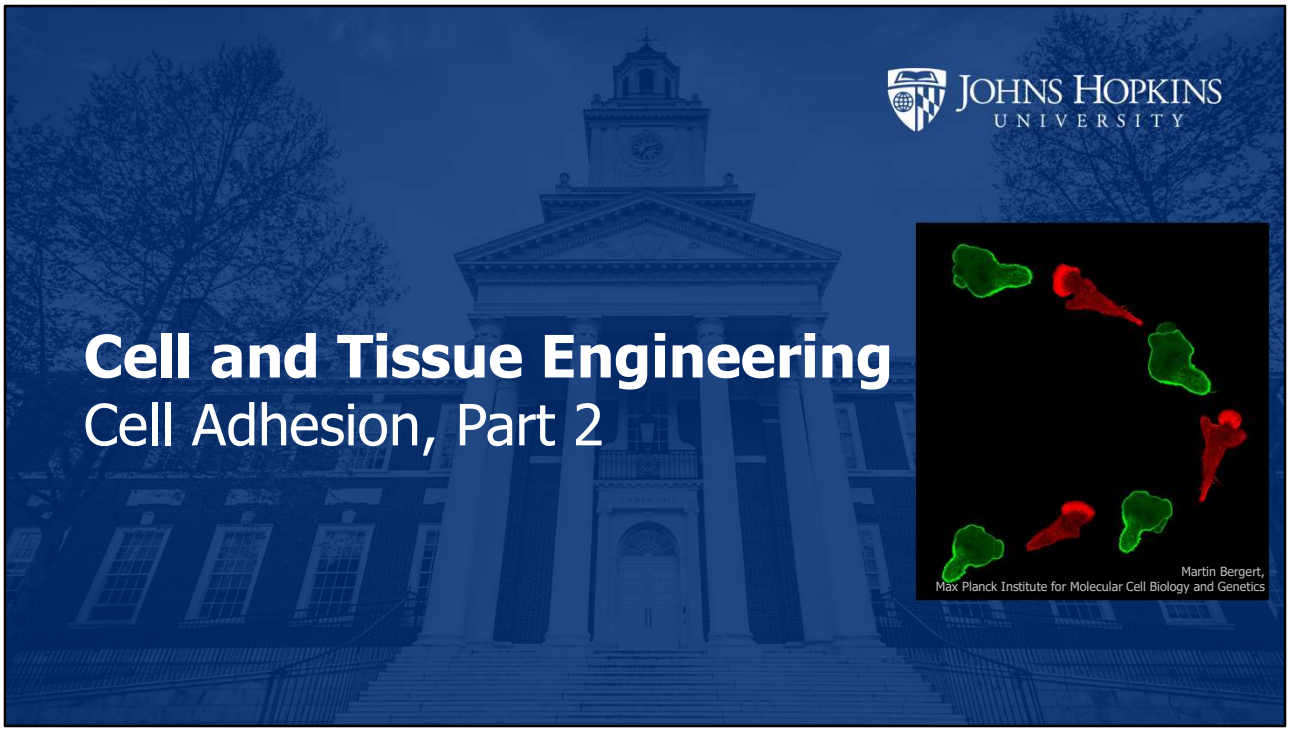
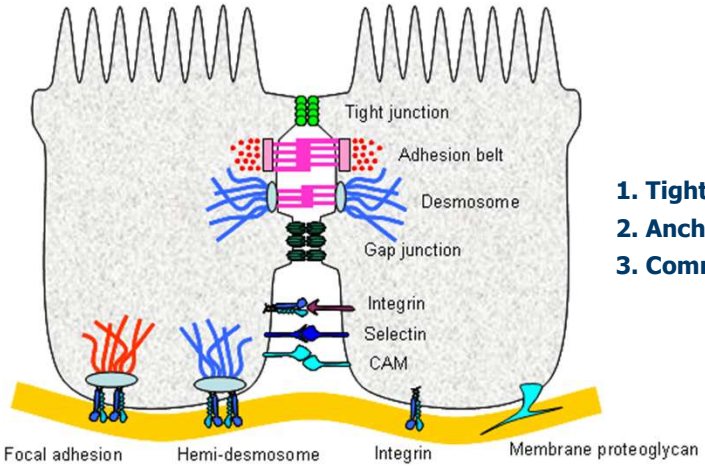


Welcome to Cell and tissue engineering - Cell adhesion part 2. In this this lecture we are going to focus on specific types of cell adhesions.

