Tissue Engineering
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Lecture - 01
Introduction to Tissue Engineering - Part 1

We will start with the basic Introduction for Tissue Engineering today. So, we briefly looked at the course content, and I also said what tissue engineering was. Today we will go into depths, so we will have a few classes where we discuss the introduction to tissue engineering.

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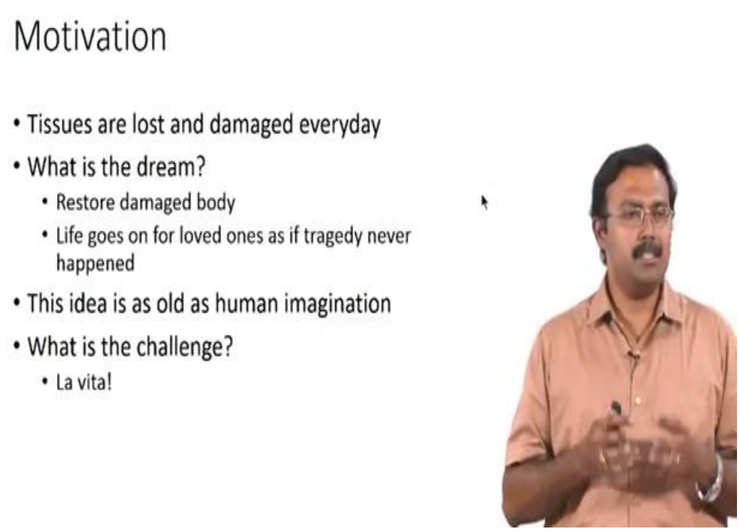

What is the motivation for tissue engineering? What do we really want to do? Tissues are lost and damaged every day, right? So, it could be due to injury, disease or congenital malformations, and so on. Due to different reasons, the tissues are usually damaged, and you want to restore these damaged tissues. Your dream is to restore it so that that life can go on forever. Especially for loved ones, and we want to make sure that tragedy never strikes us, right? So, we do not have to go through the pains of whatever the process is.

This idea itself is not new; Obviously, it should have come to a human being when the first death occurred, or when the first lost limb occurred. So, why have we not been able to achieve it? Because we always had dreams. we as humans wanted to fly, so we have been able to invent the airplane and so on; Most of our dreams, we have kind of achieved it, at least.

Whereas here, this is one of the most fundamental dreams. So, we want to create another life basically; so, why we have not been able to do it? The simple reason is the challenges life; Life itself is very complicated and beautiful. See, we do not think about it. Most of us here have biology or biotechnology background. So, we do know some of the things about how life starts, but we do not sit back and think about it.

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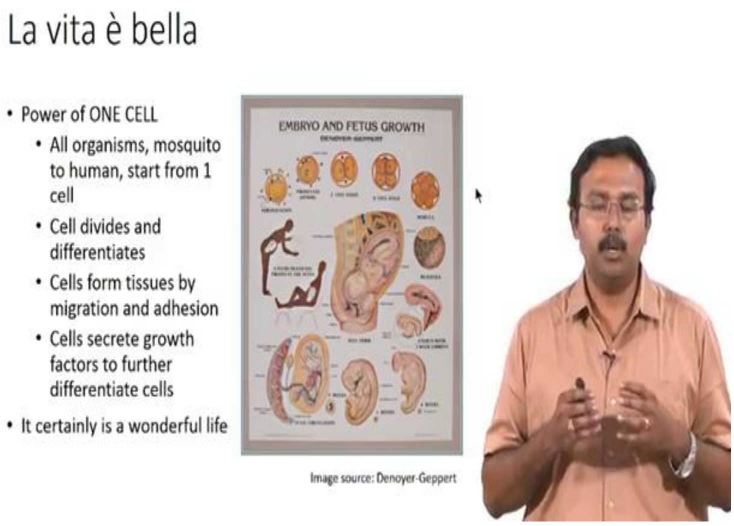

So, think about this. What I have shown here is basically, what I call the power of one cell. All organisms, whether it is a mosquito or a human being, start from one cell. It is unique, the single-cell divides and starts differentiating to form different tissues.

So, it starts migrating and differentiates to form various types of tissues. It could be a skin tissue or a bone tissue or cartilage or a heart tissue and so on. All these migrations and differentiation have to happen over a period of time. And eventually, it develops into the right organism; a human being or an elephant or a mosquito. All of these originate from this one cell within a concise period of time.

If you were to take humans, it takes only 282 days for a cell to become a fully-grown baby; That is a very short period of time, considering our life spans and the life span of the earth itself, it is a very very small period. And within that time there is such regulated control, which is phenomenal; Almost always we get proper development.

And that requires so much control over how the cells migrate, how the cells divide, how the cells differentiate, and so on. For us to first understand what is happening, itself has been a challenge; we still do not fully understand what is happening and why it is actually happening the way it is happening. For us to first understand and then to actually recreate it, is the challenge of tissue engineering.

So, to create an entire human is entirely out of the question at this point. But to create tissues, can we understand enough to know that what is required for creating this tissue. And that itself is a big challenge. So, that is where the field is, and we are working on it. We need to understand some of the fundamentals. Because when tissue engineering started, it actually had a lot of promises which were made.

Because it was primarily just engineers, who are starting it with some doctors, we probably did not have enough of an understanding of the complexities associated with basic biology. So, there was one paper which promised to deliver a heart in a Petri dish by the turn of the century, and this paper was published around 1993. So, within 7 years, people thought that they could create a heart in a petri dish.

What they thought was you take the material, you put the cells, you will have the heart. It turned out, it was not that simple, and people are still struggling to get even a beating tissue. Recently, about a year and a half back, there was this huge rage, which was the videos were forwarded where a small piece of tissue which was beating was created.

