Introduction to Cell Biology
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Plasma Membrane: Discussion Session

Professor: So let us begin with the first hand that went up and if you have a question, please put your hand up and I will come to you one at a time. Sarthak you are first online, go for it.

Sarthak: Sir, is this the movement of those lipids, in the sea of lipids that cause the protein to move or it is the protein that actually moving itself.

Professor: So the sea of lipids has its own inherent mobility. Now the proteins may be bound to different things and we have not come to that yet, but the cytoskeleton that is present underneath the lipid bilayer, cytoskeleton is this kind of the dome that I showed you, so it is a network that is underneath. And imagine now if you take a mesh like that and you cover it with lipids, the lipid is kind of sitting on the cytoskeleton.

So lipid is moving constantly, the receptors, the proteins that are present on the membrane, can inherently move as part of the lipid, the movement of the lipid is what allows for them. Remember, all of this is through different ionic and other interactions that exist. So it is possible for the protein to have those kinds of interactions with lipids that will allow it to jiggle around in the membrane.

Now the protein could also be anchored to something on the inside of the cell or on the outside of the cell and that could move it around inside the lipid as well. So both from outside and from inside the proteins movement would be regulated, but if none of that is present, and the protein is just sitting in the membrane, then chances are it will kind of keep wriggling around and there will be a slight amount of movement as a result of movement of the movement of the lipids.

Sarthak: So the movement of intrinsic lipids can, intrinsic proteins can also happen, the proteins embedded inside the…

Professor: Intrinsic proteins is what we are talking about, these are intrinsic to the membrane, if that is what you mean?

Sarthak: No, no, I was talking about the extrinsic protein that was…

Professor: What is extrinsic, you mean the extra cellular?

Sarthak: No, the one that was shown in the video that was…

Professor: That bound to the outside membrane?

Sarthak: Yes sir.

Professor: Okay, so all anything that is anchored to the membrane can have movement, inherently because of the membrane, but they can bind things and that can also regulate their movement, both outside as well as inside.

Sarthak: Okay sir, thank you, sir.

Professor: So I am not sure I am going to pronounce your name correctly. So can you tell me how I pronounce your name?

Ajinkya: Ajinkya, sir.

Professor: Okay, go for it.

Ajinkya: Sir, are the lipid rafts only restricted to the cell membrane or are they present?

Professor: Good question. Actually, this is a bit of a contentious issue, so because, we are having a discussion today, I will tell you a little bit more about it, which is that, so far the presence of these rafts has come with some question mark, a lot of the data that exists for these domains, has come from studies that people have isolated the plasma membrane, and seen that there are certain parts of lipids that have very different biochemical and biophysical properties as compared to the rest of the membrane.

So when you try to separate them, these lipids actually are much lighter, and will float up on a gradient on a sucrose kind of gradient that people use for separation and that is how you will be able to detect those. Now one of the problems here is that those lipids and the ones that have, that are lighter, and can float differently, could have been created because of the lysis of cells.

And so there is always that question mark of did this exist in cells or did they happen when we started isolating these or breaking up these cells? Then there were studies which actually looked at proteins, and labeled them and these are very interesting studies, where you label a single protein, and then you watch its movement on the plasma membrane.

And what they noticed is some proteins that have a tendency to go to lipid rafts, have a more restricted movement, so they move, but they move within kind of an invisible boundary. Now in that movie the inner life of the cell, they have clearly marked what the cholesterol region looks like and made it a slightly different color from the rest, so you can tell that this exists. But in the real membrane, there is no way to know this.

So the only way to know is if a protein for example, when it is moving moves in a restricted space and you now know that there is a boundary of some kind and which could be the lipid raft, a lot of this has almost exclusively be done been done on the plasma membrane, simply because being able to see live a membrane inside the cell and watch a protein move inside, it is not something we have accomplished still.

