

Antibiotic Disruption of Commensal Microbiota Alters Signaling in Orthodontic Tooth Movement

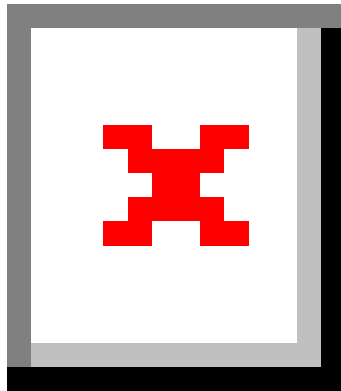
2023 Research Aid Awards (RAA)

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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:*

Antibiotic Disruption of Commensal Microbiota Alters Signaling in Orthodontic Tooth Movement

Award Type

Research Aid Award (RAA)

Period of AAOF Support

July 1, 2023 through June 30, 2024

Institution

University of North Carolina at Chapel Hill

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

Tung Nguyen, Shannon Wallet, Christina Graves, R. Balfour Sartor

Amount of Funding

\$6,000.00

Abstract

(add specific directions for each type here)

Refer to uploaded document

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".

AAOF_Resultsandinferences.pdf

See attached uploaded file.

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

Aims of the proposal were modified within reason due to resource constraints, collaborator turnover and in a discovery-guided approach to optimize the potential significance of results.

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?*

AAOF funding has made a substantial contribution to furthering my career. Without the support of AAOF, my research project would not have been possible. Basic science projects require adequate resources to appropriately plan and execute and are few and far between in orthodontic master's projects. This support allowed me to develop as both a clinician and a researcher and provided the flexibility to maximize my creative potential through digging deep to find the most meaningful next step in my research. AAOF support has enabled me to improve on my ability to critically review present literature and expand this information into new unanswered questions. Presenting my data at research conferences provided abundant opportunities for networking, learning and growing as a professional within the orthodontics community. I will forever be grateful for the support provided by AAOF.

Accounting: Were there any leftover funds?

\$0.00

Not Published

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

No, more studies are required to elaborate on mechanistic underpinnings of results for publication. Due to resource and collaborator constraints, this work will not be continued.

Presented

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

J. Gerasco, E. Kay, C. Graves, L. Jacox, T. Nguyen, S. Wallet. Antibiotics Alter Fibroblast-Osteoclast Signaling in Orthodontic Tooth Movement. AADOCR/CADR General Session 2023, Portland, OR, USA

J. Gerasco, C. Graves, L. Jacox, T. Nguyen, S. Wallet. Antibiotics Alter Fibroblast-Osteoclast Signaling in Orthodontic Tooth Movement. UNC ASoD Research Day 2023, Chapel Hill, NC, USA

J. Gerasco, E. Kay, C. Graves, L. Jacox, T. Nguyen, S. Wallet. Antibiotics Alter Fibroblast-Osteoclast Signaling in Orthodontic Tooth Movement. AAO Annual Session 2023, Chicago, IL, USA

Was AAOF support acknowledged?

If so, please describe:

yes, the AAOF was acknowledged in an acknowledgements section in each presentation.

Internal Review

Reviewer comments

Reviewer Status*

File Attachment Summary

Applicant File Uploads

- AAOF_Resultsandinferences.pdf

Doxycycline alters periodontal ligament fibroblast signaling and morphology in an in vitro model of orthodontic tooth movement