So, it has taken us more than 25 years to create that small tissue, and valves are a whole another ball game. There are so many challenges which were not foreseen. And as we started doing more and more, people have started realizing; there are a lot of challenges associated with this field. People are trying to address them, and that is where we as researchers should contribute.

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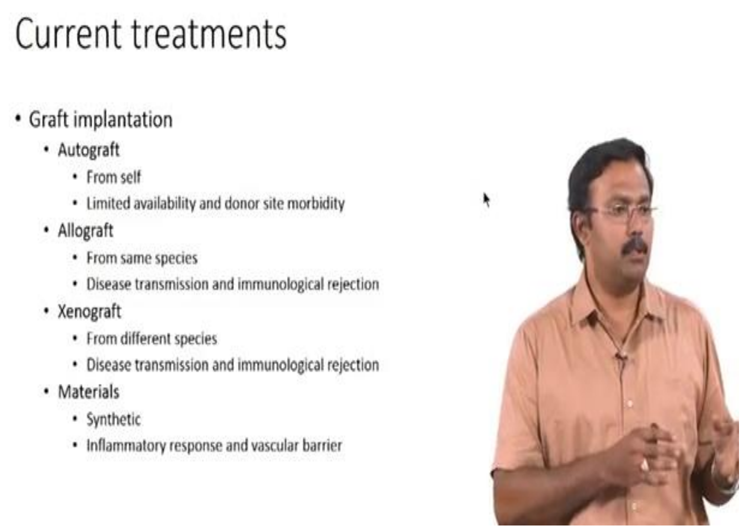

Currently, people do treat damaged tissues. So, there are different techniques you can use. So, graft implantation is the primary approach. So, there are different types of grafts; you can have an autograft which is basically from yourself. Here the advantage is, it will not get rejected because it is part of your body; Hence, it is not going to get rejected. But the problem is there is very limited availability; it is not easily accessible because you will have only limited tissue in your body, and we cannot completely harvest a particular tissue.

For example, if you have diabetes and you want to replace your pancreas; then you do not have another pancreas, you cannot take it from your own body. So, you need to get it from an allograft, which is another person from the same species. Here, there is a risk of disease transmission; there is a higher availability, but there is always a risk of disease transmission and rejection. This problem persists, even with transplants which have been very well established. So, what is the most common transplant that you can think? Organ transplant?

Students: Livers.

Liver.

Student: Heart valves, kidneys.

The kidney is probably the most common one. The liver is also done, but it is a much more complicated procedure than the kidney. Also, heart valves were done using cadaver heart valves, but people use from other animals as well. So, that would be a xenograft; where you take from a pig or a cow, and you take them for your transplantation.

If you are talking about an organ transplant like kidney, which has been well established for almost half a century now. Even for that, people still have to take immunosuppressive drugs for their life; that puts them at risk of getting infected at any point.

So, it is a severe problem even to have one of the most well-established surgeries. That is a problem with allograft; And xenograft obviously, the risks are going to be much higher compared to allograft; because you are now talking about a different animal altogether. Your chances of disease transmission and immunological rejection are significantly higher.

Hence, the last option is using synthetic materials; People use polymers, metals, and so many other types of biomaterials for implantation. However, this also has inflammatory responses, and there can be a vascular barrier. Cells may not infiltrate, for example, if you are using a hip and joint replacement which is made up of metals; Cells are not going to infiltrate.

It is not a biologically active tissue you have placed; what you have is just a mechanically supportive device. So, that causes some discomfort, and there can always be complications because of that. In some cases, like where you have plates and screws for broken bones; you might have to go back and remove them because there might be some immunological issues.

These kinds of problems exist with the graft implantation, but that is not the only reason you want to do tissue engineering. Because tissue-engineered products can also have similar problems, right? Because you are also going to use synthetic materials or materials which are not common in your body. And you are probably going to use cells which are not your own. Tissue-engineered products could also have the same kind of problems; then why do tissue engineering. The answers?

Student: Maybe it is the best chance for us to mimic the living cell condition in the body.

Ok so, probably you can get a closer tissue which is closest, but would not an allograft be the closest? An autograft would be the best, but autografts might not be available. So, if I can get it from another human being, that is God's creation.

Student: limited source.

Ok, limited source; yes.

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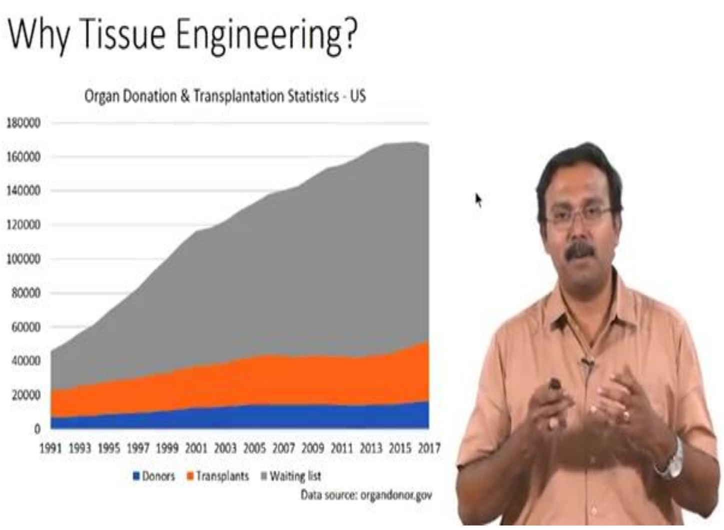

So, the major problem is this; This is the statistics from the US, you can see how the trends have been when it comes to the number of transplants, number of donors and the number of people in the waiting list. The grey curve you see is the number of people on the waiting list, and the orange one is the transplants and blue is the donors.

