Introduction to Complex Biological Systems
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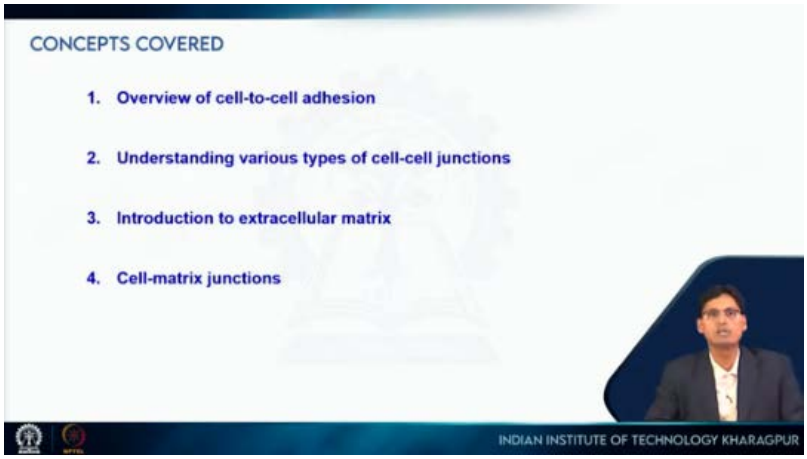
Lecture 29
Cell Junctions and extracellular matrix

Welcome to the online NPTEL course on Introduction to Complex Biological Systems. In this lecture, I am going to discuss cell junctions and the extracellular matrix. So, mostly I will be covering these major points. The overview of cell-cell adhesion and understanding various types of cell-cell junctions, followed by an introduction to the extracellular matrix, and finally, the cell-matrix junction.

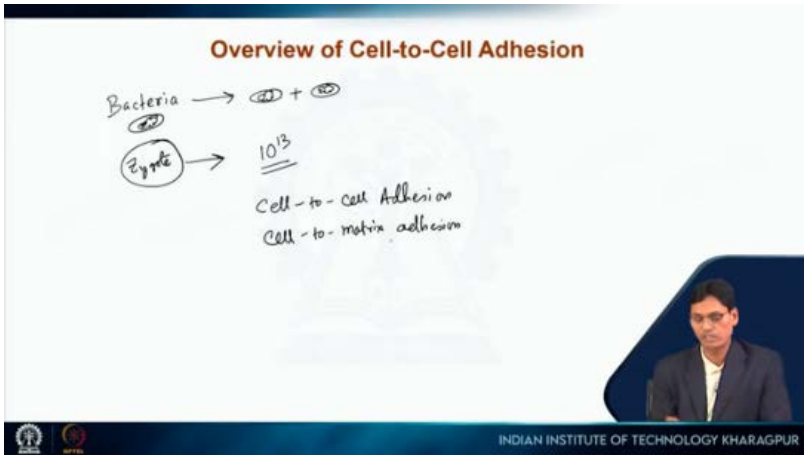


So, let me briefly discuss the overview of cell-to-cell adhesion. Cell-to-cell adhesion is a prerequisite for multicellular organisms like humans and plants. Now, if you see unicellular organisms like some bacteria or even some unicellular eukaryotes like amoeba, in those systems, whenever the chromosomes or the genome are getting replicated, and if nutrients and all other factors inside the cell are fine, then the cell will divide and give rise to two cells. If we consider bacteria, whenever the chromosome duplicates, it will give rise to two bacteria after division, and this is the same for unicellular organisms in eukaryotes also. But for eukaryotic systems where organisms are multicellular, for example, humans, it is much more complex. All of us started from a single cell, say we are starting from a zygote.

So, now when it divides and finally, I mention that in an adult human being, approximately we have 10^{13} cells, but almost all of those cells are somehow attached to each other in some ways. So, that is why cell-to-cell adhesion is very important for multicellular organisms. Not only for multicellular organisms, I would say even for some prokaryotes, for some bacteria, it is sometimes very important. When some bacteria infect us, they colonize in the human body; they also need to attach to the host cell surface. So, they get attached to some molecule present on the host surface, so this is also cell-to-cell adhesion, but this is some kind of pathogen and host interaction. Pathogens are getting attached to the host cell.

But in this lecture mostly I will be discussing cell-to-cell adhesion in the context of our own body, mostly in the mammalian system, specifically the human system, and how cells adhere together. That is the major focus of today's class. So here I mention only that there are approximately 10^{13} cells. If you consider some cells, for example, some immune cells, they are traveling through our blood and other fluids. So they are not constantly adhered to a particular site, but they also dynamically adhere as and when required. So you can understand that cell-to-cell adhesion is also a very dynamic process.

Here we are going to discuss mostly cell-to-cell adhesion and cell-to-matrix adhesion. Adhesion in the context of mostly animal cells, specifically mammalian cells, and most specifically, let us see the adhesive properties of epithelial and connective tissues. So, epithelial cells, for example, during our last discussion in the previous lecture. During that time, for example we discussed intestinal epithelial cells. So, if you see any epithelial cell.