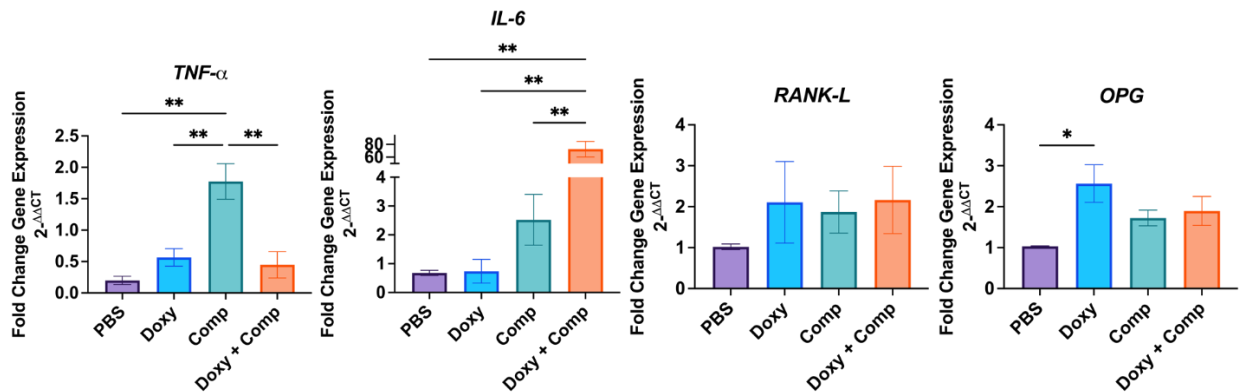


Figure 1. Doxycycline alters key osteoclastogenesis genes after 24 hours of compression. Compression of periodontal ligament fibroblasts expressed increased pro-inflammatory genes TNF- α and IL-6 at 24h. Doxycycline reversed the effect seen in TNF- α and exacerbated the effect on IL-6. While Doxycycline increased baseline expression of OPG, this effect was normalized under compression conditions. * $p < 0.05$, ** $p < 0.01$; $n = 3$ biological replicates, 2 technical replicates. Normalized to GAPDH. One-way ANOVA with Tukey's test for multiple comparisons.

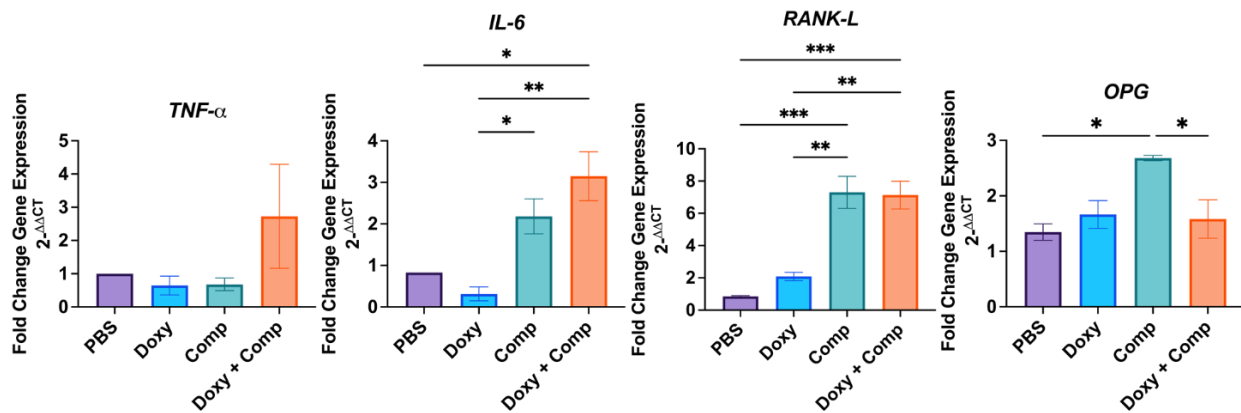


Figure 2. Doxycycline alters key osteoclastogenesis genes after 72 hours of compression. Compressed periodontal ligament fibroblasts expressed increased IL-6, RANK-L and OPG and no change in TNF- α after 72h. Doxycycline caused a trend toward increased pro-inflammatory cytokines IL-6 and TNF- α under compression. Doxycycline decreased compression-induced OPG expression. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; $n = 3$ biological replicates, 2 technical replicates. Normalized to GAPDH. One-way ANOVA with Tukey's test for multiple comparisons.

