

## AAO Foundation Award Final Report

Principal Investigator	Petros Papagerakis
Co-Investigator	Jeanne Nervina
Secondary Investigators	
Award Type	BRA (Biomedical Research Award)
Project Title	Role of orai1 in osteoblast differentiation and function
Project Year	2012-2014
Institution	University of Michigan
Summary/Abstract (250 word maximum)	<p>Orai1 is a plasma membrane protein that forms the pore of the calcium release activated calcium channel. Humans with mutated orai1 present with hereditary combined immunodeficiency, congenital myopathy and anhidrotic ectodermal dysplasia. Consistent with the human phenotype, orai1 knockout mice present immunodeficiency, ectodermal dysplasia but also defected mineralized tissue formation. However, orai1 knockout mice suffer by severe lethality that prevents full characterization of orai1 functions. Objective: To evaluate orai1 role during mineralized tissue formation using mouse models and in vitro assays. Results: Our data shows strong expression of orai1 in mineralized matrix secreting cells. Knockdown of orai1 expression decreases cell proliferation and results in RNA expression levels changes of key genes regulating matrix deposition and mineralization. Osx-specific conditional knockout of orai1 results in severe bone, enamel and dentin dysplasia. Conclusions: This study provides insights in the expression pattern of orai1 during mineralized tissue development. It also highlights the importance of calcium signaling in controlling cell proliferation and differentiation but also matrix deposition during development.</p>
Were the original, specific aims of the proposal realized?	The original 1 and 3 are being finalized. However, the obtained orai1 ob/ob mice have a high lethality and only can be examined in embryonic stages. Therefore, we were unable to realize the specific aim 2. Nevertheless, AAOF funding allowed us to increase our knowledge regarding orai1 function during mineralized tissue formation.
Were the results published? If not, are there plans to publish? If not, why not?	A paper with our findings is submitted and currently under review at the Journal of Developmental Dynamics. AAOF is acknowledged for providing funding.
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?	An oral presentation has been awarded to the next IADR/AADR meeting to be held in Boston in March 2015. This study has the title "Orai1 expression and roles in mineralized tissue formation" and is authored by Zheng L, Zinn, V, Nervina J, Papagerakis S, and Papagerakis P. This presentation summarizes the phenotype of the mineralized tissues in orai1 ob/ob mice.
To what extent have you used, or how do you intend to use, AAOF funding to further your career?	The majority of the data generated will be used to support a NIH grant application in 2015.