Introduction to Cell Biology
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Motor Proteins in Cell: Discussion Session

Professor: Vaishnavi has a query, Vaishnavi can you go first?

Vaishnavi: Yes, sir is it that each individual motor protein moves in a particular route and carries a particular type of vesicle? Is it very unique and specific or can a single motor protein perform different functions?

Professor: So, a single motor protein could do different functions. So, something that moved from here to this particular point, now has the capability to go bind two different strands of say actin and I mean, here it walked and carried something reached a certain point. And now here, it does a slightly different function, because that is what is required. So, there is no direct evidence right now to suggest that a motor protein that carries a vesicle and carries that just carried a vesicle of a particular kind will carry only that kind of vesicle and will not do anything else. So, there is flexibility here and they are used as per their requirements.

Vaishnavi: Sir, so how do they know what to do or where to bind?

Professor: They do not actually. So, that is the that is why for example, directionality when we talked about I think we are inherently thinking they somehow know okay, this is plus sign, this is minus sign, this is inside, that is outside. If it is a very small motor protein in the context of a big cell, the only thing it sees and knows is its immediate domain. So, it is responding and doing things in the context of that immediate domain. So, that is why the context of size for example, when you looked at the microtubule strand and a motor protein working on it, you can see what the size of the strand is likely to be and how big or small the motor protein is.

So, the motor protein is not thinking plus and I have to reach this, motor protein till I have energy, I will keep doing this. And as I keep doing this, whatever I am bound I will carry and walk in one particular direction. So, there are things that can regulate the rate at which motor proteins move. Different motor proteins could have as I said, the size of the stroke could be variable, the speed therefore, at which they move things could be variable, there are regulatory mechanisms that suggest that depending upon the availability of a motor protein, which means if this is a particular pathway, that requires things to be carried very quickly,

inherently there are more motor proteins available there that can move things faster as compared to some other part site inside the cell.

So, a lot of it is governed by the local concentrations of things, including motor proteins and the kind of cargo that exists around them. So, there is not anything to suggest that this motor protein actually goes looking for a specific kind of cargo, it is doing its thing depending upon the availability of cargo, availability of motor protein there is binding and once binding happens, they do their thing. Medha next to you.

Medha: Sir, my question is kind of related to Vaishnavi's in the sense like what helps to, so, if you have a vesicle that starting off at one end of the cell and say it needs to get to like a very specific organelle that the other, does it follow a path that is tailor made for it or like simplistically is it like different stops along the cytoskeleton path where a lot of different?

Professor: See it could be very differentt stops, it could be a very direct route. It depends on what is happening at the cell at that point of time. It depends on what kind of motor proteins are available and bound to that particular cytoskeleton component at that point of time. So, some of this is fine tuned by the availability of things and that availability of things could be controlled by stimuli that is coming from different places, but it is the ability of the cargo to bind to the motor protein is also controlled in the sense that this may bind to only certain kinds of motor proteins.

So, there may be so one for example, way to think about this is suppose there are plus end and minus end motor proteins present and you want this cargo to go towards the plus end. One way to regulate this would be to change, to make sure that there are more plus and binding proteins on the surface of the vesicle which means the number of a motor proteins that will be engaged, which are plus end directed, versus minus end directors directed will be shifted towards the plus end. And this cargo could move in that direction.

The other way to do this is regulate the availability of motor proteins itself. So, that means you can have, if there is a way to enrich or bring together plus end motor proteins in that particular area, have 10 times more plus end motor proteins than minus end motor proteins. Even if the cargo distribution on the surface is such that they can bind plus or minus. The fact that the motor protein density is variable could allow for movement to take place in one direction.

So, there could be many ways to do this. But it is not clear, if there is a very defined purpose to say that, I am this vesicle, I am going to go find this particular motor protein. And I know this motor protein is not going to talk to anything else. And will just walk with me. Suppose, for example, a vesicle is being carried. And everything is about relative affinities. Everything is about and you have seen that, across the board. So, what if this motor protein, encounters another cargo that binds with significantly more affinity.

Does this motor protein once it holds this cargo, does it kind of keep holding it without letting it go? Or that does that depend on the relative affinity? Which means that to go apart, come back, go apart, come back. And if that is happening? If there is now a cargo that binds and does not let go. Can this motor protein actually shift? Like carry something to a particular point and then kind of, go bind something else, so it is possible? So, all those permutations combinations are happening. And despite those permutations combinations, the cell is able to drive movement of something in a direction that it needs.

And that is the remarkable aspect of this. So, how does it understand all the variables to achieve the endpoint it needs? It is still a mystery. So, we do not completely understand that. Prerna, can you go next?

Prerna: Sir, you mentioned that different cells could have different flavors of myosins and dynein kinesin and so I want to ask that, is it that cell inherently carries this information that okay this variety of myosin, it has to make this number? Or is it develops over time? Or is it like it can also change over time?

Professor: Good question. It is possible that it can change over time. It is possible that, obviously, these are all regulated by genes, the expression of genes is controlled, and the expression of genes is controlled by many parameters. So, depending upon where the cell is, in the cell cycle pro. For example, the regulation of gene expression is affected, whether it is seeing an external stimuli, not seeing an external stimuli could regulate gene expression. There is so many parameters.

