

Role of Cellular Senescence in Alleviating TMJ Degeneration

2020 Grants

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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 Cellular Senescence in Alleviating TMJ Degeneration

Award Type

Biomedical Research Award (BRA)

Period of AAOF Support

July 1, 2020 through June 30, 2023

Institution

University of Nebraska Medical Center

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

Dr. Ming Xu

Amount of Funding

\$30,000.00

Abstract

(add specific directions for each type here)

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".

Our findings demonstrate that biweekly administration of D+Q improves subchondral bone turnover, alleviates cartilage degeneration and pathological conditions, and increases bone volume in TMJs from old mice. Of note, the benefits on the TMJ cartilage by senescent cell clearance is similar to the knee cartilage, as previous studies showed that transplantation of senescent cells impaired knee cartilage morphology and clearance of senescent cells in aged or osteoarthritis knee alleviated cartilage pathology. Despite slightly different starting ages (23 vs 24 months), we observed similar changes in TMJs by D+Q in both male and female mice, indicating little sex difference as regards the benefits of D+Q in TMJs in aged animals. It is possible that D+Q alleviates TMJ dysfunction through mechanisms beyond the clearance of senescent cells, since both D and Q have pleiotropic effects. In this study, D+Q treatment was intermittent with 3 doses every 2 weeks and TMJs were collected 7 days after last dose of D+Q. Because both D and Q have short elimination half-lives (<12 hours), the effect we observed was most likely due to mechanisms that are long-lasting and do not require continuous presence of the drugs to inhibit or activate certain enzymes or pathways. Moreover, D+Q seems to only have effects on old mice, but not on young mice (which contain few senescent cells), indicating age-specific benefits. All these pieces of evidence are consistent with the possibility that D+Q mitigates age-related TMJ degeneration at least partially through eliminating senescent cells. It is still unclear how D+Q increases cartilage thickness and bone turnover (increased AP and TRAP signals) in old TMJs. We found that Bmp2 level increased with aging (consistent with previous findings, while DQ has little effect on Bmp2 level in either young or old TMJs, indicating that D+Q might not work through Bmp2 pathway. Future experiments are needed to further investigate these underlying mechanisms. Although the TMJ morphological features differ between human and mice our study here provides preclinical evidence that D+Q has potential to improve TMJ tissue homeostasis in mice with aging and likely lays the foundation for clinical trials to treat TMJ degeneration in old age.

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

Yes

Were the results published?*

Yes

Have the results of this proposal been presented?*

No

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

AAOF has been very instrumental in supporting my career. Due to AAOF continued support, I was recruited to UNMC to lead the research and head the department

Accounting: Were there any leftover funds?

Published

Citations*

You indicated results have been published. Please list the cited reference/s for publication/s including titles, dates, author or co-authors, journal, issue and page numbers

Senolytics alleviate the degenerative disorders of temporomandibular joint in old age. Aging Cell.

Was AAOF support acknowledged?

If so, please describe:

Yes

Not Presented

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

AAOF grant was used to generate preliminary data for an R03 and R01. I was successful in obtaining an R03 and an R01 with the preliminary data gathered due to support from AAOF

Internal Review

Reviewer Comments

Reviewer Status*

Approved

File Attachment Summary

Applicant File Uploads

No files were uploaded