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AAO Foundation Final Report Form (a/o 6/30/2019)

In an attempt to make things a little easier for the reviewer who will read this report, please consider these two questions before this is sent for review:

- *Is this an example of your very best work, in that it provides sufficient explanation and justification, and is something otherwise worthy of publication? (We do publish the Final Report on our website, so this does need to be complete and polished.)*
- *Does this Final Report provide the level of detail, etc. that you would expect, if you were the reviewer?*

Please prepare a report that addresses the following:

Type of Award, e.g., Orthodontic Faculty Development Fellowship Award, Postdoctoral Fellowship Award, Biomedical Research Award, Center Award, Educational Innovation Award, Program Award, Research Aid Award

Orthodontic Faculty Development Fellowship Award

Name(s) of Principal Investigator(s): **Eliane H Dutra**

Institution: **University of Connecticut Health**

Title of Project: **BMP2 mediated anabolic effect of intermittent PTH on the mandibular condylar cartilage.**

Period of AAOF Support (e.g. 07-01-19 to 06-30-20): **07-01-18 to 12/31/19**

Amount of Funding: **$20,000**

Summary/Abstract :

Objectives: The objectives of this project were to gain insights into the cellular and molecular mechanisms by which Intermittent Parathyroid Hormone (I-PTH) administration exerts its anabolic effects in the mandibular condylar cartilage (MCC). Our hypothesis was that PTH acts through BMP2 as an anabolic mediator, leading to increased cartilage thickness, increased matrix synthesis and increased cell proliferation and differentiation. **Materials and Methods:** ***In-vivo:*** Forty-eight male and female BMP2 fl/fl, AGC-CreERT2 Cre-positive (Conditional BMP2 deletion in the chondrocytes of the MCC mouse model – BMP2 CondKO) and BMP2 fl/fl, AGC-CreERT2 Cre-negative (Control group) mice were used. Four-week-old mice were injected with tamoxifen and, at 12 weeks of age, mice were injected with I-PTH daily for 2 weeks. Micro-CT and histological analysis of the MCC and subchondral bone were performed in I-PTH injected mice and compared to non-treated controls (saline injection). ***In-vitro:*** We utilized 20 3-week-old triple transgenic mice (Col1a1 X Col2a1 X Col10a1). Primary chondrocytes from the MCC were dissected and plated in micro mass cultures. Chondrocytes were treated daily with PTH or regular media. The mRNA expression of genes relevant to chondrogenesis was examined by qPCR.
Results: ***In-vivo*** **results:** Micro-CT analysis revealed significant increased bone density in I-PTH treated mice in comparison to saline control mice. There was no significant difference between BMP2 CondKO and control mice, suggesting that the conditional deletion of BMP2 did not affect the effects of I-PTH. Histological analysis suggested similar results, I-PTH increased MCC thickness in both BMP2 CondKO and Control mice**.** ***In-vitro*** **results:** To further understand the molecular mechanisms behind the effects of I-PTH in the MCC, we examined the mRNA expression of genes relevant to chondrogenesis in primary chondrocyte micro mass cultures treated with PTH by qPCR. There was no significant difference between PTH treated chondrocytes and control groups in the expression of *Col2a1*, *Fgfr1* and *Fgfr2*. However, we observed a significant decrease in *Ihh* and *Bmp2* and a significant increase in *Fgf2, Fgfr3,* and *Sox9,* suggesting I-PTH affects chondrocyte proliferation and differentiation. Moreover, we found a remarkable decrease in *Col10a1* and *Alp,* important markers for cartilage mineralization. **Conclusion:** Our results suggest that the effects of I-PTH in the mandibular condyle of mice are not primarily determined by BMP2. The I-PTH effects in the MCC may be controlled by the *Fgfr3* signaling.

Detailed results and inferences: **Complete manuscript has been submitted for publication.**

1. If the work has been published please attach a pdf of manuscript OR
2. Describe in detail the results of your study. The intent is to share the knowledge you have generated with the AAOF and orthodontic community specifically and other who may benefit from your study. Table, Figures, Statistical Analysis and interpretation of results should be included.

Respond to the following questions:

1. Were the original, specific aims of the proposal realized? **Yes**
2. Were the results published? **Manuscript has been submitted and it is under revision.**
    a. If so, cite reference/s for publication/s including titles, dates, author of co-authors, journal, issue and page numbers: **N/A**
    b. Was AAOF support acknowledged? **Yes**
    c. If not, are there plans to publish? If not, why not? **N/A**

3. Have the results of this proposal been presented? **Yes**
    a. If so, list titles, author or co-authors of these presentation/s, year and locations: **Results were presented at the 2019 Burstone Presymposium in the Indiana University in October 24th 2019.**
    b. Was AAOF support acknowledged? **Yes**
    c. If not, are there plans to do so? If not, why not? **N/A**

4. To what extent have you used, or how do you intend to use, AAOF funding to further your career?

The AAOF funding has helped me to generate data for NIDCR and AAOF grants submission and to publish key manuscripts.

Accounting for Project; i.e., any leftover funds, etc.

There was no leftover funds left.