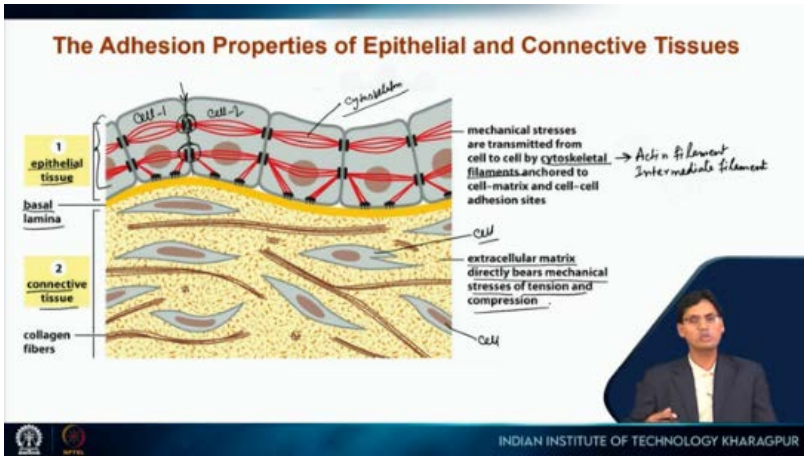


So here these are epithelial cells, as you can see; this is the epithelial cell layer and now, those epithelial cells are attached to each other. So, you can see here; this is the attachment site. If this is cell 1 and this is cell 2, you can see they are attached here, and some cell-to-cell junctions are present here also.

In addition to that, these red fiber-like things are nothing but the cytoskeleton. So, you can see here that the mechanical stresses are transmitted from cell to cell by cytoskeletal filaments. So, cytoskeletal filaments here can be actin filaments or intermediate filaments, which you have already learned in different lectures on cell biology. As you can see, in our body, different types of tension, stress, pulling forces, and other forces are sometimes generated because of our movement and many other reasons. But during that time, this mechanical stress can be tolerated.

So, what I am trying to say is that in the case of epithelial tissue, these cytoskeletal filaments, which are present and anchored to the cell matrix and cell-to-cell adhesion sites, are the major load-bearing components. On the contrary, if you see in the case of connective tissue just beneath the epithelial cell layer, as you can see, this is the basal lamina on which our epithelial cells are attached, and just below it, we have some connective tissues. So, in connective tissues, you can see that the cells are arranged in a slightly different way. These cells are not very compact and are not very much attached to each other, as you can see here. So, this is one cell, and here is another cell.

Those cells are actually surrounded by some extracellular matrix, which I will discuss in more detail. So, now, in this case, in the case of connective tissue, the extracellular matrix directly bears the mechanical stresses of tension and compression. So, this is the major difference between epithelial tissue and connective tissue. So, examples of connective tissue would include tendons, bones, and other similar structures. As you already know, examples of epithelial tissue include the intestinal epithelium, our skin layer, and many other parts of our body. Now, a little more detail about cell-to-cell and cell-to-matrix junctions.



So, first of all, I should explain a little bit about what a matrix is because when I was showing that epithelial layer of cells, those cells are just attached one by one. But below that layer, we have some kind of matrix, and that matrix is nothing but mostly different types of proteins and carbohydrates. These are secreted by cells, particularly cells present in connective tissues, and they form some kind of jelly-like or gel-like structure. Sometimes, fibrillar proteins are also there. All together, they form the extracellular matrix or cell matrix. Now, if you see here, I would say this is cell number 1, cell number 2, and cell number 3, as you can see. These are again some epithelial cells, and they are present consecutively. Now, if you see those cells, for example, cell 1 and cell 2. So, this site is the apical site, and the basal site is getting attached to the basal lamina.

So, this is our basal lamina, and this is the apical site, and this is the basal site. Now, from the top, if we see from the apical side, at the very beginning, we have this kind of junction which seals those cells together. So, for example, if I consider these to be intestinal epithelial cells, then this part should be the lumen of the intestine. So, we have some fluids, some nutrients, and so many things. So, then if those cells are not sealed through tight junctions, then some material can enter through the space between two cells. So, that is why tight junctions basically seal this gap. So, this is the tight junction, followed by two different types of junctions, those are the adherens junction and the desmosome. So, together, the adherens junction and desmosome are referred to as cell-to-cell anchoring junctions. They somehow anchor two cells together. So, if you see the adherens junction, some proteins are involved there. I will discuss this in more detail soon.

So, those proteins from those two cells from the adjacent cells actually interact through their extracellular domain and through their intracellular domain, they interact with the cytoskeleton. So, as you can see in the case of adherens junctions, whatever proteins are involved there, they interact through actin filaments. Similarly, in the case of desmosomes, if you see whatever proteins are involved there, they interact through their cytoplasmic tail to intermediate filaments. So, those two cells are now physically attached to each other through this procedure

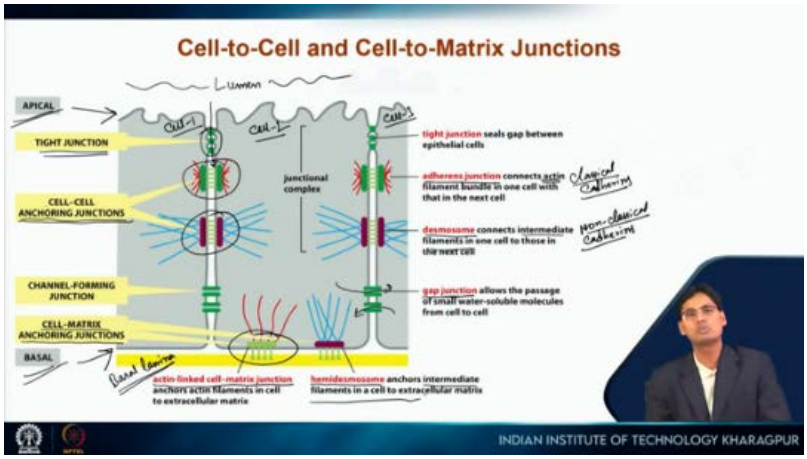
and particularly, as I already mentioned, these adherens junctions and desmosomes, these types of junctions together we call anchor junctions or anchoring junctions. In the case of adherens junctions, the major proteins involved there are classical cadherins. So, cadherins are a very big group of cell adhesion molecules that we have in our body, almost more than 100 different types of cadherins, and they are majorly categorized into classical cadherins and non-classical cadherins. In the case of desmosomes, cadherins are non-classical cadherins. They are involved in these desmosomes. Now, we have another type of cell-to-cell junction that is called a gap junction, as you can see this is a gap junction.