The transplants are higher than the donors because a donor can donate more than one organ right. So, this is the trend, and the gap seems widening from 1991 to 2017. And the problem is; this is for a developed nation like the US, where you have 54 percent of the people registered for organ donation.

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So, we will start with history; This is something which you would see in any tissue engineering book; not exactly these images, but you would see images of Chimera. So, this is to say that people have been dreaming of enhancing organs and enhancing tissues and so on. This is basically what people start within a tissue engineering book.

So, I always felt why we should start with the Greek mythology; why not our own mythologies; so, this is something we have all seen. And I would also go to the other mythologies and show how similar our imaginations have been. But the cool thing is people have actually dreamt of this; people have thought of xenografts, right? Lord Ganesha is a xenograft, technically right?

So, why I said that disclaimer again was, I am not saying a xenograft was performed. It is something which people want, and people have been thinking about, right? This is what people were trying to do, so the images I have are a Lord Ganesha and Lord Narasimha. So, Narasimha was just an avatar, who came down with the head of a lion and so on.

Ganesha was proper xenograft where the head was chopped off, and then restored by elephant head; The other two things which you see, the Kamadhenu and Yali are more of mythological creatures which are designed based on what we think is cool, what features you would like to have, right?.

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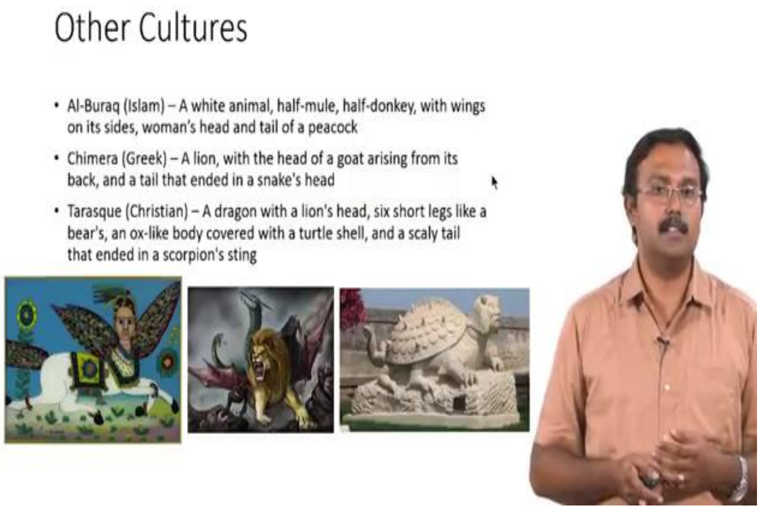

Why I said there is similarity is, look at the other cultures; the one you see here which is Al-Buraq; so this is a mythological creature by Islam. And you see that it is a white animal half mule, a half donkey with wings on its sides and a women's head and tail of a peacock; it looks eerily similar to Kamadhenu right. So, Kamadhenu instead of a mule, they imagined it to be a cow; cow being the sacred animal for Hindu mythology and a women's head with the feathers and peacocks tail and so on.

You see that people were thinking along the same lines. Chimera is very similar to what you would see as Yali; Yali is a Tamil mythological creature. So, if you go to any of the temples, the older temples in Tamilnadu; you would be able to see Yali; so, these are there on all the pillars of the temple. So, Chimera has something similar; Chimera is a Greek mythological creature which is a lion with the head of a goat from its back and a tail with the snake's head.

And actually, Yali is also that; Yali has the lion head, and the tail is actually a snake, but you also have teeth from an elephant. It is almost like, you wanted to look at all the cool features, put it them together. Tarasque is a Christian mythological creature, and it is a dragon with a lion's head and a bear's legs; ox-like a body covered in a turtle shell and so on. So, why I show this is because to understand what people imagined and what people thought of doing. Because people were looking to enhance tissues, people were looking to add additional features to what would improve a regular animal.

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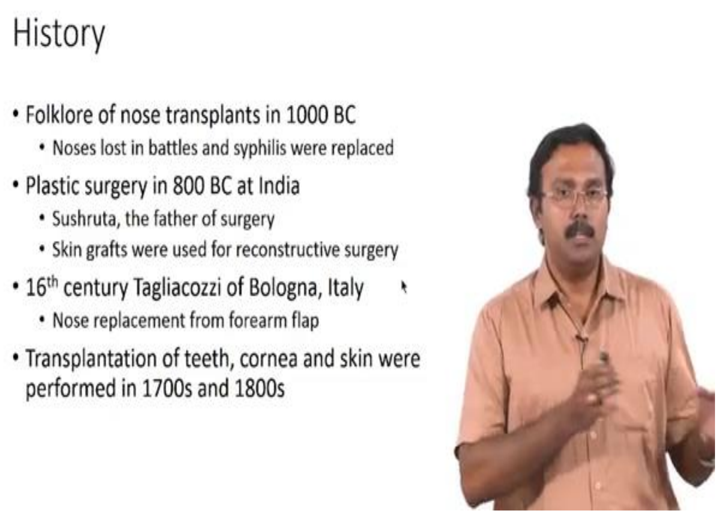

So, leaving beside mythological history; if you were to go into real history, there are folklores of nose transplants which happened in 1000 BC. So, 3000 years back, people had lost noses because they were in battles and they got syphilis.

And if you have syphilis, it proceeds to extreme cases, where you lose your extremities such as nose and ears and things like that. So, losing a nose was a problem because you looked ugly when syphilis happened. So, people wanted to replace that, and they tried to put transplants. The officially recorded plastic surgery was done here in India, and Sushruta, who is considered as the father of surgery did this at 800 BC.

