



CELL ADHESION MOLECULES

DEPARTMENT OF PERIODONTICS

KARPAGA VINAYAGA INSTITUTE OF DENTAL SCIENCES

What is a cell???

- Cells are basic unit of all living organisms

Cells



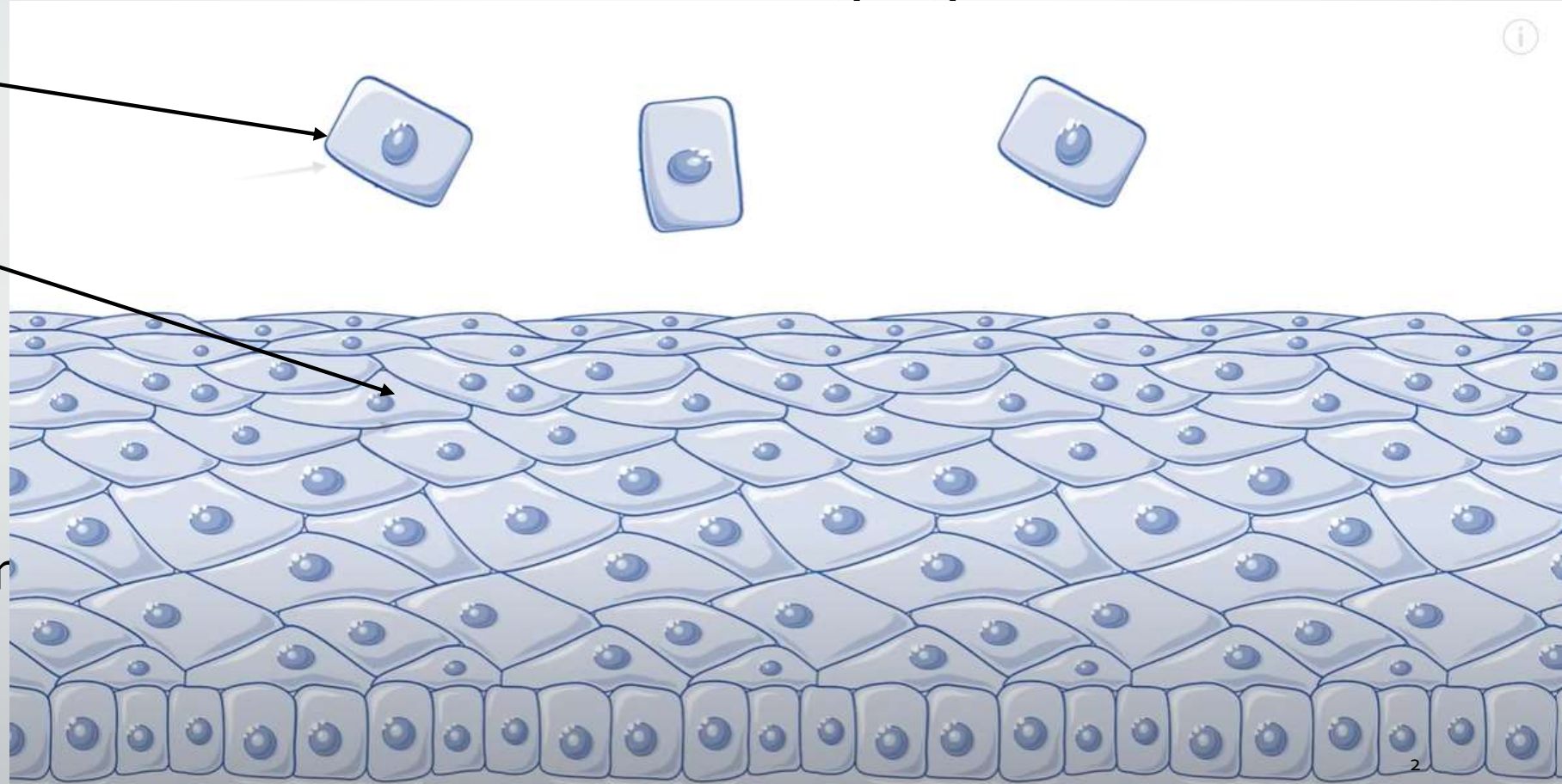
Tissues



Organ



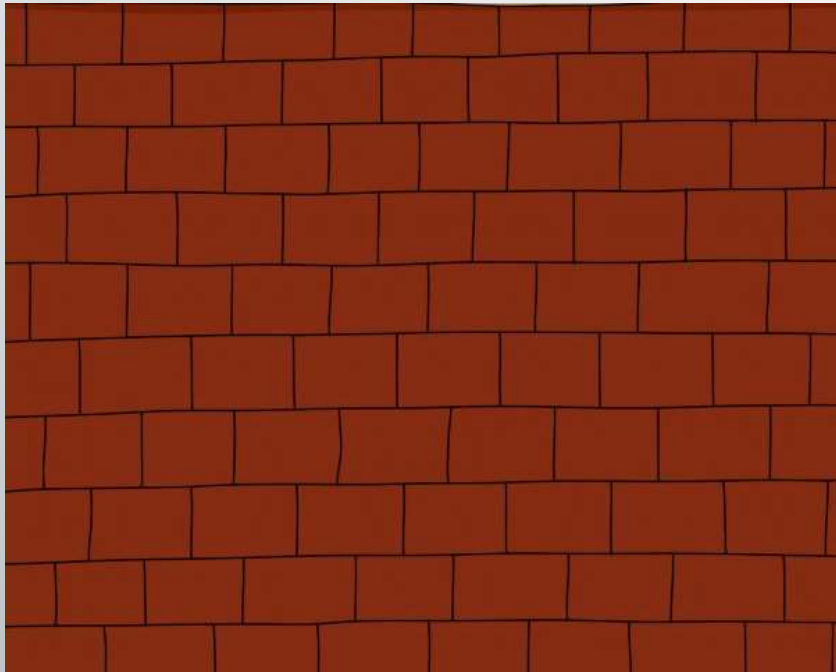
Organ system



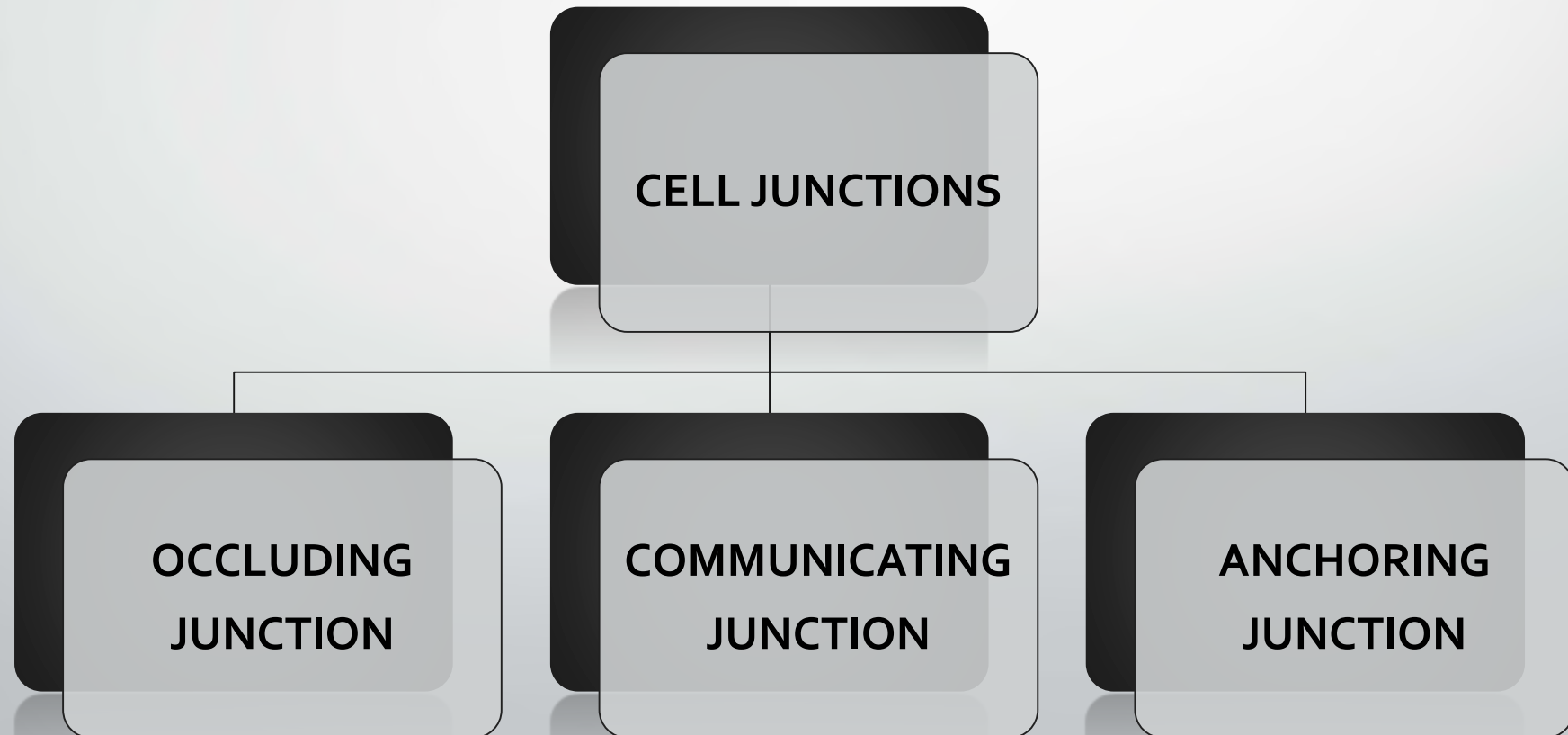
TYPES OF TISSUES:

