Advances in Additive Manufacturing of Materials: Current status and emerging opportunities

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Lec 29 Introduction to Biological System

I am continuing my lecture on introduction to biological system, particularly I will start with the cell fate processes. So cell fate essentially means that how one cell type can transform to another cell type and this I will be explaining you using the example of stem cells. And in the last lecture I think I completed the cell signaling processes involved in the cell fate processes as well as the apoptosis and necrosis as the two pathways for the cell death process. Now stem cells, stem cells I think many common people in the society they heard of stem cells either by reading newspapers or by news on the television and so on, because stem cells have revolutionized the healthcare treatment around the world. So what are the stem cells? Stem cells are unspecialized cells. What it means that stem cells on their own does not have any unique function or any special function physiological function but it has different attributes which makes stem cells so attractive across the different healthcare domains.

One is that differentiate to show or differentiate to essentially form different specialized cells or to show or to demonstrate specialized functions and the word differentiation essentially means differential gene expression. So this is one of the cell fed processes that I have introduced you in the earlier lecture. So you have the cell proliferation is one cell fed processes, cell differentiation is another cell fed processes. Another attributes of the cells just by virtue of being cells, it has the ability to divide, certainly it should be there.

But at the same time, it has the ability to renew themselves for long periods of time. And this particular property is called stemness. So, one is the stemness and one is the differentiation ability of the cells. Now what you see here this you have a quiescent stem cells like you know they then becomes an active stem cells. So these active cells they can do they can follow one of the two pathways.

One of the pathways it can go to self renewal process. And self-renewal process it can go to then it can divide and so on. So, these are multiple stem cells or if you give some biophysical and biochemical stimuli for the stem cells, they can undergo differentiation. I repeat stem cells on their own they do not have any specialized functions, but it has the unique ability to undergo differentiation to either neurogenesis. Neurogenesis, that means

it is the process of differentiations to the functional neurons.

I repeat the phrase called functional neurons. So it is the process of differentiation to functional neurons. That means the differentiation to neurons itself is not sufficient unless you show that these neurons also can function like a natural neurons which is contained in the nervous system. It can undergo differentiation to osteogenesis, osteo means bone. I mentioned to you earlier, osteo means bone.

Osteogenesis essentially means stem cells undergo differentiation to bone cells. Adipogenesis, adipogenesis essentially means it is adipocytes, this is fat cells. Osteoblast I have mentioned you earlier this is bone cells. This is called adipogenesis that when stem cells undergo differentiation to fat cells. Chondrogenesis essentially chondro anything chondrocytes essentially means it is a cartilage cells.

So, when stem cells undergo differentiation to cartilage cells, it is called chondrogenesis. So, these are like 4 different examples as how stem cells can be differentiated to form different type of functional cells and then it is called neurogenesis, osteogenesis. At the same time I will also mention that in many scientific study, when people show that stem cells are differentiated often their electrophysiological functionalities often not reported. So without showing that functionality of the differentiated cells, we cannot say that differentiation is complete and then mature cells have formed at the end of the differentiation process. Which are the factors which govern the stem cell differentiation because I mentioned that differentiation is a cell-fate processes and I am explaining you using the example of stem cells.

Like mechanical or electrical stimuli, for example, over at least for last 15 years or so we have been working on the electric field stimulation of stem cells and we have shown that electric field in combination stimulation in combination with the substrate functionality can drive the stem cells through different differentiation pathways. You can use soluble factors like you know there are there are different chemical compounds or there is differentiation inducers, which can be added to the culture medium And these differentiation inducers are essentially you know arguably they should be different whether when you essentially allow the stem cells to undergo differentiation to bone cells or neuron cells and so on. So depending on which pathways you want to activate, you have to use that pathway specific differentiation inducers. Third one is the surface topography, like you can see that this is a step kind of things, right. So, this step function like there is a specific group height, the group depth, you allow stem cells to be contained in these particular groups and that actually topography will influence the cell fate processes.

Another one is stiffness and then depending on typically if it is a osteogenesis. like bone formation or bone cells differentiation is favored on elastically stiff substrate, okay. So, when the biomaterials or scaffolds are elastically stiff, often it promotes osteogenesis and bone formation. This is like known in the scientific community. Like tissue, as I mentioned that tissue is essentially a collection of tissue is tissue composed of, that I have written, self-assembly of similar cells of identical origin with the ability to perform a specific physiological function.

