To the editors of *Nature Medicine*,

My team and I are tremendously thrilled to present to you our manuscript entitled “Genetic and inflammatory signatures associated with worse prognosis in hospitalized patients with severe SARS-CoV-2 infection with and without diabetes.”

In this article, we performed a retrospective cohort study of 182 hospitalized patients with and without COVID-19 (110 versus 72) patients and with and without diabetes (67 versus 115 patients). Leftover blood samples from these patients were analyzed for RNA sequencing, cytokine and chemokine levels, and ACE-2/DPP-IV levels. After analysis, a total of 19,909 protein-coding genes were found, with 14,223 genes demonstrating a sufficient number of hits for further analysis. RNA sequencing analysis was performed with the DESeq2 R package based on a negative binomial distribution for differential gene expression. Of these genes, 18 were differentially expressed in COVID patients compared to non-COVID patients; 2 were downregulated and 16 were upregulated. 431 genes were differentially expressed in diabetes patients versus non-diabetes; 45 were upregulated and 386 were downregulated. 5 genes were differentially expressed between both analyses: GRASP, KRT8, MYZAP, PRKG1, and SMIM24.

This study is, as far as we are aware, the largest gene profiling analysis of blood samples of COVID-19 patients. The results provide insight into altered gene expression patterns in patients with and without COVID-19 and with and without diabetes and highlights potential 1) markers for more severe disease and 2) disease progression pathways that may be future targets for treatment. We hope that the results of this study will increase the research into specific gene-protein pathways related to COVID-19 to better elucidate the mechanisms of related risk factors.

This article is an original retrospective cohort study approved by the institutional review board. All authors fulfilled authorship criteria and were critical to this research. The manuscript has been reviewed and approved by all authors. It is not under consideration for publication elsewhere and has not been published in full or in part. There have been no prior discussions with editors from *Nature Medicine* regarding the manuscript.

Thank you again for your time and consideration of our manuscript and we look forward to hearing back from you soon.

Sincerely,

Marshall Yuan