- Epithelial tissues
- Connective tissues
- Muscular tissues
- Neural tissues

EPITHELIAL CELLS

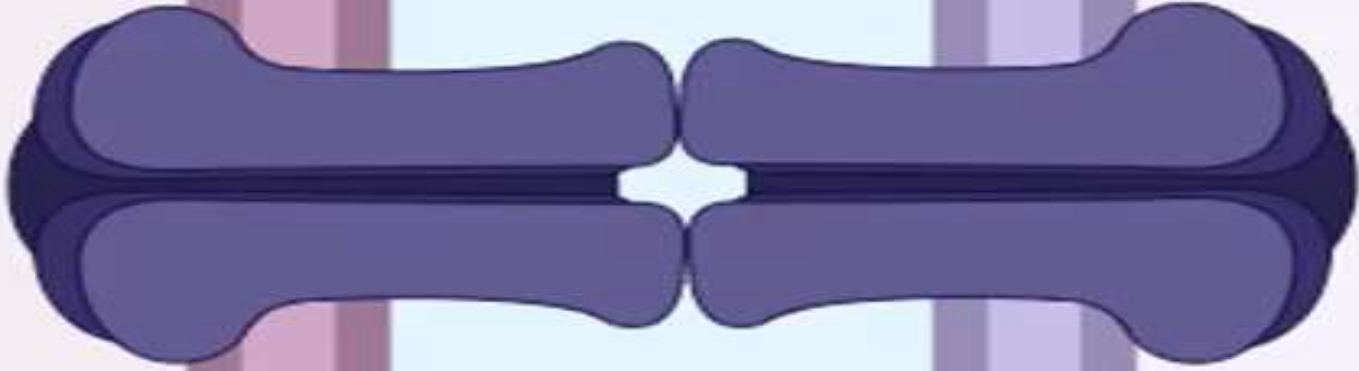


CLASSIFICATION OF CELL JUNCTIONS





Tight junction



GAP junction

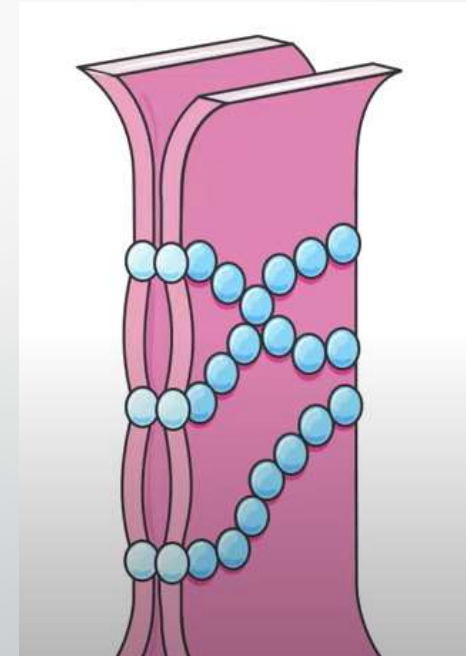


Adherence junction

CELL JUNCTIONS

OCCLUDING JUNCTION

- Tight junctions/*zona occludens*
- Apical surface
- Functions:
 1. Rigidity
 2. Prevents cellular leaking
 3. Maintenance of polarity



IN GINGIVA:

Found only in the oral epithelium.

- FUNCTIONS:

1. Mechanical rigidity

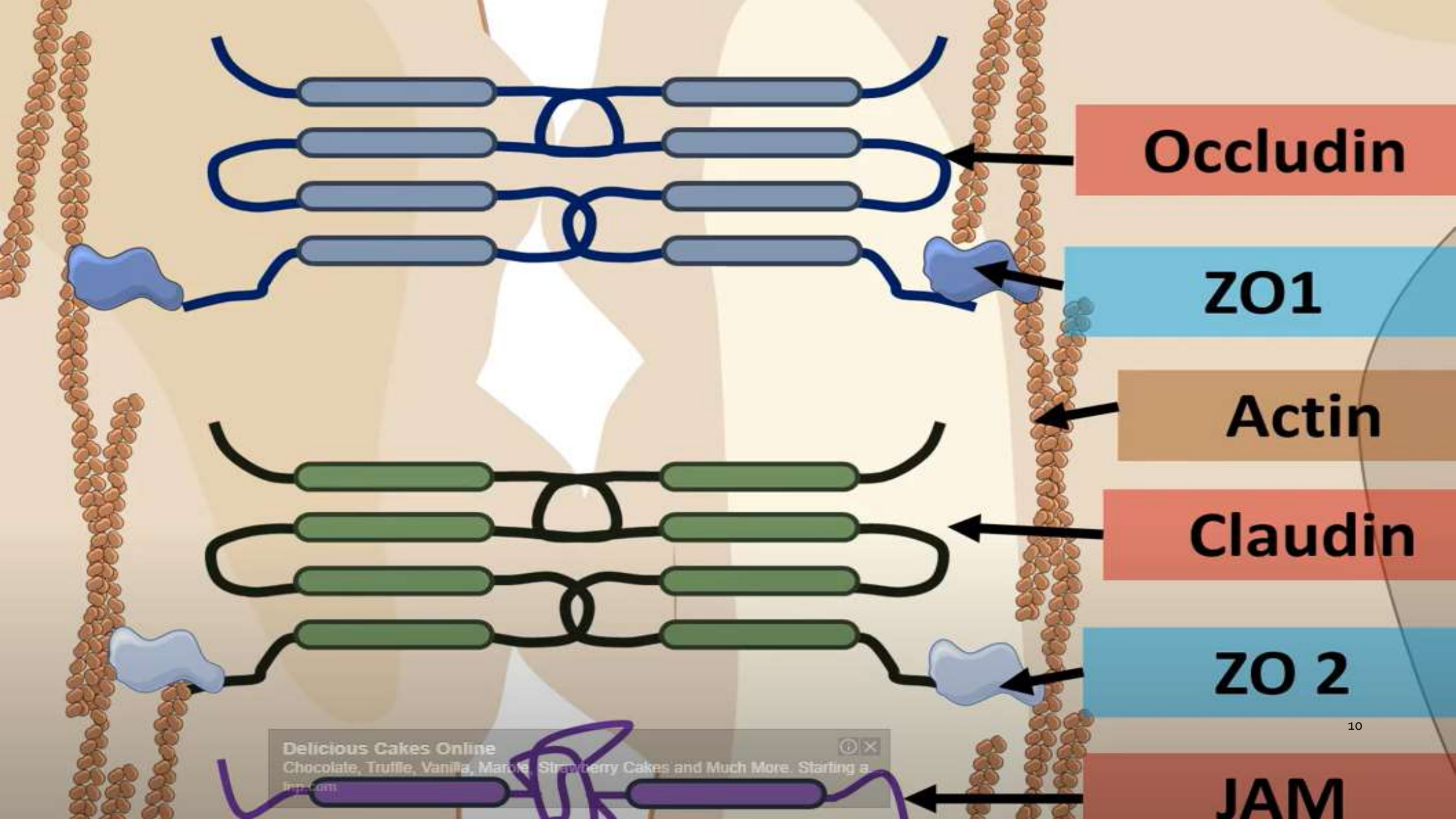
2. Impermeability

3. Maintenance of polarity

4. Regulation of cellular behaviour

STRUCTURAL PROTEINS

- INTEGRAL MEMBRANE PROTEINS:
 1. Claudins
 2. Occludins
 3. Junction adhesion molecules
- MEMBRANE PLAQUE ASSOCIATED PROTEINS:
 1. ZO
- ACTIN FILAMENTS AND OTHER INTERCELLULAR COMPONENTS



Occludin

ZO1

Actin

Claudin

ZO 2

JAM

- **CLAUDINS:** Small Tetraspan proteins.
Transepithelial electric resistance (TEER)
In gingiva- claudin-1 and-2
- **OCCLUDINS:** large tetraspan proteins.
- **JUNCTION ADHESION MOLECULES:** single span membrane protein
Ig superfamily.