Three types of functionally different cell adhesions



1. **Tight Junctions**
2. **Anchoring Junctions**
3. **Communicating Junctions**

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php.med.unsw.edu/au

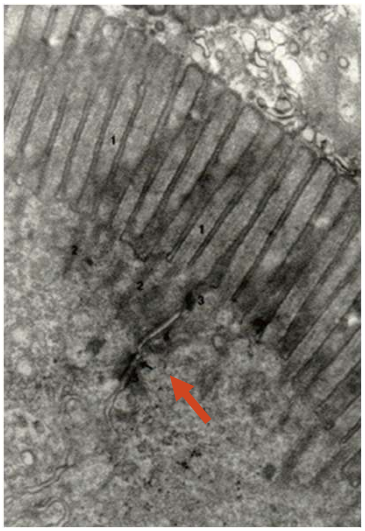
In the last lecture, we discussed tools that can measure cell adhesion strength. These tools can measure many different adhesion types. Lets take a look at some of these adhesion types.

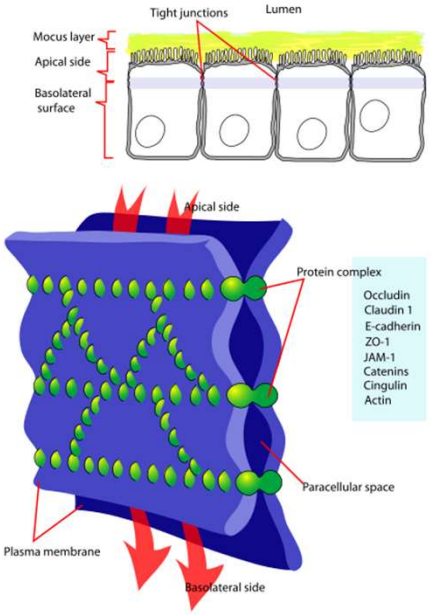
There are three categories of cell adhesion in the body. Tight and anchoring junctions which are mechanically active, and communicating junctions are for signal transmission via the exchange of molecules from the cytoplasm of one cell to the cytoplasm of another cell.

You can see a tight junction here at the defining the apical and basal surfaces of this cell, some anchoring junctions here including cell-cell adhesion belts, desmosomes, and integrin matrix adhesion.

And finally the gap junction here which we discussed earlier in the context of action potential propagation.

1. Tight junctions form barriers





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Wikipedia.org; http://www.biologie.uni-hamburg.de

We won't spent time on tight junctions here since we've already seen these this semester.

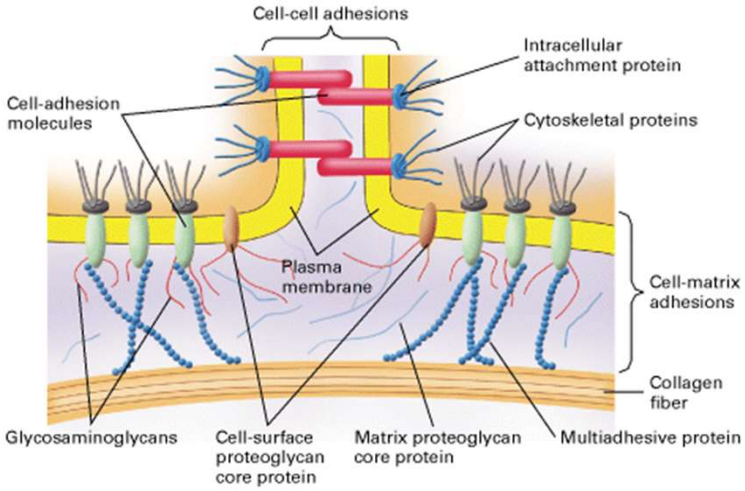
I'll only remind you that this type of cell-cell adhesion is used to form barriers like those needed in epithelial tissues. The membranes of two adjoining cells are so tightly fused that in this junction that they can be impermeable to molecules and even fluids. Tight junctions are composed of many proteins as you can see listed here. The permeability of the junction depends on the density of these proteins within the junction.

