Direct Comparison of Glycans and their Isomers Derived from SARS-CoV-2, SARS-CoV-1, and MERS-CoV Recombinant Spike Glycoproteins

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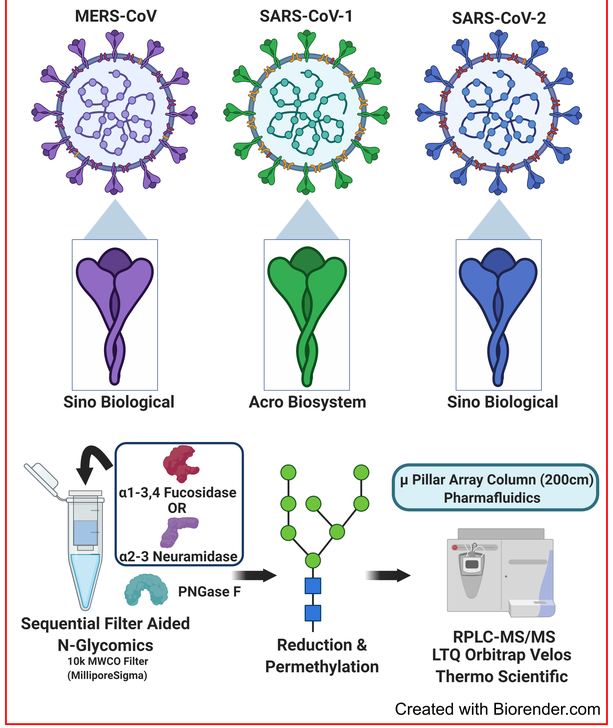
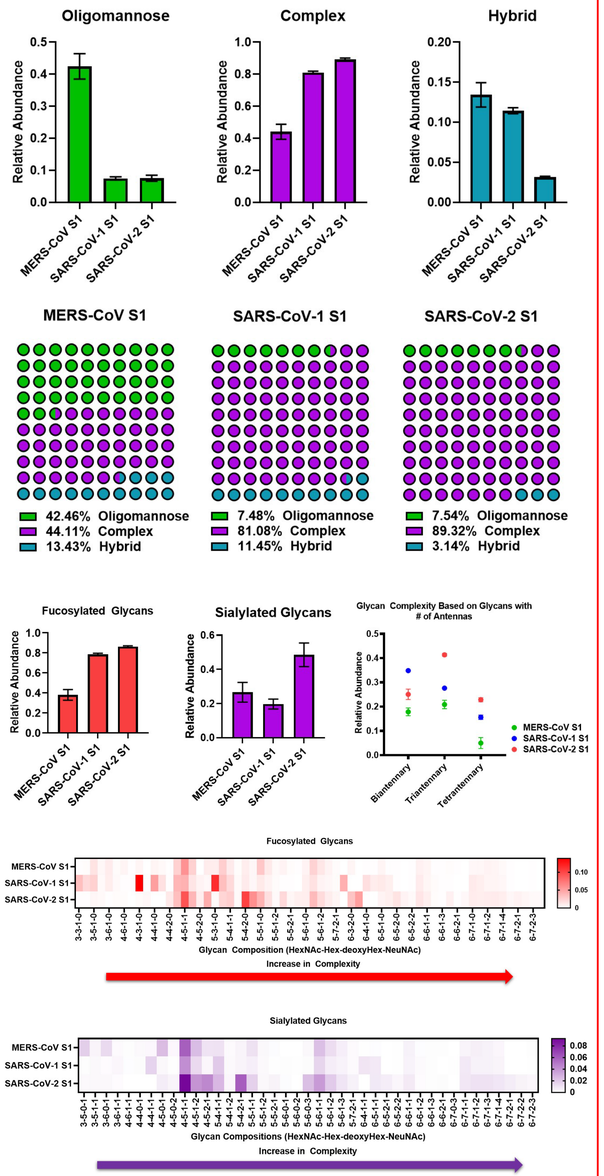
Introduction

