**Metatransciptomic multivariate analysis of bronchoalveolar lavage fluid amongst patients with COVID-19**.

**Abstract:**

In order to better understand the potential relationship between COVID-19 disease severity and microbial community dynamics / functional profiles from a hologenome standpoint, we conducted a multivariate comparison of publicly available human bronchoalveolar lavage fluid (BALF) metatranscriptomes samples amongst COVID-19 (*n*=48), community acquired pneumonia (*n*=25), and uninfected patients (*n*=32). Our overarching hypothesis was that there is a potential informative relationship between the BALF microbiome and the severity of  COVID-19 disease onset and progression. After read filtering and batch effect sample removal, the remaining SARS-CoV-2 viral and microbial reads were taxonomically classified (Kraken2), functionally characterized (SeqScreen), and analyzed for multivariable associations with linear models (MaAsLin2) in association with the occurrence of COVID-19 disease and death. Among our cohort of n=105 subjects, there were n=48 with COVID-19 disease; deceased comprised *n*=20 while survived were another *n*=19). After controlling for differences in publication and study design, we observed significantly unique taxonomic and functional changes to the hologenome associated with COVID19 disease and death.  Specifically, we observed notable functional profiles within microbial communities through which analysis of predicted proteins and gene ontology terms were predictive of outcome severity amongst COVID-19 profiles. Collectively, while this data does not speak to causality nor directionality of the association, it does demonstrate a significant relationship between the human microbiome and severity of COVID-19, rendering further testable hypotheses that warrant further investigation.