Here, he tried to use skin grafts to create reconstructive surgery; which is what is being done even now. When you try to do skin grafts, that is what an autograft would be. An autograft being, somebody goes through a burn injury, you take the victim skin and try to apply on the wound. Can you think of another autograft other than skin?

Student: Sometimes, we use the saphenous vein.

Ok.

Student: During bypass surgery.

Yes, bypass surgeries usually use your own vein, and that would be an autograft too. And there is actually a long gap between 800 BC and 16th century; there is not much of a record of what has happened between that time. But in the 16th-century people tried to build nose replacements using the forearm flaps. Transplantation of teeth, cornea, skin were all performed in the 1700s and 1800s.

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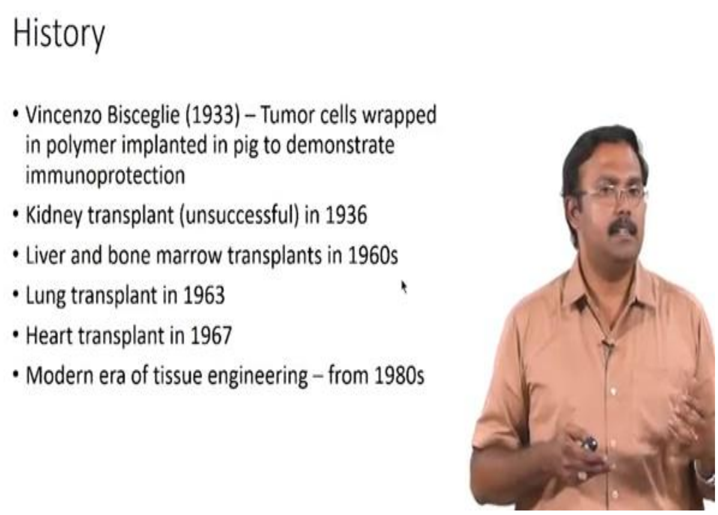

And in 1933, people were looking at immune rejection, and they were trying to understand how you can protect some implant from an immune system; so, what they did was they took tumor cells and wrapped it using a polymer.

They implanted it in a pig to show that this polymer can prevent immune rejection. The kidney transplant was first done unsuccessfully in 1936, and liver and bone marrow transplants were done in the 1960s and so on. A lung transplant was done in 1963, a heart transplant in 1967. Thus, a modern era of tissue engineering itself started sometime in the 1980s, and this is a very recent development.

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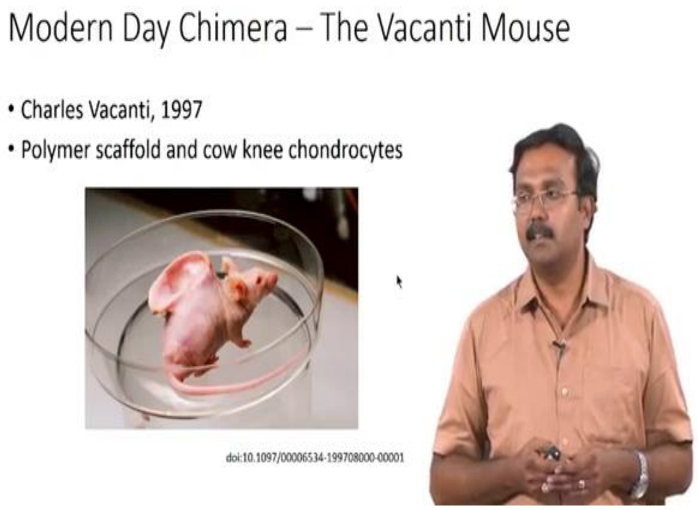

So, this is a modern-day Chimera; Charles Vacanti actually did it and what he did was he took a polymer scaffold and seeded it with cow knee chondrocytes. Chondrocytes are cells which are there in cartilage, and you put that in SCID mice; this is an immune-deficient mice and showed that you could create an ear.

Obviously, this is not a functional ear; this should only be for plastic surgery, just for the aesthetic reasons. It cannot help you with listening or anything, but it was a start, and this was done in 1997; there have been many other recent studies.

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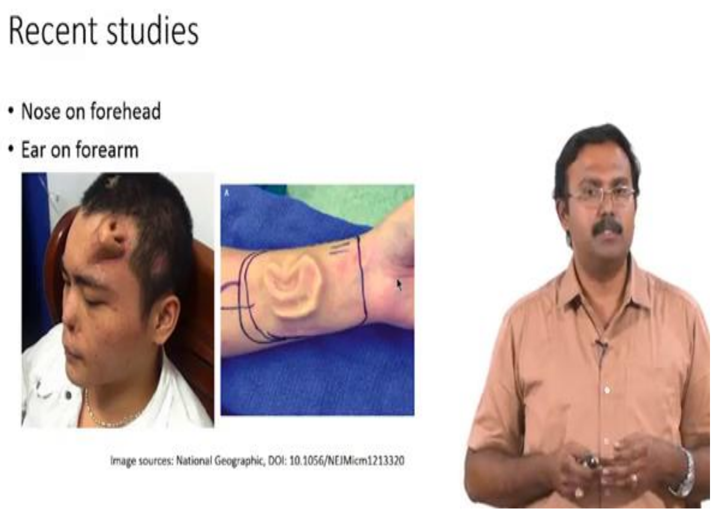

I do not know if anybody has seen this image where you see the forehead having a nose. So, this was on the first page of the Hindu; maybe a couple of years back. This was done in China; A guy met with an accident and lost his nose. Then, the Chinese doctors decided to put a polymer scaffold on his forehead and let the cell seed themselves and create a new nose. And this was eventually transplanted to his nose, and I hope he is healthy.