So, here they are basically channel-forming junctions. So, the previous two, adherens junctions and desmosomes, their main property is to keep those two cells together physically, and through those proteins, they are finally attached to the cytoskeletal material, as I already mentioned. But in the case of channel-forming junctions, the example is a gap junction. From the name, you can understand that some gap is there. So, those two cells are directly communicating with each other. They can send some small, water-soluble molecules from cell number 2 to cell number 1, for example, similarly from cell number 3 to cell number 2. They can directly transfer some of the small molecules, not very big things, not very high molecular weight proteins or nucleic acids because of the pore size. I will discuss this in more detail later, but this is a gap junction.

Apart from this cell-to-cell junction, there are four types of cell-to-cell junctions. I already mentioned that they are the tight junction, adherens junction, desmosome, and gap junction and we also have some cell-matrix junctions. So, as I already mentioned, the epithelial layer should be attached to some substratum, some kind of layer called basal lamina. So, as you can see in this case, for example, this cell-matrix junction is an actin-linked cell-

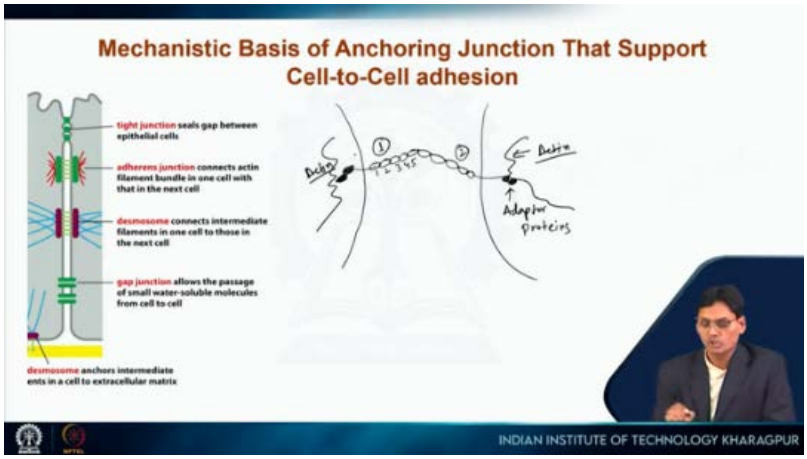
matrix junction. So, some proteins are again linked to the actin cytoskeleton present inside the cell.

So, some proteins present in the extracellular matrix are interacting with some other proteins present on the cell surface, and finally, they are getting attached to the actin cytoskeleton. Similarly, in the case of hemidesmosomes, this is again, intermediate filaments are involved in this case. So, that way, I hope that you understand that cell adhesion means cell-to-cell adhesion and, at the same time, cell-to-matrix adhesion. Now, very briefly, I will discuss the mechanistic basis of anchoring junctions, that means, particularly I will focus on adherens junctions that support cell-to-cell adhesion. So, all these four types of cell junctions I already explained.



So, if you see something like this, I would say this is one cell and this is another cell. So, now, what happens with cadherins? So, cadherins, particularly classical cadherins look like this. They have five extracellular domains, as you can see here those are one, two, three, four, five. So, five extracellular domains are present in cadherins. So this is classical cadherin, and another cadherin here, for example, if I say this is cadherin-like something, cadherin one, cadherin two, some cadherin molecules coming from the next cell, but cadherin should be the same kind of cadherin molecule involved in this interaction. So, here is the classical cadherin. When they are interacting through their extracellular domain, at the cytoplasmic site, through some adapter proteins, for example, these adapter proteins will be finally attached to the actin cytoskeleton through adapter proteins. So the adapter proteins will be finally attached to the actin cytoskeleton through adapter protein.

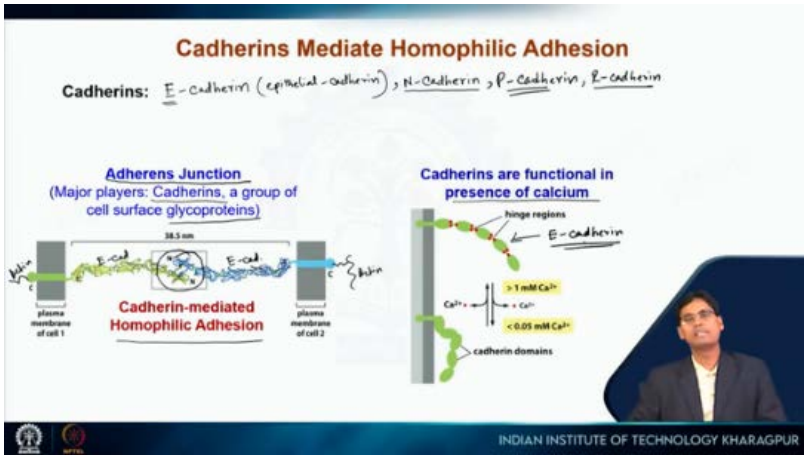
So, now, I hope that you understand how this interaction through cadherin to the extracellular domains finally helps to adhere these two cells together. But only on the cell junction side, not just one cadherin from this cell and one cadherin from the adjacent cell interact. Many cadherin molecules together assemble and form a very large complex, and thereby they can support cell-to-cell adhesion. Here, cadherins mediate homophilic adhesion. Homophilic means, here I would say, the same cadherin interacts with, as I told you, we have more than 100 different types of cadherin. For example, I would say, like major cadherin, classical cadherin, for example, E-cadherin. This is very common. So, here E-cadherin means this is epithelial. E stands for epithelial because it was first discovered in epithelial tissue, and it is also predominantly present in epithelial tissue.



