CELL SOURCES FOR CARTILAGE TISSUE ENGINEERING

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Adult stem or progenitor cells have now been detected in most tissues of the body, including those relevant to the musculoskeletal system – bone marrow, bone, periosteum, cartilage, synovium, adipose and muscle. The cells of most tissues have been shown to have at least chondrogenic, osteogenic and adipogenic differentiation potential, and in some tissues, certain subfractions with greater differentiation potential are now described. Despite these advances, the relationship between the various cells of the different tissues is unclear, as is their relative importance in the field of regenerative medicine. There still remains a need for specific markers for these stem cell populations. Furthermore, to harness the therapeutic potential of stem cells for the treatment of skeletal pathologies, novel technologies need to be developed to isolate these cells effectively and efficiently.

Comprehensive comparative analyses, in vitro and in vivo, of the differentiation capability of the various adult stem cell populations are still lacking. Thus, it is still unclear which particular cell source provides the cells most applicable to a given tissue therapy. Comparisons of this type are also needed to address the notion that sorted populations will provide a better differentiation result in either ex vivo or in vivo tissue engineering and tissue regeneration. Indeed, it has to be considered that the sorted populations may actually be less useful because other cell types present in less purified populations may be beneficial for a given differentiation process to succeed.

Complicating the analysis done to-date is evidence that age- and gender-related differences may also play a role in the relative effectiveness of the isolated cells. For autologous human cell therapies, an added complication is the health status of the patient, which some evidence suggests can influence the number and potency of the stem cells isolated from various tissues. For this reason, several efforts are underway to isolate human stem cell populations that can be used as universal donors, taking advantage of the immune privilege that has been reported for these cells.

Even with optimized isolation and expansion methods for these cells, the field of stem cell-based therapies for skeletal tissues still faces many other challenges. We have yet to develop appropriate tissue engineering or tissue regeneration strategies that can be utilized in the clinical setting. The early promise shown in the preliminary studies of skeletal tissue engineering has been tempered by the realization of the complexity of stem cell interactions within implants, and with host tissues, which must be understood if we are to provide effective regenerative tissues for skeletal pathologies.

Scientists have developed a host of in vitro systems to investigate these issues. For example, our laboratory developed the in vitro system now widely used for the chondrogenic differentiation of stem cells. Variations on this system have been developed for different cell sources and applications. The system was originally developed in a scaffold-free format. However, for tissue engineering of implants on the scale needed for human cartilage pathologies, scaffold-based stem cell chondrogenesis has been widely investigated.

It was quickly appreciated application of biomechanical forces to the developing tissues in vitro would influence the composition and organization of the implants produced. Thus, the mechanobiology approach to skeletal tissue engineering has evolved. However, with the increasing sophistication comes increased cost. Despite the challenges, some of the first products of this field are now making their way into clinical trials.