Introduction to Cell Biology Professor Girish Ratnaparkhi and Professor Nagaraj Balasubramanian Department of Biology Indian Institute of Science Education and Research, Pune Lecture 49 Endomembrane System of Cells: Discussion Session - 1

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Professor: Deep, you have your hand up, you have a query?

Deep: Yes, Sir, quite a few lectures ago, when we were discussing about the cell membrane, and like the membranes of different organelles, you had shown a picture that showed that the membrane was quite different from each other, like the organellar membrane were different, but here are each and every membrane is very interacting, like it is interacting a lot with each other. For example, membrane of Golgi, and membrane of the plasma membrane is very different. But like the membrane of Golgi, is only going and attaching itself as vesicles.

Professor: what is common between those membranes?

Deep: lipid bilayer is common.

Professor: It is a big commonality, see, the thing here is that obviously, each of these components, each of these endomembrane systems will have differences in the organization of their membrane. That in part, for example, when we come to the Golgi, and we look at each compartment of the Golgi, we will also see that, between compartments, there could be differences in the composition of the membrane, it is not fully known what extent of

difference there is, but there could be some lipids that are very unique to certain compartments.

And these may be vital for many reasons. One, they could influence, for example, the architecture of the membrane, they could also play an important role in allowing proteins, for example, that are part of the membrane to work and function in a certain unique way. But the critical thing in all of this is that the fact that they are lipids, is allowing for these membranes to talk to each other in a way that would have been very difficult otherwise, had they all not had this feature of being made up of lipids.

So yes, the composition could be different. And for example, when a vesicle gets delivered to the plasma membrane, once it integrates into the plasma membrane, these lipids also now move around and it will get diluted in the sea of lipids, that is at the plasma membrane. And so, this eventually, kind of regularizes, if I may call it that, to become the composition that is the plasma membrane,

So, it is one of the ways to think about distinguishing these compartments is also these small subtle differences that exists. So, there are a lot of lipids that will be common, that will be present in most lipid membranes, but there will be some lipids which will be unique to certain compartments.

Professor: Vardha your query?

Student: Varad

Professor: Varad, sorry, yeah

Varad: So, in the video that I have seen so many times of the cell, it was shown that the mitochondria keep moving between the cytoskeleton and cytoskeletal components determine what shape the mitochondria will take and it is vary. So, if the Golgi apparatus also have a varying shape, or at least.

Professor: Yes actually, they do and I will show you some images in the coming lecture particularly, we study the Golgi in my lab in the context of cells, when they are adherent versus when the cells are detached. And there is a very dramatic reorganization of the Golgi. And the really interesting thing is that reorganization of the Golgi happens almost entirely dependent on the microtubule network so, the Golgi opens up. And the really interesting thing is when it opens up, all the pieces of the Golgi are actually moved apart along the microtubule tracks.

So, when we take a suspended cell and then we play it back, and the cell attaches. This all these Golgi pieces that have floated away all come back into a compact structure. And that coming back happens along the microtubule tracks. So, if we break up the Golgi by detaching a cell, and all the components disperse, and then we break the microtubules and then, ask the Golgi to come back again by replacing the cell.

You know what happens? Nothing comes back. So, you are right in thinking about this way that these components are all tied to the Golgi. Many of the motor proteins that we talked about are actually vital in keeping the Golgi components, right next to each other as well. And I am not going to get getting into the detail of how this is regulated. But motor proteins and cytoskeleton elements are very vital for the architecture and functionality of many of these endomembrane components.

Professor: Ajinkya, please go ahead. Ajinkya

Student Ajinkya: Yes, Sir, am I audible?

Professor: Yes, excellent.

Student Ajinkya: So, my question is that when the transport vesicle reaches a plasma membrane, how does it open up?

Professor: So, there is a very elaborate mechanism that is in place. See, because it is not that trivial to fuse one lipid membrane to another lipid membrane. And it is because you raised it, I am discussing this right now, but there are a set of proteins, which are actually part of the plasma membrane and part of the vesicle as well, that allow for one docking, because there has to be binding versus there are 2 events here.

