**Université des frères Mentouri Constantine 1**

**Département de Biologie Animale**

**specialité Immunologie Cellulaire et Moléculaire Master I**

**Matière : Signalisation moléculaire et cellulaire**

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# Chapter II

## Adhesion Molecules

### Introduction

Cell surface adhesion molecules play vital roles in numerous cellular processes. Some of these include:

Cell growth, differentiation, embryogenesis, immune cell transmigration and response, and cancer metastasis. Adhesion molecules are also capable of transmitting information from the extracellular matrix to the cell.

There are four major families of cell adhesion molecules.

These are the immunoglobulin (Ig) superfamily cell adhesion molecules

(CAMs), integrins, cadherins, and selectins.

## 1-The immunoglobulin (Ig) superfamily cell adhesion molecules

### A-Definition

The Ig superfamily CAMs are calcium-independent transmembrane glycoproteins. Members of the Ig superfamily include the intercellular adhesion molecules (ICAMs), vascular-cell adhesion molecule (VCAM-1), platelet-endothelial-cell adhesion molecule (PECAM-1), and neural-cell adhesion molecule (NCAM).

### B-Structure of Ig superfamily CAMs

Each Ig superfamily CAM has

1-an extracellular domain, which contains several Ig-like intrachain disulfide-bonded loops with conserved cysteine residues

2- transmembrane domain

3- intracellular domain that interacts with the cytoskeleton (Figure 1).

### C-The role of Ig superfamily CAMs

Typically, they bind integrins or other Ig superfamily CAMs. The neuronal CAMs have been implicated in neuronal patterning.

Endothelial CAMs play an important role in immune response and inflammation.

## 2- Integrins

### A-Definition

Integrins are membrane receptor . They formed a family transmembrane proteins calcium- dependent.

### B- structure of integrins

Integrins are a transmembrane molecules have two domains intracellular and two domains extracellular. They are non-covalently linked heterodimers of alpha and beta subunits.

The subunit alpha has two chains linked with disulfide bridge and a globular head expresses binding sites for divalent cation.

The subunit Beta has

1- Extracellular chain which has domains rich in cystein linked with tripeptide sequences RGD ( Arg - Gly- Asp) presented in laminine and fibronectine.

2- Intracellular portion interact with actin filaments by intermediate proteins Taline - Vinculine and α - actinine ( Figure 2).

### C- localization of Integrins

Integrins are located on the surface of , leukocytes , platelets and basal lamina of the epithelium .

In human integrins α2 β1 , α5 β1, α6 β1 linked with sequences Arg- Gly- Aps located on fibronectine molecules.

### D-The role of integrins

Integrins on cell surface are inactive but they will activated by chimical signal so when they will activated integrins could linked with extracellular molecules binding sites located in lamina , in the matrix ( fibronectine , laminine collagen IV) (Figure3) and Ig superfamily CAMs.

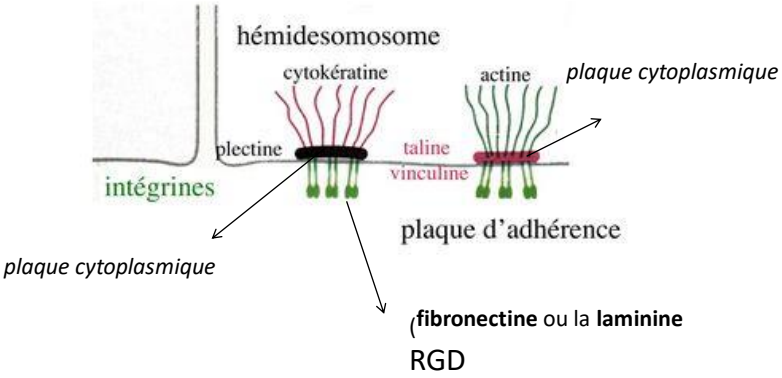



Figure 3: The interaction between integrin and MEC .

## 3-Cadherins

### A-Definition

The cadherins are glycoprotein , calcium - dependent adhesion molecules . The three most common cadherins are neural (N)-cadherin, placental (P)-cadherin, and epithelial (E)-cadherin. All three belong to the classical cadherin subfamily. There are also desmosomal cadherins ( Desmocollin and Desmoglein ).

التركيب الجزئي

بقعة لاصقة Macula adherens

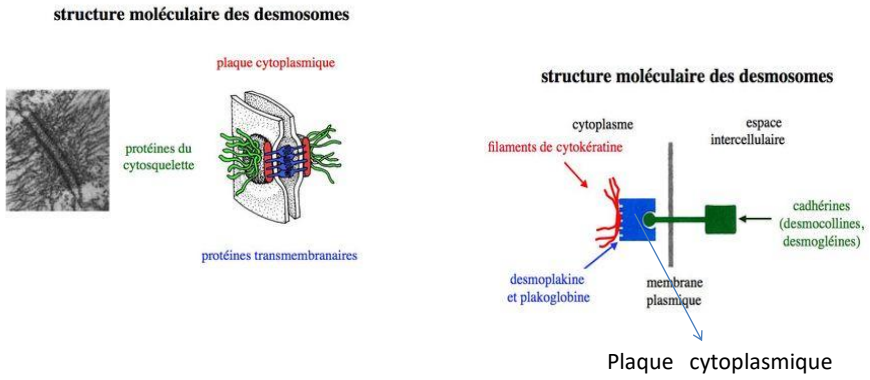



Figure 4: The desmosomal cadherins (Desmocollin and Desmoglein ).