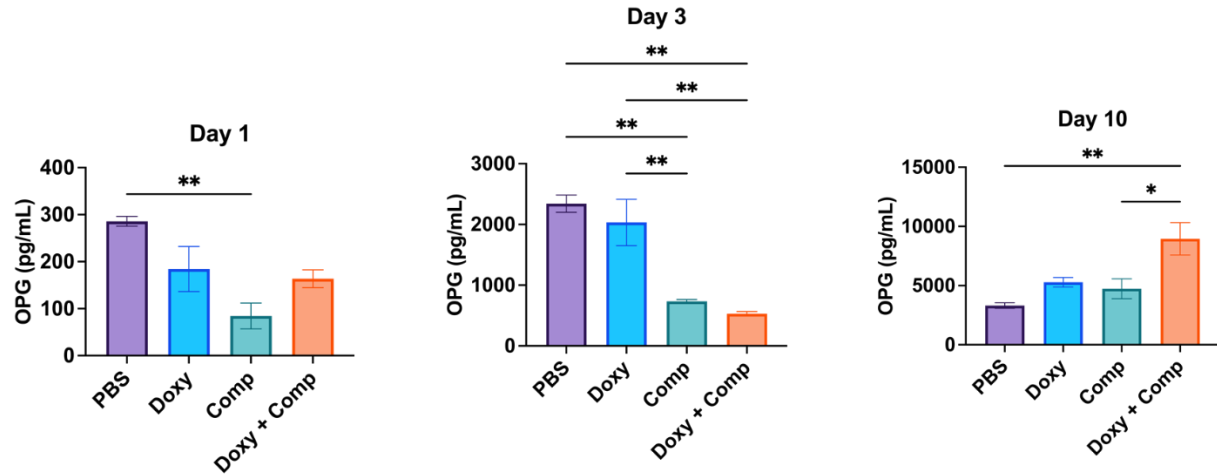


Figure 3. Doxycycline had minimal effects on secreted OPG and until day 10, where doxycycline significantly increased compression-induced OPG. * $p < 0.05$, ** $p < 0.01$; $n = 3$ biological replicates, 2 technical replicates. Concentrations extrapolated from regression based on standard curve. One-way ANOVA with Tukey's test for multiple comparisons.

