Definitions

• **Nanotechnology:** The use of materials and systems whose structures and components exhibit novel and significantly changed physical, chemical and biological properties by gaining control of structures at the atomic, molecular, and supramolecular levels.
  
  – 1 nm = 1 billionth of a meter

• **Tissue Engineering:** 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.”
Tissue engineering

• **Goal**
  To enable the body to heal itself by introducing an artificial transient microenvironment that the body recognizes as “self”, and in turn uses to regenerate “neo-native” functional tissues

*How do we do this?*
Direct a population of cells to form a living tissue, structurally and functionally indistinguishable from that found in nature
Tissue Engineering - Components

- Cells
- Biomaterial/scaffold
- Factors/Signals

Engineered Tissue
Role of Scaffolds

• Present a surface/structure that closely resembles the extracellular matrix (ECM)

• Surfaces that could maximize favorable biological responses (cell-matrix interaction, Protein-matrix interaction)
TE : Challenges

• **Enormous**
  – Generate, insert, maintain functional tissue
  – Biological and Engineering Challenges

• **Dynamics vary**
  – Tissue to tissue
  – Macroscopic structure
  – Composition
Scaffolds used for Tissue Engineering

- Biocompatible
- Biodegradable
- Interconnected porous structure
In Vivo – Ulnar Defect
Extracellular Matrix

- Hierarchical structure with nano-sized features
  - Figures not shown
Cell Responses to ECM

• ECM-Instructive capacity
  – Information encoded in the matrix architecture forms a multidimensional map
• Cells use this map to guide their behavior
• Information expressed as signaling gradients – chemical distributions/differential expressions of ECM components/topology
Hierarchical Assembly

- Multifunctional nature – Consequence of ECM’s modular and hierarchical architecture
- Cell-matrix interactions modulated by multiple binding domains, chemistry and topography of the various ECM constituents
- Dynamic 3-D inter-relation is constantly kept in balance and influenced by both internal and external stimuli
Structure of Bone

- Hierarchically structured
- Nanoscale features
- Properties depend on architecture at all levels of hierarchy
  - Mineralized fibrils in bone

*Figures not shown*
Can Nanotechnology Provide An Alternative Platform To Fabricate Constructs that closely mimic the ECM
Nanofabrication

Electrospinning

Self assembly

Phase separation

Figures not shown

Figures not shown
Electrospun nanofibers as tissue engineering scaffolds
Can nanofeatures modulate cell functions
Human Mesenchymal Stem cell Proliferation and Differentiation on Nanoscale HA-PLAGA Matrices

HMSC Proliferation

Alkaline Phosphatase activity
Human fibroblast cells on nanofibers
Effect of fiber diameter on cell proliferation
Ectopic bone formation in mice

In vivo 3D micro CT scans showing ectopic bone formation using nano-and micro fiber matrices
Why does the Nanostructure increase cell growth?

• Nanophase Ceramics, Metals, Polymers, Composites
  • Increase In Vitro Functions of Mammalian Cells: Regeneration
  • Dynamics of cell material interactions occurs at all levels
    – Cells interact three dimensionally when the matrix feature size is smaller than the size of the cells
Uniqueness of Nano

- Increased Number of atoms and crystal grains at their surfaces
- High surface area to volume ratio
- Altered Surface energy

- Figure not shown

Webster et al., Expert review Medical Devices, 2004
Why does the Nanostructure increase cell functions?

- Initial Protein Interactions with Nanophase Materials: Putative Cause

- Figure not shown

Webster et al., Expert review Medical Devices, 2004
Nanomaterial Surfaces

• Altered Protein Adsorption
  – Improved wettability
  – Similar sizes

• Increased unfolding of proteins

• Promotes availability of specific cell-adhesive epitopes

• Figure not shown
Books Edited

1. Biomedical Nanostructures
   - Edited by: Kenneth E. Gonsalves, Craig R. Halberstadt, Cato T. Laurencin, Lakshmi S. Nair

2. Nanotechnology and Tissue Engineering: The Scaffold
   - By: Cato T. Laurencin, Lakshmi S. Nair
Conclusions

Nanostructured scaffolds

• Better mimic the structure of the ECM
  – Potential advantages in promoting cell responses
• Combining surface chemistry & biomimetic topography – better design strategy
Conclusions

• Better designs to improve biomechanical properties
• Study the mechanism of cell interaction with nanostructures/impact of structures on biological system
• Development of cost effective/reproducible nanofabrication techniques
• Novel high resolution in situ imaging and analysis tools
Thank You