Not only do these junctions stop movement of materials between cells but they also restrict the movement of membrane bound proteins from one side of the junction to the other. For example certain membrane bound transporters on the apical side cannot move past the junction to the basal side. This means that the apical and basal surfaces can function uniquely.

This TEM shows the tight junction immediate beneath the villi of intestinal epithelial cells.

2. Anchoring junctions are mechanical links

Cell-cell AND cell-matrix adhesions



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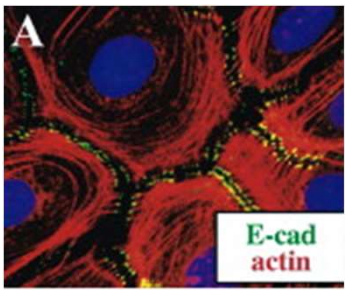
Anchoring junctions include both cell-cell and cell-matrix adhesions. These are mechanically active links that incorporate the cytoskeleton allowing for force transmission.

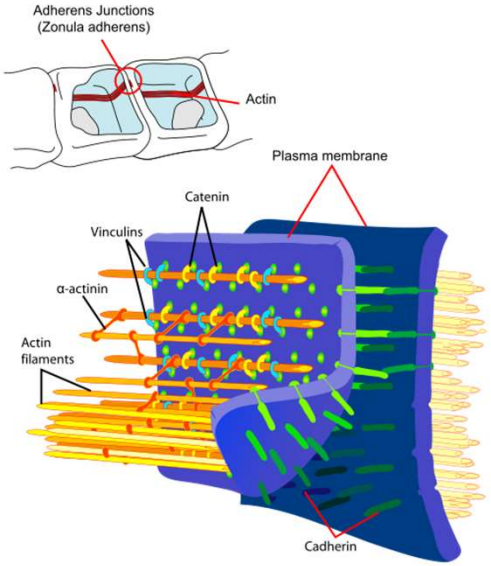
Here are the top you can see an example of a cell-cell adhesion, and here at the bottom you can see an example of cell-matrix adhesion.

2. Anchoring junctions are mechanical links

Types of anchoring junctions

- **Adherens Junction**
- Desmosome
- Hemidesmosome
- Focal contact





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Wikipedia.org; Vaezi, et. al., 2002

Let's take a closer look at one type of anchoring cell-cell junction, **the adherens junction**.

From the top image you can see these junctions form a contractile band around the cell (dark red line).

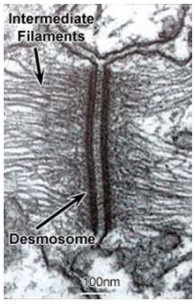
To do so they must incorporate the actin filaments of the cytoskeleton. From the lower panel you can see there are a host of other proteins involved as well including **cadhereins** on the extracellular side, AND **catenins**, and **vinculin** and crosslinking protein **alpha actinin**.

