MEK/ERK cascade, PD98059, to characterize the necessity of each pathway for osteogenesis.

METHODS: hMSCs were cultured in osteogenic media on Col-GAG or MC-GAG scaffolds. Scaffolds were untreated or treated with the DMH1 or PD98059 at 50 mM for 4 days, 14 days, 24 days, 4 weeks, and 8 weeks. Gene and protein expression were measured using quantitative RT-PCR and western blot analysis. Scaffolds were subjected to histochemical and micro-computed tomographic analyses.

RESULTS: Inhibition of the BMPR signaling pathway inhibited Runx2 and BSPII gene expression of primary human mesenchymal stem cells (hMSCs) on MC-GAG. In contrast, inhibition of the MEK/ERK axis downregulated BSPII expression on Col-GAG independent of Runx2 expression. While inhibition of the BMPR signaling pathway resulted in decreased mineralization on both Col-GAG and MC-GAG, inhibition of the MEK/ERK axis only affected mineralization on Col-GAG. When the mechanistic details were evaluated in greater detail, inhibition of the BMPR pathway reduced both Smad1/5 phosphorylation and Runx2 protein expression on both MC-GAG and Col-GAG. Inhibition of the MEK/ERK axis downregulated phosphorylation of ERK1/2 and JNK1/2 without affecting Smad1/5 phosphorylation or Runx2 expression.

CONCLUSION: Interactions between hMSCs and collagen-based materials result in mechanistic differences in osteogenesis. Activation of the canonical BMPR signaling is required for osteogenic differentiation and mineralization of hMSCs on Col-GAG or MC-GAG. The MEK/ERK cascade, intimately tied to JNK activation, is necessary for Runx2-independent osteogenesis on Col-GAG, while completely dispensable in osteogenesis on MC-GAG.

Adipose-Derived Stromal Cells Demonstrate Superiority over Bone Marrow-Derived Stromal Cells in Bone Healing by Enhancing Vasculogenesis in a Murine Model of Irradiated Mandibular Fracture Injury

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INTRODUCTION: Over 60,000 new cases of head and neck cancer were diagnosed in the U.S. in 2016. Radiation is commonly required to reduce recurrence rates and improve survival; however, complications after radiation, including poor bone healing and osteoradionecrosis, contribute to the significant morbidity associated with this disease process. The current standard of treatment of such complications is limited to free tissue transfer. Given the significant morbidity associated with these procedures, it is important to examine the utility of cell-based therapies as a potential translational treatment to promote bone regeneration for irradiated patients. Adipose-derived stem cells (ASCs) and bone marrow derived stem cells (BMSCs) represent translational therapies that can improve osteogenesis. We recently demonstrated that ASCs are superior to BMSCs in enhancing bone healing using a segmental defect model in the rat mandible. We hypothesize that differing mechanisms of action between the two cell types contribute to the superiority of ASC’s to enhance bone healing.

METHODS: BMSCs and ASCs were harvested from male Lewis rats (n=3), plated at a density of 200,000 cells/well, and treated with osteogenic differentiation medium. Alkaline phosphatase stain was performed to evaluate osteogenic potential. Vascular endothelial growth factor (VEGF) was also measured and compared. Finally, ASCs and BMSCs were cocultured with human umbilical vein endothelial cells using a transwell system to study the paracrine effect of these two cell types on vasculogenesis. Student’s t-tests were used to compare the osteogenic and vasculogenic potential of the two groups.

RESULTS: ASCs had significantly less osteogenic potential than BMSCs (11.8 ± 0.9 vs. 16.3 ± 0.4; p<0.05). Conversely, ASCs were significantly more vasculogenic than BMSCs based on VEGF release (3,573 ± 87.4 vs. 1607.0 ± 45.0; p<0.001). These findings translated to significantly greater tubule formation in transwells treated with ASCs.
compared to BMSCs on video microscopy. The properties of ASCs that resulted in enhanced vasculogenesis are associated with enhanced bone formation in vivo and improved healing in our segmental defect model.

CONCLUSION: ASCs and BMSCs enhance bone formation via different mechanisms. While to enhance bone healing as described in this study, the mechanism of a vasculogenic intermediate may hold greater promise in creating a translational therapeutic that more proficiently promotes bone healing and remediates the ravages of radiation injury.

33 Condylar Fractures in 28 Children: Demographics, Treatment, Outcomes, and Long-Term Growth

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INTRODUCTION: The condyle has been described as an important growth center for the mandible. Fractures to the condyle could affect occlusal relationships, jaw growth, and orofacial functions. To date, there have been few reports assessing long-term growth after pediatric condylar fractures.

METHODS: This is a retrospective study at the Children’s Hospital of Pittsburgh (2000–2016). Patients with condylar fractures identified by ICD-9 code and with >1y follow-up cephalograms were included. We examined demographics, mechanism, management, and cephalometric. Age- and sex-matched control values were obtained from the Bolton Cephalometric Standards.

RESULTS: There were 28 patients (18 male, 10 female). Average age at injury was 7.53y (age group 0-6y, n=13; 7-12y, n=13; 13-18y, n=2). Average follow-up was >5years. Thirteen were bicycle-related, 7 were high-speed injuries (ATV, MVC), and 8 were falls. Fractures involved the head of the condyle (47%), neck (41%), or both (13%). Eighteen patients received conservative management (rest, physical therapy; 6 underwent external stabilization, i.e. jaw bra); ten underwent closed reduction (with elastics or MMF). Nineteen patients had a complication related to the fracture; this mostly involved slight deviations of dental midline or chin point and occasional asymptomatic clicking with mouth opening. One patient, who had the most severe fracture, had malpositioned hardware.

Lateral cephalograms were compared to Bolton cephalometric norms. Z-scores were used to compared published Bolton standard normative data to our patients’ SNA, SNB, ANB, gonial angle, ramal height, and body length. Frontal cephalograms were used to internally compare injured and uninjured hemimandibles (bilateral fracture were omitted). The average ratios of ramal height, body length, and articular to menton distance were, respectively, 1.01, 0.94, and 1.00, indicating very minimal differences between hemimandibles.

CONCLUSION: We present the longest-duration follow-up found in current literature assessing mandible growth in patients who suffered condylar fractures prior to skeletal maturity. Our cohort demonstrates minimal operative intervention, minimal complications, and no obvious growth abnormalities. Frontal cephalogram ratios demonstrate nearly equal hemimandibles and lateral cephalogram differences approximate the standard deviations from the Bolton standards. Our data challenges the growth disturbances reported in existing pediatric condylar fracture literature.

A Review of Frontal Sinus Fractures and Associated Ocular Complications - The McGill Experience and Novel Treatment Algorithm

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