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Poster Title: Investigating the paradoxical effect of oral aspiration on the lung microbiome using computational and in-vitro modeling

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Abstract: Lung microbial communities play critical, but under-characterized roles in health. Bronchoalveolar lavage (BAL) samples from patients with severe pneumonia provide a rare window into lower respiratory tract ecology. Analyses of these samples have identified distinct microbial community states that correlate with patient outcomes. Notably, more oral-like lung microbiomes are associated with improved outcomes, presenting a paradox: aspiration occurs routinely in health yet can also contribute to pneumonia itself. This raises key ecological questions regarding the context by which oral immigration is beneficial or harmful and whether communities reflect intact transfer or selection-driven restructuring within the lung.

To address this, BAL samples from pneumonia patients were analyzed using amylase as a proxy for salivary input. Samples were stratified by amylase content. Increasing amylase was associated with elevated neutrophil percentages, consistent with controlled immune engagement. A Bayesian mixture model (SourceTracker) estimated that oral contribution to lung communities increased with amylase but remained modest (~35%), supporting a model of seeding followed by environmental filtering. 16S rRNA sequencing revealed no differences in alpha diversity but significant beta diversity shifts, with enrichment of oral-associated taxa. To explore persistence mechanisms, genus-level oxygen tolerance profiles from BacDive were mapped onto BAL communities using relative abundance. Increasing amylase was associated with increased anaerobic and microaerophilic representation. Consistent with the oral cavity, where polymicrobial aggregates support coexistence of aerobic and anaerobic taxa, similar organization may generate localized oxygen gradients that enable anaerobic persistence within the lung.

To further investigate these findings, a controlled bioreactor platform is under development. A 10-member consortium of lung-associated species was cultured under lung-mimicking versus nutrient-rich conditions with dynamic oxygen control. Lung-like conditions enriched *Rothia*, reduced *Streptococcus*, and promoted aggregate formation, while nutrient-rich favored *Corynebacterium* and *Staphylococcus*. Together, these findings support a model in which lung microbial communities are shaped by oral immigration and lung-environment filtering.