CHAPTER 9

Cell Guided Tissue Regeneration in Biologically Derived Materials at the Molecular Interface

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Summary

Most currently available biomaterials used in areas of reconstruction, repair and artificial devices are not designed to regenerate tissue but to cover or fill defects and/ or perform a mechanical function. A regenerative or responsive biomaterial is defined as one that recruits wound healing and precursor cells to form new viable tissue *in vivo* by stimulating and guiding the body's *in vivo* regenerative potential.

But, at what level of the tissue is regeneration controlled? It is suggested that a single cell must be given local control of its microenvironment at the cell adhesion nano-interface (~30-100 nm), where the cell forms its adhesions and perceives the biomaterial. The only way this control can be achieved is by using a responsive biomaterial system that is defined as one whose chemical composition responds to the biochemical factors (e.g. proteases) secreted by cells during regeneration, whose chemical composition permits the storage of water and growth factors, whose fibril nano-structure and mechanical properties allow for the attachment of cells at cell-material interface, and most importantly maintain a mechanical force balance between adhesions and the matrix nano-fibrils, whose structured 3-D assembly from nano to micro to macro can bear the *in vivo* mechanical loading.

This chapter identifies structural parameters and molecular linkages of the extracellular matrix that contribute to the internal mechanics of the cell and regulate a remodeling of an implanted biomaterial at the nano-interface.

The concept of nanoscale regulated tissue regeneration is introduced by identifying various parameters of the biomaterial scaffold that would allow a cell to remodel the biomaterial without the addition of any growth factors, or other regulatory molecules by being influenced by composition, intermolecular linkages, nanostructure, nanomechanics of the biomaterial, and the biological/ chemical/ mechanical balance at the cell-biomaterial interface.

KEYWORDS: Tissue Regeneration, Three-Dimensional Nanostructure, Biological Macromolecules, Cell Nano-mechanics, Biomaterial, Nanomaterials, Nanotechnology, Nanomedicine.