

AAO Foundation Award Final Report

Principal Investigator	Dr. Kyungsup Shin
Type of Award	Postdoctoral Fellowship Award
Period of Support	07-01-17 to 06-30-20 (with 1 year NCE)
Amount of Funding	\$99,424
<p>Summary/Abstract: As a preliminary study, we have demonstrated the effect of soluble calcium (Ca^{2+}) concentration on cell viability and transfection efficiency when combined with polyethyleneimine (PEI)-plasmid DNA complexes. This combination can be specifically applied to further enhance the differentiation of bone mesenchymal stem cells (BMSCs) by using the combination of PEI-plasmid bone morphogenetic protein 2 (PEI-pBMP-2) and altered Ca^{2+} as compared with PEI-pBMP-2 alone. The osteogenic potential of combining matrices and protein growth factors has been well documented, however, improvements are necessary to achieve optimal therapeutic benefits upon clinical translation. In our main study, gene-activated matrices (GAMs) have been tested for bone regeneration <i>in vitro</i> and <i>in vivo</i> using rat calvarial defect model. Both <i>in vitro</i> and <i>in vivo</i> studies were performed to determine the optimal mode of gene delivery. After 6 weeks, the calvarial defects were retrieved to assess bone formation and tissue quality through histological and micro-CT analyses. The optimal GAM was PEI-pDNA complexes embedded in the calcium phosphate coating produced by SBF, which increased total bone formation by 39% compared to 19% for control samples. A follow up <i>in vivo</i> study was performed to optimize the ratio of growth factors included in the GAM. The optimal ratio of pBMP-2 to pFGF-2 was determined to be 5:3 in terms of bone formation after 6 weeks of implantation. These studies demonstrated that collagen matrices biomimetically mineralized and activated with plasmids encoding FGF-2 and BMP-2 can optimally improve bone regeneration outcomes.</p>	
Were the original, specific aims of the proposal realized?	Yes, the specific aims redirected and proposed in the progress report and the NCE request have been tested. The outcomes have been presented and published.
Were the results published?	<ol style="list-style-type: none"> 1) Kyungsup Shin, Timothy M. Acri, Sean M. Geary, Aliasger K. Salem, “Biomimetic Mineralization of Biomaterials Using Simulated Body Fluids of Bone Tissue Engineering and Regenerative Medicine”, <i>Tissue Engineering Part A</i>, 23(19-20):1169-1180, 2017 (AAOF PFA support was acknowledged in the ‘ACKNOWLEDGEMENT’ section of the article) – 1st author 2) Timothy M. Acri, Kyungsup Shin, Dongrim Seol, Noah Z Laird, Ino Song, Sean M. Geary, Jaidev L. Chakka, James A. Martin, Aliasger K. Salem, “Tissue Engineering for the Temporomandibular Joint”, <i>Advanced Healthcare Materials</i>, (8)1801236, 2018 (AAOF PFA support was acknowledged in

	<p>the ‘ACKNOWLEDGEMENT’ section of the article) – Joint 1st author</p> <p>3) Timothy M. Acri, Noah Z Laird, Sean M. Geary, Aliasger K. Salem, <u>Kyungsup Shin</u>, “Effects of Calcium Concentration on Nonviral Gene Delivery to Bone Barrow-derived Stem Cells”, <i>Journal of Tissue Engineering and Regenerative Medicine</i>, (13):2256–2265, 2019 (<u>AAOF PFA support was acknowledged in the ‘ACKNOWLEDGEMENT’ section of the article</u>) – corresponding author</p> <p>4) Timothy M. Acri, Noah L. Laird, Leela R. Jaidev, David K. Meyerholz, Liu Hong, Aliasger K. Salem, <u>Kyungsup Shin</u>, “Non-viral gene delivery embedded in a biomimetically mineralized matrices for bone tissue engineering” submitted to <i>Tissue Engineering Part A</i> and currently under review (<u>AAOF PFA support was acknowledged in the ‘ACKNOWLEDGEMENT’ section of the manuscript</u>) – corresponding author</p>
<p>Have the results of this proposal been presented?</p>	<p><u>INTERNATIONAL CONFERENCES/MEETINGS</u></p> <p>1) Timothy M. Acri, Sean Geary, Aliasger K. Salem, <u>Kyungsup Shin</u>, “Impact of Calcium Concentration on Transfection Efficiency and Osteogenic Differentiation”, 2018 IADR/AADR/CADR Annual Meeting & Exhibition, Fort Lauderdale FA, March 2018 (<u>AAOF PFA support was acknowledged in the ‘ACKNOWLEDGEMENT’ section of the poster</u>)</p> <p>2) Timothy M. Acri, Sean Geary, Aliasger K. Salem, <u>Kyungsup Shin</u>, “Effect of Calcium Concentration on Non-Viral Transfection of Bone Barrow-Derived Stem Cells”, 2019 American Association of Pharmaceutical Scientists (AAPS) PHARMSCI 360, San Antonio TX, November 2019, (<u>AAOF PFA support was acknowledged in the ‘ACKNOWLEDGEMENT’ section of the poster</u>)</p> <p>3) <u>Kyungsup Shin</u>, Timothy Acri, Aliasger K. Salem, “Non-viral Gene Delivery on Mineralized Matrices for Bone Regeneration”, 2019 IADR/AADR/CADR General Session, Vancouver, BC, Canada, June 2019 (<u>AAOF PFA support was acknowledged in the ‘ACKNOWLEDGEMENT’ section of the poster</u>)</p>

	<p>4) Timothy M. Acri, Sean Geary, Aliasger K. Salem, <u>Kyungsup Shin</u>, “Impact of Calcium Concentration on Transfection Efficiency and Osteogenic Differentiation”, abstract accepted and abstract/poster archived in JDR for 2020 IADR/AADR/CADR Annual Meeting & Exhibition, Washington DC (meeting canceled due to COVID-19), (<u>AAOF PFA support was acknowledged in the ‘ACKNOWLEDGEMENT’ section of the poster</u>)</p> <p><u>OTHER LOCAL/UNIVERSITY MEETINGS</u></p> <p>1) 2018 Iowa Section of the AADR Research Day 2) 2019 Iowa Section of the AADR Research Day 3) 2020 Iowa Section of the AADR Research Day (<u>AAOF PFA support was acknowledged in the ‘ACKNOWLEDGEMENT’ section of the posters</u>)</p>
<p>To what extent have you used, or how do you intend to use, AAOF funding to further your career?</p>	<p>This PFA funding allowed me to conduct the proposed experiments. Over the years of support, the outcomes of this study have been presented at the national/international meetings, and published in a number of peer-reviewed journals. More importantly, this PFA support enabled me to generate preliminary data that have been used to apply for multiple federal grant applications such as the NIH/NIDCR (R03, R21).</p>