We can do this for cell surface, but we cannot do it inside. So does it happen in other membranes? We do not know. Is it possible? Maybe. So that is not a very clear answer, but that is where we stand as far as our understanding now goes. Goraksh, am I pronouncing that name correctly?

Goraksh: It is Goraksh.

Professor: Goraksh, go ahead.

Goraksh: My doubt was regarding them was endosymbiont theory, a prokaryotes have been existing for a long time and the first event that happened was a 2 billion years ago, which was the Archaean engulfed the bacteria. So and this happened simultaneously at various locations globally. So…

Professor: We do not know this.

Goraksh: In the BBC video they stated that.

Professor: Well, that does not necessarily mean they know. See, the thing is, it could have happened in many places, it could have happened in one place, it could have happened over a few million years also each of these events, the fact that there is nothing to suggest that these events happened in one place or in a very short span of time. And remember, in the big scheme of things, short span of time could be a few million years, we are talking in billions right now. Go ahead.

Goraksh: So was there a trigger event that caused this to happen at 2 billion years ago, was that an external driving force? It could have happened at any time…

Professor: Yes. It is possible, we really do not know. It is possible that there was some conditions that came together that allowed for this. It is possible that, you like for example, one simple condition is such a bacteria that, has a reasonable amount of energy producing capability and an archaea to be in the same pool and at a particular temperature that allowed for this kind of entry to happen and for them to be stable.

See, it is highly possible that these events kept happening, they kept happening in different forms, they kept happening with different combinations, and only the combinations that were viable and had environmental conditions that supported that viability may have survived. So it is highly possible that this chance event kept happening on and off and the version that we now have is whether that is one is the origin of one event is very difficult to say.

So a lot of these are kind of unanswered, we really do not know. We are making some very calculated guesses here and even the idea that this could have happened is now based on some of this information that now is more factual than before. But it could have happened in multiple places, many times it could have failed, many times.

It could have gone through one or two generations and then given up because the environment may have changed, all those possibilities exist. What we do know that an event of this kind should have happened for what we see today. So I hope that kind of gives you a very pragmatic answer, I am not being, very…

Goraksh: Yes, sir.

Professor: Very forward in this. I am being a little practical about it, and saying that, let us be cautious rather than too optimistic that, but it could have and it is very difficult to know this. So it is possible that these things are happening even as we speak now and it is just a question of us now looking for them.

And obviously, what the cell that we have now is something that is a derivative of something that happened many millions of years ago, but what is happening now could lead to something, which could be relevant a few million years, a few billion years from now we do not know. K.K. all yours? What is your query?

K.K: Yes sir, my doubt was that since a brain of an individual helps him to interact or perceive his environment, so can we consider the cell membrane to be equivalent to a cell's brain?

Professor: Sure, see the thing is that, this, we have a tendency to kind of want to put these things under compartments or categories that we are comfortable with. And some of the challenge in learning about this and all, even going forward, not just in this class in other classes, is also to do away with some of those pre-established notions.

That there could be something that need not be the brain, the cell does not need a brain, there could be many different things that could act as a brain or there could be no brain, it could be all very intuitive. And so it is very difficult to kind of compartmentalize these this way and say this is the equivalent of this. And I know we have a tendency to do this, because we are just comfortable with that, but my suggestion to you is do not walk that line.

Do not go thinking, should I be thinking about this as the brain, no, think of it as the cell membrane and think of what the cell membrane is capable of doing. Because there are other things inside the cell that also do their own important part in making the cell what it is and allowing it to work and function the way it is.

But it is perfectly fine to feel this way and I am just kind of encouraging you to kind of go to this place where you are not having to think about it this way.

K.K: Yes sir.

Professor: So try that okay. Piyush over to you.

Piyush: Sir, as we explain the origin of eukaryotes from prokaryotes only and we explained the presence of mitochondria and chloroplasts from the endosymbiont theory, but sir, like in eukaryotes, most of the organelles have membrane So how do we explain the presence of membranes on them and like in the prokaryotes there was no nucleus type thing, there was no…

Professor: Nucleus is not there, but membrane is there no.

