

AAOF Award Final Report

Principal Investigator	Zongyang Sun
Co-Investigator	
Secondary Investigators	
Award Type	Biomedical Research Award
Project Title	Enhance Alveolar and Symphyseal Bone Surface Growth with Autologous Stem Cell Sheets
Project Year	July 1, 2014-December 31, 2016
Institution	The Ohio State University
Summary/Abstract (250 word maximum)	<p>Background: This project investigated the effects of autologous mesenchymal stem cell (MSCs) transplantation on mandibular bone surface growth. Methods: First, MSCs were isolated from tibial and mandibular bone marrow of four 4-month-old pigs, cultured and compared for their proliferative, osteogenic differentiation and gene expression. Then, MSCs were fabricated into cell-sheets using temperature-sensitive plates and examined for cell viability. Finally, autologous mandibular MSC sheets were surgically transplanted onto the buccal surface of molar extraction sites and mandibular symphyseal surfaces on one side of five 4-month-old pigs, with the contralateral (control) side only received sham surgery. Six weeks later, the buccal cortical bone geometric size, bone volume fraction (BV/TV,) mineral apposition rate (MAR) and tissue mineral density were assessed by blinded raters using radiographic (CT) and histological methods. Results: Pig mandibular and tibial MSCs were generally similar in gene expression at the mRNA level, but mandibular MSCs proliferated faster, showed stronger osteogenic differentiation and expressed significantly higher BMP4 expression than tibial BMSCs. Both MSCs could be readily fabricated into cell sheets, but the mandibular MSCs were faster. MSC viability was poorer in multiple-layer sheets than in single-layer cell sheets. After <i>in-vivo</i> transplantation, all parameters measured demonstrated higher values on the experimental side than the control side, but most pair-wise statistically analyses were insignificant at an $\alpha=0.05$ level partially due to relatively high variability among animals. Conclusion: Our data confirm the feasibility and potential to use mandibular MSCs in cell-sheet form for <i>in vivo</i> transplantation for bone surface growth.</p>
Were the original, specific aims of the proposal realized?	<p>The following specific aims were included in our proposal (with approved revision of SA1 in 2015).</p> <p><u>S.A.1 In Vitro Aim: Optimize fabrication of bone marrow derived mesenchymal stem cell (BM-MSC) sheet for in vivo application.</u></p> <p><i>S.A.1a: Compare BM-MSC derived from jaw and long bone for their proliferation and osteogenic differentiation capacity.</i></p> <p><i>S.A.1b In Vitro: Develop a high-throughput and reliable method</i></p>

	<p><u>to prepare 3-layer BM-MSC sheets for in vivo application.</u></p> <p>These experiments have been completed and the data have been presented/published (thesis) and submitted for journal publication.</p> <p><u>S.A.2: In Vivo Aim: Examine the effects of autologous BM-MSC sheet transplantation.</u></p> <p><u>S.A.2a: Compare buccal alveolar surface growth between post-extraction sites treated with and without autologous BM-MSC sheet transplantation.</u></p> <p><u>S.A.2b: Compare bone modeling of the facial symphyseal surfaces with and without transplantation of autologous BM-MSC sheets.</u></p> <p>These experiments have been completed. The data will be presented at the 2017 IADR meeting and included in future publications.</p>
<p>Were the results published? If not, are there plans to publish? If not, why not?</p>	<p>Part of the results have been published in a thesis: L</p> <ul style="list-style-type: none"> • Lloyd BR. Comparison of bone marrow mesenchymal stem cells from limb and jaw bones: The Ohio State University; 2016. <p>A manuscript has been accepted:</p> <ul style="list-style-type: none"> • Lloyd BR, Tee BC, Headley C, Emam HA, Mallery SR, Z S. 2016, Similarities and differences between porcine mandibular and limb bone marrow mesenchymal stem cells. Archives of Oral Biology, under review. <p>We are also in the process of preparing two more manuscripts based on the data from in vivo experiments for publication</p>
<p>Have the results of this proposal been presented? If so, when and where? If not, are there plans to do so? If not, why not?</p>	<p>Yes, the results have been presented as an oral presentation:</p> <ul style="list-style-type: none"> • Lloyd B, Tee BC, Headley C, Mallery SR, Emam HA, Z S. 2016, Comparison of BM-MSCs from Limb and Jaw Bones, J Dent Res 95(Spec Iss A). 2016 AADR meeting, Los Angeles, CA <p>Two more presentations will be given at the 2017 IADR meeting:</p> <ul style="list-style-type: none"> • Mu S, Zhou YC, Tee BC, Emam HA, Sun Z. Effects of BMSC Transplantation on Extraction-Site Alveolar Bone Growth. 2017 IADR meeting, San Francisco, CA • Swan A, Tee BC, Zhou YC, Emam HA, Sun Z. Effects of BMSC Transplantation on Mandibular Symphyseal Surface Growth. 2017 IADR meeting, San Francisco, CA
<p>To what extent have you used, or how do you intend to use, AAOF funding to further your</p>	<p><u>For my career, this funding has:</u></p> <ul style="list-style-type: none"> • Helped us to find that mandibular MSCs are likely better than long bone MSCs for craniofacial bone regeneration. Based on these data, our future tissue engineering studies for

career?

craniofacial bones will focus on using mandibular BMSCs.

- Brought us great opportunities for publications, grant applications and collaborations with other investigators.