But the other one you see is an ear on a forearm. So, this has been done multiple times now; Recently it was done for a US army officer; I do not remember her name, but anyway she lost her ear in combat, and they grew an ear on her forearm and replaced it. Again, it is only for aesthetic reasons. I do not think it provides the functionality, but it has been reasonably successful.

And there was an article which basically said forearm is the best place to grow an ear or something like that. So, people have been quite successful in doing that. So, these are the more recent studies that probably happened within the last 5 years or so.

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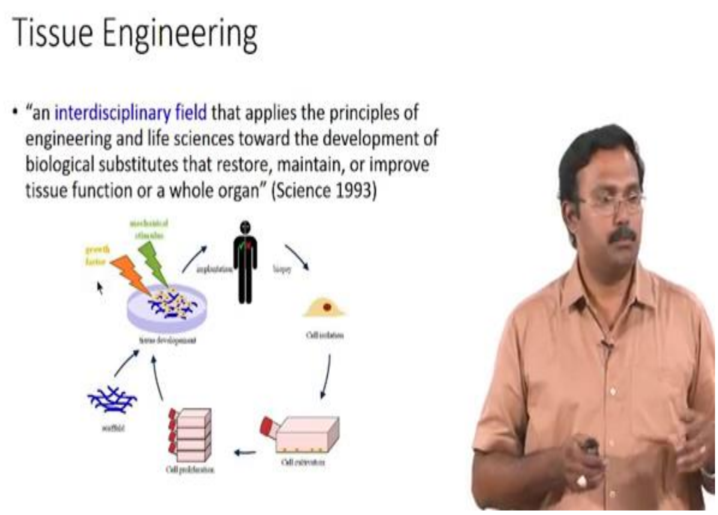

What is tissue engineering? The paper defined the term itself in an article published in Science, 1993. This was written by Robert Langer and Joseph Vacanti; Joseph Vacanti is different from the Charles Vacanti; they were not related. So, Joseph Vacanti is a medical doctor, and Robert Langer is a chemical engineer.

So, these two people came together to write a paper; This was a review article which was published in 1993. So, they defined tissue engineering as an interdisciplinary field that applies the principles of engineering and life sciences; towards the development of biological tissues that restore, maintain or improve tissue function or a whole organ; This is what the definition itself is.

So, what you see here is basically an image from Wikipedia. So, there is damaged tissue, and you take some cells out of that person; then, culture the cells, you get enough of the cells, put them along with a scaffold and give them the signals. With everything combined, you now should have a fully functional tissue; which should replace the damaged tissue and the person is recovered after that.

So, that is what this image represents; this is exactly what you try to do. The challenges are, identifying what type of cells; how to isolate the cells; how to culture the cells; how to design scaffolds; how to make sure the cells attached to the scaffolds; how to make sure the scaffolds do not get rejected; what kind of signals should be provided; and what time it should be provided; at what rate it should be provided; whether it should be provided in sequences or not; and what are the biophysical cues are required; and then with all that hopefully it will have the function to the end ok. So, that is the idea; the challenges in the steps which have been shown here.

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The first term in this definition was interdisciplinary field right. So, it is also one of the hot tags to have, but it is truly an interdisciplinary field, and it was defined as an interdisciplinary field 25 years back; it is not because you want to get funding; so we call it interdisciplinary right. Why do I say it is interdisciplinary? What disciplines do you want, what expertise do you want?

Student: Life sciences, materials science.

Ok, life sciences, material sciences.

Student: Doctor; get medicine expert.

Medicine; Ok, what else?

Student: Mechanical engineer

Ok, mechanical engineers, you also have to justify why you are saying all these, but we will get to that.

Student: Chemist.

Chemistry, ok.

Student: It is developmental biology.

Ok, So developmental biology.

Student: Also, maybe synthetic biology.

Synthetic biology; Ok, anything else that you can think of?

Student: Aesthetic biology.

What?

Student: Aesthetic.

Aesthetic biology?

Student: Like aesthetic experts.

Ok, so aesthetics. So, are you from engineering design?

Student: Someone who knows it like from the art side for ethics.

Ethics, from; from what side?

Student: The arts; humanities.

Oh, humanities ok; humanities is different from arts.

Student: Chemical engineer.

Ok, thanks; otherwise, I will be wasting my time.

Student: Instrumentation.

Ok, so let us first justify why we have all this. So, life sciences; it is quite obvious we are working with the living system; thus, we should have life sciences. So, why specifically development biology?

Student: Because if you want to regrow some kind of cells, you can make the cells into tissues by using stem cells.

Ok.

So, development biology is the domain which actually says how tissues are developing. If you have an understanding of that, hopefully, you can recreate it. So, what about material sciences; why do you want material sciences?

Student: Biocompatible main thing, the materials whatever we are taking it should be biocompatible.

So, why do we even need materials?

Student: Of course, we are dealing with polymers because of many of the things;

Why should we use polymers? So, why should we even use materials; why not just use cells?

Student: As a medium for cells, scaffold

Mammalian cells are adherent cells; they need a substrate to which they can adhere to; they cannot just grow like suspended bacterial cells; so that is why we need materials. So, why do you need a material scientist?

Student: there are some of the materials which can be biocompatible in nature.

Ok.

Student: So, material sciences people can know what are the materials that can be actually biocompatible in nature.

They can design the materials which would be compatible and also functional. So, it is not just compatibility; compatibility can just mean that it is not toxic; It should also require some functionality with that; why do we need medical experts?