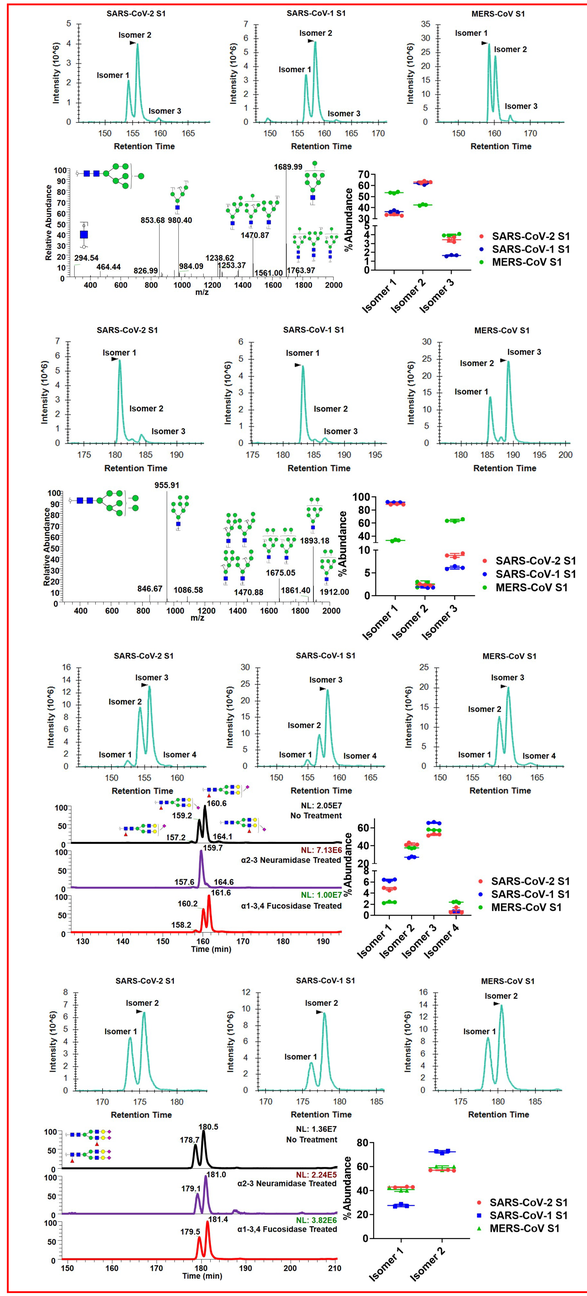
COVID-19 is a disease caused by human infection of SARS-CoV-2 virus thought to have originated from China. Currently, the virus has infected more than 5 million people and killed more than 170,000 people in the United States alone as of August 19th, 2020. The pathology of SARS-CoV-2 has been documented previously as the spike protein (S Protein) on the viral membrane attaching to the angiotensin-converting enzyme 2 (ACE2) protein on human cells. S proteins can be categorized into 2 parts: S1 and S2. While the S2 protein is associated with membrane fusion, the S1 protein is involved in the initial attachment of the virus to host cells. The S1 protein is also heavily glycosylated, a state that protects the SARS-CoV-2 virus by acting as a sort of "Glycan Shield" [1, 2]. Due to the uniqueness of this adaptation, the glycosylation of the SARS-CoV-2 S1 protein has been previously investigated [3-6]. However, there never has been a direct comparison of glycosylation between previous epidemic coronaviruses (SARS-CoV-1 and MERS-CoV) as well as glycan isomers of their glycan shield. Glycan isomers are important feature of viral transmissions and their functions have been well documented previously with flu virus variants [7]. Here in this work, we demonstrate direct comparison of glycosylation between the current pandemic coronavirus and the other two previous epidemic coronaviruses as well as the isomers of their glycans using LC-MS/MS.

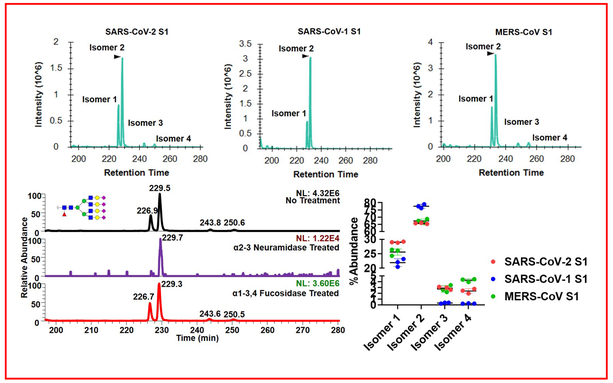
Method



Results







Conclusion & Future Works

In this work, we demonstrated glycan complexity, types, compositions and various isomers derived from S1 proteins from three different coronaviruses. Both SARS coronaviruses revealed significantly more complex glycans while MERS showed high abundance of oligomannose. SARS coronaviruses also exhibited high abundance of fucosylated glycans. SARS-CoV-2 however, revealed significantly more glycans with sialic acids in comparison to other two coronaviruses. Moreover, SARS-CoV-2 glycans unveiled to be more complex with more antennas on their glycans. This work is the first time ever to demonstrate glycan isomers from S1 proteins of coronaviruses. It could be feasible that the high false positive rate of antigen tests targeting S proteins may be due to the complicated glycan isomers presenting on the protein. Therefore, wild type SARS-CoV-2 S protein glycosylation should be investigated and compared with recombinant proteins to further validate and produce more reliable diagnostic tests.

References

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