Animal Physiology
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Lecture - 12
Skeletal Muscle Formation

Welcome back to the 2nd lecture of week 3. So, as I told you in the previous lecture while starting the week 3 that next 15 classes, we will be dealing with muscle nerves and somewhere in between we will talk about a small tail piece of conjunction of a skeleton and the muscle in the form of appendicular and axial skeleton and appendicular and axial muscle and the articulations. So, if you recall back where we stopped in the last class.

So, I give you three examples beating of your heart, you playing basketball or whatever games you like where your muscle is getting lot of a stretch and the third thing you are eating food and I told you that these three are orchestrated by muscle, the muscle lining, your elementary canal or digestive track which is termed as the smooth muscle. When the bowlers of food moves along these elementary canals or the digestive track, you do not even feel that there is something moving along your body, ok.

That is so I can settle and so smooth how they are yet when you take your hand and touch out here, you feel there is a lub-dub sound and if you cannot feel like that he just put a stethoscope, I will be able to feel it. So, there is big chunk of organ which is beating and there are no bones in it. The suspended out there in your thoracic cavity which is called the heart and these muscles which are having lot of stretch and I told you the fundamental difference between them, if you look at from a very holistic point of view is the force generated by them and the force which is directed ring to the displacement. You can stretch most of your skeletal muscle.

So, one underline thing what we came is it is not all muscles cover the bones point. One second, these three different muscles have different force dynamics and we concluded the class saying that in order to understand what are those dynamics, one has to understand that development of the muscle in the first thing once you understand just like the street corollary is that when we have to talk about the bone, we have to understand how it develops from the cartilage because initially it was the cartilage. So, now, let us move on to understand the development of the muscle.

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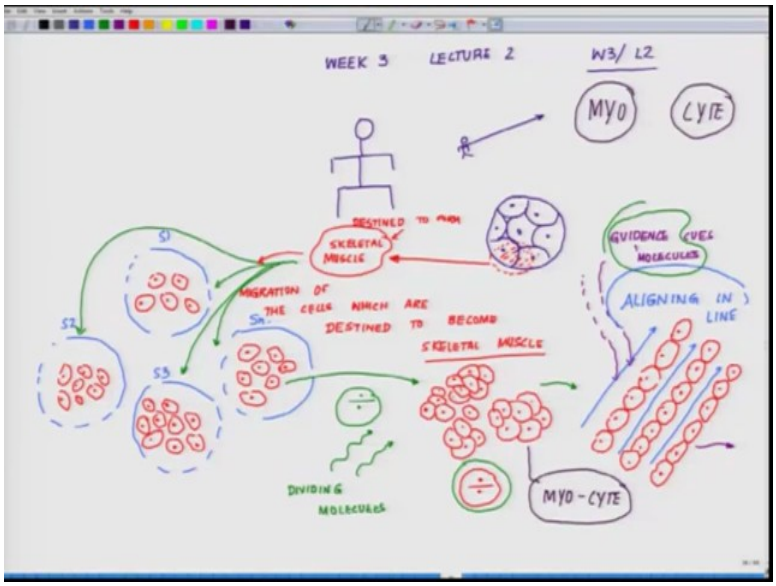

So, today we are into week 3 and this one is lecture 2, right lecture 2. So, W 3 slash l 2, this is where we are.

Now talking about the development of the muscle: so I told you in the previous class that the classic example what will be taking will be of the skeletal muscle and later as we will be talking about the cardiac muscle, we will talk about the features of the cardiac muscle and while we will be talking of the digestive system, we will talk about the future of the smooth muscle. So, muscular development just like the week cartilage develops pretty early in the mother's womb, muscle development also happens pretty early. So, when the embryo develops there are certain classes of cells which are destined to become muscle, ok.

So, these cells migrate to their specific places can be on top of the bones. Since we will be talking about not bones, the cartilage precisely because it is a cartilage from where the bones are formed and yet some which forms the beating organ, the heart and the ones which form the elementary canal what happened after that. So, those cells, you say for example, I say this is cartoon of a human being, right. So, say for example, say when we are in our mother's womb like say for example, I blow it up something has to form something has to form a muscle to it. So, what happens here? So, those say for example, in this embryo which is a mass of cell like this among these mass of cell see for example,

some of them a lot like this is destined to become muscle or let say they are destined to become a skeletal muscle.

