpha IIb\beta 3, \alpha 5\beta 1$  |
| Disintegrins          | $\alpha v\beta 3, \alpha IIb\beta 3$   |
| Fibronectin           | $\alpha 2\beta 1, \alpha 3\beta 1, \alpha 4\beta 1, \alpha 4\beta 7$<br>$\alpha 5\beta 1, \alpha v\beta 3, \alpha v\beta 5, \alpha v\beta 6$ |
| Fibrinogen            | $\alpha v\beta 3, \alpha 5\beta 1, \alpha M\beta 2, \alpha IIb\beta 3$   |
| ICAM-1                | $\alpha M\beta 2, \alpha L\beta 2$   |
| ICAM-2,3,4,5          | $\alpha L\beta 2$  |
| V-CAM                 | $\alpha 4\beta 1, \alpha 4\beta 7$   |
| Vitronectin           | $\alpha v\beta 1, \alpha v\beta 3, \alpha v\beta 5, \alpha IIb\beta 3$   |
| von Willebrand factor | $\alpha v\beta 3, \alpha IIb\beta 3$   |
| L1                    | $\alpha v\beta 3, \alpha v\beta 5, \alpha 5\beta 1$  |









# Cross-talk between cell adhesion molecules

**Cadherins**

**Integrins**

**Syndecan-4**