Piyush: But in the organelles, how do we explain the presence of membrane in eukaryotes in presence of membrane…

Professor: So the prokaryotes did have membrane, the prokaryotes had, see, the fact that there is a cell membrane seems to be the first big thing that has happened. And even if you did not have a cell inside or all the components of a cell inside the fact that you could now have a self-assembling lipid ball that has a hollow center means there is an outside.

Then there is an inside, this may have the beginning, this may have been the beginning of how cells, or the idea that you could have something inside that now works and does things, which is the early kind of precursor to a cell may have originated. So thus the prokaryotes have a cell membrane, it is just looks very different.

So that is why for example, the mitochondria lipids are very similar to the lipids that are in bacteria, which is suggesting that the bacteria do have lipids, they do have a cell membrane and in many cases, like the mitochondria, mitochondria actually has a double layer, which means it has an outer membrane that probably came from the cell that engulfed it, and it had an inner membrane that actually came from the mitochondria from the prokaryotes and both are present now in this version that we see inside cells. So there is a membrane. Dhairya.

Dhairya: Good morning sir.

Professor: Morning.

Dhairya: You mentioned when you were discussing the lipids present in the bile in the cell bilayer and the mitochondrial bilayer, that they have slight differences.

Professor: The cell no, no could you repeat that again?

Dhairya: In the cell membrane and the mitochondrial membrane lipid present have slight differences with sort of…

Professor: Yes, great.

Dhairya: But the mitochondria has 2 bilayers. So would not only one of those have a different composition?

Professor: Good question. Good question. So will you go look this up to find out whether when I talk about the mitochondrial lipids, am I talking about the inner membrane or am I talking about the outer membrane or over millions of years does the outer and the inner membrane of the mitochondria actually shuffled lipids to reach a equilibrium, where the outer and the inner membrane have similar composition in terms of the distribution of lipids that

may have come from an early engulfing cell versus like lipid that could have come from a bacterial membrane.

So the question to ask would be, one is the outer leaflet and inner, not outer leaflet, the outer membrane and the inner membrane in the mitochondria. One is their composition comparable and second, can lipids actually be exchanged this way? I did not talk about this because this is going into more detail, but even in the bilayer that the plasma membrane or other membranes, lipids tend to flip and they can do this.

So there are enzymes that actually regulate this also. And so it is possible that what came with almost a very unique microbial membrane over millions of years, went back and forth, went back and forth and now both the outer and the inner membrane in the mitochondria have unique composition from the rest of the plasma membrane.

And the reason it is unique is that they both have remnants of the bacterial lipid that originally came with this, there is a possibility that there was a point of time where there was a distinct difference between the outside and the inside, that there was no bacteria lipids there, and all bacterial lipids were here.

But right now the version that we have does that exist there too or has this back and forth happened between these two membranes to now make them more uniform? Very good question, can you look up and find out what you find and this is something we can take up. Like Vaishnavi has an answer for us, this is something you will come back to us as well.

Dhairya: Okay sir.

Professor: Thank you, Deep have a query?

Deep: Yes sir, if we take the case of proteins, the like, the building blocks or amino acids and they are joined by peptide bonds, what is the bond between the two lipids in this liquid bilayer like, why are they joined?

Professor: So they are not joined together, in lipids the interactions are much more transient. In many cases they are electrostatic interactions, they in some cases, their interactions with proteins, for example, may have slightly higher propensity, but otherwise the lipid is made up of interactions that are fairly mild, but just strong enough for them to be assembled, into a layer, that they can be sufficiently close to each other and stay together, so to speak.

So this, the idea of making a ball, for example, only happens if there is an energy there is a way for that energy to get balanced out and lipids have a tendency to do that. So these are not very strong interactions, even with proteins. The thing is the fact that there are a lot of lipids and a protein is inserted in there, and it can bind to multiple lipids is possibly the reason why, if you hold a protein and pull it out of lipid, you will feel some resistance.

