Impact of differential gene expression on early innate immune responses to COVID-19 vaccination in end stage renal disease patients and healthy controls

Gingras SN [1,2],Lopez C[2], Ahmed J[2], Ball TB[2,1], Su RC[2,1], Bueti Joe[3,4,5], Card CM[2,1], Kiazyk SA[2,1], McLaren PJ[2,1]

[1]Department of Medical Microbiology and Infectious Diseases, University of Manitoba, Winnipeg, MB, Canada, [2]National HIV and Retrovirology Laboratory, JC Wilt Infectious Diseases Research Centre, National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, MB, Canada, [3]Department of Internal Medicine, University of Manitoba, Winnipeg, MB, Canada, [4]Section of Nephrology, Department of Internal Medicine, University of Manitoba, MB, Canada, [5]Health Sciences Centre, Winnipeg, MB, Canada.

Background: SARS-CoV-2 has infected more than 508 million people worldwide causing more than 6.2 million confirmed deaths since the beginning of the COVID-19 pandemic. End Stage Renal Disease (ESRD) patients are immunocompromised and at an increased risk of infection and severe disease and death. Studies have shown ESRD patients have a significantly reduced humoral and B cell memory responses to COVID-19 vaccination. However, early innate immune responses have yet to be explored in this population.

Methods: Blood was collected in PAXgene RNA Blood Tubes before (BD1) and 1-4 days post dose 1 (PD1) of COVID-19 vaccination (n=17 ESRD; 28 healthy controls). RNA was isolated for RNA-Sequencing and differential expression was assessed between groups using DESeq2. Network and gene ontology analysis will assess differences in early innate immune response pathways after COVID-19 vaccination. Detailed enrollment and follow-up questionnaires (demographics, medical history, COVID-19 history, medications, etc.) were collected from participants and cellular and antibody responses are being measured at 2 week, 6 months, and one-year post vaccination. We will assess whether these long-term responses are impacted by early, innate activation.

Results: Transcriptional profiling in response to COVID-19 vaccination identified 125 significantly differentially expressed genes (DEG) ($1.17E-08 < padj < 0.04$) and 107 DEGs ($3.13E-03 < padj < 0.05$) in ESRD patients and healthy controls, respectively. 72 DEGs were significant in both populations, 54 unique to ESRD patients and 36 unique to healthy controls. Network analysis and gene ontology analysis is currently underway to identify which innate immune responses are activated or repressed in these populations.

Conclusion: ESRD patients are at an increased risk for COVID-19 infection and severe disease. We show ESRD patients elicit a unique immune response to COVID-19 vaccination compared to healthy controls, potentially impacting the effectiveness of vaccination in ESRD patients.

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