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**AAO Foundation Final Report Form
(a/o 5/31/2017)**

Please prepare a report that addresses the following:

Type of Award

Orthodontic Faculty Development Fellowship Award

Name(s) of Principal Investigator(s)

Tate H. Jackson, DDS, MS

Title of Project

Ortho-omics: Characterization of dysbiotic shifts from oral health to disease

Period of AAOF Support

07-01-2017 to 06-30-2018

Amount of Funding

\$20,000

Summary/Abstract of Completed Project Results

AIM: Orthodontic treatment is known to increase both caries and periodontal disease risk—we posit that this risk is mediated via changes in the composition or activity of the oral microbiome. In this longitudinal pilot study among adolescent orthodontic patients, we tested the hypothesis that the introduction of fixed appliances induces taxonomic and functional dysbiotic shifts in the supragingival dental biofilm, as assessed by next-generation sequencing methods.

MATERIALS: The study cohort comprised 10 healthy orthodontic patients (aged 13-15) scheduled for treatment with fixed appliances. One trained and calibrated examiner recorded clinical measures of bleeding on probing, gingival index, and plaque index. Supragingival plaque samples were collected from facial surfaces of maxillary incisor and mandibular premolar index teeth using sterile scalers at four time points: before bonding of orthodontic appliances and at 1, 6, and 12 weeks after bonding. Samples were placed in Tris-EDTA solution and snap-frozen. DNA was isolated using a MagMAX Pathogen DNA isolation kit (ABI) and a 16S amplicon library was prepared to carry out pair-ended, (2 x250bp) Illumina sequencing. RNA was isolated using a Power Microbiome kit (Qiagen). After rRNA removal, total Pair-ended (2 x 150bp) Illumina sequencing of the pooled library was executed. After bioinformatics processing and estimation of taxa, gene family abundance, pathway abundance, and pathway coverage; diversity indices and metagenomic/metatranscriptomic correlated data were analyzed over time

and across bacterial species of interest.

RESULTS: Biofilm taxonomic diversity decreased (phylogenetic diversity, whole tree, Shannon index) in both DNA and RNA from baseline (pre-treatment) to one week (post-treatment). This shift was primarily due to a 66% relative decrease in *Corynebacterium matruchotii* and relative increases in Actinobacteria: *Lautropia Mirabilis* (86%) and *Veillonella* (32%). Concurrently, metatranscriptomic pathway abundance diversity (Shannon index) decreased. *Corynebacterium matruchotii* showed a decrease both in abundance and expression at one week, and *Veillonella* showed a marked increase in expression through 12 weeks after bonding, consistent with all participants developing gingivitis.

CONCLUSIONS: These results provide initial proof-of-principle evidence that an elective oral disease risk-increasing intervention, fixed orthodontic appliances, can induce a dysbiotic shift in both the composition and function the supragingival oral biofilm of healthy patients.

Response to the following questions:

1. Were the original, specific aims of the proposal realized?

Yes – Specifically:

- 1. The aims of the research plan were achieved. As a hypothesis-generating pilot study, initial proof-of-principle data were generated that lay the foundation for future high-impact research with the potential for funding.**
- 2. The goals of the educational plan were met as research expertise was gained from NC TraCS resources and from Dr. Divaris as outlined in the original proposal.**
- 3. Teaching skills goals were surpassed. Dr. Jackson has been a key member of a committee to rebuild the UNC DDS curriculum, not just a single pre-doctoral course as outlined in the original proposal. Progress outcomes of that work have been accepted for presentation at the ADEA Annual Session in 2019.**
- 4. Intramural practice has allowed Dr. Jackson to achieve the goals of the Clinical Skills Plan in the original proposal, including the presentation of interdisciplinary orthodontic care as Faculty at the Frank Brantley Update in General Practice (ADA CERP credit given to participants).**

2. Were the results published?

a. If so, cite reference/s for publication/s including titles, dates, author or co-authors, journal, issue and page numbers

Not yet – submission planned for December 2018

b. Was AAOF support acknowledged?

In the manuscript to be submitted, it is.

c. If not, are there plans to publish? If not, why not?

Yes – manuscript submission to the Journal of Dental Research titled “Fixed Orthodontic Treatment Induces Time-Varying Dysbiosis in Both Composition and Function of Supragingival Oral Biofilm” in December 2018

3. Have the results of this proposal been presented?

a. If so, list titles, author or co-authors of these presentation/s, year and locations

Yes –

2018. TH Jackson, F Teles, J Roach, A Morgenstern, K Divaris. Fixed Orthodontic Treatment Induces Time-Varying Supragingival Oral Biofilm Dysbiosis. IADR Annual Session. London, England.

2018 Morgenstern A, Divaris K, Teles F, Jackson TH. Shifts in The Oral Biofilm of Patients with Known Oral Health Risk Factors: A Microbiome and Transcriptome Level Pilot Investigation. American Association of Orthodontists Annual Session. Washington DC.

2018. Morgenstern A, Divaris K, Teles F, Jackson TH. Orthodontic Treatment Induces Time-dependent Oral Dysbiosis. DRRD. Chapel Hill

- b. Was AAOF support acknowledged?
Yes
 - c. If not, are there plans to do so? If not, why not?
4. To what extent have you used, or how do you intend to use, AAOF funding to further your career?

Funding from the AAOF has been pivotal to my success as an academic so far. Without the Foundation's support, the research reported here would not have been possible. The Foundation has enabled me to position myself as a clinician who is also capable of meaningful and innovative research – research that has the potential to impact not only orthodontics, but also the broader field oral health care.

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

All funds were used as indicated in the proposal.

Please return to AAOF via email attachment to aaofevp@aaortho.org