Since we are taking the example of skeletal muscle, we will talk more about this skeletal muscle at this stage. Now, these muscles they destined, they have informed it at destined to form skeletal muscle. So, these cells, there is a set of cells which migrate. I am just putting those cells in red, the one which are shading them, right. For your understanding, these cells migrate to different parts where the skeletal muscle has to form. This is the first level of differentiation which happens. They are moving to different zones. So, just for the simplicity sake, I am just keeping something like this. These are the four different locations I am just putting that. So, many locations all the bones which are there, they must have move to them. So, they have migrated the first level is migration of the cells which are destined to become skeletal muscle, fine.

So, these are different sites. So, just I am putting the blue bordering as s 1, s 2, s 3 and s n. These are different sites. So, now what we will try to figure out what is happening that at specific sites, initially these individual cells reaches the site and at that particular spot, they start to divide. This is the first thing which happens the form or kind of a lump of cells like this. They dividing like this at that specific site, right. See they are now in a dividing phase and I will try to get an animation which I want to make long long time back for you. So, first and foremost thing is they undergo massive division step 1. So, now, to remember in your brain map, put the first sign that division.

After division something very interesting happen. So, this whole thing has divided, then they started to form kind of rows like this something like this. Follow my pen here, you will realize what they do next. Next there is something called alignment. So, these cells started to you know align like this. It is a very interesting thing. I am in if you see it under tissue culture dish, it just look amazing the way they align it. I had the privilege and great fortune and blessings to do this kind of experiment. So, I have seen them in a real life and it just in a dish, they look phenomenal like this, this started to align, ok.

So, while I am drawing this up, it should strike the first thing which should strike your mind is what are those molecules which help them to form this kind of alignment, it is almost like a rope has. If they are aligning like a row, those of you were from villages, they must have seen when this jute or you know different hemp or something form a

kind of you know fiber like this, you know pull the fiber out of it almost like you are pulling fiber, these cells align. So, let us go back what all we did in the embryo. There are cells which are distain to become muscle. Step 1, those cells which are to stain to become muscle migrate to real specific locations wherever they have to form is collect. In this case, we are talking skeleton muscle. We will talk later about the cardiac and these smooth muscles.

At this point just concentrate on this skeleton muscle. Those cells migrate to that specific region say for example; something has to form these muscles of my body, right. So, they will migrate here, they will you know scattered round the bone or the cartilage where which is present at that stage what were stage of development and that is the setting on then these small lumps which will be formed, they started to divide as I showed you. So, if you see it here, they are dividing. That is why I kind of put that signature for you. They are dividing. After dividing they are moving for the alignment, they are aligning in line. This is a beautiful alignment which is happening you know.

Now, what I was trying to tell you it must strike you, what are those molecular players who tells them that you have to align like this. It would not align like this. These are some of the biggest challenge of modern biology who tells them all these things, how they know, they have to align like this, if you strike, it should strike your brain. That you know there has to be certain molecular players which are present here, they have to present here what telling that may know this is the guidance cue. These are called the guidance cues or guidance molecules.

Now, you realize that why those first week are so important. I told you that all these organizational cues are very important who tells them there has to be some form of guidance; otherwise they cannot align like this. So, this is the first level of self assembly which happens. They align. The next thing what happens is even much more interesting, they have aligned. Now, these individual cells which are present there now you see this now let me go to the next page to tell you exactly what happens.

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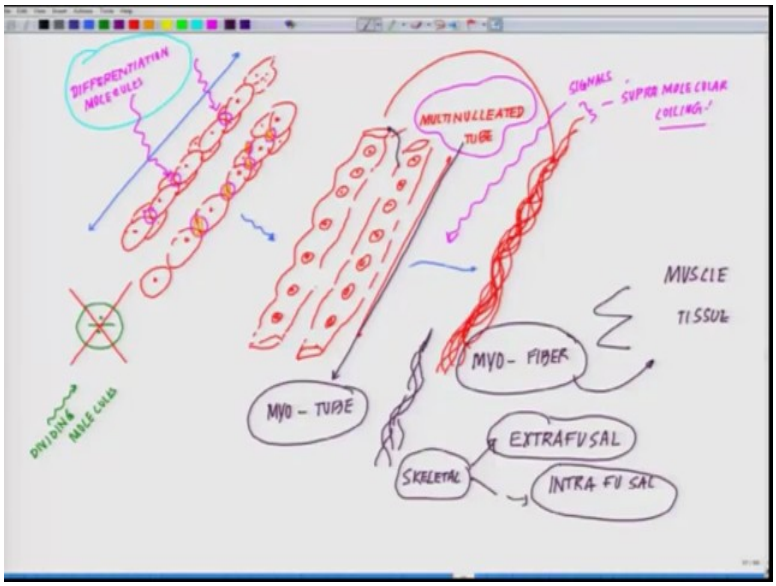

So, I do it up to this, right. These are the individual cells which are present out here with their individual nucleus and they are aligning like this.

