Introduction to Tissue Engineering

S. Swaminathan
Director
Centre for Nanotechnology & Advanced Biomaterials
School of Chemical & Biotechnology
SASTRA University
Thanjavur 613 401
Tamil Nadu

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1. What is tissue engineering?

Tissue engineering is defined as "*the application of the principles and methods of engineering and life sciences toward the fundamental understanding of structure function relationships in normal and pathological mammalian tissue and the development of biological substitutes to restore, maintain or improve tissue function"* – Y.C. Fung.

"*The application of biological, chemical, and engineering principles toward the repair, restoration, or regeneration of living tissues using biomaterials, cells, and factors alone or in combination*" – C. T. Laurencin.

From these definitions, it is clear that tissue engineering has the potential to address the organ failure and tissue loss. This is because current clinical approaches for restoring the organ or tissue function are organ transplantation, surgical reconstruction, or use of prostheses. However, each treatment strategy has its own merits and demerits.

For example, organ transplantation is only treatment at the end stage of organ failure. This procedure involves mainly remove the failed organ from the patient and replaced with the procured organ for transplantation. With today's medical advancement, it can be done for any organ – liver, kidney, heart, etc. But this whole procedure should follow legal and ethical considerations. Organ transplantation society encourages the use of organs donated from the cadavers instead from the living donors in order to reduce the risk for living donors while transplantation. Although such therapies have merit to save the lives of thousands, shortage of donor organs and tissues as the patient waiting list number has increased per year tremendously; and requirement of immunosuppressant limits its potential to address organ failure crisis.

In case of surgical reconstruction, there is no possibility of immune rejection because of the use of patient's own tissue (autologous). However, autologous grafting chiefly requires surgery at donor site; even limited supply, inadequate size and shape (Complaint mismatch) with donor site morbidity restrict its use towards tissue loss. In some cases of organ failure, say for example loss of hand; or loss of leg; patients are advised to use artificial prostheses. But they are biologically non functional and they do not behave physiologically as a true organs. Examples are artificial heart, heart valves, prosthetic hip, and artificial breast. But these materials are subject to fracture, wear, toxicity, inflammation, which could induce the long term complications and rejections at the later stage.

Hence limitations of existing therapies provoke the search of new technologies or therapies as tissue engineering to combat the organ failure and tissue lose crisis. Prof. Cato T. Laurencin defined Tissue Engineering as "*the application of biological, chemical, and engineering principles toward the repair, restoration, or regeneration of living tissues using biomaterials, cells, and factors alone or in combination*".

2. Tissue Engineering Triad

Biomaterials, cells and growth factors are known as the "Tissue Engineering TRIAD".

There are three different strategies that could be adopted for the regeneration of new tissues. In the first approach cells can be used as therapeutic agents to restore the functional tissue. This approach mainly involves the isolation of cells from different cell sources (autologous, allogenic; syngenic and xenogenic) and even use of stem cells using a special technique called stem cell therapy, placing them in the site of interest for improving the tissue function.

The second approach involves the exogenous delivery of growth promoting substances like growth factors using the carriers (polymeric or lipidemic) can stimulate the endogenous stem/progenitor cells for the specific differentiation thereby replacing the lost cells or tissues.

The third approach is to use artificial 3-dimentional scaffolds or matrices for the growth of cells where cells can be either recruited from the host tissue *in vivo* or seeded *in vitro*.

We will now see from the animation below as to how biomaterials, cells and growth factors can be used alone or in combination to regenerate bone.

