Clinically Relevant Strategies for Treating Cartilage and Meniscal Pathology

Editorial Comment

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Millions of surgeries are performed every year in attempts to treat defects of articular cartilage or damaged or diseased menisci. While many treatment options are currently available to surgeons, none consistently affords long-term preservation of fully functional tissues or prevents the development and progression of osteoarthritis. As such, there is an urgent need for strategies that can restore the architecture, geometry, physiology, and material properties of deficient articular tissues such that full joint function is realized and maintained in the long term. Biologic strategies using the principles of tissue engineering appear to hold the most promise for accomplishing these goals. In pursuit of regeneration of specific tissues, it is vital to remember the “joint is an organ” and all tissues and related pathology must be considered when trying to develop clinically relevant procedures. Therefore, we have assembled a series of articles that explore both meniscal and articular cartilage regenerative strategies.

Cartilage and meniscus are related soft-hydrated tissues that share load-bearing responsibilities in the knee. Both exhibit limited reparative capacity due in part to their avascular nature. For articular cartilage repair, living allografts offer a treatment. Cell-based approaches remain an important area of research, with autologous cell implantation techniques used clinically. To meet clinical

demand for coverage of larger lesions or articular surfaces overcome with degeneration or traumatic injury, these strategies are not practical and generally necessitate arthroplasty. For meniscal repair, surgical removal of damaged regions is the current standard of care. One treatment strategy, most often using a multidisciplinary approach, is to grow clinically relevant grafts in the laboratory for use in cartilage and meniscus repair.

Efforts focused on mimicking grafts for focal defect repair are serving as a foundation for those aimed at scaling up to large defects suitable for replacing even entire articular surfaces. The successful scale up to biologic arthroplasty systems that would replace metal and plastic with engineered living components is confronted by major challenges related to tenuous nutrient support and inability to mechanically protect the nascent and sometimes fragile biologic systems.

Basic science efforts, in vitro culture studies spanning to animal models, provide fundamental insights that bolster translational efforts to the clinic. Musculoskeletal researchers are faced with a conundrum when choosing between the use of clinically relevant human cells where in vivo testing is not practical and cell sources are mostly limited to adult sources or the use of an animal model system where in vivo studies are permissible and cell sources can be readily attained from tissues of varying age. This choice is further complicated because translation of findings from animal to human systems (or even other animal models) is often convoluted, thereby prompting many research groups to work with parallel human and animal model systems.

Conserved across species is an inherent ability of cells derived from younger sources to outperform cells from more mature sources in strategies for regenerative medicine. As such, research is often aimed at capturing the

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Fig. 1 Clark T. Hung, PhD, is shown.

higher biosynthetic activities of immature cell sources, including exploration of stem cells (embryonic or adult) and in vitro priming techniques of adult cells. Included in these strategies are chemical and biophysical stimuli, applied perhaps via direct medium supplementation or cell coculture systems, or sophisticated bioreactors, which are aimed at modulating cell phenotype and tissue development in culture. As the in vivo environment is much more complex than the culture environment, researchers must aim to recapitulate what they believe to be the most salient aspects that can promote and direct functional tissue development.

In addition to possessing mechanical properties to survive implantation into the harsh joint-loading environment, other measures of tissue function, such as their metabolic response to anabolic- and catabolic-inducing agents and to physical stimulation, need to be compared to that of native

Fig. 2 James L. Cook, DVM, PhD, is shown.

cartilage or meniscus to assess the full spectrum of their biofidelity. Ultimately, cartilage or meniscal repair is aimed at eliminating pain and durably restoring diarthrodial function. Considering the former is necessarily omitted as an outcome parameter in culture laboratory studies, it is important to incorporate measures of pain (eg, clinical scoring or measurement of gait) with in vivo work through judicious choice of animal models that provide clinical evaluative measures complementing standard imaging, histology, mechanical, biochemical, and molecular analyses.

As normal human tissues are limited in their availability, functional engineered tissues derived using human cells may serve dual functions, as test beds for in vitro screening of agents (eg, pharmacologic drugs aimed at mitigating arthritis and inflammation) and as clinical tissue grafts for restoration of joint function.