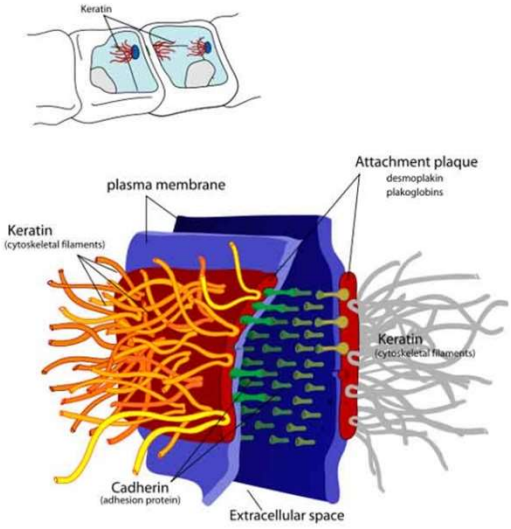
In the Florescent image on the left you can see skin epithelium cells (keratinocytes). The stain in this image shows **e-cadherein** in green colocalizing with **red actin cytoskeleton**, resulting in yellow adherens junctions between the cells.

2. Anchoring junctions are mechanical links

Types of anchoring junctions

- Adherens Junction
- **Desmosome**
- Hemidesmosome
- Focal contact





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Wikipedia.org; histology.leeds.ac.uk

Desmosomes are another example of a cell-cell anchoring junction that links to the **intermediate filaments** of the cell instead of the actin filaments.

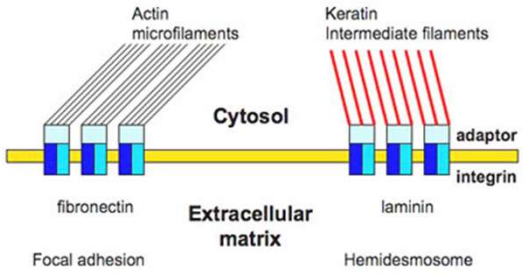
Instead of appearing as bands, these exist as dense plaques or clusters, as you can see on the upper right image.

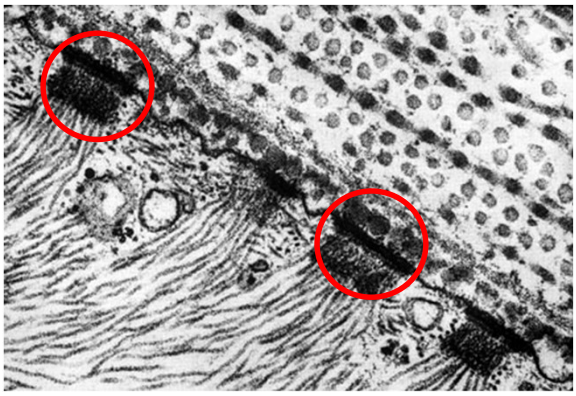
These adhesions are found anchoring muscle cells to one another and also in the epithelium tissues of the body. This junction links muscles cells together to form one contiguous piece of muscle.

2. Anchoring junctions are mechanical links

Types of anchoring junctions

- Adherens Junction
- Desmosome
- **Hemidesmosome**
- **Focal contact**





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micro.magnet.fsu.edu; downstate.edu

The last two types of anchoring junctions we'll look at are **hemidesmosomes** and **focal contacts** or focal adhesions – These are both cell-matrix contacts.

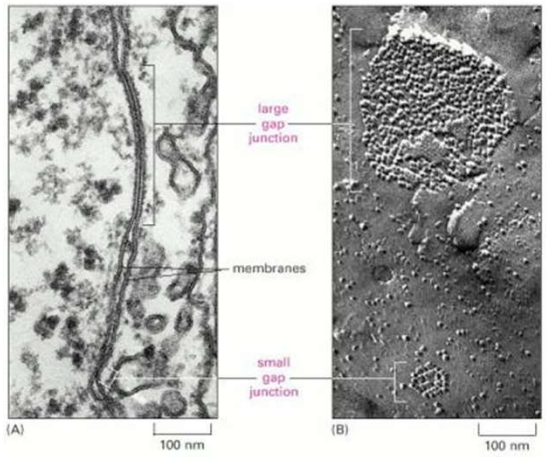
Like desmosomes, **hemidesmosomes** link to **intermediate filaments** and like adherens junctions, **focal contacts** link to the **actin cytoskeleton** as you can see in the image on the left.

