

Role of Geroscience-Guided Therapeutics in Oral Health Problems of Aging

2023 Orthodontic Faculty Development Fellowships (OFDFA)

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FollowUp Form

Award Information

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?*

Title of Project*

Role of Geroscience-Guided Therapeutics in Oral Health Problems of Aging

Award Type

Orthodontic Faculty Development Fellowship Award (OFDFA)

Period of AAOF Support

July 1, 2023 through June 30, 2024

Institution

University of Nebraska Medical Center

Names of principal advisor(s) / mentor(s), co-investigator(s) and consultant(s)

Sumit Yadav

Amount of Funding

\$30,000.00

Abstract

(add specific directions for each type here)

attached

Respond to the following questions:

Detailed results and inferences:*

If the work has been published, please attach a pdf of manuscript below by clicking "Upload a file".

OR

Use the text box below to 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 also be attached by clicking "Upload a file".

In this study, we propose to target both cellular senescence and intermittent loading to alleviate degenerative disorders of the TMJ with aging. Our hypothesis is that concurrent administration of senolytics and mechanical loading will have a synergistic anabolic effect on the cartilage of TMJ. Five groups were included: 1) Vehicle, 2) Senolytics(D+Q), 3) Mechanical loading, 4) D+Q with mechanical loading, 5) D+Q with botox injection. Micro-CT analysis revealed a significant bone mineral density(BMD) decreased in D+Q administration with botox injection comparing to D+Q administration alone or D+Q administration with mechanical loading. For the D+Q administration with botox injection group, the cortical porosity looks increased but there was no significant and had high variation. We observed an increased TRAP expression(indicator of osteoclast activity) in the group of D+Q administration with botox injection in comparison with all other groups. This finding also reflected on the micro-CT data which showed lower BMD. Alkaline phosphatase(AP) is an enzyme marker for mineralization. Our previous studies have shown an age-related decline of AP signal in subchondral bone area in old TMJs, as well as significantly increased AP activity in TMJs with D+Q treated old mice. From AP staining in this study, we have found the same result. Additionally, we observed increased AP expression in the mechanical loading alone and D+Q treated with mechanical loading group. In the D+Q treated with botox injection group, there was a shift of expression with AP staining(mineralization) layer moving toward the condylar surface, suggesting the mineralization was migrating towards the superficial layer of mandibular condylar cartilage, invading the unmineralized portion of cartilage. We next performed toluidine blue(TB) and Safranin O staining to assess the cartilage thickness and overall pathological changes. Similar to our previous finding, the D+Q treatment increased the cartilage thickness comparing to vehicle treated group. The condylar surface was also more intact with D+Q administration. With aging, there is a decrease in the number of chondrocytes/cells and their inability to maintain the synthetic activity. The level of the cartilage cellularity determines the tissue volume that is being maintained and has significant implications for cartilage repair and regeneration. We have noticed cellularity was increased with D+Q treated and mechanical loading group, the combined D+Q administration and mechanical loading group increased cellularity profoundly(Fig. 3). In the D+Q treatment with botox injection group, the chondrocyte phenotype looked different than other group and the integrity of cartilage was altered. Similar to other aged tissues, D+Q administration significantly reduced RelA(v-rel avian reticuloendotheliosis viral oncogene homolog A, is also known as p65) expression level, however, the expression was increased when applied mechanical loading. Our results suggest that mechanical loading augments the beneficial effects of senolytics on the cartilage of TMJ in old age while unloading has negative effect on the MCC and subchondral bone of TMJ.

Were the original, specific aims of the proposal realized?*

Yes

Were the results published?*

No

Have the results of this proposal been presented?*

Yes

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

The funding has helped me on setting up my research lab and supported me traveling to present my research result. Additionally, the funded research allowed me to generate data for future grant application.

Accounting: Were there any leftover funds?

Not Published

Are there plans to publish? If not, why not?*

Yes, we are preparing the manuscript.

Presented

Please list titles, author or co-authors of these presentation/s, year and locations:*

- 1) Synergistic Effect of Senolytics and Mechanical Loading on TMJ Cartilage. Po-Jung Chen, Aiyi Liu, Eliane Dutra, Ming Xu, George Kuchel, Sumit Yadav 2024 IADR/AADOCR/CADR General Session & Exhibition, New Orleans, LA, USA
- 2) Synergistic Effect of Senolytics and Mechanical Loading on TMJ Cartilage. Po-Jung Chen, Aiyi Liu, Jonjei Ku, Eliane Dutra, Ming Xu, George Kuchel, Sumit Yadav 2024 TAO APOC, Taipei, Taiwan

Comment: The AAOF commends your accomplishments in this completed study. We look forward to your published results in the public domain of orthodontic and craniofacial research to advance our specialty's future.

Was AAOF support acknowledged?

If so, please describe:

Yes, AAOF support was acknowledged in the poster/oral presentation.

Internal Review

Reviewer comments

Reviewer Status*

Approved

File Attachment Summary

Applicant File Uploads

No files were uploaded