**B- Structure of cadherins**

1-The extracellular domain consists of several cadherin repeats, each is capable of binding a calcium ion.

2- The transmembrane domain

3- The intracellular domain which is interact with actin filaments by the intermediate protein intracellular the α, ß, and γ catenins ( Figure 5).

**C-Role of Cadherins**

Cadherins are intimately involved in embryonic development and tissue organization. They exhibit homophilic adhesion**.**

## 4-Selectins

**A-Definition**

The selectins are a molecules belonging to a family consisted from three members include :

1-(P)-selectin ( CD62) elaborated in platelet , megacaryocyte

and endothelium vascular cells; P selectin is performed and stored for rapid release in the granules of platelets or the weibel – Palade bodies of endothelial cells but in the latter P-selectin is expressed only after cytokine activation its target are neutroplils , monocytes , eosinophils , lymphocyte and some tumour cells.

2- (E)-selectin ( CD62E) is produced by endothelial cells after cytokine activation and its counter -receptors are on neutroplils , monocytes , eosinophils , lymphocyte and some tumour cells.

3- (L)-selectin ( CD 62 L) expressed on leukocytes and its target cells are activated endothelial cells.

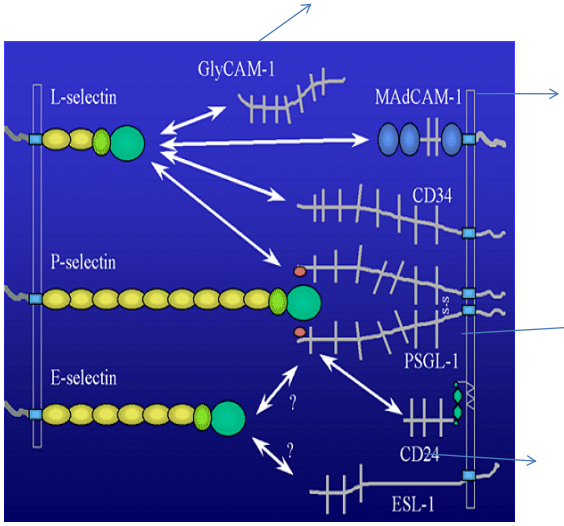
**B-The selectins ligands**

All three selectins can recognize glycoproteins and/or glycolipids containing the tetrasaccharide sialyl-Lewis$^x$ (sialyl-CD15). This tetrasaccharide is found on all circulating myeloid cells and is composed of sialic acid, galactose, fucose, and N-acetyl-galactosamine ( Figure 5).

Though Slex has been considered to be potentially useful as an anti- inflammmatory agent and its synthesis on large scales has been developed for clinical evaluation this natural saccharide can only be used in its injectable form for acute symptoms as it is orally inactive and unstable in the blood stream.

The search for novel Slex mimetics with simpler structure , higher affinity for the receptor , and better stability against glycosidases especialy fucosidase and sialidase.

(Glycosylation-Dependent Cell Adhesion Molecule),




(Mucosal Addressin Cell Adhesion Molecule)

P-selectin Glycoprotein Ligand expressed on blood cells and contains the sialyl-Lewis$^x$ tetrasaccharide.

CD24, which appears to be important for tumor cell binding to P-selectin.

Figure 5 : Shows the ligands for selectins.

**C- Structure of selectins**

The selectins have

A-Extracellular domains, each consists of

1- Carbohydrate recognition domain ( CRD).

2- Growth factor (EGF)-like motif.

3- A short repeated domain related to complement-regulatory proteins.

B-Intracellular domain

Following the transmembrane region, the selectins have a short cytoplasmic domain( Figure 6).

**D-The role of selectins**

Selectins aid in leukocyte extravasation

1-Endothelial activation causes P-selectin to be displayed on the cell surface.

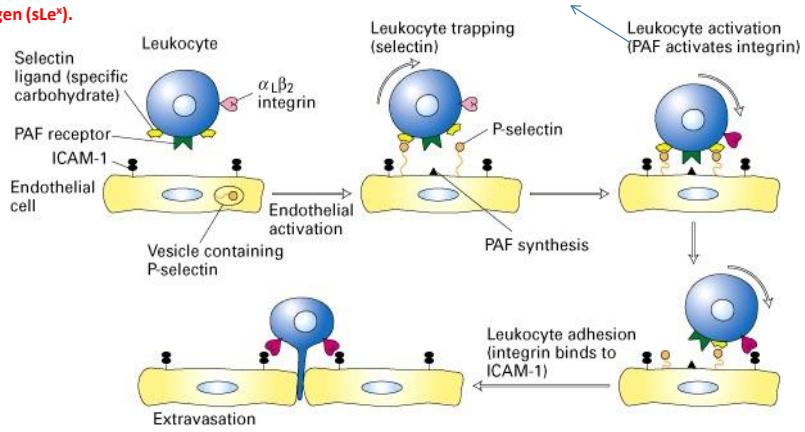
2-Leukocytes are trapped by the P-selectin.

3-Endothelial cell signals leukocyte through platelet-activating factor (PAF) to activate alphaL-beta2 integrins.

4-AlphaL-beta2 integrins on the leukocyte bind to I-CAM on the epithelial cell and activate the loosening of the tight junctions as leukocyte passes between epithelial cells ( Figure 7).

-Endothelial cell signals leukocyte through platelet-activating factor (PAF) to activate alphaL-beta2 integrins.

sialyated Lewis X antigen (sLe$^x$).




activate the loosening of the tight junctions as leukocyte passes between epithelial cells.

Figure 7 : Leukocyte extravasation