Student: To execute it.

To execute it. So, that is there.

Student: To perform clinical trials and stuff.

So you are reducing them to technicians; they are more useful than that. So,

Student: Our end goal is to put it in the human body.

Ok.

Student: And they have an understanding of it.

Ok, you are getting information about the anatomy and physiology sure.

Student: And they will be required for surgery.

Ok, for implanting the material, you need a surgeon ok; what else? They are the ones who can identify the problem; so, it starts from them. So, see many times what happens is we as engineers do not really know the need. Some of the requirements, we just take it for granted; we do not think it is a significant need, but turns out they are actually important needs.

Recently, I was talking to a doctor. He is a dentist. So, he was saying there is a severe problem in dental issues, where people undergo cancer; especially, bone cancer. And you need to have some small-diameter vascular graft which has to be placed. And engineering those have been a big challenge, and he was looking to understand what would be the issues there.

I would not have thought of vascular grafts as an application for dental procedures and especially in cancer patients. I would have thought of it for the usages in cardiovascular procedures. So, those kinds of things we might not know because those were the guys who are actually doing it every day right. So, it is crucial to have a conversation with them. There was another doctor who gave a talk here sometime back.

So, he actually was talking about the heart valves. So, I do not know if anyone of you has seen a heart valve, not of real one like the mechanical heart valves, have you seen a photograph or anything. So, the mechanical heart valve basically looks something like a regular heart valve with the flap, and there is a cylindrical metal which is covered by a cloth. So, this cloth is usually present, so that it can be sutured to the patient and it will key hold it in the proper place.

So, the metal which comes in contact with the blood, all that the flaps which come in contact with the blood, all that is entirely biocompatible and people try to coat it with different materials to ensure that it is compatible. But this cloth was something which was causing a problem, but without a cloth, they could not implant it. Otherwise, it will get displaced. Finally, these guys were sitting together and with a group of engineers and they figured, just remove the cloth and put holes in the cylinder. And that holds it in the proper place. It removes a major limitation which has been causing clogs and clots in the implant.

So, it is a very simple solution, which was proposed by an engineer, but nobody would have guessed that there was a problem there; unless a doctor came to them and said that hey this is a problem. So, doctors are very useful in identifying the problem; so why mechanical engineers?

Student: If you are designing blood vessels and the flow dynamics of the blood when and how it could impact.

Ok.

Student: Every designer has modeled for it so that we can probably test it before we implant it. Or if you are modeling anything for bones, so will the material which we were using be able to take on the stress which would be applied on it once implanted or any other body movements that can affect implant actually. Will it be able to perform all the different,

Yeah.

Student: Case in which we can move.

The mechanical stresses which our tissues go through have to be understood. And you need some expertise in that, and there are also mechanical signals which can actually regulate how the cells migrate and cells differentiate; so, that also needs to be looked at. There are different aspects where a mechanical engineer could contribute. See we are all standing upright right; it is actually the worst thing to do.

It is not good for your knees; it is not good for your joints; you are putting all your body weight on your ankles, which are probably crying for you to sit down. You are much better off when you walk in force because your stress in your body weight has distributed much better. So, you are going through severe stresses, and this needs to be understood, and this might have to be emulated for making it into viable tissue. So, mechanical engineers can help you there. So, chemistry; why chemistry?

Student: I do not know whether is clarity or not, but that there are prosthetic arms and all which can detect whatever if the person thinks in a particular way that is reflected in the fingers; So, a chemist understands chemical signals to be used in that way?

I do not know exactly what is being used to get that; I have also seen lectures where that is possible. But I do not think it is chemistry, and it is more with electrical engineering because it is not that it is being implanted in their body for them actually, to have a chemical connection. It is mostly just put on top of an amputated arm or something. So, I would think it is more about the electrical signals rather than chemistry.

Student: Nervous system.

Yeah. I do not have enough understanding of the electrical engineering aspect actually to comment on that. But that brings to an aspect where electrical engineers can also be useful because you have nerves and heart which have electrical signals and also muscles. So, all these things have electrical signals which are being processed.

So, chemists can be very useful because they are the ones who can tell you how to design materials. So, that is one major step where they can help you, and they can help in how actually to functionalize materials. So, you need to know what chemistry is required for actually functionalizing a material and so on. And aesthetics yeah that is quite obvious and humanities as you said; for ethics, it could be useful to have a humanities person, but probably I would like to bring them at the end of the project so that they do not kill the project on day one.

So, chemical engineers are basically working in this domain for a long time because they have the expertise concerning polymer engineering and also for transport, fluid mechanics. So, chemical engineers know a little bit of everything.

When I joined chemical engineering; one of my professors used to say this ‘chemical engineer can speak chemistry to engineers and engineering to a chemist,’ so that you can basically show off as if you know something; even when you do not. So, you can fool people that way. Anyways, you actually know a little bit of everything; They can contribute, at least I hope I can.

