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Comprehensive transcriptomic analysis of a pediatric COVID-19 cohort uncovers new role for OTOF upon SARS-CoV-2 infection

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Objectives:

Numerous studies have been undertaken to understand the immune response upon SARS-CoV-2 infection enabling characterization of key genes and pathways involved in Coronavirus disease 2019 (COVID-19). Majority of COVID-19 transcriptomic studies have been performed on adult cohorts, providing first insights into the immune response upon infection. Children infected with SARS-CoV-2 typically experience a milder disease course compared to adults. To better understand the immune differences upon infection, we performed a comprehensive bulk transcriptomic analysis on whole blood of a COVID-19 cohort comprising both pediatric and adults from the ages of 2 weeks to 40 years old. Probandes were grouped into either Healthy (n=36), COVID (n=42), Non-COVID (n=44) or MISC (n=8).

Methods & Results:

In our age-associated analysis, 4 genes show strong differences in expression values in COVID compared to healthy controls; MMP8 decreases with age while OAS1, OAS2 and LY6E increases with age. When controlling for the effect of age, differential gene expression (DGE) analysis revealed 246 genes to be significantly differentially expressed in COVID compared to healthy controls, including known COVID-19 biomarkers such as IFI27 and SIGLEC1. Interestingly, our analysis revealed a marked upregulation of Otoferlin (OTOF) expression in the COVID cohort. OTOF is a protein coding gene associated with non-syndromic hearing loss. Emerging studies have shown OTOF to play a role within the type I interferon pathway in response to viral infections. To understand the role of OTOF in our cohort, both bioinformatics and functional analyses, focusing on the effects of OTOF in influencing viral entry and binding to host cells, are ongoing where we hypothesize OTOF to inhibit viral entry specifically in myeloid cells.

Conclusions:

A complete characterization of the function of OTOF, specifically in a SARS-CoV-2 infection context, will provide new mechanistic insights into the role of OTOF and potentially a new target for future therapeutics.