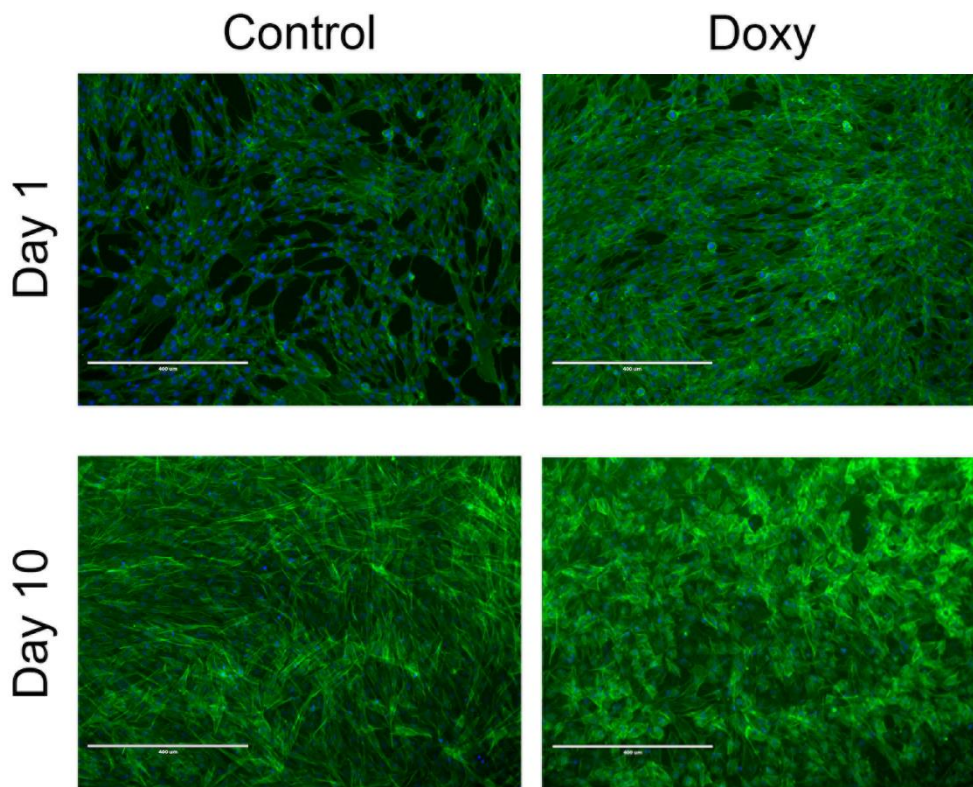


Figure 4. Doxycycline alters morphology of compressed periodontal ligament fibroblasts. Doxycycline treatment of compressed periodontal ligament fibroblasts results in rounded rather than traditional spindle morphology. The effect is more pronounced over time. Scale bar 400μm.

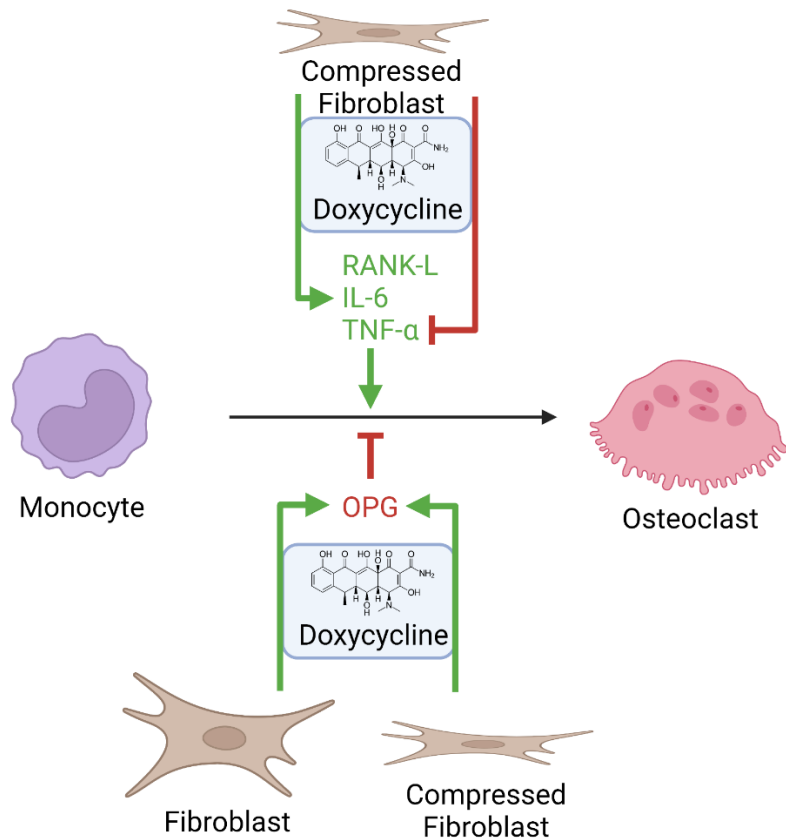


Figure 5. Doxycycline may reduce OTM via reduction of osteoclastogenesis through stimulation of OPG

Interpretation of results:

Doxycycline alters expression of key osteoclastogenic genes in fibroblasts, both at baseline and under compression. We observed reduced compression-induced TNF α and increased compression-induced IL-6. In addition, there was increased baseline OPG expression in response to doxycycline at 24h, but this effect normalized under compression. Gene expression alterations were not sustained beyond 24h, however, both protein secretion and morphological changes were observed at 10d. Because orthodontic tooth movement persists for years, this key finding suggests that future in vitro experimentation of periodontal ligament fibroblasts to study orthodontic tooth movement should be carried out beyond the traditional 24h timeline. At 10d, doxycycline increased secreted OPG, a key anti-osteoclastic protein. In addition, a dramatic morphological change was noted at 10d, where fibroblasts appeared more rounded rather than their traditional spindle-shaped form. These data suggest that doxycycline alters the normal compression response in periodontal ligament fibroblasts and may limit osteoclastogenesis and ultimately tooth movement.