So, this is the textbook definition of tissue. Then tissue is derived from a French word means "to weave". So weave means that means the tissue essentially contains a fabric. It is a kind of a biological fabric. which is contained in any functional organs.

So what are the major components of tissue? Tissue must contain cells. Tissue must contain extracellular matrix. I think you have got some basic fundamentals of the cells. What are the characteristics of eukaryotic prokaryotic cells? I will also explain your extracellular matrix in the subsequent slides. So tissue in a broad can be described as a collection of cells and ECM that performs a given function.

So, depending on whether it is a epithelial tissue, its function is different. Whether bone tissue, its function is, if it is a neuron, its function is, if it is a cardiac tissue, its function is different. And due to the presence of both minerals like inorganic component here calcium phosphates like hydroxyapatite or collagenous proteins like organic components, mineralized tissues. So, mineralized tissues example is bone, bone has very good combination of strength and toughness and stiffness. So, you already remember the strength, toughness and stiffness if you have a stress versus strain plot.

So, typically if it is a viscoelastic type of deformation like a polymer, so it has a this kind of , so the area under the curve is called toughness. So, the slope of the initial part it is called it is a measure of stiffness. So, slope of the initial curve is called elastic modulus and it is a measure of stiffness and strength means what is the kind of maximum load bearing capability. All these 3 terms has been sufficiently explained in some of the earlier lectures of this course. So, what are the 4 major tissue types? The 4 major tissue types essentially are mentioned here and you can see in these 4 major tissue types I have mentioned epithelial tissue like which provides protection and composed of very tightly spaced cells and with characteristic cell shape typically it is of cuboidal shape as I have shown you before.

Connective tissue, it is a more, it offer mechanical support and it is a fibrous tissue and it is made up of cells separated by non-living material like extracellular matrix. So extracellular matrix contains proteins and so on, so these are like non-living material.

Muscular tissue it is like a muscles and it has an active contractile tissue and it produce to produce force and cause motion and these actually movement within internal organs and 3 different type of organs it will form is a skeletal muscle tissue, cardiac muscle tissue, smooth muscle tissue. Then fourth one called nervous tissue, it provides control and it controls the body function by nervous organs like brain, like spinal cord. So, this is the central nervous system or peripheral nervous system.

CNS stands for central nervous system, PNS stands for peripheral nervous systems. So, if PNS is damaged, it is often repaired by or regenerated by some of the 3D printed scaffolds. People have done several experiments, several studies around the world. Central nervous system, if it is damaged often human patients their mobility will be impaired. So and also in CNS neural tissue forms the brain and spinal cord.

If there is a spinal cord injury that is that can be very very fatal. And PNS forms are cranial nerves and spinal nerves and inclusive of the motor neurons, okay. So these are like very basic introduction to major tissue types that I think one needs to know. some biological description from the textbooks or adapted from this particular source, connective tissue like bone, tendon and fat. So, you can see that cells are dispersed.

You have this very closely spaced epithelial cells that will form epithelial tissue like skin surface. You have a muscle tissue like cardiac muscles, smooth muscles and skeletal muscles and you can see that these are like well straited muscle tissue, muscle cells and you have a nervous tissue, it is called brain, spinal cord and nerves. So, you have a cardiac muscles, smooth muscles, skeletal muscle, you have skin surface, you have a lining of hollow organs, you have a bone, tendon and fat. So you have a nervous tissue so these are like 4 different tissue structures that we need to kind of know. So this is just to show that you know how myoblast or muscle cells they fuse together and they form a muscle tissue.

So myoblasts when they are determined to form the muscle tissue then they start proliferating right. So if you have a myoblast cells like muscle tissue cells it starts doubling up proliferate then it starts aligning. So alignment is one of the major things and once it starts aligned then they form the multinucleated cells right. So that individual cells have more than one nucleus and then when it forms maturation when it undergoes maturation then the you can see these different fibers form in the extracellular matrix because then it will form a mature muscle tissue. So this is starting from myoblast going to the myotube this is called myotube.

In this process you can see the proliferation and differentiation process that actually cooperate well to form the myotube formation. So, I repeat mononucleated muscle cells

or myoblast cells, they undergo proliferation, then undergo fusion to form multinucleated cells, they undergo maturation in the process of differentiation process, they form that myotubes forms which has a very well aligned structures and also it is multinucleated characteristics. Now, extracellular matrix has been mentioned to you before, but what you see here very clearly, so these are kind of this is one cells like the way I am hatching it, so this is a cytoplasm of a cell, right. As the name suggests extracellular matrix essentially means it is the structure, biological structure which is there or which exists outside the cell, okay. And what you see the extracellular structure also has some kind of a collagen fibers, fibers like structure.

