Applicant Name (Last, First): Atsawasuwan, Phimon

PREVIOUS AAOF AWARDS AND OUTCOMES

Award Type:	OFDFA 2012 (T.M. Graber teaching Fellowship Award) (Use abbreviations defined in guidelines: OFDFA, PFA, BRA, CA, EIA, RAA, etc.)		
Title of Project:	Ameloblastin Affects Cranial Bone Morphogenesis via Fibronectin and Heparin-Integrin Complex Pathways.		
Role in Project:	Principal Investigator	**Amount of Funding:**	$ 15,000
Period of Support:	July-1-2012 (Month-day-year) to June-30-2013 (Month-day-year)		
Outcomes: - Cite/describe any: 1. Publications 2. Presentations (organization, location, date) 3. Follow-up grants or awards	Publications: 1. Atsawawuwan et al. Ameloblastin inhibits cranial suture closure by modulating MSX2 expression and proliferation. PLoS One. 2013 Apr 4;8(4):e52800. doi: 10.1371/journal.pone.0052800. 2. Atsawasuwan et al. Expression and Function of Enamel-related Gene Products in Calvarial Development. J Dent Res. 2013 Jul;92(7):622-8. doi: 10.1177/0022034513487906. Epub 2013 Apr 26. The abstracts are attached.		

Repeat the above, as appropriate to provide a complete history of AAOF award funding.

Final report for OFDFA 2012

Phimon Atsawasuwan
Assistant Professor, Department of Orthodontics
University of Illinois at Chicago

Award Type: OFDFA
Title of Project: Ameloblastin Affects Cranial Bone Morphogenesis via Fibronectin and Heparin-Integrin Complex Pathways.
Role in Project: Amount of Funding: $ 15,000
Period of Support: __July, 1st, 2012_____ **to** __June, 30th, 2013____

The T.M. Graber teaching fellowship award 2012 from AAOF funding allows me to further investigate my projects and successfully published my results in **PLoS One** and **Journal of Dental Research** as follows: I would like to express my gratitude to AAOF for the funding.

PLoS One. 2013 Apr 4;8(4):e52800. doi: 10.1371/journal.pone.0052800.

Ameloblastin inhibits cranial suture closure by modulating MSX2 expression and proliferation.

Atsawasuwan P, Lu X, Ito Y, Zhang Y, Evans CA, Luan X.

Brodie Laboratory for Craniofacial Genetics, Department of Oral Biology University of Illinois College of Dentistry, Chicago, Illinois, United States of America.

Deformities of cranial sutures such as craniosynostosis and enlarged parietal foramina greatly impact human development and quality of life. Here we have examined the role of the extracellular matrix protein ameloblastin (Ambn), a recent addition to the family of non-collagenous extracellular bone matrix proteins, in craniofacial bone development and suture formation. Using RT-PCR, western blot and immunohistochemistry, Ambn was localized in mouse calvarial bone and adjacent condensed mesenchyme. Five-fold Ambn overexpression in a K14-driven transgenic mouse model resulted in delayed posterior frontal suture fusion and incomplete suture closure. Moreover, Ambn overexpressor skulls weighed 13.2% less, their interfrontal bones were 35.3% thinner, and the width between frontal bones plus interfrontal suture was 14.3% wider. Ambn overexpressing mice also featured reduced cell proliferation in suture blastemas and in mesenchymal cells from posterior frontal sutures. There was a more than 2-fold reduction of Msx2 in Ambn overexpressing calvariae and suture mesenchymal cells, and this effect was inversely proportionate to the level of Ambn overexpression in different cell lines. The reduction of Msx2 expression as a result of Ambn overexpression was further enhanced in the presence of the MEK/ERK pathway inhibitor O126. Finally, Ambn overexpression significantly reduced Msx2 down-stream target gene expression levels, including osteogenic transcription factors Runx2 and Osx, the bone matrix proteins Ibsp, Coll, Ocn and Opn, and the cell cycle-related gene CcnD1. Together, these data suggest that Ambn plays a crucial role in the regulation of cranial bone growth and suture closure via Msx 2 suppression and proliferation inhibition.

J Dent Res. 2013 Jul;92(7):622-8. doi: 10.1177/0022034513487906.

Expression and Function of Enamel-related Gene Products in Calvarial Development.

Atsawasuwan P, Lu X, Ito Y, Chen Y, Gopinathan G, Evans CA, Kulkarni AB, Gibson CW, Luan X, Diekwisch TG.

Brodie Laboratory for Craniofacial Genetics, University of Illinois at Chicago, IL 60612, USA.

Enamel-related gene products (ERPs) are detected in non-enamel tissues such as bone. We hypothesized that, if functional, ERP expression corresponds with distinct events during osteoblast differentiation and affects bone development and mineralization. In mouse calvariae and MC3T3 cells, expression profiles of enamel-related gene products (ERPs) correlated with key events in post-natal calvarial development and MC3T3 cell mineralization. Developing skulls from both Amel- and Ambn-deficient animals were approximately 15% shorter when compared with those of wild-type controls, and their sutures remained patent for a longer period of time. Analysis of Amel- and Ambn-deficient calvariae and calvarial osteoblast cultures revealed a dramatic reduction in mineralized nodules, a significant reduction in Runx2, Sp7, Ibsp, and Msx2 expression, and a reduction in Alx4 in Amel-deficient calvariae vs. an increase in Alx4 in Ambn-deficient calvariae. Analysis of these data indicates that ERP expression follows defined developmental profiles and affects osteoblast differentiation, mineralization, and calvarial bone development. We propose that, in parallel to their role in the developing enamel matrix, ERPs have retained an evolutionary conserved function related to the biomineralization of bones.