Transitioning from Nanomedicine to Picomedicine: What's on the Horizon ?

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Statement of Purpose: Inspired from biological systems, nanotechnology has already revolutionized medicine including improving the prevention, diagnosis, and treatment of numerous diseases. This talk will summarize efforts over the past decade that have synthesized novel nanoparticles, nanotubes, and other nanomaterials to improve medicine. Efforts focused on the use of nanomaterials to minimize immune cell interactions, inhibit infection, and increase tissue growth will be especially emphasized. Tissue systems covered will include the nervous system, orthopedics, bladder, cardiovascular, vascular, and the bladder. Due to complications translating in vitro to in vivo results, only in vivo studies will be emphasized here. Materials to be covered will include ceramics, metals, polymers, and composites thereof. Self-assembled nano-chemistries will also be emphasized. However, while significant promise has been made in using nanomaterials in medicine, particularly regenerative medicine, some problems remain (such as toxicity and manufacturing). This talk will further provide the latest concerning nanoparticle toxicity and manufacturing issues. Moreover, this talk will also introduce a new research direction in picotechnology which may generate materials even better for medicine that what nanotechnology has accomplished.

Methods: For orthopedic applications, numerous 3D tissue engineering scaffolds have been fabricated using polymers, ceramics, and metals. Osteoblast (bone forming cells) functions including adhesion (up to 4 h), proliferation (up to 5 days) and differentiation (up to 21 days) on different 3D tissue engineering scaffold topographies were systematically investigated [1]. Moreover, using a standard rat-calvarial defect model, 3D tissue engineering scaffolds were implanted and topographical effects on bone formation assessed. Similar studies have been conducted for cartilage applications using chondrocytes (cartilage producing cells) and rabbit osteochondral in vivo assays.

For anti-cancer implications, nanopatterned poly(lactic-co-glycolic acid) (PLGA, 50:50 PLG/PGA, wt%) 3D surfaces with similar surface chemistry but different topographies have been fabricated. Nanopatterned PLGA substrates were investigated for their ability to inhibit numerous cancer cell functions, including osteosarcoma, breast epithelial adenocarcinoma cell (MCF-7), and lung epithelial cancer cell adhesion, proliferation, apoptosis and vascular endothelial growth factor (VEGF) secretion using standard techniques [2].

For cardiovascular applications, 3D PLGA:carbon nanofiber (CNF) composites were formulated as a novel type of cardio-patch to promote cardiomyocyte (heart muscle) growth [3]. In this study, PLGA and CNF weight ratio densities were altered to investigate changes in cardiomyocyte functions including adhesion (up to 4 h), proliferation (up to 5 days), and protein (fibronectin and vitronectin) adsorption.

Results: For all materials, traditional methods such as scanning electron microscopy (SEM), Raman spectroscopy, and water contact angle measurements verified similar scaffold surface chemistry and wettability but varied topographies. Cytocompatibility in vitro and in vivo assays demonstrated enhanced osteoblast functions (including adhesion, proliferation, intracellular protein synthesis, alkaline phosphatase activity and extracellular calcium deposition) on nanostructured compared to nano-smooth 3D tissue engineering constructs. An SEM study of osteoblast attachment helped to explain the topographical impact substrates have on osteoblast functions by showing altered filopodia extensions and migration rates. Similar results have been observed for cartilage. In a novel manner, efforts have been made develop in situ sensors which can provide real time information on tissue growth.

Nanopatterned PLGA samples for cancer applications demonstrated for the first time significantly decreased cancer cell functions (including decreased proliferation rate, increased apoptosis and decreased VEGF synthesis) on 23 nm featured PLGA surfaces compared to all other PLGA surface topographies fabricated (specifically, nanosmooth and submicron rough 300 and 400 nm surface-featured PLGA surfaces) without the use of chemotherapeutics. In contrast, healthy cells proliferated more on the 23 nm featured PLGA surfaces compared to all other PLGA samples.

For cardiovascular applications, in vitro analysis indicated greater surface area and nanoroughness when increasing CNF ratio amounts until they reached a 25:75 [PLGA:CNF (wt:wt)] ratio where the surface roughness at the nanoscale decreased. Vitronectin and fibronectin adsorption assays showed greater initial adsorption on 3D scaffolds with greater nanoscale roughness which may provide a mechanism for greater cell responses on such nanostructured scaffolds.

In a move towards picotechnology, we have stimulated atoms in nanomaterials to control electron distributions to further increase surface energy. We have seen that through such control at the pico-level, we can achieve the best tissue growth.

Conclusions: Nanostructured polymers, metals, and ceramics promote bone, cartilage, anti-cancer (bone, breast, and lung), and cardiovascular applications. Recent studies controlling electron distributions at the picolevel have further promoted tissue growth.

References:

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