Similarly, we have N-cadherin, which is mostly found in neuronal tissue, mostly on nerve cells. It is also present in some other tissues, for example, in heart muscle. But it was initially discovered in neurons, neuronal cells, that is why its name is N-cadherin. Similarly, we have P-cadherin, which is present in the placenta, and R-cadherin, which is predominantly present in our retina. So, these cadherins interact in a homophilic fashion, that means E-cadherin interacts with E-cadherin, similarly N-cadherin interacts with N-cadherin, and that way they support cell-to-cell adhesion. Here, you can see that this is an adherens junction, as I already explained. These two cadherins, although you can see here in different colors for clarity, I would say this is E-cadherin and this is also E-cadherin. The same molecule, E-cadherin, but they are coming from two adjacent cells, and they interact through their N-terminal extracellular domain, and on the C-terminus, they should be attached to some actin cytoskeleton, the actin bundle.

Similarly, here also, they will be attached to the actin cytoskeleton. So, that way cadherins mediate this homophilic adhesion and I already mentioned that cadherins are the major group of cell surface proteins, and particularly, they are glycoproteins, meaning some carbohydrates are also attached to this protein. That is why they are called glycoproteins. So, during translation, we get the polymer of amino acids. But after some post-translational modifications, some carbohydrate groups are also attached to this protein for their special function and also for their stability. Another important aspect about cadherin is that their function is dependent on calcium. So, calcium is very important for their function. As you can see, this is what cadherin looks like. I would say this is again, if I say this is E-cadherin, so E-cadherin, N-cadherin, they look very similar like this.

They have five extracellular domains: one, two, three, four, and five. In between those domains, they have calcium. These red dots you can see are the calcium ions, and they are very important. If you deplete calcium or take it out, the cadherin structure will collapse, and they cannot mediate cell-to-cell adhesion. Even the name 'cadherin' comes from calcium. The first two letters here are because they depend on calcium. During the discovery, when scientists understood that they only work in the presence of calcium, they named it 'cadherin'. Now, some interesting experiments I am going to discuss are about cadherin and how it helps in the development of tissues. Cadherin-dependent cell-to-cell adhesion guides the organization of developing tissue. In this figure, whatever you can see now is the sorting of cells.

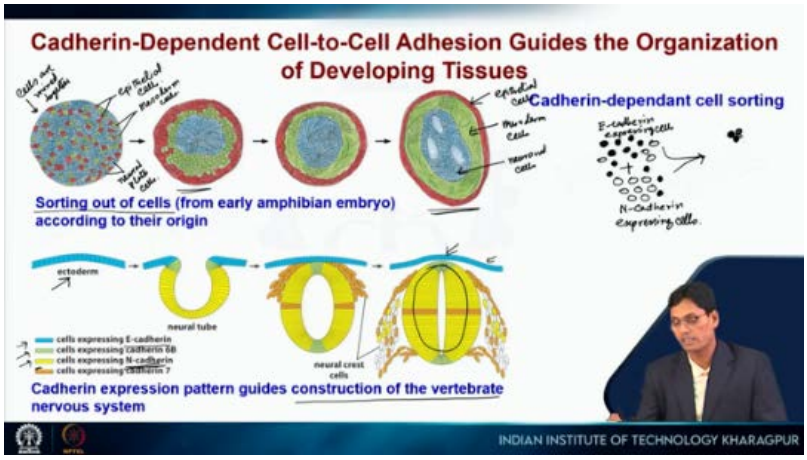


So, what scientists did was take cells from an early amphibian embryo. An amphibian embryo means, I would say, a frog embryo or a salamander embryo. They took those cells and somehow mixed them together. After taking those cells, they just mixed them together. As you can see here, this is the initial point of the experiment where cells are mixed together. Here, as you can see, these red cells are epithelial cells, and these green cells, as you can see here, are mesoderm cells. These blue cells you can see here, for example, this one and many others, are neural plate cells. That means they are part of the developing neuronal tube. You can consider them that way. Neural plate cells are mixed together, and now, when those cells are there and given some time, you can see the organization is slowly changing. As you can see, those cells are getting sorted out by themselves. Here, you can see this is almost reminiscent of the embryo structure. Why? Because, as you can see after all these steps, all those epithelial cells are now on the periphery.

Similarly, the mesoderm cells are present just beneath the epithelial cell layer, and the neuronal tube cells, the neural plate cells, are inside. These are neuronal cells. So, as a result, which is true during the development of a frog embryo itself, how does it happen? A lot of research has found that this is because of cadherin itself. Cadherin helps in the sorting out of those cells and organizes the developing tissue in this way. So, if I explain this figure, you will understand even more clearly. As you can see, this is the ectoderm layer, and then you can see during the neural tube formation. Here, we are trying to explain the cadherin expression pattern and how it guides the construction of the vertebrate nervous system. So, as you can see here, the neuronal tube formation is taking place. During that time, the similar type of cadherin stays together, and finally, the ectoderm layer gets separated. You can see the neuronal tube is already formed here and here, this is kind of in color code. We are mentioning different types of cadherin majorly present in this cell. As you can see, the ectoderm cells have a very high level of E-cadherin, and you can see that E-cadherin is present in these ectoderm cells. This is getting separated from the neural tube, and in the neural tube, mostly you have N-cadherin, as I already mentioned. N-cadherin is majorly present in neuronal tissue. As you can see, this is yellow color code here, so this is almost everywhere, the neuronal tissue. This is the brief idea of how cadherin helps in tissue organization, and the basic idea is where this is coming from. This is a very simple experiment someone can perform, something like this. That cadherin-dependent cell

sorting, if I say, those cells which I am drawing now, these black color cells, those are E-cadherin expressing. E-cadherin expressing cells, and now these cells which I am not filling in. So, these are N-cadherin expressing cells.