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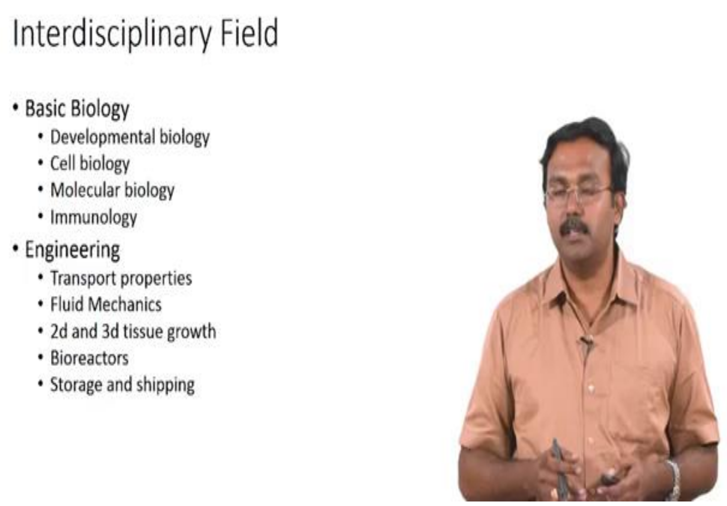

So, we will go into some of what we have already mentioned. We will see what else; I have basic biology. In that, you had mentioned developmental biology. You also would like to have cell biology and molecular biology because you are ultimately want to know how the cells are to be cultured and if they have to be engineered in some way and immunology because ultimately you want to know what the rejection process would be and how you can prevent that.

Engineering, I have just clubbed all engineering's together and put it as transport properties, mechanics 2d, 3d tissue growth, reactors, and even storage and shipping; so, wherein industrial engineer would be useful right.

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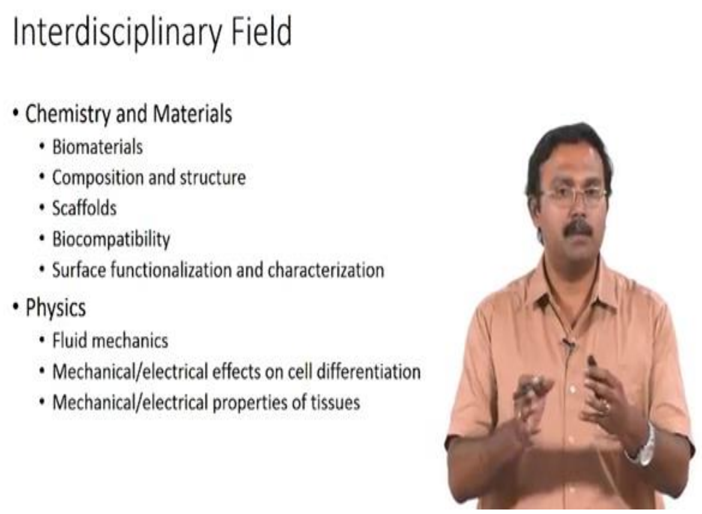

So, chemistry and materials people have clubbed together because they kind of works hand in hand because you want to design biomaterials; look at compositions and structures; how the scaffolds can be biocompatibility, surface functionalization, and characterization.

Any time you prepare a material you have to characterize it thoroughly to understand it fully; you need to have enough expertise in chemistry, without that you would not be able to understand what you see from an FTIR or an XPS and so on. So, then I would have to spend a little more time on the characterization aspects. It is crucial to understand how you can characterize biomaterials.

Physics people are also useful because they also have understandings of the fluid mechanics, mechanical and electrical effects on cell differentiation, electrical properties of tissues, and so on. So, I am just clubbing them all together as a physicist.

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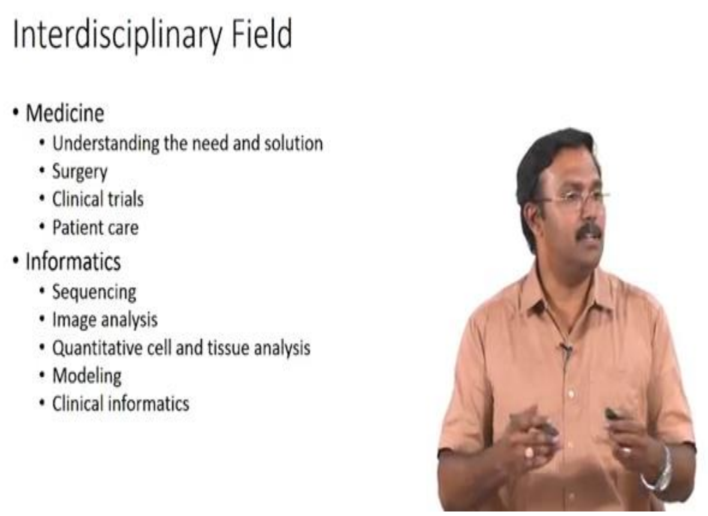

In medicine for understanding the need and solution, surgery, clinical trials, patient care after surgeries, and so on, you need medical professionals. Last but not least is informatics for any kind of work which happens today, you do need informatics people, it could be for sequencing, image analysis, quantitative cell and tissue analysis modeling or even clinical informatics and so on.

For different reasons, you need different people, and all of these people have to come together actually to make it into a viable industry. So, this kind of cross-pollination is required for the field to emerge and be a more successful thing. That actually is one of the major challenges in the field.

Because it is challenging for people to communicate when they do not speak the same language; where people with different kinds of training usually do not speak the same language. So, you go and talk to a basic biologist; the way they think would be very different from the way an engineer would think. And even a traditional research-based engineer or industry-based engineer, they are going to think very differently.

I like to narrate this story. I do not know if you guys have already listened to the story before, but you might have to listen to it again. So, when I was a Ph.D. student. The head of the department at that time he had his Ph.D. in transport phenomena related to done downstream, drying and all those things. So, he went into an industry job. It was a polymer wire manufacturing company.

They have a system where there was an extrusion of this polymer wire, and it was being spun on a spindle in an X shaped fashion. What happened was a wet polymer wire coming out and deposits on the spindle. And as it was spun out, there was like some difference in the thickness depending on which part of the spindle it was being assigned. Some places were thicker, and some places were thinner because there was a little bit of stress because of this wet pulling.

