

Systems Biology Approach to Analysis of the Oral Microbiome in HIV-positive Opiate abusers

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In HIV+ opiate users periodontal diseases is further aggravated by synergistic effects of Opiates with HIV antiretroviral drugs. We evaluated the oral microbiota in saliva/gingival plaque samples obtained from HIV+ Opiate+, HIV+ Opiate-, HIV- Opiate+ and HIV- Opiate - patients by genomic and proteomic profiling using RNA-seq and other state of the art NGS methods. Investigation of salivary and gingival plaque microbiota will likely lead to predictive markers for dental caries-risk patients and highly sensitive diagnostic markers of periodontal conditions. We hypothesize that opiate abuse causes significant perturbations in the oral microbiome, that contribute significantly to inflammation and can damage the barrier between the oral mucosa and the bloodstream, triggering systemic disease and immune system dysfunction. We evaluated the following specific aims: **Aim-1a**: Evaluate the effect of opiates on the biodiversity of the oral microbiome in Opiate users with and without HIV **Aim-1b**: Identification of specific microbiota that cause periodontitis, and evaluate their association with immune factors such as levels of pro-inflammatory cytokines. **Aim-2**: Epigenetic analysis in host DNA to determine genome-wide methylation profiling to help unveil the epigenomic regulation and related biomarkers relevant to HIV disease and opiate abuse. **Aim 3a**: Data mining using translational bioinformatics to identify biomarkers for periodontal disease progression and identify correlations with opiate abuse. **Aim 3b**: Analysis of the temporal progression of functional modules of dynamic data (e.g. biodiversity of oral microbiome, epigenomic data, immune regulation) in the patient groups above. Our preliminary results showed the microorganisms most associated with periodontal diseases in HIV+Opiate+ patients included *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema* species, which are termed the "red-complex". HIV-specific DNA methylation patterns were identified which could be used as biomarkers for prediction of response to varying degree of exposure to both ART and Opiates.