So, but inherently, for a cell, depending upon, how it is regulated, the expression of certain motor proteins is happening. Does it mean it cannot express a certain motor protein at all, maybe, it has something that has blocked that expression. It could also be that the expression of certain motor proteins happens at very specific times. And that also could be a regulatory factor here? So, it is fine tuned in more than one ways. But that is the remarkable thing that,

the more we understand about this, we realize that or we at least, begin to appreciate the complexity with which the cell is working.

And for all these, hundreds or thousands of pieces, to kind of all have these variable varying capabilities to be regulated by many ways. For a particular class of proteins to come together and do something very, very unique for the cell at a given particular point of time, requires a level of fine tuning that is just amazing. And, and that is what the cell is able to do. We do not completely understand everything about how that control is mediated, but we know it exists.

And as we understand more, we realize how complex that is how subtle it can be and how many different ways it can be controlled. Sanjay, next query.

Sanjay: Sir. I just wanted to ask what happens when a motor protein reaches an end?

Professor: Good question. So, see, one possibility is that the motor protein, just hands over the cargo to something because now something else is binding the cargo with much greater affinity than the motor protein. So, it is like, does the motor protein keep walking and the cargo is stuck here? And then at some point of time, the cargo just detaches. We actually fully do not know. We do not know, what exactly is the handing over mechanism like? We also do not know what happens, does the motor protein then just keep on walking? Does it pause for some time now?

See, as long as energy is available, it has the capability to keep going. So, chances are it keeps going. So, are there motor proteins that are empty with no cargo that are walking around? Probably there are. But considering the crowding that exists, does a motor protein really have that much space to walk for a significant amount of time without actually binding anything? Probably unlikely. So, some of this because we have limited by what we can see and how we can see. We are only now beginning to understand. The fact that two motor proteins can tug on the same vesicle and pull in this direction and this direction.

And the relative force with which they pull and the number of motor proteins that are attached, which will eventually determine which direction it goes. It was discovered maybe a few years ago, 4, 5 years ago. Roop's lab here in Roop Mallik's lab in IIT Bombay. Roop was in TIFR before. Roop's lab is they study lipid droplets and their ability to bind to motor proteins. And they made this discovery using those lipid droplets.

So, it is, there is…

Professor: A lot of this is still being discovered. Amruthamshu, am I saying that correct?

Amruthamshu: Yes, sir. So, after the kinesin molecule goes to the plus end with the vesicle. Was it recycled again, for further usage?

Professor: So, this is kind of the question of what happens to the dropping off at the cargo. I think, there could be many ways to do this possible. One possibility is that the motor protein is just broken up there. And then, brought back, it is possible that that motor protein now goes to a different strand and starts doing something else. We do not completely know. We do not completely know whether there is a like a defined mechanism says that only this will happen.

So, it could be very specific. And this is among the questions that people are trying to find out, saying, how do you optimize functionality if it goes in one end? Now, if it had the capability to walk back the same way and now suddenly become a motor protein that goes this direction maybe, this will be of interest. But that does not happen for most of the motor proteins. So, what does it do? It just falls off the edge? We actually do not know. Dhairya, next question.

Dhairya: Good morning sir, you responded to Vaishnavi and Medha regarding the direction of travel.

Professor: Quick question, get to the question.

Dhairya: Basic thing is, you said that motor protein travel is independent to the larger picture it is governed by the local surroundings of a motor protein. So, is it like an emergent phenomena?

Professor: Could be and if you know what an emergent phenomena is, which probably many people may not know yet. It could be. So, the short answer is yes. Next question.

Christopher: Hello sir. My name is Christopher sir. So, my question was about actin and myosin. I have heard them in the context of muscle contraction is the exact same thing?

Professor: Yes, same thing.

Christopher: So, do they work very similarly, in both cases? Or is there a differences in the motor protein version or not?

Professor: No, they do actually the same thing. All they do is that they bind and they move. And in the context of muscle, that is what drives everything. And this is the remarkable thing that these systems are repurposed in so many different ways. The microtubule network that goes from the center towards the out and acts as a highway in cells in a dividing cell does this and then pulls. Same machinery, same players, completely different outcomes.

Christopher: So, how does the so how does the myosin organizing the filaments they do?

Professor: It does not. It binds to actin only, it is largely, connecting actin strands.

Christopher: They do not become filaments.

Professor: No, they do not. Absolutely no. Aniak, next query.

Aniak: As you said that there is also traffic on the microtubules. And there could be multiple motor proteins on the same microtubules. How does one microtubule motor protein know that there is another motor protein?

Professor: It probably does not. It just does its bit. Now, if there is something that affects it, only then does it know. Like, for example, if there is a cargo and this motor protein is walking with it. And there is another motor protein that binds it and walks with it in the other direction. It is only when that it is not able to move forward, will it probably not know, but at least feel the fact that it is actually getting pulled in the other direction.

So, it is not trying to find out what is around it and how to, it does its own thing. And in the process, if something else happens, its functionality is affected. And that is all there is to it.