Now, at this stage, there are two things which happen. So, they have aligned like and longitudinal manner. Some of these cells even further divide while in align state further division happening, it almost form a three-dimensional rope kind of thing and then, its division stops. There is no more division. Division sees us there is no further division. Now, what happens is there are two cells which are touching each other. You see this. So, look at this, I am drawing in pink. You see this; they are contact points, right. I am circling them. These contact points are lost. What does that mean? That means, instead of having individual cells like this attaching together, this whole thing becomes one common almost if you keep on adding them, a small cell like this and there are the contact point are lost. What it looks like? It will look like a complete tube.

So, think of it. Now, let me go to the next level like now these contact point are now getting merged. I am showing in even now orange colour, these contact points are lost. So, what you essentially will be landing with is something like this. Initially as if it is like a tube like structure and with the individual nuclei as if it forms a multi nucleated structure, a multinucleated tubes and there is no, you will not be able to figure out which cell is which one. So, what you get is multi nucleated tube and there are several such

tubes which are formed and say three-dimensional tube is as I told you, they are almost in a three-dimension form like this.

There are several such multinucleated tubes. So, now out here you have such long tubes. So, that is why I give you the analogy of those of you are from village or goes to village or goes to rural places, where they pull this strings you know from him from jute from any sources you know and in any other several places or even though those where they put the self threads, you will see how they are formed. They have individual threads and then, they pull up together you know they turn them, coil them, super coil them and likewise and so on so forth.

It is almost like your thin tubes like this with lot of nucleus and then, with multi nucleus and nucleus are range nuclei, sorry nucleic or arrange like this next thing is another interesting thing which happens. Once these tubes are form, these tubes come close to each other and form something called exactly what happens in the formation of the thread. They form a super coiling. So, in other words these are different. So, now I am just showing it in one line. The individual tubes I am showing in one line, they come like this. They form a super coiled structure like this and I will call there are specific names for it. So, these are lot of tubes which are coming close to each other and forming a super coiled assembly, right. Does not it look very interesting?

So, this is how in case of a skeletal muscle, it happens. Now, we have talked about anything about the molecular players, but what we figured out is that at this stage also the first I told you in the previous slide. If we go back to the previous slide, there are guidance molecules. From here the guidance molecule which guides these individual progenitor cells to move to their specific sites and out here, they get a signal to you know divide.

So, it means they are dividing molecules which are present there dividing molecules and these dividing molecules further in conjunction with the guidance molecules tell them to align in a specific line. There are further division or may not be further division, but the next thing what we know is that this division molecules, dividing molecules stop. There are no more dividing molecules are allowed and what you get is there are molecules which pictures in here which tells.

So, this is the new set of molecule that these are another set of differentiation molecules which tells these muscles or tells these muscle cells to lose their identity and form what we call as the tube like structure, what we termed as the multinucleated tube. So, at different point we see differentiation molecules or different molecular players which are doing it. Next what we know there another series of signaling which is coming, molecular signals which are telling them to form supra molecular coiling. So, you see that every point there are you need signal molecules guidance cues dividing signals, non-dividing signals, merging signals, coiling signals which are involved in it and that is what the whole molecular physiology is all about. Deciphering, discovering these things because any mistake in any of these things could lead to difficult diseases like muscular dystrophy and so many other things, ok.

So, now what are the scientific terms for all this thing. So, still by the way I still have not touched upon how the force is generated all we come slowly into it. First of all, you have to get a mind map of what is happening. Now, let me introduce the scientific terms for each one of these. Now, let me go back to the previous slide. These cells which are destined to become muscle are called anything to do with muscle is designated by this word called myo and anything which is dealt with cell if called cyte.

So, these cells are called myocyte. Muscle cells create you guys. Next these myocytes align together, divide this myocytes, divide and then align together. There is alignment of the myocytes as you could see in the previous slide out here. Alignment of the myocytes followed by formation of a multinucleated tube and this multinucleated tube is called myo coming from muscle tube.

Now, these different myo tubes align with each other at different level. Some of them like you know merge like this, they are merging like this as well as they are merging like this. So, end to end they are adding together or merging like this forming a super coiled assembly. This formation is called myo fiber. So, we started with the progenitor cells which went to their specific location in the cartilage during development followed by the generation of series of myocytes, cytes, and the cells which are destined to become muscle.