But a lot of the protein-protein interactions, for example, are far more stronger, as compared to lipid-lipid interactions, and I am putting it very loosely, what kind of interactions lipids have, what is the kind of energy requirements that they have? Sai, go ahead.

Sai: Yes sir I was meaning to ask about the mitochondria that we discussed yesterday. How does the cell like I have read that the number of mitochondria per cell depend on how active the cell is? Your skeletal muscles tend to have more mitochondria because they are used more like, they need more energy. So I was wondering if the mitochondria itself senses the lack of energy and replicates like an autonomous body or like it gets a signal from somewhere and…

Professor: Good question. So one question to ask, which I think you have indirectly asked and I was hoping somebody will is if this is a bacteria that is inside a cell does it divide?

Sai: I know it does, but then does it sense the surroundings itself and divide or does it get the signal from somewhere like the nucleus?

Professor: So obviously, it must be getting multiple cues, the mitochondria now is thought to talk to pretty much everything inside the cell. So it is highly possible that there are cues that it is reading the mitochondria also has a lot of proteins that are involved, it talks to the cytoskeleton, it talks to the ER, it talks to the Golgi.

It talks to the nucleus, it talks to the plasma membrane, and receptors that are present everywhere could talk to the mitochondria to tell it what to do. So this regulation may be more complex, and some we know, some we do not know, but clearly there are cues coming from many places to tell the mitochondria what to do.

Sai: Okay sir.

Professor: So and if your query, read a little bit more. See, the thing is, it is very difficult for me to cover everything about mitochondria here in this 1 or 2 lectures, but there is a lot of

content that is available and if you cannot find something, first look up and part of the idea is to kind of teach you guys how to look things up and we will do that on this Monday class.

And if you still cannot understand something, see finding information in today's age is not difficult understanding it might be. And so look for this information, if something in that source is not very clear, then come back and write to me, and I will be happy to see if I can help you understand that better.

Sai: Yes, sir. Thank you.

Professor: Okay, thank you. Akshusma, I am also not sure I pronounce your name correctly. Sorry…

Akshusma: Yes sir, you pronounced it correct. Sir, I wanted to ask that you told the lipid phospholipid bilayer they fold themselves into spheres in order to have a energetically favorable state. And you also told that this is a reason for the presence of the bilayers in that, so I just wanted to ask that how you related that.

Professor: So see the fact that there is a compartment that is created the moment the energetically favorable state for us for a sheet of lipids is to kind of become this automatically this allows for segregation of outside and inside. So the ability to create this kind of a structure which has something hollow inside.

One means that there are a bunch of things that can get trapped inside and as a result the inside could now start behaving very differently from the outside, the fact that the outside is undergoing change, as long as this bilayer is intact and is able to keep the insides safe there could be changes that are happening in the inside which will allow for this to develop differently.

And so this ability to create segregation from between outside and inside a sphere of lipids will be able to do more readily, which is why I was suggesting that the fact that that is an energetic energetically favorable state may have had contributions to why the cell that as we know it could have a lipid bilayer as the membrane because that separation between outside and inside such a structure could facilitate. Kinjal, please go ahead,

Kinjal: Sir, about the peripheral proteins on a larger ones in an already formed cell, if we want to create our peripheral protein and move it to the like the extracellular region, like how is it like as a whole protein moves to the lipid membrane or is it divided into parts and like…

Professor: So the whole thing gets carried and the really nice thing is that all these internal organelles like the ER, mitochondria, could all are all lipid based. And so when a protein is synthesized, it is integrated into the lipid, and now it is carried with the lipid. Now one of the really interesting things you will see when we talk about how stuff is carried from the Golgi is remember that it comes as a vesicle, and then it fuses with the plasma membrane.

