SELECTED TALK:

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Exploring a role for ABO antibodies in the association between ABO blood group and COVID-19 susceptibility

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Purpose: In the current COVID-19 pandemic there is a recognized association between ABO blood group and susceptibility to SARS-CoV-2 infection, where blood group A (ABO-A) individuals are more susceptible to infection than ABO-O individuals. Antibodies to blood group A antigen (glycans) are produced naturally in ABO-O individuals but not in ABO-A individuals. It has been hypothesized that anti-A antibodies may have specificity for A-glycans (or A-like glycans) on the heavily glycosylated SARS-CoV-2 spike protein (SP), which may result in viral neutralization in ABO-O individuals. Here we sought to explore this hypothesis by investigating binding of ABO antibodies to recombinant SARS-CoV-2 SP.

Methods: An inhibition assay was used to examine ABO- and SP-antibody binding to soluble SP (recombinant S1+S2). Recombinant SARS-CoV-2 SP was produced in HEK293 cells (ABO-O). Antibodies to ABO glycans (and the related glycan galactose-α-1,3-galactose (α-gal)) and SARS-CoV-2 targets were assessed using a multiplex bead-based assay developed in our laboratory consisting of BSA-conjugated A and B subtype glycans I-VI and α-gal, and SARS-CoV-2 recombinant SP (S1 subunit or S1+S2 heterodimer), receptor binding domain (RBD), and nucleocapsid protein (NP). Plasma (1/50 dilution) obtained from a COVID-19-infected ABO-O individual and from a COVID-19-uninfected/unvaccinated ABO-O individual were incubated for 1 hr at 37ºC with and without soluble SP (0-80 nM) before addition to ABO and COVID Luminex beads followed by secondary fluorescence-tagged antibody to detect IgG ABO and SARS-CoV-2 antibodies.

Results: When COVID-19 convalescent plasma was incubated with increasing concentrations of soluble SP, there was a dose-dependent decrease (up to 90%) in detection of IgG anti-RBD and anti-SP (S1+S2, S1) antibodies. However, there was no change in the levels of detected IgG anti-NP, indicating the specificity of inhibition to SP-specific but not third-party antibodies. Plasma from a uninfected ABO-O individual showed no detectable COVID antibodies. Following incubation with SP, plasma from both convalescent and uninfected/unvaccinated ABO-O individuals showed a dose-dependent decrease (up to 20-25%) in IgG anti-A and anti-B (all subtypes) as well as α-gal antibody.

Conclusion: In a preliminary analysis using an inhibition assay we found a marked decrease in IgG anti-SP antibodies following incubation of convalescent plasma with soluble SP, consistent with anti-SP antibody binding to soluble SP. Further, we found that IgG anti-A and anti-B of convalescent or uninfected plasma decreased after incubation with soluble SP, suggesting some of these antibodies may recognize soluble SP. Studies are ongoing to determine whether ABO antibodies bind SP produced by either ABO-O-derived cells or ABO-A cells.