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Hylonome

Perspective Article

Summary – Joint regeneration using functional tissue engineering

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This session examined how degenerated joints might be reconstructed through tissue engineering. The term "tissue engineering" was first used at a National Science Foundation sponsored meeting in 1987. More recently, at another National Science Foundation workshop, the following definition was proposed:

"...the application of principles and methods of engineering and life sciences toward fundamental understanding ...and development of biological substitutes to restore, maintain and improve [human] tissue functions."
[http://www.nsf.gov/od/lpa/nsf50/nsfoutreach/htm/n50_z2/slct_shk.htm]

This session included five speakers with topics ranging from basic aspects of bone regeneration and gene expression at the bone-implant interface (**Virdi**), osteolysis at the bone-implant interface (**Schwarz**), issues affecting cartilage repair (**Sah**), *in vitro* testing of biomaterials useful for skeletal tissue engineering (**Lim**) and *in vivo* testing of tissue engineering constructs (**Guldberg**). The organizing theme was joint reconstruction. Most of the research described by the participants was, therefore, geared toward biological substitutes for joint structures, especially those involving damage to articular cartilage or bone.

Some may consider inclusion of traditional joint replacement as not fitting in the context of functional tissue engineering, but I would argue that joint replacement is best viewed as an early, successful step toward biological reconstruction of joints. One of the ideas of tissue engineering is that any biomaterials used will eventually be replaced by natural tissue. In the case of joint replacement, however, researchers are not concerned with eventual replacement of the biomaterials (plastics and metals) by natural tissues, thus somewhat simplifying the problem. A current major concern is establishing and maintaining durable interfaces between the permanent replacement components and the host skeleton. The initial fixation is mechanical but the regenerative potential of the host bone can be enhanced so that biological fixation takes over sooner, and in theory, might provide a long-lasting viable interface. Wear debris from articular surfaces and other interfaces (e.g., connections between modular pieces) can induce osteolysis and disrupt the biological connection between the host skeleton and implant, threatening long-term function of the reconstructions. Thus, there has been considerable interest in assessing this phenomenon radiographically and devising therapies for treatment so that the need to revise the joint replacement is minimized.

Although not yet ready for replacement of joints that have been largely destroyed by diseases processes such as osteoarthritis, already there is considerable use of osteochondral allografts and other treatments, including transplantation of expanded chondrocyte populations, to repair focal defects in articular joints. As with joint replacement, one of the areas of major concern is how to establish long-lasting connections at interfaces, especially those between the regenerated cartilage and native cartilage and host bone. Reconstruction of cartilage and bone through cell transplantation or other means provides an interesting model for thinking about what the design goals need to be. In other words, what are the most important aspects to target – for instance, is return to function with relief of pain (the clinical goals) dependent upon reconstitution of mechanical properties and tissue architecture?

It became clear in the discussions surrounding each talk, that the field is lacking good models to translate knowledge about cell-cell or cell-biomaterial interactions *in vitro* to the behavior of tissue engineered constructs *in vivo*. In some ways, this is simply a revival of a long-standing controversy in biology – the relative merits of *in vitro* and *in vivo* models. Perhaps, the idea of predicting *in vivo* behavior from *in vitro* studies is too ambitious and the *in vitro* work should be viewed as a means of detecting possible mechanisms that might be important *in vivo*. In that way, the model and appropriate questions that can be addressed with the model (whether *in vitro* or *in vivo*) can be more carefully defined.

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