And when it does that and it opens up the inside actually becomes the outside and that is the case of protein that is present that is synthesized in the Golgi has to have the conformation inverted, which means when it is a vesicle coming out of the Golgi, the outside of the protein is actually inside the vesicle.

And the reason it is designed in this way that eventually when it goes in fuses, the inside of this vesicle becomes out. And now this protein this part of the protein that should be outside is actually facing outside. So a lot of the proteins that are synthesized are brought together and delivered to the plasma membrane that does not mean protein-protein interactions do not happen on the plasma membrane, they do happen on the plasma membrane, and proteins can come together there as well.

Kinjal: And when they are degraded or like, when they are nonfunctional like how do we degrade them, we have to bring them inside the cell….

Professor: Degradation is a completely different process, so you go look this up of how proteins are degraded, they are very complicated mechanisms for how proteins are brought in and degraded. And there are very elaborate mechanisms to do it and I am not getting into that at this point. As I said, go look this up. Sanskriti over to you.

Sanskriti: Sir, am I audible?

Professor: Yes.

Sanskriti: Sir, my question is about the class before the last class. In one of the slide it was mentioned that prokaryotes have a higher surface area to volume ratio as compared to the eukaryotes, and that is why their metabolism is high. I was wondering how surface area to volume ratio could have affect them…

Professor: Metabolism not per se, but the surface area essentially means that there is a greater region of contact. See, remember, these are prokaryotes do not have a higher metabolism than eukaryotes, if that is what you are suggesting, that is not what I implied. What I was saying is

that because these are very tiny, the fact that any increase in surface area that happens means that the extent of contact with their environment is better.

And a lot of the energy sources for these prokaryotes come from the environment, which means that, that contact and surface area that they have could be hugely beneficial for them to get access to more energy, more resources from the environment and that might serve them well, which is why the surface areas is better.

Now in a eukaryotic cell, which is inherently bigger, that surface area is already expanded and obviously, that is beneficial, but it is also has its own way of generating energy, so both are working now in the favor of the eukaryotes, So the prokaryotes, having this increased surface area could be beneficial in these respects to keep them, to get for to make sure that they get more from their environment. Kedar, that go for it.

Kedar: Sir, when cell was evolving, how the water enter inside the cell because the plasma membrane has hydrophobic tails, so it creates a barrier for water,

Professor: When you have a lipid membrane that does this and becomes a ball. Remember that lipid membrane is floating in water? Outside inside everywhere is water. And when you do this and make a ball what is inside is water. So because it is in an environment of water any sphere it forms like this, will trap water inside. It is as simple as that. Hoka over to you.

Hoka: Sir, I was looking up for like if viruses came before prokaryotes and I found that it is still like there is no consensus yet on whether but is there or like are there any examples of like…

Professor: I do not know

Hoka: Viruses behaving like endosome….

Professor: I do not know actually. So this could be a completely different area of reading and we are really not touching viruses at this point, it is like a completely whole. Sneha.

Sneha: Sir, I wanted to tell you that in the last lecture, you told me to find about the centrioles that is present in both, so sir I found that…

Professor: And what did you find?

Sneha: Sir in prokaryotes they are not well developed, they have many of them have single membrane nucleus. So….

Professor: No, what about centrioles?

Sneha: Yes sir, so nine plus two pattern is not present in prokaryotes, not in…

Professor: Are there centrioles at all in prokaryotes?

Sneha: No, they are not.

Professor: Do prokaryotes have cytoskeleton?

Sneha: Yes, they have.

Professor: They have cytoskeleton?

Sneha: No, so they do not have.

Professor: They do not have a cytoskeleton, I think it all depends on my reaction looks like. So why do not you do one thing, the next class is going to be about the cytoskeleton. And so why do not you look up now that you found out whether centrioles are present, find out centrioles are attached to the mitochondria to the microtubules.

So find out if there are no centrioles are there microtubules in cells in prokaryotes? Okay, look this up, because this is this will lead to a very interesting answer that is why I am asking you to look it up, okay. So we will stop here guys.