ANCHORING JUNCTIONS

- CROSS TALKS
- Lateral surface of cell
- Intercellular gap of 15-20 nm – contain proteinaceous strands.
- Aid in intra and intercellular communication.
- Regulates cell proliferation, differentiation and survival.

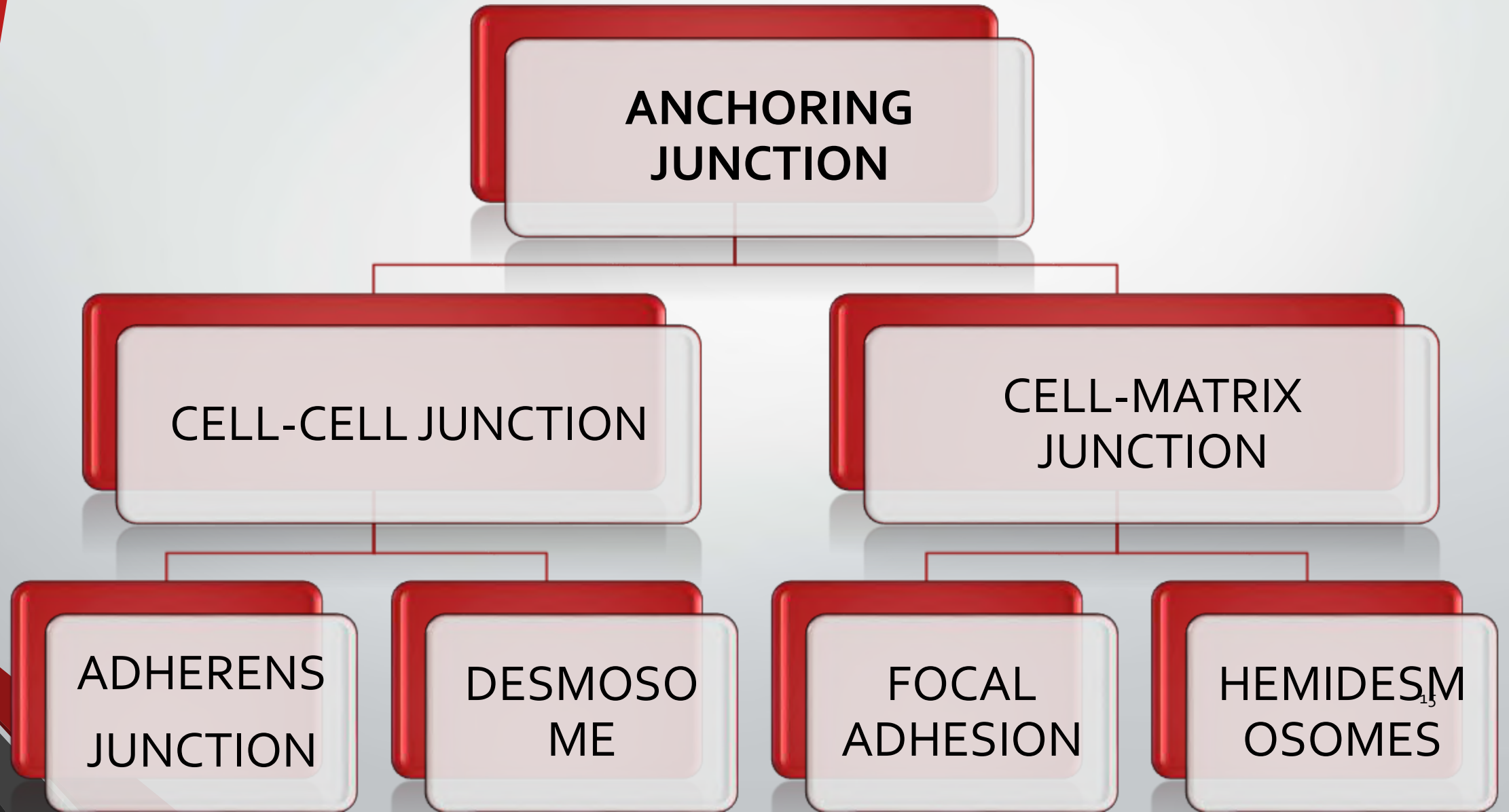
IN GINGIVA

- Determines the cell size and shape of gingival cells to form an intact barrier.
- Cell proliferation – intracellular signals
- Regulates keratinization.
- Future development of tight junctions

STRUCTURAL PROTEINS

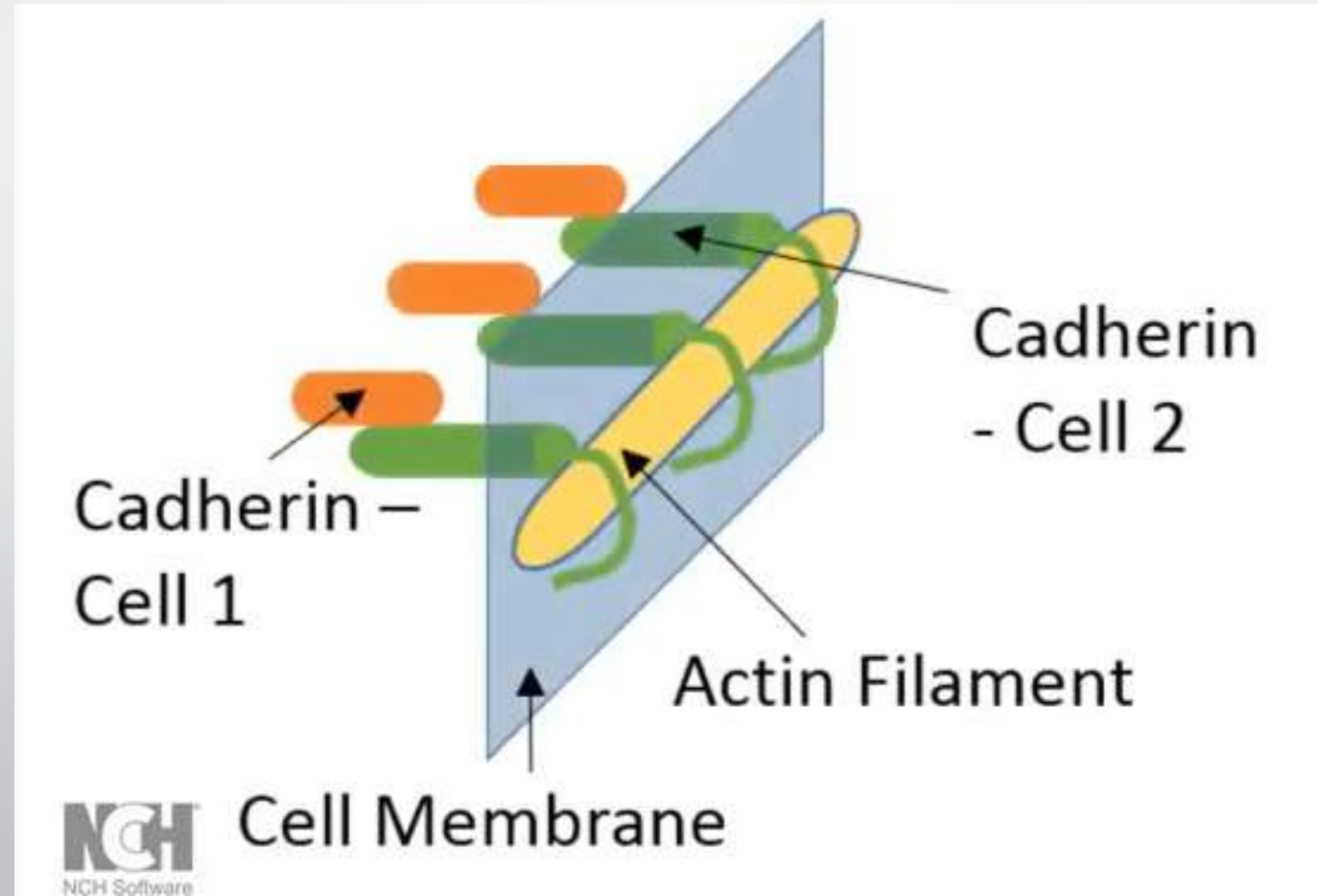
- Transmembrane adhesion protein : predominantly *cadherins* or *integrins*.
- Intracellular component: *actin* or *intermediate filaments*.
- Anchoring proteins: bridge between cytoskeletal components and TMAPs. EG: ***catenins in adherens junction & non-classical cadherins in desmosomes***.
- Extracellular ligand : *fibronectin, laminin* or *integrins*.

