Nanoparticles as Modulators of Cell Shape and Function

review of presentation given by Dr. Prasad Shastri of Vanderbilt University

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Dr. Shatri's research group at Vanderbilt has been engaged in tissue regeneration studies, specifically with growth factors and stem cell based therapies.[i] One application is found in generating new bone in vivo by what is called a bioreactor, an artificial space within the body where the body's natural healing mechanism.[ii] The future goal of this work is realizing the engineering of tissue and whole organs. This article does not reach those heights, but rather approaches those same issues at the level of the cell and how stress applied to it modulates the cell's function.

Factors Impacting Cell Function: stress changes shape of a cell, which in turn changes its contact relationships with other cells and changes the cell's chemistry, changing its functioning. When a cell is cultured in a medium, upon a material, that material sometimes has a marked effect upon the way the cell grows, or even enters into stasis. The way it grows can be physically marked to an anisotropy in the material or in its proliferation. Dr. Shastri's group wanted to investigate the degrees of change by first searching for a way to establish a baseline for independent control of surface topography.

There are many methods for influencing the size, shape and function of a cell, but each of these methods reported in the journals is very specific to the material/cell interaction. The problems of the variety of responses appears to be chemistry related, but the investigators chose to examine the possibility that a simple consideration such as surface roughness and texture of the material had a large role in the material/cell interaction: surface oxidating plasma, ion-beam etching, acid treatment, electrostatic deposition, or chemical modification. All are specifically useful, but too specific for a general solution to controlling surface topography.

Advantages of nanoparticle assemblies as functionalization tools are in their periodicity and regularity, plus their ability to self organize. Dr. Shastri's group found that in their investigations that nanoparticles within a size range of 50 ηm to 100 ηm provided effects that were highly separable from other materials with well defined surface characteristics. Nanoparticles also bring the advantage of being predictable in both their manufacture and application.

One such material drawn from the biomaterials engineering field is acid etched titanium that is widely used for bone replacement structures. The acid etched surface produces a roughness that provides a large surface area for bone adhesion. Another material Dr. Shastri's group chose for comparison was glass. One of the conclusions drawn from these comparisons of materials is that their chemistry doesn't matter so much as the physical, surface topography and at the nanoscale it is the most significant.

In this regard of scale, Dr. Shastri's group investigated a range of roughness, expressed as a metaphor of ping-pong ball to beach ball sized features in relation to a human scale of texture. All such features at the nanoscale, and within the methods of their construction, are eminently suited to a fine level of control for replication. The size range had been established through tests that revealed their candidate materials outperformed conventional materials that have already demonstrated wide application with high success.

These measures of performance were against metabolic activity where 300% to 400% gains were observed. Alternately, the investigators also found they could inhibit growth and hold cells in stasis by modulating the roughness features. Where in a bone scaffolding site the emphasis is naturally focused upon cell proliferation, here too the nanoscaled biomaterials outperformed conventional biomaterials. The differences were not nearly as dramatic, but certainly a doubling in proliferation could be observed.

Conclusions drawn from this research include biological responses in cells can be controlled by surface bound physical cues; surface topology is dominant factor and nanotopology is significant.

i ***http://www.blackwell-synergy.com/doi/abs/10.1111/j.1525-1594.2006.00307.x***

ii ***http://www.pnas.org/cgi/content/abstract/102/32/11450***