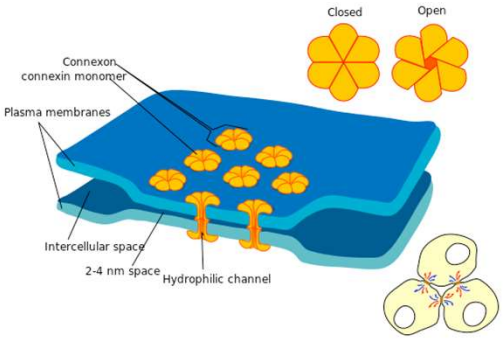
Hemidesomosomes are used to connect epidermal cells to the underlying basal lamina while focal adhesions are used in migration. You can see an example of Hemidesmosomes in the right image.

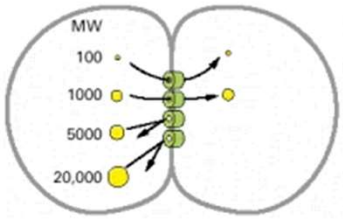
We'll hear more about **focal contacts** later on when we discuss migration, as these are the contacts that help cells generate the necessary traction forces for movement.

3. Communicating junctions regulate passage of chemical/electrical signals between cells

Gap Junctions







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Wikipedia.org; Mol. Biol of the Cell, 4th Ed., Alberts

All cells except **blood and skeletal muscle** communicate with **gap junctions.**

12 connexin proteins together form a junction channel, six proteins each in the neighboring cells, which forms the channel. These channels allow small ions and water soluble proteins under 1000 daltons to pass.

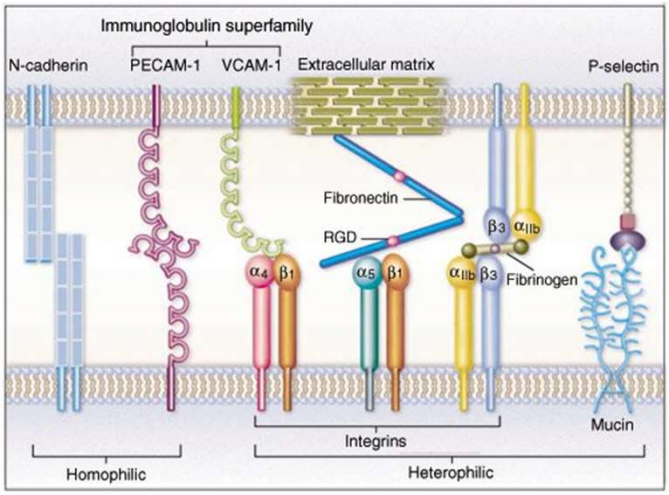
All channels are not the same however and the unique connexin composition determines what can pass through and therefore what functions the junction regulates.

These junctions are most often thought of in coordination of electrically excitable cells, but they are just as abundant in non-excitable cells where they act to smooth out coordinated cell behaviors by evenly distributing signaling molecules among a large population of cells.

Cell-Adhesion Receptors

Four Major Families

1. **Integrin**
2. **Cadherin**
3. Ig-like CAM
4. Selectin



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labs.idi.harvard.edu

Now that we've talked in briefly about the different adhesion types lets look more closely at some of the adhesion receptors they use.

There are four major families of adhesion receptors – this image shows you examples of each. It also indicates if the bonds are **homotypic**, that is they bind each other, or **heterotypic** meaning they bind a different molecule.

Here you can see **N-cadherein** binding to **another N-cadherin**, homophilic.

On the right you can see **P-selectin** binding to a **mucin** or a different receptor. This is heterophilic.