CLASSIFICATION



ADHERENS JUNCTION

- Predominant in gingival epithelium.
- Major component – Ca dependant CAM : cadherin;
- Also has nectin – Ca independent protein



DESMOSOMES

- Macula adherens
- Proteins –
 1. outer core: Desmoglein, Desmocollin → cadherin super family.
 2. Plaque proteins: Desmoplakin, plakoglobin, plakophilin.

IN GINGIVA

- Mechanical resilience to cell.
- Regulate cell behavior by transmitting intracellular signalling via the intermediate filaments.

CELL- MATRIX JUNCTIONS

- Diffusion through basal lamina.
- Focal adhesions
- hemidesmosomes

FOCAL ADHESIONS

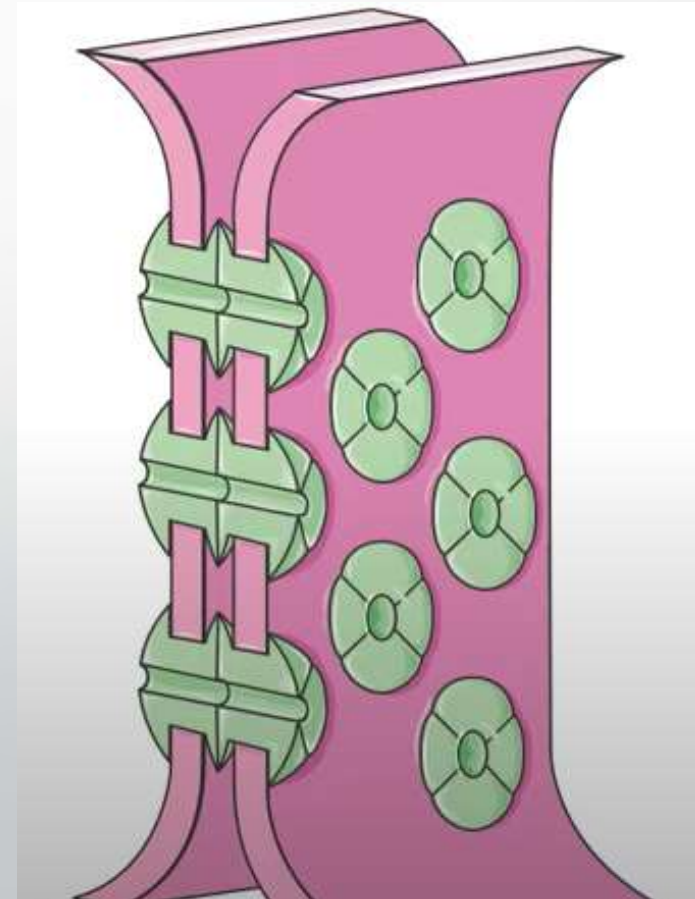
- Focal adhesions are actin-enriched adhesive domains found in many cultured cells, including fibroblasts, endothelial cells, synoviocytes and chondrocytes .
- Interlukin-1 signalling through focal adhesion as they are enriched with tyrosine phosphate.

HEMIDESMOSOMES

- Adhesion of epithelial cells to basal lamina.
- Two sets of proteins – intracellular and extracellular proteins
- In gingiva: outer and junctional epithelium
- In outer epithelium it is found in basal layer – for nutrition from connective tissue.
- In junctional epithelium in internal basal lamina- attachment to CEJ.

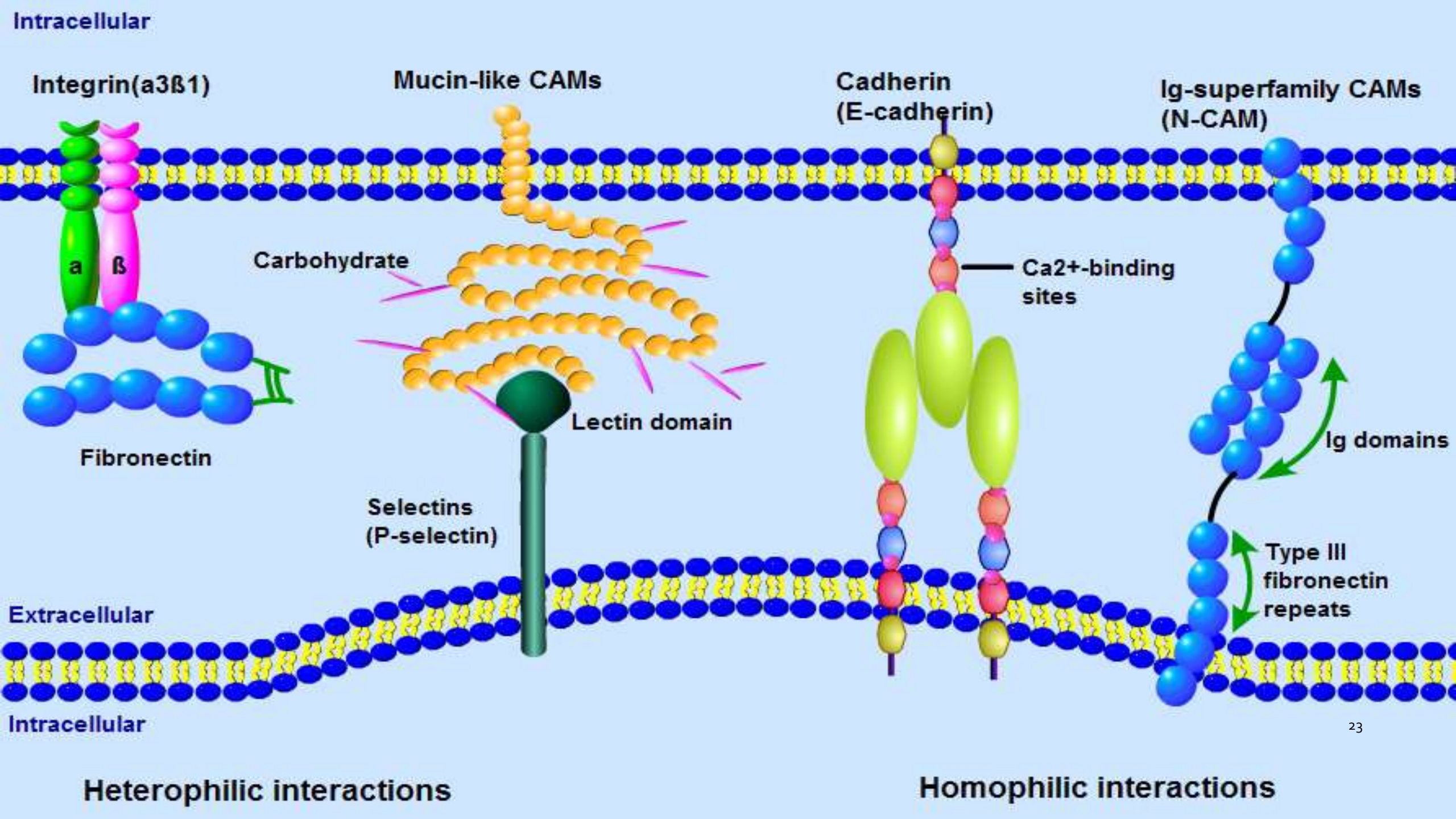
GAP JUNCTIONS

- Structural protein – *connexin*.
- *In gingiva:* CONNEXIN 43 .
- Predominantly found in outer epithelium



CELL ADHESION MOLECULES

- Glycoproteins.
- Mediates adhesion of cells to each other or to the extra cellular matrix.
- Four classes of CAMs :
 1. Cadherins
 2. Selectins
 3. Integrins
 4. Immunoglobulin super family



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graph TD; CAM[CAM] --- CD[Calcium dependent]; CAM --- CI[Calcium independent];
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CAM

