Is a tissue-engineering approach effective for the treatment of osteoporotic bone defects?

Osteoporosis (OP) is a disease that affects the formation, maintenance, and density of bone. OP is also associated with an increased risk of bone fracture. For those people/patients facing a traumatic injury or tumor removal in the skull, diseases like OP can greatly affect the body's natural ability to repair damaged bone. OP affects 44 million people in the United States alone, with the highest prevalence in women (~80% of all cases). A better understanding of injuries to the skull, along with the effects of OP on the healing process, is important for discovering mechanisms of bone formation that are impaired and effective treatment methods and also for developing a better understanding of the effects of OP.

The purpose of this study was to evaluate the effectiveness of adult stem cells from adipose tissue (ASCs) as a mechanism for repairing bone damage in rat skulls. Commonly, stem cells from bone marrow (BMSCs) are used for repairing bone but, due to the difficulty of cell isolation, pain associated with extraction, and low number of stem cells, this choice may not be the best for future clinical applications. ASCs are easy to harvest and cause only slight discomfort to the patient. This study sought to answer two main questions about bone formation and OP. 1) Compared to normal rats, do ASCs from OP-induced rats alter their ability to proliferate and change into bone? 2) Can insertion of ASC based tissue constructs into the damaged skull of normal and OP-induced rats help heal the injury?

For the first question, the ability of ASCs was assessed in both normal and OP-induced rats. Adipose stem cells were taken from both populations and expanded outside of the body in culture flasks. These flasks were subsequently subjected to specific chemicals that encouraged the cells to transform into bone-like tissues or adipose-like tissues. The results of this study showed that ASCs from OP-induced rats may actually have a lower osteogenic, i.e. bone-forming, potential (decreased alkaline phosphatase and bone gamma-carboxyglutamic acid-containing protein) than normal ASCs, though gene expression during later stages of expansion (runt-related transcription factor 2 and secreted phosphoprotein 1) may suggest otherwise. The proliferation (total cells grown during expansion) and number of generations (how many times the cells replicated) were similar between the normal and OP-induced groups.

The second aim of the study was to determine how ASCs affected bone growth *in vivo* (in living rats with skull injuries). All rats had two cranial holes created which were then seeded with ASCs in a scaffold (a 3D structure used to house cells and simulate native tissue constructs), just the scaffold without cells, or left empty as a control. These three conditions were evaluated over both 6- and 32-week periods after initial surgery. The results indicated that, at the 32-week period, normal ASC and scaffold treatment was more effective than the scaffold alone, while the OP-induced group had no significant difference between the ASC and scaffold group compared to the scaffold group alone. Significantly though, both treatments involving the scaffold in the OP-induced

rats resulted in a larger bone mass density increase than the normal rats.

Cell expansion demonstrated that the characteristics of ASCs from normal and OP-induced rats are slightly different (changes in osteogenic gene expression), but aspects of cell growth and expansion were similar. The *in vivo* studies showed that treatment of bone defects in OP-induced rats was effective, providing hope for human treatment in the future.

Quincy Hathaway *and* ***Tyler Pizzute***
Stem Cell and Tissue Engineering Laboratory
Department of OrthopaedicsWest Virginia University
Morgantown, USA

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A comparison of tissue engineering based repair of calvarial defects using adipose stem cells from normal and osteoporotic rats.
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