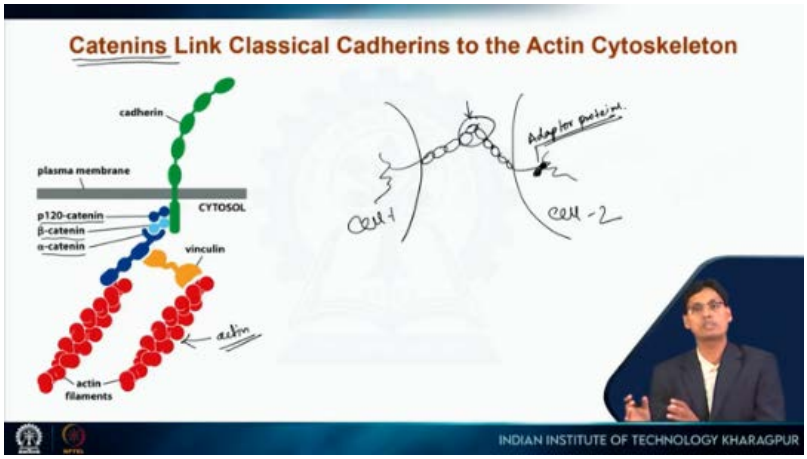
Now, if you mix together these two cells, then you will be saying that you mix them together. So you can say something like this in this scenario that everything is mixed together, the N-cadherin expressing cells and E-cadherin expressing cells, but they will be sorted out soon. Those E-cadherin expressing cells will form a cluster. They are expressing E-cadherin, and N-cadherin expressing cells will also be sorted out. This is the basic logic of those things whatever I have just explained in these two different types of scenarios.



Now, what is happening inside the cytoplasmic site when cadherins interact? So, as you can see here, another group of proteins as I previously mentioned some adapter proteins, because sometimes it is very difficult to remember so many names here. That is why I just mentioned adapter proteins, but those are the catenins. Catenins link classical cadherins to the actin cytoskeleton. So, this is cell 1 and cell 2, and now if you say this is one catenin, this is another catenin. Now, they actually interact with this actin cytoskeleton here, as you can see that this is actin and through the cadherin, they directly cannot bind to the actin cytoskeleton, they need some adapter proteins, and those adapter proteins here, so these are adapter proteins.

For example, different types of catenin like p120 catenin, beta catenin, alpha catenin. Nothing will happen if you forget those names, but the overall idea that is why I am drawing here is that when catenins are interacting through their extracellular domain. At the same

time, through their cytoplasmic domain, through some adapter protein, they are physically attached to the actin cytoskeleton, thereby two cells are interacting together. So the catenin-catenin interaction is here, catenin-catenin interaction is generally a very weak interaction, but it is a dynamic interaction. So, that is why to support this weak interaction and to make it physiologically relevant. So, that cells can be attached together, cells can adhere together, many catenin molecules assemble together, and thereby they perform physiological function. That is all.



Now, like whatever I mentioned, that is mostly about anchoring junctions. I specifically explained more about adherens junctions, but this is almost the same thing for desmosomes also, which is also one type of anchoring junction. But now I am going to discuss the tight junction. So, it is also very important. Not just keeping cells together, they are attaching two cells together at some places, but particularly on the apical side of the cell. In addition to that, they also play an important role in the cellular task force, which is very important. Again, this example you can consider in the context of intestinal. Epithelium, so I am taking the intestinal epithelial layer as a model organ, a model tissue system to explain this thing. So, it will be easy for you also. If I say a kind of similar thing and different types of explanation, different types of scientific observation, I am going to discuss intestinal epithelial cells.

So you can see this is the lumen of the gut. So, now you can see through the apical side here, you have some molecules here, nutrients, water, all those things are present inside the intestine, but they can easily pass here. In between two cells, we have some space. In

between two cells, but this material present in the lumen should not enter in between cells. So, that is why I would say the tight junction is present. The tight junction somehow seals this portion. You can see here they are sealing this portion, sealing this portion, so nothing can enter directly in between two cells. So, that way they are helping, and now I just mentioned that tight junctions play a role in cellular transport. So, as you can see, through intestinal epithelial cells, we absorb most things, almost everything, through the intestine from the intestine.