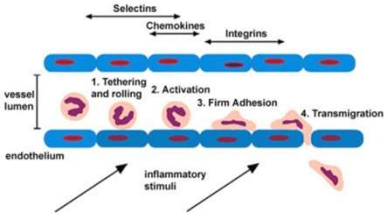
The first family we will talk about is the integrins. **Integrins** – which take part in focal adhesions, binding to the ECM -- you may recall from earlier modules that each integrin has an alpha and beta subunit

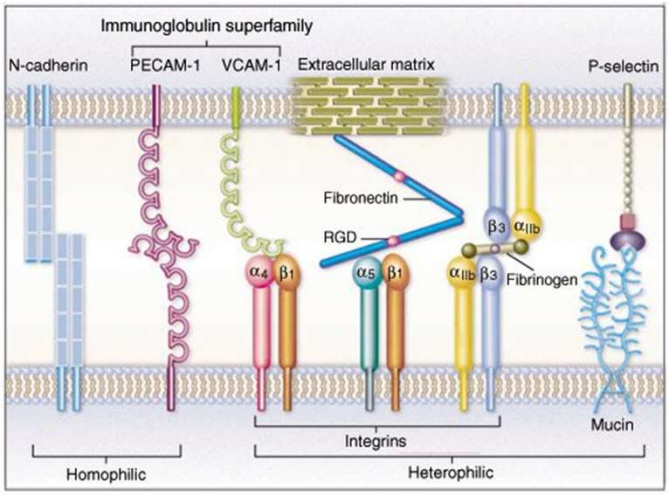
The second family is the Cadherins. **Cadherins** - we just saw in the adherens junction. N-cadherin is shown here and is found in nerve and cardiac cells.

Cell-Adhesion Receptors

Four Major Families

1. Integrin
2. Cadherin
3. **Ig-like CAM**
4. **Selectin**





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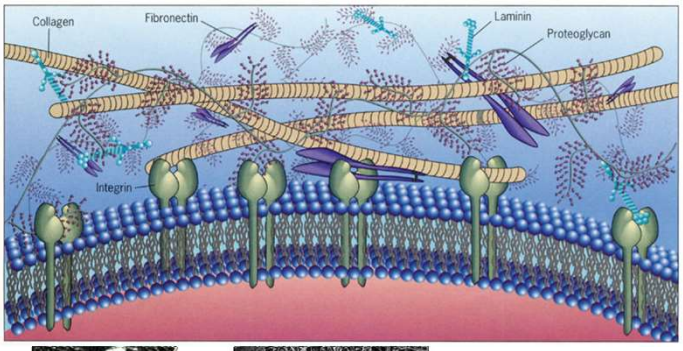
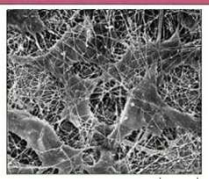
Labs.idi.harvard.edu; mpi-muenster.mpg.de

Selectins are used in the leukocyte adhesion cascade. These receptors are expressed by **endothelial cells in inflamed tissue**. When expressed, these receptors reach out into the blood stream to facilitate the **capture of leukocytes**

This last family **is Immunoglobulin or IG-Like** cell adhesion molecules. Immunoglobulin-like receptors are also used in the leukocyte cascade but not for capture – the example here of **PECAM or platelet- endothelial cell adhesion molecules** is used during transmigration of the leukocyte through the endothelial cell-cell junctions. These bonds are weaker than cadherin bonds and can more readily be broken as the leukocyte transverses in between the endothelial cells in the blood vessel wall.