Calcium
dependent

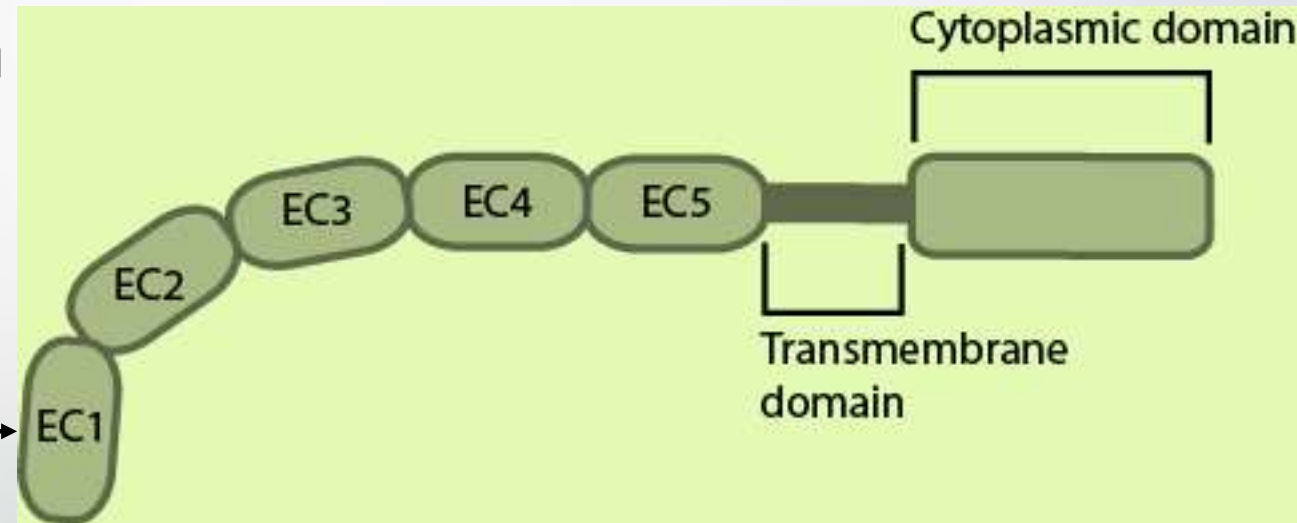
Calcium
independent

CALCIUM DEPENDENT CAMs

- Requires optimum calcium concentration.
 - Responsible for adhesion of cells to each other during their developmental stages.
- CALCIUM DEPENDENT CAMs :
 1. Cadherins
 2. Selectins
 3. Mucins

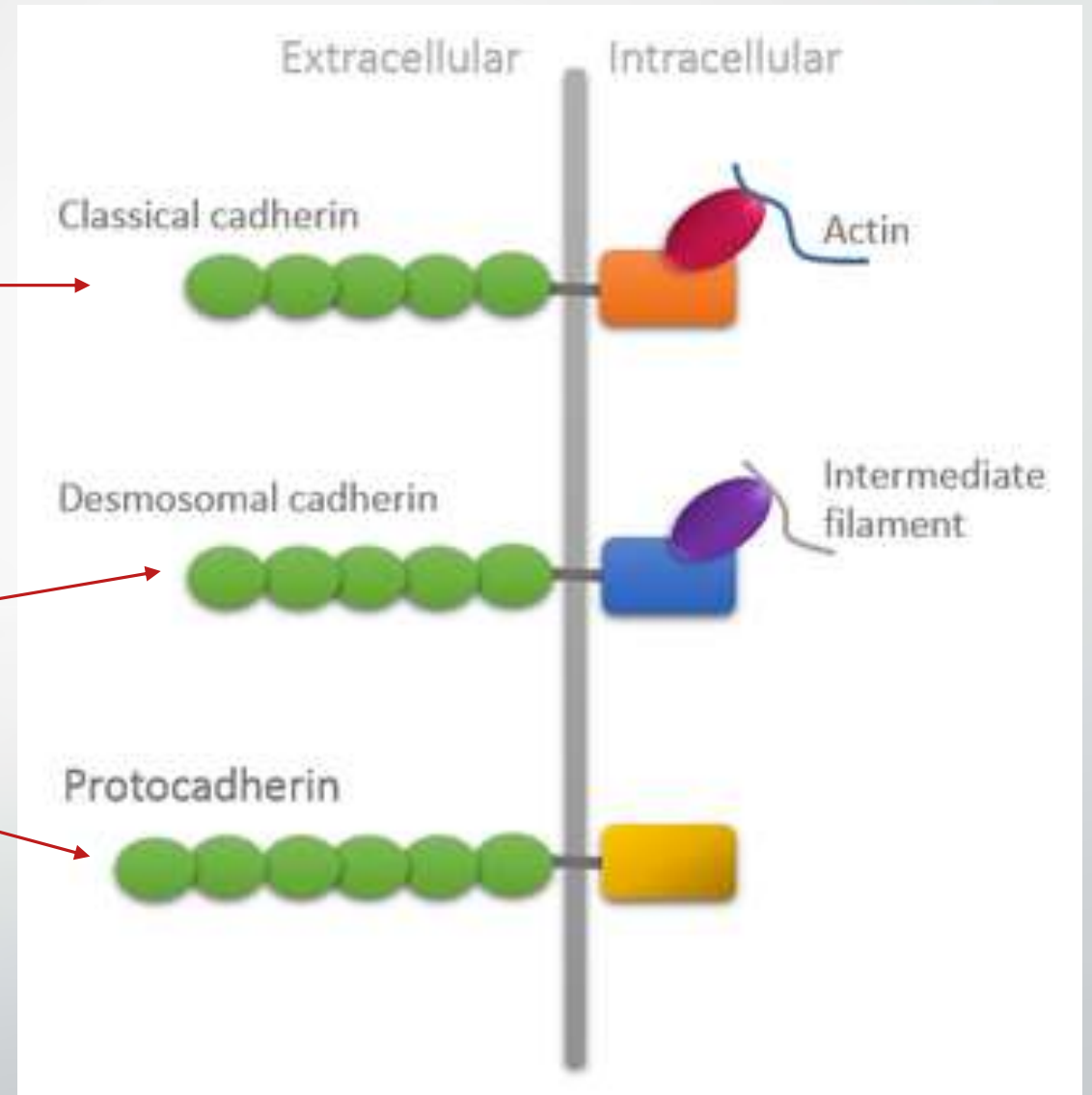
CADHERINS

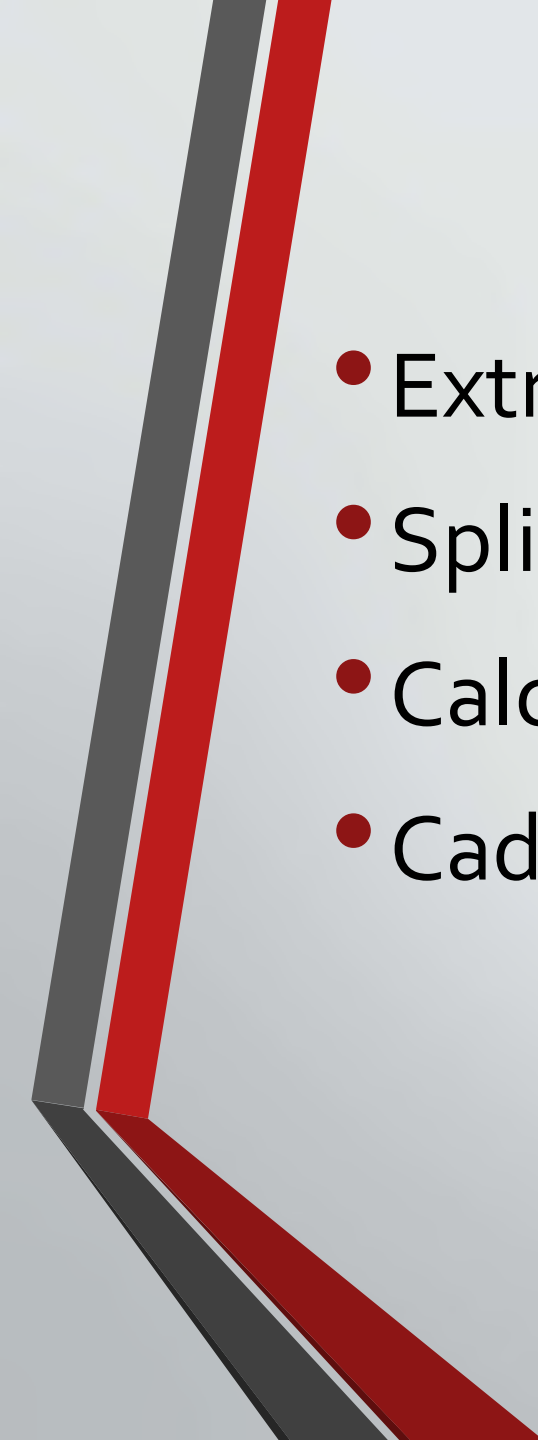
- Homophilic cell adhesion
- Adherens junction
- Extra cellular domain – amino terminal
- Intra cellular domain – carboxy terminal