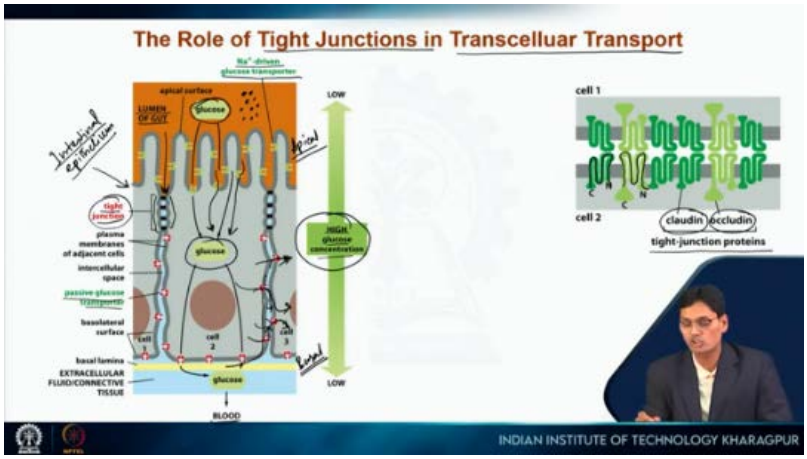
So, here particularly we are talking about glucose transport, as you can see that glucose is also present in the lumen of the gut, and now we have some sodium-driven glucose transporters on the apical side. So, this is our apical side, and this is our basal side. So, you can see some sodium-driven glucose transporters. So, as a result of that, glucose will enter here.

So, as you can see, glucose there, and glucose concentration will be high. Now those are the absorptive cells and they are absorbing glucose; they are taking glucose from the intestine. Now, this glucose should go into the other part of our body. You can see here the glucose concentration is maximum in this epithelial cell and high glucose concentration here and now, this high glucose concentration will slowly diffuse towards the other side, but here you have sodium-driven glucose transporters. So as a result of that, this glucose will not again get out into the lumen of the gut because that is not possible. But it will diffuse to the lower side, I would say, throughout the basal side, and finally, it will go into the bloodstream, and it will be carried over. Similarly, some passive glucose transporters are also present in this cell membrane that is the basolateral cell membrane.

So, this is basolateral. The basal and the lateral so that is why basolateral cell membrane. So, as a result of that, some glucose molecules will come here in this passive glucose transporter, and through there, it can also enter; it is possible to enter here. So, now directly from the gut lumen to these cells, and from these cells, it is passing, and then it is going to the blood. So, that way, it is crossing this cell; this is what we say transcellular transport, and in the same layer, when this way it is moving, this is paracellular transport.

Transcellular and acellular transport is just some kind of information that is not that important to understand cell adhesion itself. Now, what is the mechanism in the case of tight junction formation? So, as you can see, instead of cadherins, here you have different types of proteins. These are called tight junction proteins, particularly these two proteins are very important, the claudin and the occludin. One very fundamental difference between cadherins and these proteins is that cadherins cross the membrane just one time; they are single-pass proteins but here, you can see that they pass through the membrane four times. So, they pass through the cell membrane four times. So, they have multiple membrane-spanning domains or spanning regions.

So, this is our cell membrane, and similarly, this is another cell membrane. This is cell 2, and this is cell 1, and this is how tight junctions are formed. Now, the next thing is gap junctions. Gap junctions couple cells both electrically and metabolically. Why? Because gap junctions mean that these two cells are directly connected to each other by some kind of channel, as you can see. This is a direct channel. So, something can go from this cell to the other cell. Particularly, I mention here electrically and metabolically because here, a lot of ions, for example, Na^+, Cl^-, and so many ions, can move, and that is why we are mentioning electrically and metabolically, small water-soluble nutrients, for example, some glucose molecules, small amino acids, nucleotides, they can pass through this channel or through this gap junction. So, these are the ions, and then, as I already mentioned, amino acids, sugars, they can pass quickly without any problem.



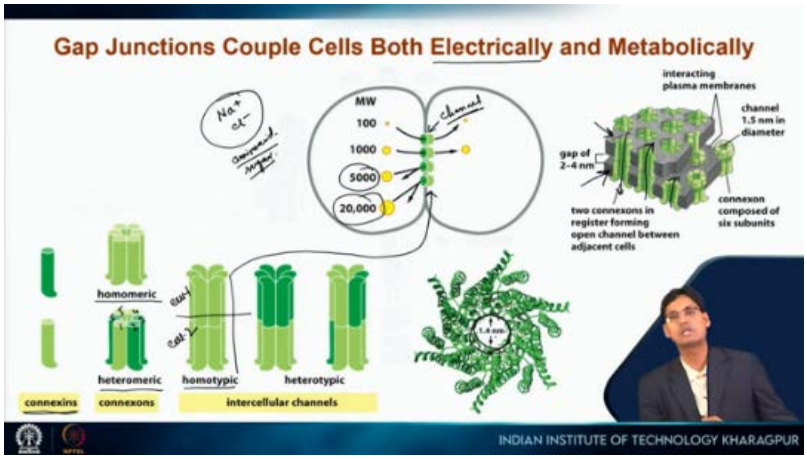
But if something is very big, I would say above 5000 Daltons, 20000 Daltons, they are much bigger than this pore size, they cannot cross. So, as a result of that, a big protein, for example, a protein or nucleic acid, cannot move through this pore. Only small nutrients and ions can move and, as you can see here, this is just in a different dimension. This figure shows one plasma membrane and another plasma membrane, and this is the channel here. As you can see, things can move in this direction. So, those are the channels, and these are the channel-forming proteins. The proteins which form these channels are called connexins, particularly in the case of vertebrates, in the case of the mammalian system.

So, these connexins form some kind of hexamer. As you can see here, connexins 1, 2, 3, 4, 5, 6 are together forming some kind of hexamer. So, it can be homomeric, which means the same kind of connexins are involved, or heteromeric, which means different types of connexins are involved together and those two connexins are forming this channel. This is the channel, which means, for example, this one, if you just rotate it 90 degrees, you will get this. So, this is from one cell, and this is from another cell. So, cell 1 and this is cell 2, that way.

