Autologous Platelet Enhanced Fibrin (APEF) Compared to APEF with Culture Expanded Bone Marrow Derived Mesenchymal Stem Cells (BMDMSCs) to Enhance Cartilage Repair in an Equine Model

Laurie R. Goodrich, DVM, PhD1, Albert C. Chen, PhD2, Natasha Werpy3, John D. Kisiday4, Paul Morley4, C Wayne McIlwraith, BVSc, PhD, DSc, FRCVS4, Robert L. Sah, MD, PhD5, Constance R. Chu, MD6.

1.California State University, Ft. Collins, CO, USA, 2UC San Diego, La Jolla, CA, USA, 3University of Floride, Gainsville, FL, USA, 4Colorado State University, Fort Collins, CO, USA, 5University of California, San Diego, San Diego, CA, USA, 6Stanford University, Palo Alto, CA, USA.

Disclosures:

Introduction: Culture expanded bone marrow derived mesenchymal stem cells (BMDMSCs) have been utilized in humans as well as large and small animal models to enhance cartilage repair[1]. In some of these studies, culture expanded cells have been placed in fibrin scaffolds alone or in fibrin scaffolds enhanced with platelets. Although the combination of BMDMSCs with an autologous platelet enhanced fibrin (APEF) scaffold would appear to provide both essential growth factors and cellular components of cartilage healing, this combination has not been scientifically studied. The purpose of this work was to investigate whether Autologous Platelet Enhanced Fibrin (APEF) Scaffold with or without bone marrow-derived mesenchymal stem cells (BMDMSCs) could enhance cartilage healing. We hypothesized that 1) the presence of growth factors delivered by platelets in a scaffold would support cartilage repair and that 2) BMDMSCs would further improve repair tissue when evaluated with arthroscopy, histology, MRI and biomechanical analysis.

Methods: Twelve adult horses had a critical-sized chondral defect made in the femoropatellar joint. One joint was repaired with APEF scaffold mixed with culture-expanded BMDMSCs and the contralateral joint had APEF alone. Second-look arthroscopies were performed at 3 months postoperatively. At one year, all defects had multiple analyses performed including arthroscopy, histology (modified O'Driscoll score system), MRI, microCT (with and without Hexabrix), and biomechanics (structural stiffness and material stiffness). Scores from the APEF versus APEF plus BMDMSC repairs were compared using Wilcoxon Signed Rank analyses with significance set at P≤0.05.

Results: Defects treated with APEF with or without BMDMSCs resulted in good to excellent integration and fill as evaluated arthroscopically and histologically although no significant differences were detected between treatment groups (Figure 1). There was a trend for greater Safranin O staining (GAG content) in defects repaired with APEF alone compared with defects repaired with APEF plus BMDMSCs. There was a trend (P=0.09) for defects repaired with APEF and BMDMSCs to have higher trabecular bone edema compared to defects repaired with APEF alone. MicroCT analysis revealed repair tissue thickness closer to the surrounding host cartilage (P≤0.05) in lesions treated with APEF alone (Figure 2). Normalizing for thickness, the material stiffness was similar, and less than normal, for the defects treated with APEF alone and APEF with BMDMSCs. While 11 out of 12 defects repaired with APEF alone had good fill, four out of twelve defects repaired with APEF with BMDMSCs developed bone within the repair tissue.

Discussion: This study suggests that APEF treatment of large osteochondral defects leads to defect fill, possibly through APEF supplying a rich milieu of growth factors. The addition of autologous, culture expanded BMDMSCs did not appear to enhance cartilage regeneration but may stimulate bone formation when placed in this scaffold. Cartilage defects appear to benefit from a fibrin scaffold that contains platelets, most likely due to the growth factor such as platelet-derived growth factor and transforming growth factor-β. Several studies have found that platelet-enriched plasma has beneficial effects on cartilage repair[2]. Additional translational studies are needed to delineate the mechanisms and efficacy of APEF in enhancing repair of osteochondral defects.

Significance: APEF may enhance cartilage healing and can be applied to osteochondral defects arthroscopically. The inclusion of culture expanded BMDMSCs into an APEF scaffold is not beneficial to cartilage repair.

Acknowledgments: NIH NIAMS RC2AR058929-01

Figure 1. Safranin O staining of a defect repaired with APEF alone (top) or APEF with BMDMScs (bottom). No difference in composite histological scores was detected between both groups.
Figure 2. Thickness of defects repaired with APEF alone or APEF with BMDMSCs. Defects treated with APEF alone had greater thickness however; when defects were normalized for thickness, repair tissue of APEF alone scaffolds had similar material properties to APEF with BMDMSCs. * denotes significance.

ORS 2014 Annual Meeting
Poster No: 1272