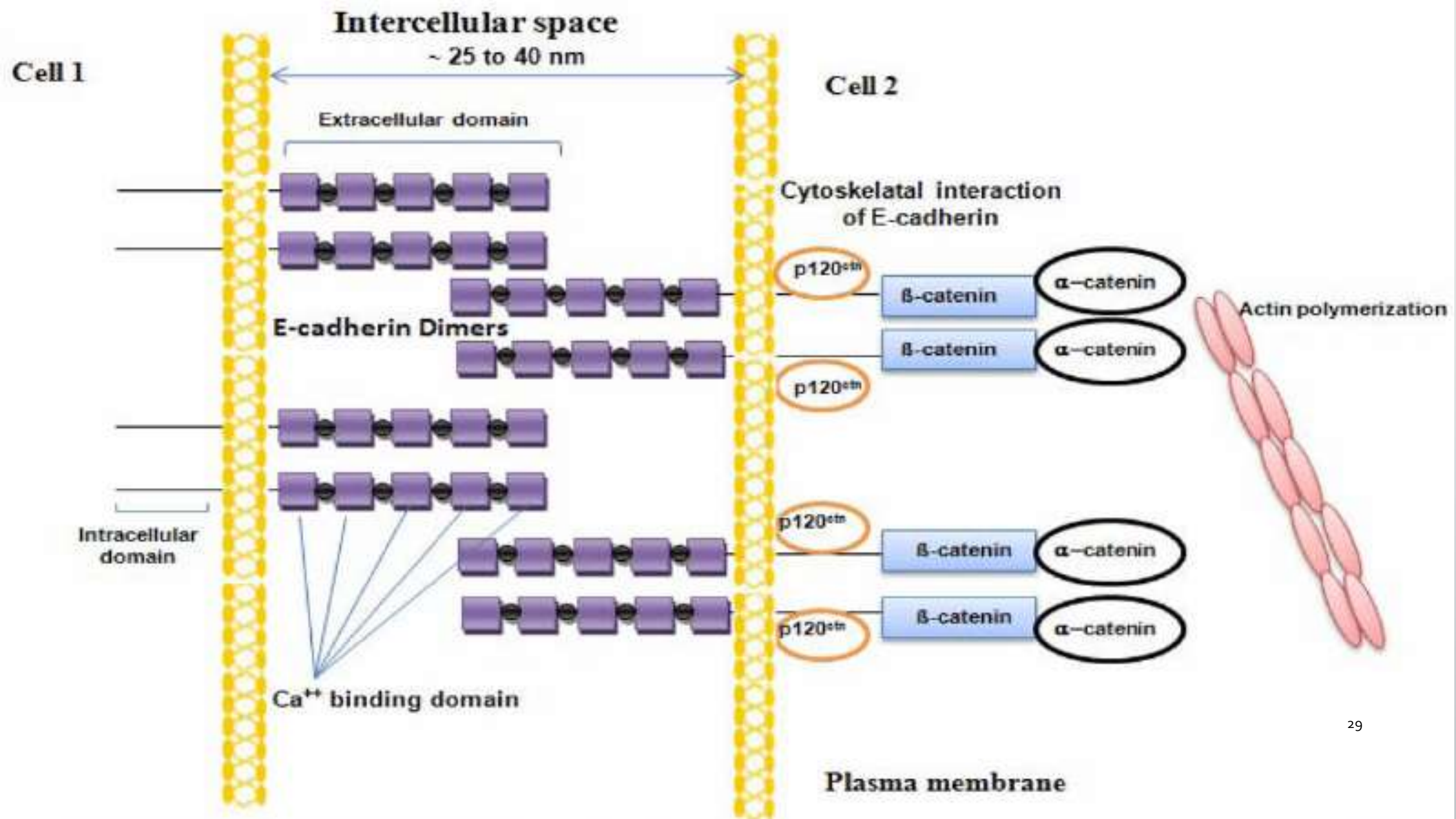


Transmembrane protein

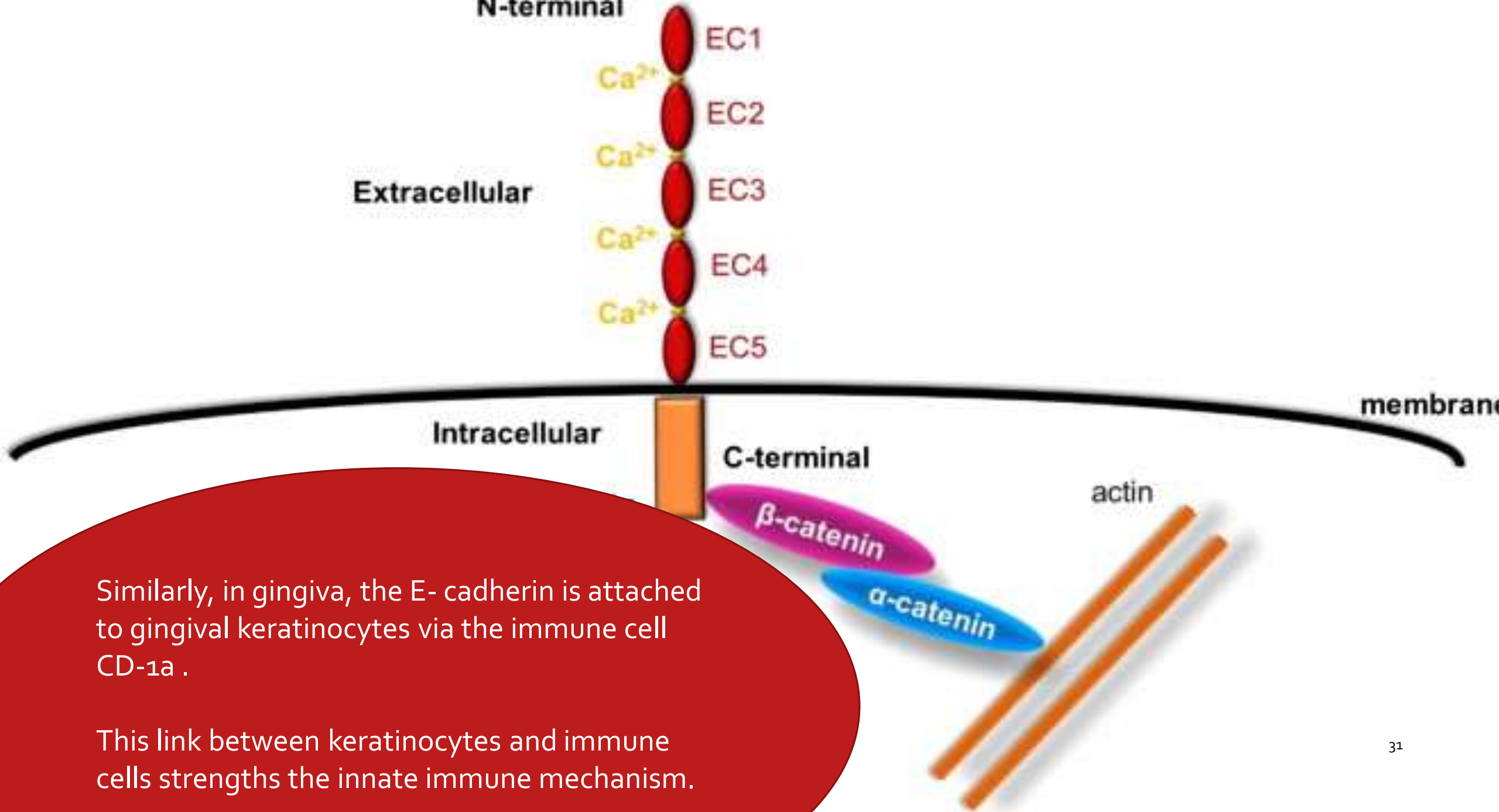
- Classical cadherins: E,P,N – cadherins
- Type 2 – neuronal tissue
- Desmosomal cadherins
- Proto cadherin



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- Extra cellular domain is composed of 550 amino acids.
 - Split into 5 homologous groups EC 1-5.
 - Calcium binding sites
 - Cadherin dimers

