Oral microbiota in relation to HIV infection and oral infection in perinatally HIV-infected adolescents

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2nd Int'l Workshop on Microbiome in HIV Pathogenesis, Treatment and Prevention

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Today’s discussion

• Oral microbiome—some background
• Do the oral microbiota differ in perinatally HIV-infected (PHIV) and HIV-exposed, uninfected (PHEU) adolescents?
• Do disease-associated microorganisms differ in PHIV vs. PHEU?
Combinatorial Labeling and Spectral Imaging FISH (CLASI-FISH)

Courtesy Jessica Mark Welsh & Gary Borisy
50-100 billion oral bacteria/person
At least 50 km (30 miles)
Swallow millions of bacteria per day
Worldwide, up to $1 \times 10^{20}$ oral bacteria
10 to 50 tons
Fill a large swimming pool
More bacterial cells ($10^{14}$) than human cells ($10^{13}$)
The Oral Microbiome

• ~700 predominant species
• So what!
• <31% have not yet been cultivated
• Specific species associated with health and disease
• Site-specificity and subject-specificity
• www.homd.org; Human Oral Microbiome Database
• Whole genome sequences for 400 taxa
• Easily accessible
• May herald oral and systemic disease
• “More complex than previously believed”
Pediatric HIV/AIDS Cohort AMP Study (PHACS)

- A longitudinal study of perinatally HIV-infected (PHIV) and HIV-exposed, uninfected (PHEU) adolescents
- Adolescent Master Protocol (AMP): Oral Disease and Type of Antiretroviral Therapy among PHIV Youth
- Goal—to examine the association between oral disease and combination antiretroviral therapy (cART) regimen among PHIV
- Clinical Results
  - cART was successful at controlling opportunistic (mucosal) infections
  - High prevalence of gingivitis and periodontal disease, but little difference between PHIV and PHEU
  - PHIV had more caries than PHEU
Specific aims-oral microbiome

1. Do the oral microbiota differ in PHIV vs PHEU?
   • What effect does HIV have on the oral microbial composition?

2. Do disease-associated microorganisms differ in PHIV vs. PHEU?
   • E.g., *S. mutans* or other caries-associated species in both PHIV and PHEU?
   • E.g., *P. gingivalis* and other periodontitis-associated species in both PHIV and PHEU?
Background

Antiretroviral therapy

- HIV infection
- Host immune suppression
- Altered oral microbiome

Influence HIV clinical course
Sampling and processing

- Excluded subjects who had taken antibiotics within three months of sampling
- 2 types of samples
  - Pooled subgingival plaque (n=289)—2 mesial buccal sites
  - Throat wash expectorant (n=296)
- Extracted DNA
- 16S rDNA NGS sequencing (MiSeq)—V3-V4 region
- Compared levels of oral microbiota
Identification of bacterial species & genera

MiSeq 441 bp, V3-V4 region, 
~50,000 reads/sample

~600 ProbeSeq species-level targets

~129 genus-level targets

Excluded low abundance taxa

Estimated diversity
Regression analysis:
Levels of microbiota in PHIV versus PHEU

"Exposure": HIV infection

"Outcome": Oral dysbiosis

- Zero-inflated negative binomial regression
- Multiple univariate models
- Adjusted for total counts, age
- Controlled FDR (B-H)
Are the same species or genera associated with caries or perio in PHIV versus PHEU?

- Logistic regression model
- Outcome is caries OR periodontitis
- Interaction term between HIV and microbiota
- Adjusted for total counts, age
- Controlled FDR (B-H)
Conclusions and future studies

• PHIV versus PHEU?
  – Many taxa differed in PHIV vs PHEU
  – PHIV microbiome seemed less diverse
  – PHIV possibly fewer “health”-associated taxa
    • Fewer *Corynebacterium, Rothia, Actinomyces*
  – HIV-infection, or its treatment, likely contributes to oral dysbiosis
• Oral disease-associated microorganisms differ?
  – No difference between PHIV and PHEU, i.e., no taxa met significance threshold level
• Future studies
  – Higher n’s, e.g., effect modification analyses underpowered
  – Sampling of specific disease sites
  – Compare with never been exposed to HIV
  – Metatranscriptomics and other ‘omics
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