Extracellular matrix components





Collagen
Fibronectin
Laminin
Elastin
Tenascin
Thrombospondin

Glycoaminoglycans
Proteogylcans

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course1.winona.edu; ecm.ucsd.edu; cc.scu.edu

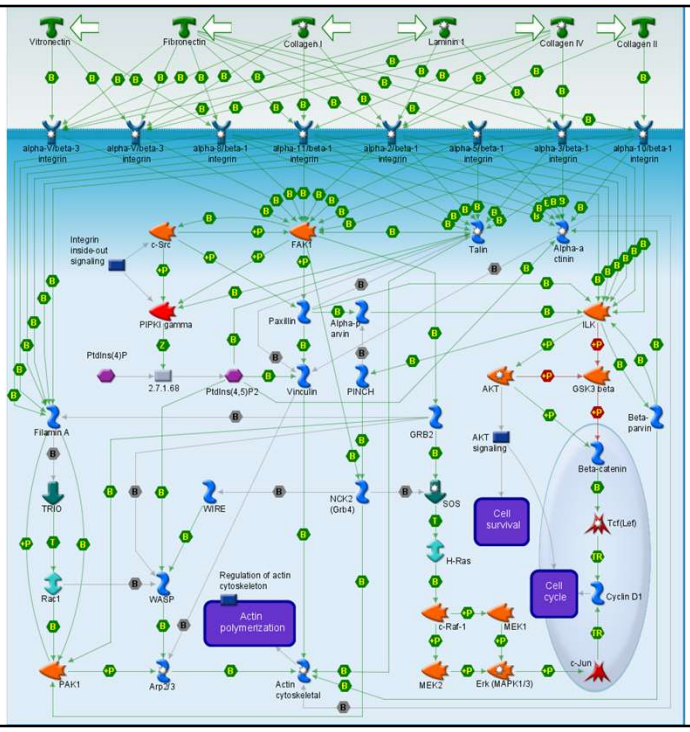
In order to talk about some of the ligands for cell-matrix adhesion we need to talk about the extracellular matrix.

We've mentioned the ECM several times in the course already. We know the the this matrix is a **scaffold** that defines the **structure** of tissues, we know that it is **secreted** and **modified** by cells, and that interacts with **adhesion receptors influencing adhesion, migration and other cellular functions** (**like growth and phenotype**).

Your text does a great job of concisely discussing the major components of ECM. You should already be familiar with these components listed on the slide from your prior biology courses. I'll leave you to the text to read about more specifics on these molecules

Cell Adhesions Signaling Role

Don’t forget that cell adhesions signal too!



As we finish covering cell adhesion, I want to touch on one last function of cell adhesions - they don’t just function in mechanical ways – that is holding cells together, holding cells to a matrix, creating a barrier or allowing for cell spreading.

They are involved in **a host of cell signaling events**. This diagram of ECM molecules binding to a integrin receptors outside of the cell (at top of image). Downstream these bindings elicite interactions with over 20 intracellular proteins and causing changes to protein assembly like actin polymerization here as well as behavioral changes like survival and proliferation (purple boxes).

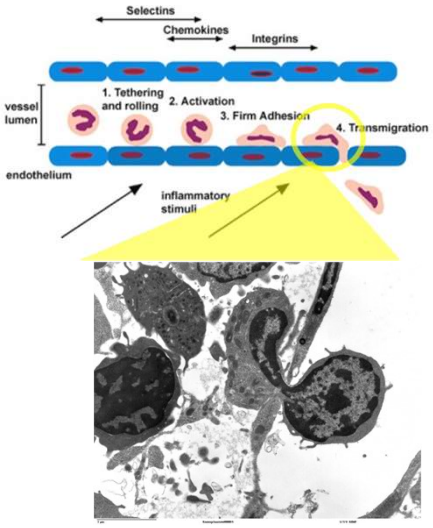
Rewind and review

Types of adhesions

- Tight Junctions
- Anchoring Junctions
- Communicating Junctions

Four Major Families of adhesion receptors

1. Integrin
2. Cadherin
3. Ig-like CAM
4. Selectin



Lets take a second to review what we've covered in this lecture.

We covered the **types of adhesions** and the four families of **adhesion receptors** present in the body.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