These myocytes align with each other to form a multinucleated structure called myo tubes. These myo tubes with respect to mycytes have lost the individual identity of the

cells because they all have collage together and form a tube light structure. These myo tubes align with each other, both or the proximal and rear end like this tube, tube to multiple tubes attached together as well as from sidewise.

So, there was sidewise attachment. They were attachment like this, right. One top of each other as well as like this and then, they form a super coil assembly like this and those super coil assemblies are called muscle myo fibers and these multiple myo fibers, this integration or the summation of these multiple myo fiber form what you call as muscle tissue.

Now, I am going back to the first slide.

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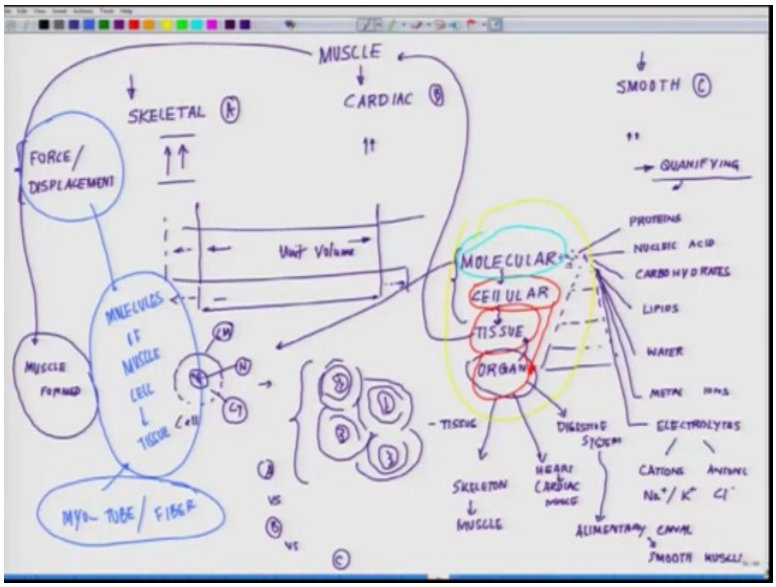

When I told you that if I now look at this one. So, we started with the cellular players, we talked about the formation of the tissue and eventually it form the organ. You see at every level, there will be an organizational setup, but mind it what I have as of now I have not touched because I am going slowly on it because who are the molecular players, right because it is the molecular player who will determine. So, I have given you some hint about the molecular players out here, but those molecular players who are involved in as a guidance molecule as a dividing molecules as these differentiation molecules, but still I have not told you which are those molecules which are involved n the process of generating different kind of force.

So, what we will do in the next class in this structure, we will again revisit this whole development process, right. We will revisit this development process and we will talk about those molecules which are involved in generating the forces and based on that, one can classify the muscle at different point. Even there is skeletal muscles are further classified into two forms of muscle which will come later, but just for your understanding saying because whenever you consult a book or something, you will come across these two words Extrafusal muscle and Intrafusal muscle.

These both are classifications of skeletal muscle who will come into this what are extrafusal muscles and what are intrafusal muscle, but at this stage, do not get confused. Please do not get confused. The whole idea of this course is to kind of you know making simple for you. So, there if you pick up any book, you should be able to understand there what you are really looking at and most important for me is you understand this, this organizational setup. This organization setup is very important. How much so ever simple it looks like, it is here if you understand this whole ball game, you will be able to develop your own story, you should be able to formulate your own research problem.

So, what we will do next is, what are the individual molecular players which are present in myocytes? The first one is the myocyte, right which over a period of time get transformed in order to distinguish a myo tube form for skeletal muscle, a myotube form for cardiac muscle, a myo tube form for smooth muscle or even within is skeletal muscle, a myo tube form for extrafusal fiber, myo tube form for intrafusal fiber or intrafusal muscle or extrafusal muscle.

So, today if I had to summarize what we did, we talked about the cellular differentiation, how the cells joint together to form a tissue like a structure or a tissue call muscle tissue, right. In the next class what we will do? We will talk about the molecules which are present in these muscles which led to the formation of the tissue and thereby giving it that feature what we talked about in the very previous class is force generation and correlating it with the molecules of muscle cell actually is called muscle tissue, and all these things happen at the level of myo tube slash myo fiber.

So, let us again take the clock back myocyte. This is one technique terminology. You should remember myocyte lead to the formation of myo tubes. You remember that different myocytes attached together and this myo tubes joint align together sometime

like this on top of each other as well as from sidewise, from myo fibers and multiple myo fibers from muscle. Keep this in mind and this framework is good enough or rest of your light to develop the story about muscle.

So, next class we will talk about the molecular players who are involved in this game.

Thank you.