AAO Foundation Award Final Report

Principal Investigator	Sumit Yadav
Co-Investigator	
Secondary Investigators	
Award Type	Biomedical Research Grant
Project Title	Studies of Cell Lineage in TMJ Condylar Cartilage
Project Year	2013-2014
Institution	University of Connecticut Health center
Summary/Abstract (250 word maximum)	**Objectives:** Mandibular condylar cartilage is a secondary cartilage, derived from periosteum and contains undifferentiated mesenchymal progenitor cells. However, little is known about the differentiation potential of these progenitor cells. Therefore, we report a genetic linage tracing approach to identify and chase the progenitor cells in the mandibular condylar cartilage. **Materials and Methods:** We used tamoxifen inducible αSMACreERT2 transgenic mice and when crossed with Ai9 reporter mice, provided a system in which the fate of progenitors (SMA9+) can be traced. Additionally, we looked at the cell surface markers for the progenitor population at 2days and 17days after tamoxifen administration. **Results:** SMA9+ cells were only found in mandibular condylar cartilage but not in articular and growth plate cartilage. SMA9+ cells were found in 4 weeks, 4 months and in 8 months old mice. SMA9 labeled cells represents a highly dynamic progenitor cell population that is capable of proliferation and differentiation into mature cell types in mandibular condylar

	cartilage. At day 2 and day 17 cells were positive for CD105 and Sca1 and negative for CD31and CD45. **Conclusion:** αSMACreERT2 cells appear to constitute a specialized cohort of progenitor population that is capable of proliferation and differentiation into mature cell types in mandibular condylar cartilage. The discovery of SMA9+ cells as a progenitor of MCC could open clinically important areas of future investigation and can be used for regeneration of MCC in degenerative disorders of temporomandibular joint.
Were the original, specific aims of the proposal realized?	Yes. We finished all our specific aims
Were the results published? If not, are there plans to publish? If not, why not?	One of the research papers has been submitted and has been under revision and we are submitting the second paper by the year-end.
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?	The results of the proposal will be presented in **International Association of Dental Research, Boston- MA, March 2015**. We have submitted the abstract. Please see the abstract below: **Title:** BMP2 Signaling in Mechanical Loading of Mandibular Condylar Cartilage **Authors: Raman Koul, Zana Kalajzic, Sumit Yadav** **Objective:** The mandibular condylar cartilage remodels in response to mechanical load by regulating chondrogenesis and endochondral ossification, in order to achieve a balance between mechanical load and the remodeling capacity of the mandibular condylar cartilage. The purpose of this study was to examine the effects of static

	compressive loading on the mandibular condylar cartilage. We hypothesized that BMP2 signaling plays a key role and is required for sensing of mechanical loading in mandibular condylar cartilage. **Method:** Four weeks old double triple transgenic mice (Dkk3 X Col2A1 X Col10A1) were divided into two groups: (1) Unloaded, (2) Loaded (5 days with 50cN of compressive force). All the animals were injected with Ethynyl Deoxyuridine (EDU) 24 hours before euthanization. Immunohistochemistry, gene expression, microCT and rate of proliferation were analyzed and compared. **Result:** Our histology indicated a significant increase in the number of the Dkk3 and Col10A1 expressing cells in the loaded group. There is increased BMP2 and Sox 9 expression, increased chondrocyte proliferation, but decreased SOST expression. Moreover, there was significant increase in the bone volume fraction and the trabecular thickness in the loaded group. **Conclusion:** The increased expression of BMP2, is associated with the adaptive remodeling of the mandibular condylar cartilage after static compressive load.
To what extent have you used, or how do you intend to use, AAOF funding to further your career?	I am planning to submit my K08 grant to NIDCR in the February of 2015. I used the AAOF grant to get the preliminary results and publications. The grant was very useful and will help me in becoming a independent investigator.