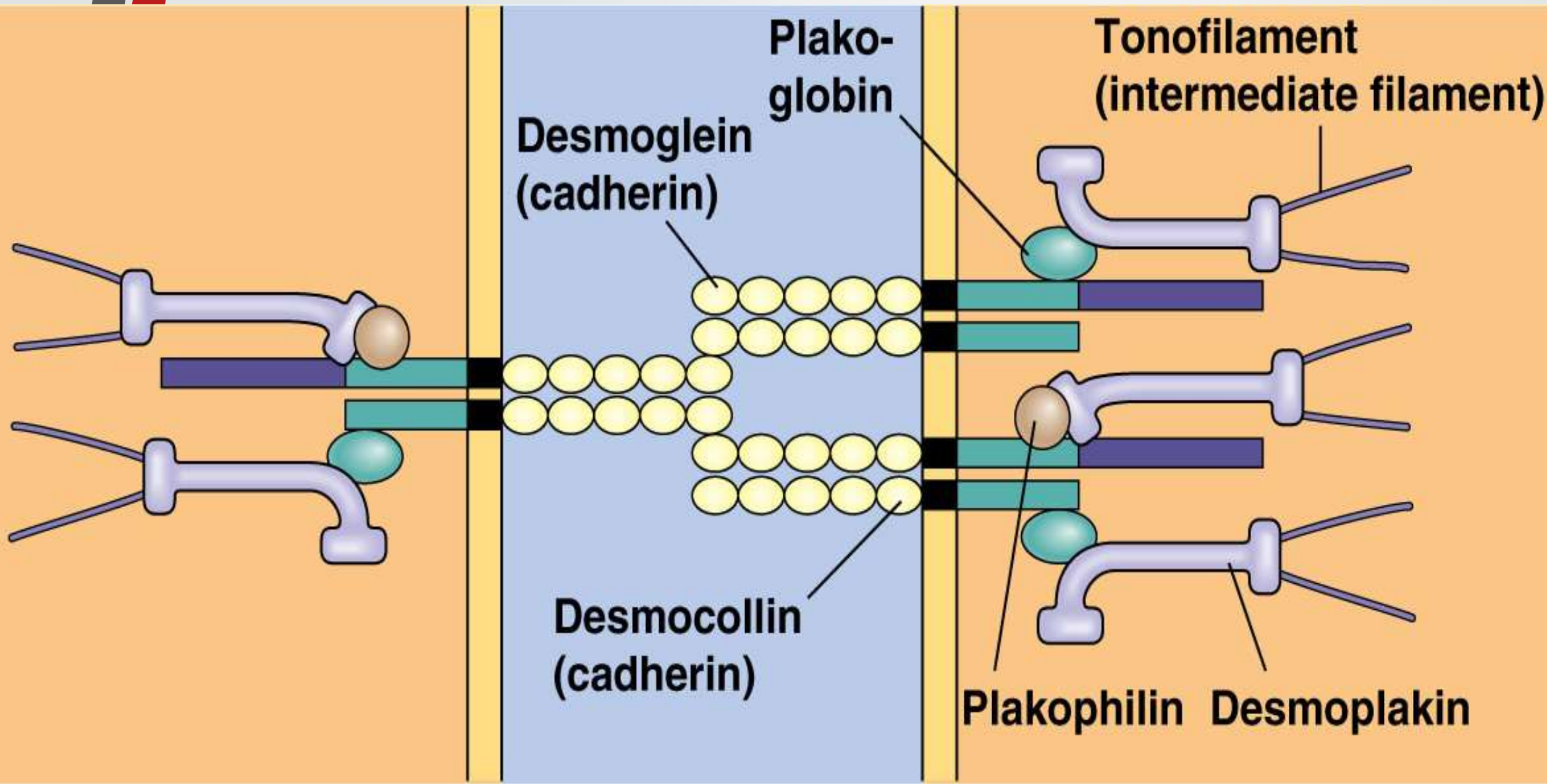


- Intra cellular domain of cadherin binds with the cytoskeletal component through catenins.
- Also mediated by calcium ions.
- Catenins are proteins that comprises of α , β , γ (plakoglobin) members.
- Cadherins are attached to the actin filaments through the catenins



Similarly, in gingiva, the E-cadherin is attached to gingival keratinocytes via the immune cell CD-1a .

This link between keratinocytes and immune cells strengthens the innate immune mechanism.



ROLE IN GINGIVAL EPITHELIUM

- *In health*

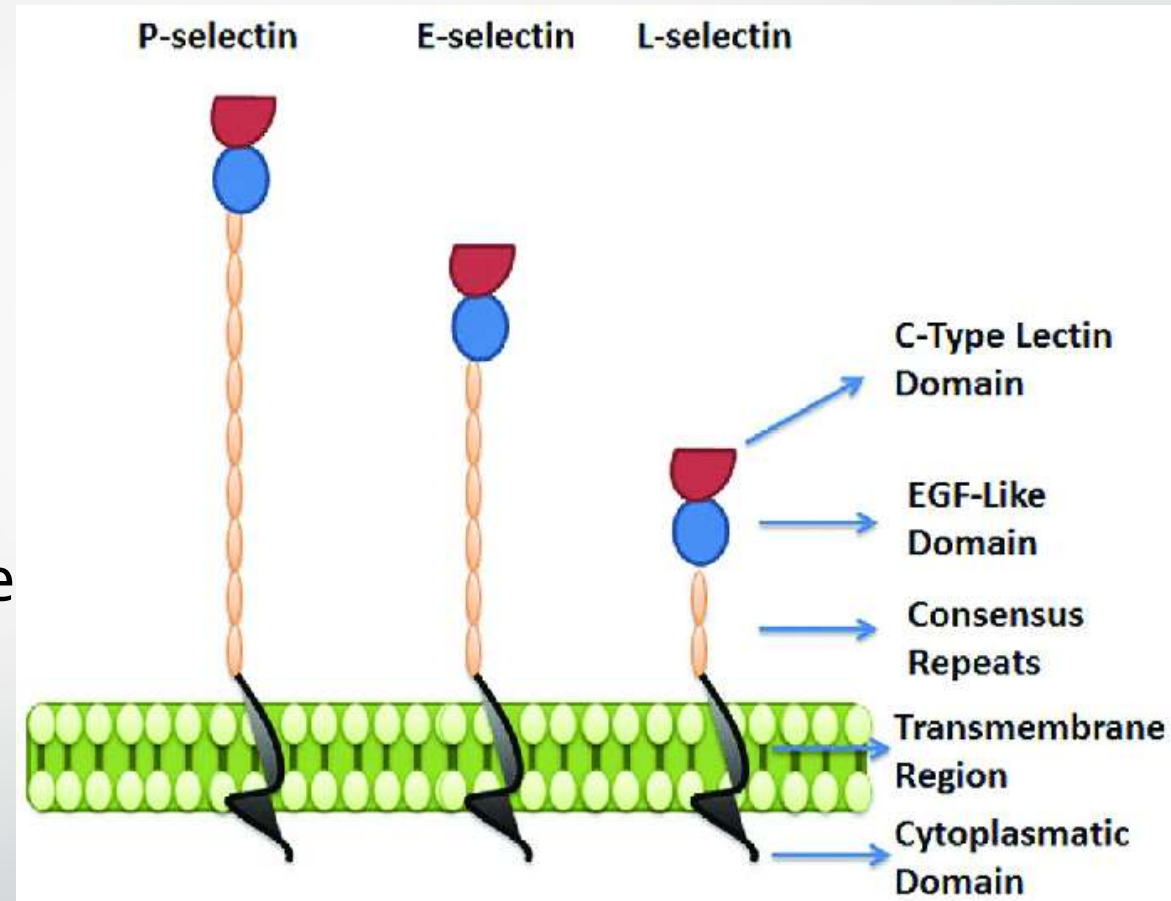
1. Effective mechanical barrier
2. Regulating the behaviour of gingival epithelium-keratinocytes

- *In gingivitis*

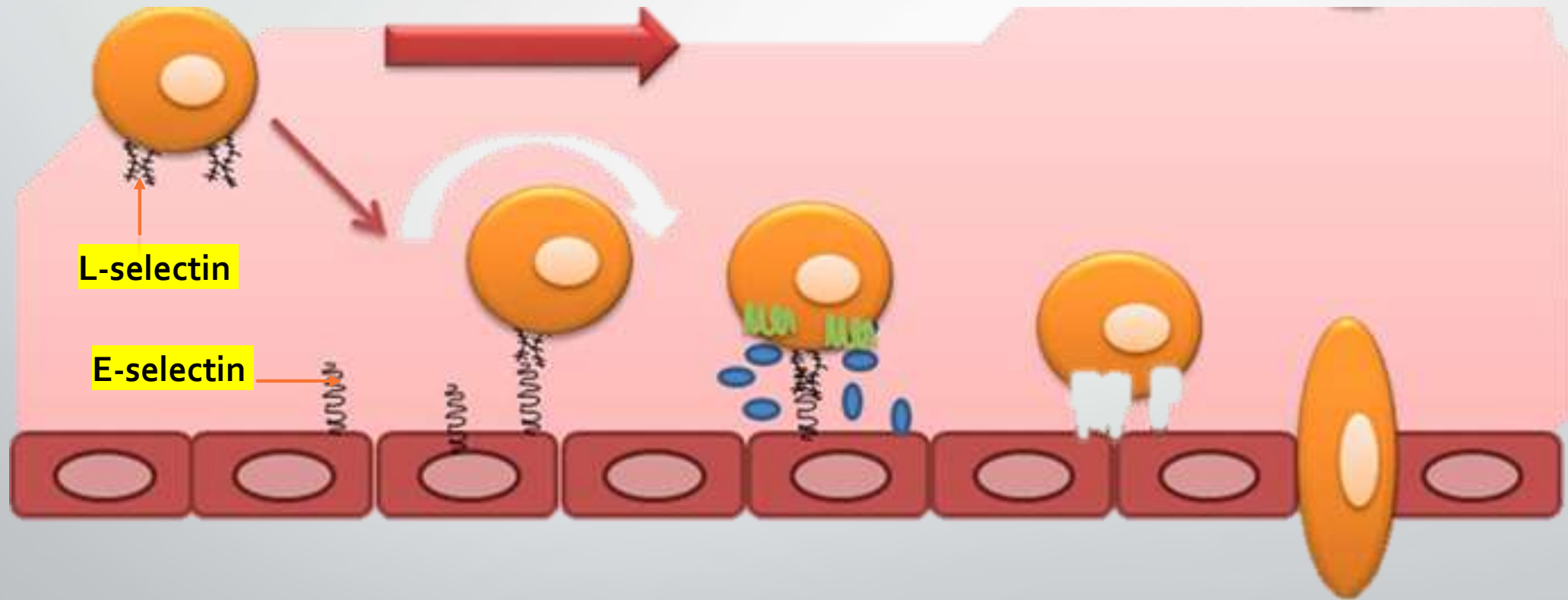
1. Reduced expression of E-cadherin in pocket epithelium.
2. Gingipains- disruption of E-cadherin assembly.