You have a proteoglycan complex and proteoglycan molecule. And if you have a fibronectin type of a protein that I have mentioned earlier when I was explaining you the protein adsorption of the biomaterial substrate, it is a fibronectin adsorption and this is called transmembrane protein. So, this is called transmembrane protein. Essentially, these protein structures are integrin proteins. These are like integrin proteins which essentially extends or which extends between the extracellular space to the intracellular space, intracellular cytoplasm.

So, these are like integrins, okay. And this is the nice bilayer structure of this transmembrane protein. This is the lipid bilayer. And this lipid bilayer also contains, you remember, this kind of channels like voltage-gated potassium channel and sodium-potassium channel and so on. So, extracellular matrix in a sense it contains collagen, elastin fibres, proteoglycans, fibronectin, laminin and integrins. So, these actually constitute extracellular matrix.

So, it has typically molecular weight of around 10 to the power 5 to 10 to the power 6. It essentially represents interconnected network of macromolecules. It essentially non-living macromolecular structures and multimodal like processes cell binding domains that means this particular fibrous structure has multiple sites which will anchor the cells, which will facilitate the cells to adhere or to get attached to the extracellular matrix, this kind of anchoring sites. ECM is over time as the different type of cells, they establish their cooperative movement, extracellular matrix is synthesized, they are secreted, they are oriented and they are modified by the cells itself and they can regulate the cell fate processes through binding of a class of receptors called integrins that I have mentioned. What are the cell fate processes that we have mentioned that adhesion, spreading, cell shape change, cell shape change or cell migration, cell differentiation and cell apoptosis.

So, these are like some of the cell fate processes that I have been mentioning to you, right. So, let us move on to more on the last point. section of this particular set of lectures on introduction to biological system and materials for human healthcare. Now what you

see in this particular slide is a human skeleton structure right and this human skeleton structure if you see that from top to bottom, so head to knee, head to toe, what we call head to toe, many parts of the human body at different anatomical locations can be reconstructed or repaired or regenerated. I repeat the term can be reconstructed or repaired or regenerated.

by synthetic material components or synthetic materials which are produced outside the human body like implants, like scaffolds and so on, again I will define those things in the subsequent slides and these materials which will form the scaffolds or which will form the implants, they are called biomaterials and whatever I have shown You before like 3D printing of metals for the stainless steel 316, titanium 6, aluminum 4, vanadium, they are classic example of that. classic example of biomaterials which are used in different parts of the human body for the purpose of that reconstruction or repairing or regenerating the damaged tissue, tissues in that specific anatomical location. So, if you see the cochlear implants for the hearing impaired patients, the cochlear implants actually is used inside this. Many elderly patients you will see that they use cochlear implants. So, that is a medical device and that contains the biomaterials and implants.

Then you have a dental implants, I will show you one such examples on in the context of 3D printing of ceramic dental implants, there I will introduce more details about dental implants in particular. Then you have a shoulder prosthesis, if the shoulder joints had to be reconstructed, we need to use the implants. Pacemakers when the cardiac functionality is not synchronized in elderly patients or the patients with problems in the cardiovascular system, then pacemaker is to be inserted to synchronize the cardiac motions. So, that is also an example of the medical device, you have a spinal implants like instead of central nervous system or kind of spinal cord injury injured patients then you need to you need to insert the implants, this is the place. Acetabular components in the total hip replacement, total hip arthroplasty, total hip joint replacement or knee joint, many patients have knee surgery like a total knee joint replacement, some human patients they undergo some accidents so some part of the leg there they need some metal plates this is for use for bone fixation in the hand injury they have also that prosthetic limb.

So what I am trying to show you and then another life threatening disease is kind of cardiovascular problems if somebody's heart attack or some coronary artery diseases or you know plaque in the arteries then it has to be dissolved or that has to be essentially that has to be cleared then they use that coronary stents, artery stents again these artery stents are made up of the either nickel titanium alloys or titanium alloys and so on. What I am trying to tell you from head to toe different parts of the human body can be reconstructed or repaired or regenerated by synthetic materials and implants. So I stop here and then I will continue in the next class from this part onwards. Thank you.