

Chapter 17

Nanotechnology and Its Use in Tissue Engineering

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ABSTRACT

Tissue Engineering is an emerging field with promises for a better future. It is a blend of biology and engineering. Millions of people lose limbs and body parts as the results of tragic accidents. Patients with diabetes, ischemia, suffer from non-functional pancreas, heart. Tissue engineering plays a major role in their lives. Instead of organs donated voluntarily (long waiting is a problem here), tissue engineering has the potential to come up with replacements. The combination of nanotechnology with engineering and biology has made some excellent improvements. In this chapter, the aim is to provide very basic knowledge about the art and science of blending tissue engineering with nanotechnology. At the same time, it highlights related fields like issues of biocompatibility, fate of nanoparticles, side effects, work with stem cells, etc.

INTRODUCTION

It is hard to part with a family member or a friend, so is the pain of accepting the loss of limb for good. Be it an accident or a surgery, losing a limb imparts several problems to the regular day-to-day functional behavior. A relatively new field in science ‘tissue engineering’ (Langer & Vacanti, 1993) comes with the promise of repairing and replacing non-functional or amputated limbs with great efficacy. For a high blood pressure patient it is very likely to have heart blockage due to blood clotting; as a result blood pressure increases rapidly. Conventional treatment includes regular blood thinning pills, exercise and controlled diet, but there is no surety to avoid bigger blockages

and heart attack. Thanks to the advancement in science: in past few decades it has been possible to overcome these issues by a bi-pass surgery or by dilating arteries using a stent. Again here tissue engineering comes into picture. This field is blend of medicine, science and engineering where synthetic implants are put into non-functional or missing limbs while keeping in mind several issues like biocompatibility, biodegradability, chances of immunorejection etc. The implants reproduce the functionality of the missing limbs and the victim can enjoy a normal life up to a considerable period of time.

Building up tissues needs proper niche like blood vessels to allow nutrient and gas exchange, which is the greatest source for thriving of cells,

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and a solid surface on which cells can hook on to. Material science, especially nano materials play a big role here. Nanomaterials come in different size and shape; like fibrous, disk like, circular, mesh like. These materials must have comparable mechanical strength, elasticity and rheological properties. For encouraging cell attachment and carrying different biomolecules (those act as tissue inducers) the surface chemistry should be easily tunable. Above all the materials should be preferably biocompatible, biodegradable and with very high surface area. To summarize the vast amount of research work done in the interdisciplinary area of nanotechnology and tissue engineering, this book chapter has been divided into mainly four points:

1. Scaffold.
2. Nutrients.
3. Nanoparticle.
4. Applications.

This book having focus on nanotechnology we plan to discuss part 3 in detail, still we will touch upon other key points.

WHAT ARE 'SCAFFOLDS' FOR TISSUE ENGINEERING AND HOW DO WE FABRICATE THEM

Scaffolds are critical constituent of tissue engineering. Within the tissue, cells are surrounded by ECM or extra cellular matrix which provides cell support and monitors cell behavior by cell-ECM interaction. So it is important to engineer biomaterials (scaffolds) that mimic the complexity of ECM both *in vitro* and *in vivo*. Interconnected pores having proper size help in controlled movement of drugs, nutrients and cells. Nanotechnology can be exploited to mimic the ECM by making nanofibers, nanotopographic surfaces, nanostructured scaffolds. But there are discrepancies. Naturally occurring collagen is around 50-500 nm while artificially made fibrils are of 10 μ m diameter. So improved

nanotechnological procedures are required for desired size, shape, functional properties and mechanical strength. Broadly, the procedures can be classified into two categories (i) bottom up approach where molecules gather one after another to build bigger architectures and (ii) top down approach where a larger structure breaks down to smaller nanoscale constituents. In practice there are many widely researched methods of making highly porous yet interconnected nano-scaffolds. (i) Self-assembly: where amphiphilic polymeric materials are allowed to assemble. The driving force is non-covalent, inter- and intra-molecular interactions, weak hydrogen bonds, ionic bonds (electrostatic forces), hydrophobic interactions, and van der Waals forces. For example, EAK16-II (AEAEAKAKAEAEAKAK) (Zhang et al., 1993) is the first self assembles peptide scaffold used for tissue engineering. (ii) Solvent casting and porogen leaching: This process involves the dissolution of the polymer in an organic solvent, mixing with nanofillers and porogen particles, and casting the mixture into a predefined 3D mold. The solvent is subsequently allowed to evaporate, and the porogen particles are removed by leaching (Mikos et al., 1994). (iii) Electrospinning: this technique is attractive since the polymers arising out of it have structural similarity to the tissue extracellular matrix (Bianco et al., 2009, Greiner & Wendorff, 2007). However residual solvents can be detrimental to the attaching cells. To overcome this drawback gas foaming is used to prepare highly porous biopolymer foam. (iv) Thermally induced phase separation (TIPS): this phase separation procedure requires the use of a solvent with a low melting point that is easy to sublime. For example dioxane could be used to dissolve polylactic acid, then phase separation is induced through the addition of a small quantity of water: a polymer-rich and a polymer-poor phases are formed. During quenching, the solvent crystallized and the polymer was expelled. Apart from these conventional techniques, there has been a lot of research regarding building of a

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