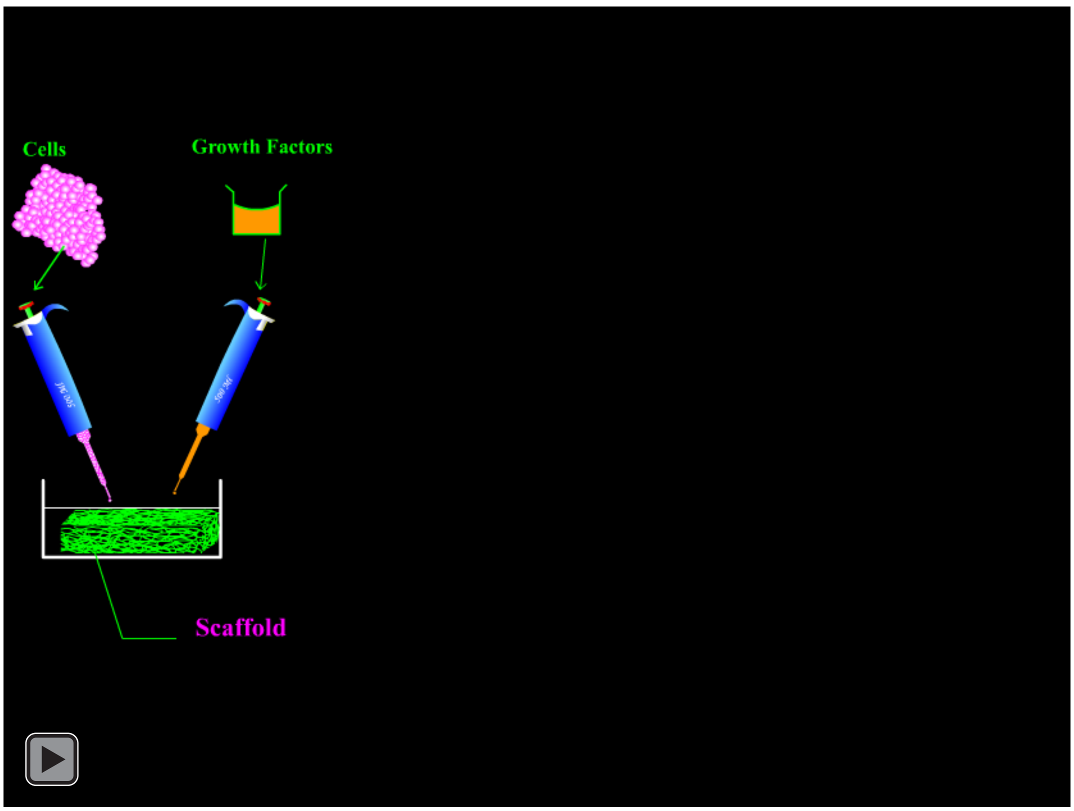

Figure 1. Tissue engineering triad

Note: Can be viewed only on Acrobat Reader 9.0 and above

Even though these strategies can overcome the problems associated with the current clinical treatments, there are few scientific challenges to construct a tissue or organ using these approaches. For example, use of cells: limited supply of autologous cells; requirement of immunosuppressant for allogenic source; disease transmission associated with the xenogenic source; ethical considerations with the use of stem cells are the major challenges in case of first approach.

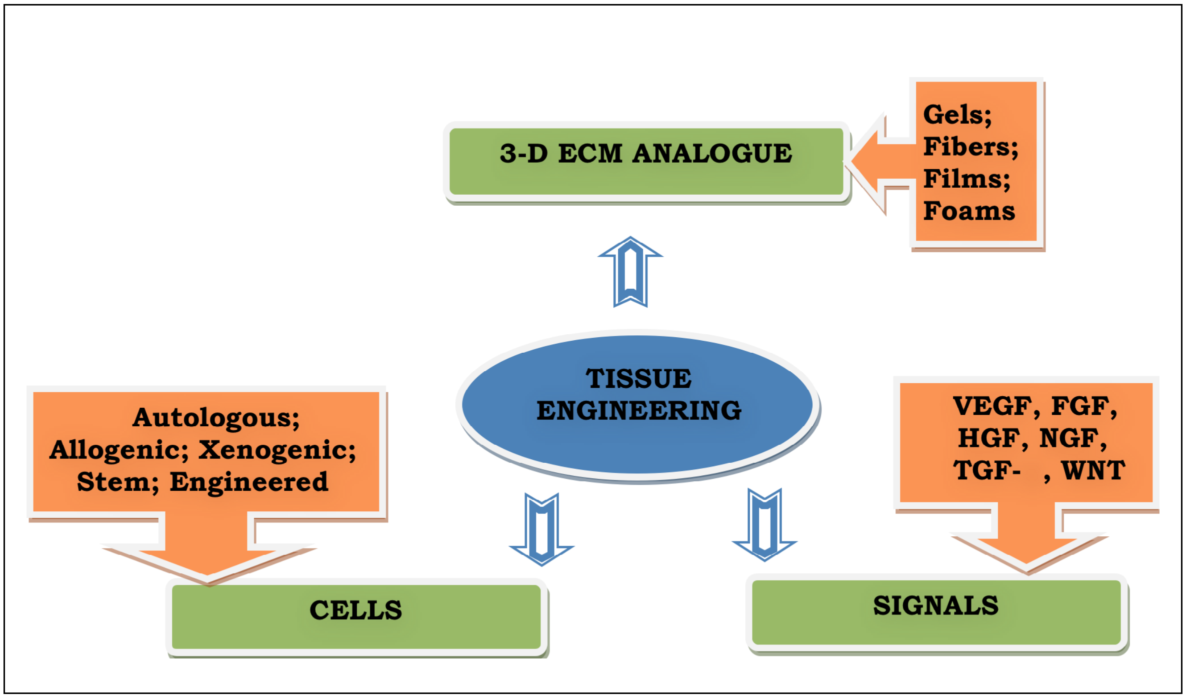

Fig 2: Tissue engineering approaches

Specific differentiation of stem cells with desired functionalities with the appropriate growth factor delivery is still unresolved question in tissue engineering. Even the third approach of tissue engineering is the development of artificial extracellular matrix (ECM) analogue towards the regeneration of specific tissue. In this, attempt to make ECM analogue with respect to chemical environment surrounding the cells within a native tissue; architecture; dimensions with signals is really tricky. Moreover construction of matrix should not provoke any immune response; toxicity i.e. it must be compatible to the host tissue; whatever the scaffold that we have prepared should control the cell fates such as cell adhesion, migration, proliferation, differentiation as like our native.

What part of the body tissue engineering replace?

• Skin	• Kidney
• Vascular tissue	• Pancreas
• Thyroid gland	• Esophagus
• Adipose tissue	• Cartilage
• Liver	• Bone
• Nerve	• Bladder

3. Challenges in tissue engineering

In conclusion, there are few challenges to be answered for the reconstruction of functional tissues. They are:

1. How do we develop a close approximate biological replica?
2. Should the tissue be produced *in vitro* implanted *in vivo*?
3. What type of scaffold should we choose?
4. How do we manufacture?
5. What cells are to be used?
6. Under what conditions can cells expand without affecting its phenotype?
7. What regulators do we use to stimulate the cell proliferation and differentiation?

Hence to answer all the questions, it is necessary to understand the basic things such as how tissue gets organized in the organ? What are the different basic types of cells? How do we classify the defects based on the tissues? How well can a tissue repair its defects? What are the components comprising the tissue?