The vesicle could keep floating around and keep bumping on the membrane and meets a place to kind of go stick to and that sticking to the plasma membrane is can be mediated by proteins that ensure that a vesicle gets delivered to a very specific site at the plasma membrane. And once that binding happens and there is a class of proteins, called the exocyst complex, which is, group of proteins that are present on the vesicle, some are present on the plasma membrane, and they bind and allow for this kind of docking to take place.

And then, there are proteins that essentially try and pinch the 2 membranes in such a way that the distance between the 2 membranes is actually reduced as much as possible. So, they pinch them in such a way that now they fuse, and now, you have the vesicle opens up and you have this entire membrane that in the membrane of the vesicle gets integrated into the membrane of the plasma membrane.

And, this is also the case when, when membranes have to be pinched off. So, if you have to make a vesicle and kind of pull it off from the membrane as well you need to be able to bring the 2 membranes of that vesicle really close to each other. And after a certain proximity the lipids now, the inherent energy of the lipids will allow them to fuse together in such a way that now you have a vesicle and the lipids that are on the plasma membrane have fused to kind of create a clean seal for the plasma membrane and the vesicle is here.

And that is only possible by bringing them together. So, the cytoskeleton obviously plays a role, but there are proteins that by themselves can create ring like structures that will squeeze the membrane sufficiently such that the 2 bilayers are close enough to allow for this to happen. So, it is a very interesting regulatory system. And there are many proteins actually involved that allow for that to happen. It is a good question.

Student Ajinka: Okay, Sir thank you Sir.

Professor: There are a couple of questions on the chat box that I am going to try and take. Just give me a minute. Let me see if there is anything everything is about bidirectionality. Somebody has asked a question.

Anand has a question saying, can motor proteins work on the lower part, or sides of the microtubules? We saw in animation that they walk on the top side here. So absolutely, they can. So, remember, that you cannot think of this space as being regulated like we would walk on a beam. I think for us gravity plays a very important role in making sure we were pulled down.

But remember, this is in a cytosol which is a fairly viscous environment. And that is also the reason why such a big vesicle can be carried by like this tiny motor protein because this vesicle is not heavy it is floating around. And this thing just has to drag it around. I think 0 gravity we see this all the time that because of the lack of gravity very heavy big objects can be moved by one person around. And it is only possible because they inherently do not have any weight in 0 gravity and so now, moving these around become easy.

So, the motor proteins will be able to walk, if you have a microtubule strand like this. They will be able to walk on all sides of the microtubule. And so, it is possible that there are motor proteins walking this way, this way, this way, all possibilities can exist. Do we Hirak as a query? Do we need less bidirectional motor proteins than unidirectional and not sure I understand the question by what do you mean by less, you need less of by

Student: Less number of.

Professor: Less number of. So, that is true that what you are in you have to make 2 kinds of motor proteins rather than imagining a situation where you have only 5 of 1 and they can go in both directions. Now you need 5 that go in one direction 5 in the other. So to speak.

So, somebody else raised it to that. You need to make more proteins to be able to do this. And there is definitely a cost factor involved there. if you have to make 10 proteins instead of 5. But what you are gaining in terms of specificity, in terms of accuracy, in terms of being less error prone, in unidirectionality.

I think might allow to say that it is worth the cost of having 2 sets of motor proteins. Can the cargo tell bidirectional motor protein in which direction it wants to go? So, that is another possibility. It is possible that the cargo itself has a regulatory mechanism that can talk to the motor protein to say, now let us switch direction which will be very cool if it is able to do it.

But at this point of time, we do not know of such a mechanism. And it is also not very clear even with classical motor proteins whether just the binding of the cargo can initiate a motor protein's walk. For the most part it is thought that motor proteins as long as they have energy will have a walk and, in the process, pick up things as they go along. In some cases, they may be attached to the vesicle to begin with and then be begin to make their walk as well.