They form this kind of channel or some kind of port. So, that things can go in and out between these two cells, and this is the extra crystallographic structure of this channel. As you can see, this is the pore dimension, and you can see here is 1.4 nanometers, the diameter here. So, as a result of that, there is a restricted movement of bigger stuff between those two cells. Now, I am going to discuss a little bit different thing here. Whatever cell-cell junction I mentioned, like I would say tight junction, then adherence junction, desmosomes, and gap junction, those are kind of more stable cell-cell junctions. But some other cell additions also happen, which are more dynamic in nature, for example. Selectins, this is another group of cell adhesion molecules. They mediate transient cell-to-cell adhesion in the bloodstream. Those cell adhesions are very transient in nature.

In this case, cadherin interacts with another cadherin, they interact with another protein. But in the case of selectins you can see that they are the cell surface carbohydrate-binding proteins. So, selectins specifically interact with carbohydrates, so that is their kind of specific feature. So, for example, there are different types of selectins also present. For example, L-selectin is present in white blood cells. Similarly, P-selectin is present in

platelets, E-selectin on endothelial cells and something like that. Now, the overall idea I would like to present is not just the name of E-selectin and P-selectin so the idea here is that the adhesion should be transient.

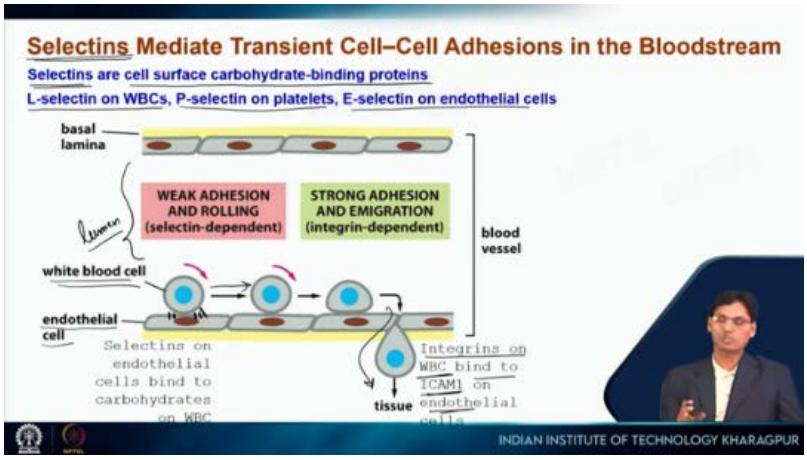


Why so? For example, you know that our immune cells, particularly if we say WBC (white blood cells), perform some kind of bohemian life. So, they are not restricted to a particular region. So, they are traveling throughout our body whenever some requirement happens, some infection, some particular site, they can go there also. So, as a result of that, they are more dynamic in nature, and they rely on selecting this kind of cell adhesion molecule. So, as you can see, this is the lumen of this blood vessel, and this is not an epithelial cell anymore. This is an endothelial cell, which is covering, I would say, the blood vessel from the inner side. This is the endothelial cell. Now, these white blood cells, they have selectins.

So these selectins are present on endothelial cells and white blood cells have some specific type of carbohydrate. They are present on WBC, and that carbohydrate and these selectins interact together. But this is not very tight adhesion; this is very weak adhesion. Still, those attached white blood cells on the endothelial surface can roll; they can go in some kind of rolling motion. And at some point in time, when integrins present on white blood cells bind to another group of cell adhesion molecules, which are a little bit different, different family members, I am not going into their details, names, and all those things. That will help that particular white blood cell to come out, or I would say to come into the tissue, as I already mentioned that white blood cells also escape this bloodstream and go to the tissue for their

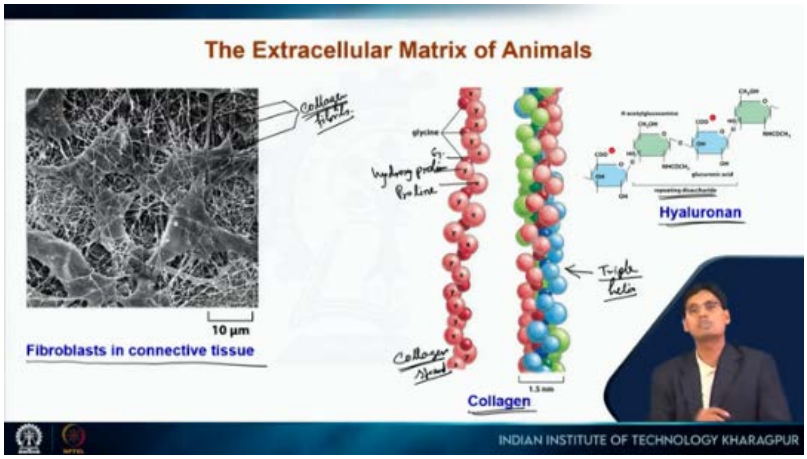
own function, for their immune function. So, as a result of that, during that, this in and out, during this, for their function, they rely on different types of dynamic adhesion.

So, that is all about, I would say, selectins and their transient cell-to-cell adjacent properties. This is just one example; there are many other examples. Now, at the beginning, I mentioned that I will talk a little bit about the extracellular matrix also. So, this is particularly the extracellular matrix of animal cells as you can see, this is fibroblasts in connective tissues. So, these like fibril-like structures, as you can see, like thread-like structures, these are actually collagen fibrils.