His boss asked him to solve this problem. So, he was fresh out of his Ph.D.; He looked at the problem, started looking at underlying transport phenomena; wrote down the Navier stokes equation and tried to solve it. So, he came up with this, and it must have been in the 60s or 70s; so there were no computers or anything.

He spent about 25 days trying to solve the problem and then went and took a nice engineering report to the management boss. Management boss then said good; you know how to implement it, let us call the worker and let us implement it. The worker was called, and he was like, that problem was solved already. Boss asked, what did you do? We just put a fan there. It was wet, that was a problem; so we just put a fan there, and it was dry, and it did not; so it is about how you think right.

Usually, you would not think of that solution because you have come to a point where that solution seems stupid to you, but that works, and that is all you need; you need a solution that would work right. So, this is an extreme example which I am giving, but between an engineer and a basic biologist; you would always find this difference.

A biologist always wants to know why it is happening; to me, I do not care as long it happens, it happens; it is good to know why it happens, but more importantly the outcome has to be there. So, the difference in this approach causes a lot of problems when you are trying to collaborate and trying to establish things.

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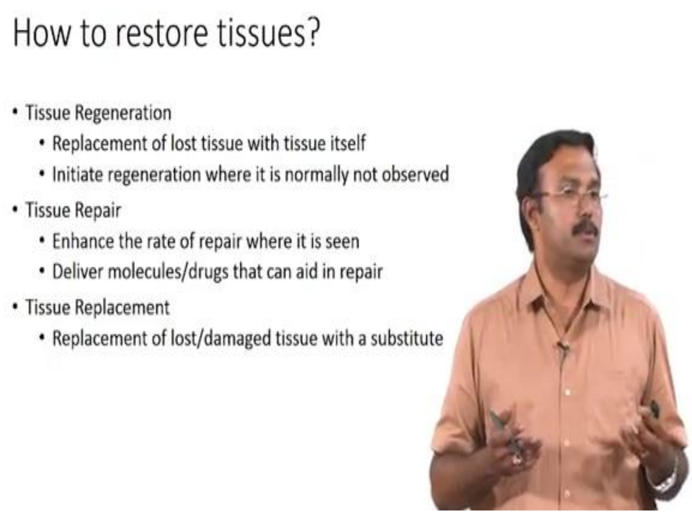

We already defined the ultimate goal is to restore tissues; how do you restore tissues? I like to call these as three R's of tissue restoration, and this is tissue regeneration, repair and replace. Regeneration is basically where you try to replace lost tissue itself and initiate the regeneration; where you normally do not observe it, you try to provide some support so that it can regenerate.

You can have tissue repair; you enhance the rate of repair where it is needed, you can also deliver molecules or drugs that can aid in repairing the tissues, and the last one is to replace. When all else fails what you do is replace the tissue; you take the tissue out and put a new substitute there. Hopefully, that will take care of the function, where the actual tissue was supposed to do. So, these are the way tissues are supposed to be restored.

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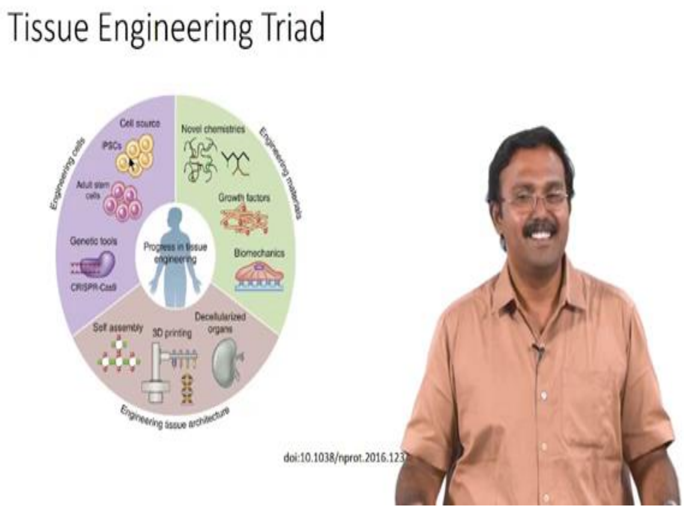

For accomplishing this, there is something called that tissue engineering triad. So, this is an updated tissue engineering triad which was published in 2016; again by Langer. So, this was published in nature protocols; Thus, the tissue engineering triad itself talks about three things; you have cells, materials, and signals.

Those are the three things here, and they have also put what the new cool aspects which have actually come out. For the cells; there are new cell sources, and there are new technologies for engineering the cells. So, you have things like CRISPR-Cas which can be used for engineering the cells; you recently have the development of IPSCs. So, what are IPSCs?

Student: Induced Pluripotent Stem Cells.

So, induced pluripotent stem cells; what are they?

Student: These are the, they take differentiated cells and reverse them back.

Somatic cells are reversed to become pluripotent by using four transcription factors; so, that is what an IPSC is. So, those kinds of cells have made sure that you can actually have personalized medicine now. So, all I would need is some tissues cells from the patient, and I can make it into a pluripotent cell and then differentiate it into the type of cells I want. So, that would give a personalized medicine.

You also have signals; Now, people have understood novel chemistries, people are looking at different growth factors, people have a better understanding of the signaling molecules which can be used and people also now understand that mechanical features and physical and electrical cues can actually help in cell differentiation. Because of all these things, we have a much better understanding of how to engineer materials for providing the desired signals.

The last, but not least; we also have very cool technologies for creating tissue architecture. Starting from self-assembly to decellularized organs to 3D printing; There are just too many technologies which have come up in the last 10 years which are now giving a lot more promise towards the field of tissue engineering; evolving into something which is entirely successful.

Thank you.