SELECTINS

- Leucocyte – endothelial adhesion
- Types – endothelium, platelets, leukocyte.
- Domains –
 1. extracellular-epithelial growth factor domain
 2. Single spanning transmembrane domain.
 3. Intracellular domain



- Aids in transmigration of neutrophils from the centre of laminar blood flow.



IN GINGIVITIS:

P.gingivalis



Suppress expression of E-selectins



Prevents transendothelial migration of neutrophils to the site of infection.



Immune suppression

INTEGRINS

- Heterodimers of α and β subunits, and the ligand binding site is composed of parts of both the chains.
- 22 integrin heterodimers
- -- **17 types of α subunits and 8 types of β subunits.**
- The diversity of integrins and their ligands in the matrix enables cells to migrate to their correct locations.
- several α subunits combine with specific β subunits.

STRUCTURE

- DOMAINS:

EXTRA CELLULAR

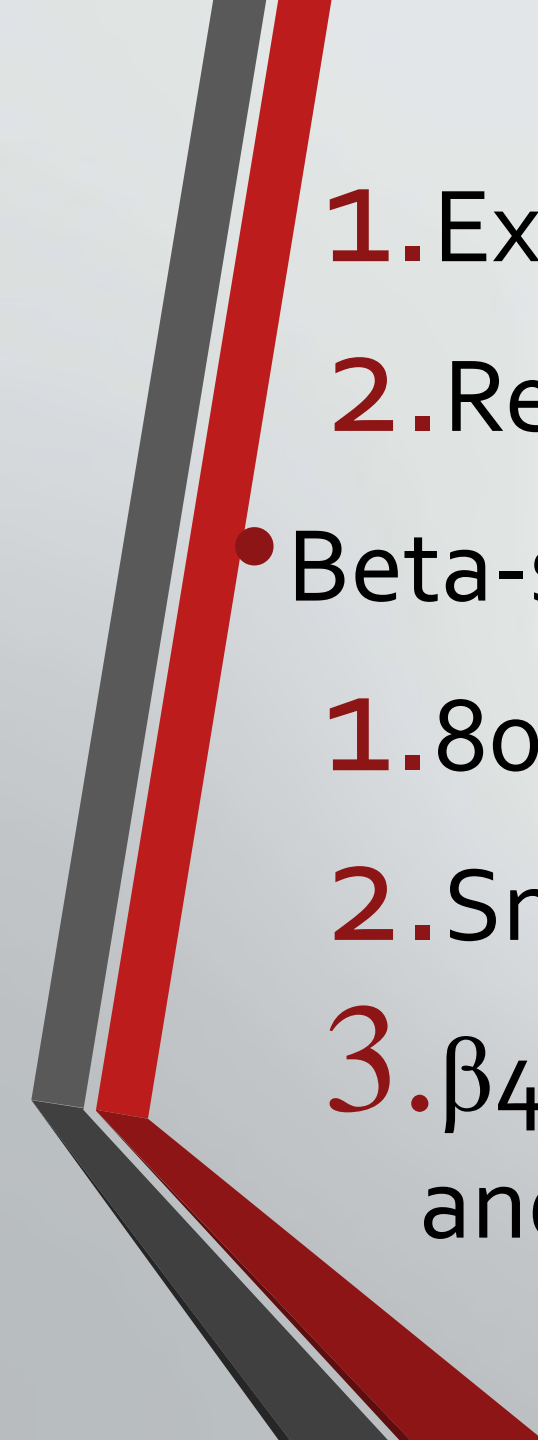
MEMBRANE ASSOCIATED

INTRA CELLULAR(Smallest)

- Alpha-subunit

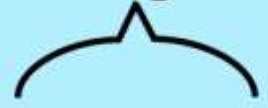
1. -1200 – 1800 amino acids

2. Structurally similar to epithelial growth factor. ³⁸

- 
1. Extracellular domains bind to calcium
 2. Requires calcium ions for activation.
- Beta-subunit
 1. 800 amino acids.
 2. Smaller than α subunit
 3. β_4 subunit has larger cytoplasmic domain and is binds to hemidesmosomes.

Binding site for extracellular ligand

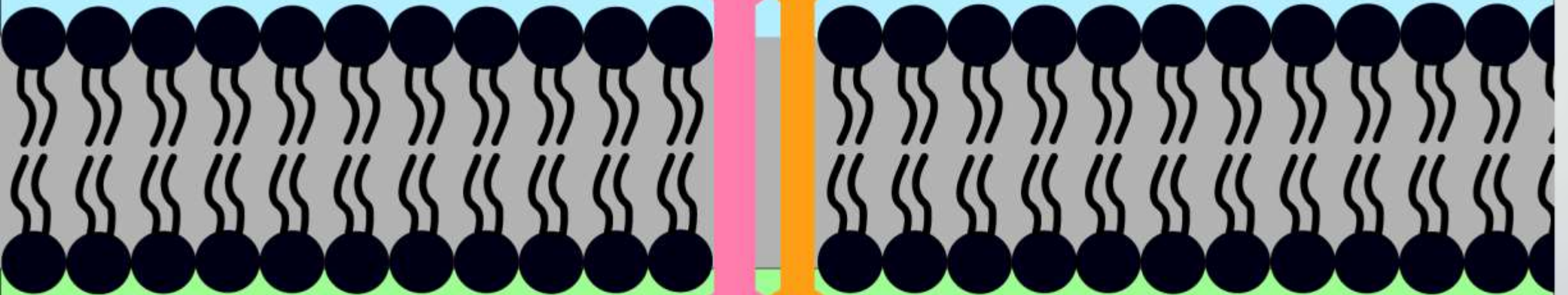
Integrin






α

β

Binding site for intracellular components



Legend:

-  = Outside of cell
-  = Inside of cell
-  = Cell membrane

FUNCTIONS

- *ADHESION:*
 1. Bind to proteins with specific amino acid sequence.
- *DIFFERENTIATION:*
 1. Transmit intracellular signals.
- *MECHANOSENSORY:*
 1. Cytoskeletal reassembly and transmission of intracellular signals.

INTEGRINS IN PERIODONTIUM

$\beta 1$ Integrins – adhesion of cells to the matrix proteins.

- ❖ $\alpha 2\beta 1$, $\alpha 1\beta 1$ – binds to collagen
- ❖ Present in gingival connective tissue and periodontal ligament.
- ❖ Mediates fibroblast adhesion to collagens
- ❖ Mediates adhesion of osteoblasts to immature osteoid matrix in alveolar bone.
- ❖ $\alpha 5\beta 1$ Responsible for PDL fibroblast adhesion to cementum attachment protein and formation of long junctional epithelium

- β_2 integrins- leukocyte integrins
 - ❖ Adhesion between ***LFA-1 and ICAM-1*** expression in junctional epithelium retain neutrophils at sulcus area.
- β_3 integrins – bone related proteins
 - ❖ Adhesion of PDL fibroblasts to OPN – ability to transform into bone like tissue when required.
- β_4 integrins – hemidesmosomes
 - ❖ Attachment of junctional epithelium to the tooth.
- β_6 integrin – mediates adhesion to fibronectin
 - ❖ wound healing
 - ❖ Regulates cell proliferation and differentiation.

IMMUNOGLOBULIN SUPERFAMILY

- IgSF cell adhesion molecules are calcium-independent transmembrane glycoproteins.
- N-CAM, I-CAM, C-CAM
- ICAM-1 is expressed on leukocytes, fibroblasts, epithelial cells and endothelial cells.
- Expression can be influenced by cytokines (IL-1, TNF- α , IFN- γ), or bacterial endotoxin.
- Hence in periodontal disease, excessive infiltration of neutrophils leads to breakdown of epithelium resulting in apical migration of JE and pocket formation.

- Cell adhesion in junctional epithelium:
 - ❖ Mediated by cell-cell adhesion molecule – (C-CAM)
 - ❖ Homophilic adhesion- unites epithelial cells to each other
 - ❖ Heterophilic adhesion- junctional epithelial cells to neutrophils.

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[Nicole Pisco](#)



- **THANKYOU...**