So, collagen is actually a protein, a kind of protein fiber, and it also gives us a lot of support, particularly in our connective tissues. It is present in the extracellular matrix. These are actually generated by the cell itself. The cell secretes this protein, and this is collagen fiber. Apart from collagen fiber, we have some carbohydrates also, for example, hyaluron. So, hyaluronic acid and then proteoglycans, all those things together form this extracellular matrix. So, as you can see here, this is hyaluron. So, this is a kind of carbohydrate, as you can see the repeating disaccharide units, and this is also present in a large amount in this extracellular matrix and also, another very important thing is collagen fiber, which I already mentioned. In the case of the mammalian system, in our body, I would say collagen is a protein fiber, but collagen is almost, I would say, 20 to 25 percent of the total protein present in our body. Specifically, collagen has a typical structure; it is a triple helix. So, three collagen strands are forming a helix, as you can see here, the triple helix of collagen.

The helix of collagen, three collagen strands, are forming a helix, and collagen has some other properties also. This is the collagen strand you can see here. This is a collagen strand; sometimes it is called the alpha chain of collagen, but here you can see some kind of repetition here, that is X, Y, and glycine. So, X is actually proline, and Y is hydroxyproline and then this is glycine. So, then it is repeating in this way, and that is kind of major, I would say, giving us a lot of mechanical strength and support in our tissues. So, this is about our extracellular matrix, and I believe this is the last slide. Now, the last thing is the integrin.

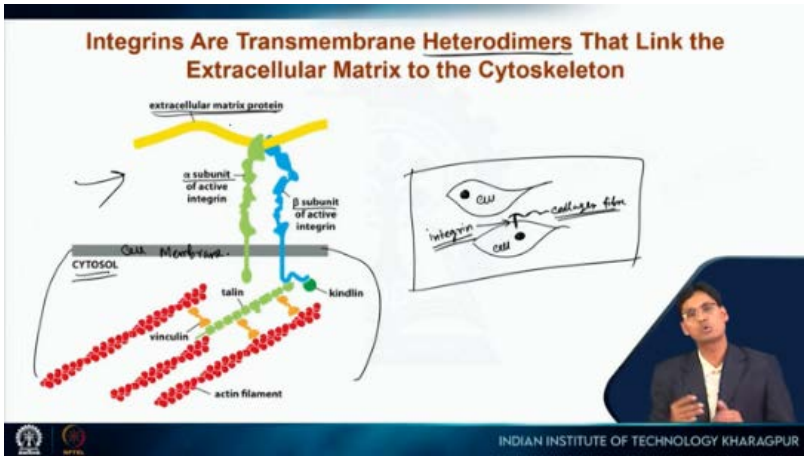


Integrins are transmembrane proteins that link the extracellular matrix to the cytoskeleton. At the very beginning, I mentioned, in the context of epithelial cells, if you consider those cells are attached together by different types of anchoring junctions, but those cells should also be attached to the basal lamina; otherwise, that layer will peel off from the surface of the connective tissue. So, they should be attached to the basal lamina. So everything should be together. So, that is why some kind of cell-to-matrix junction should also be there. So, here you can see, for example, if I mention here, this is in the case of connective tissue, not even epithelial cells. So, this is connective tissue, and this is one cell.

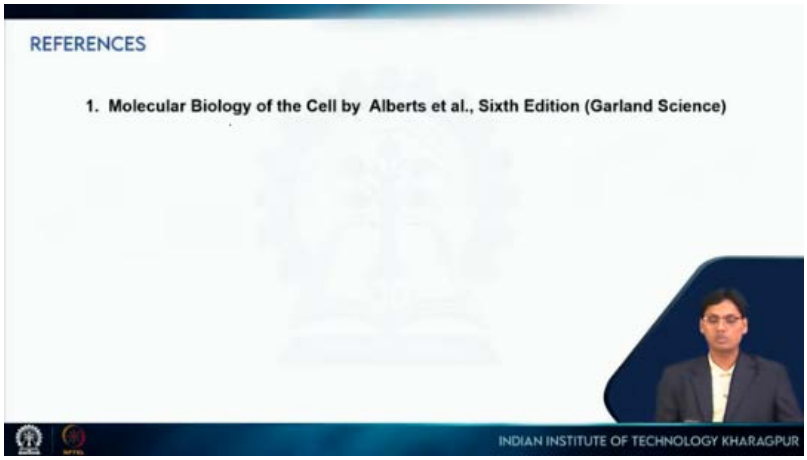
So, this is the nucleus of another cell, and this is the nucleus. So, in connective tissue, those two cells might not be together, but they are somehow attached to the extracellular matrix. So, in the extracellular matrix, you have, for example, collagen fibers are present, and also we have some other components like proteoglycans and hyaluronic acid. But here, what I am trying to say is that on this cell surface, you have some protein which is called integrin,

and this integrin is attached to the protein present in the extracellular matrix. So, that way, this cell is attached or this cell is staying together with the extracellular matrix. This is very important, just like cell-to-cell adhesion, it is also very important. So, that is why I provide you this context so that you can understand this figure itself. So, you can see this is one cell, this is one cell, and this is the cytosol, and this is the cell membrane, and now you have this integrin. So like the beta subunit of integrin and the alpha subunit of integrin, I should specifically mention here that integrins form some kind of heterodimer to define integrin. They form heterodimers and then they interact; they bind to extracellular matrix proteins.

For example, some collagen fibers like this are the extracellular matrix proteins. So, as a result of that, connective tissues, for example, are attached or they are staying together with the extracellular matrix. So, this is, I would say, all about the kind of cell-to-cell and cell-to-matrix adhesion.



We have some kind of idea, and now, for more details, you can follow this textbook, Molecular Biology of the Cell by Alberts.



Thank you very much.