

How blood group A might be a risk and blood group O be protected from Coronavirus (COVID-19) infections

by Peter Arend

In the case that *O*-glycosylation plays a key role in the pathogenesis of coronavirus infections, as was discussed already 14 years ago¹ and is currently again predicted,² this would involve the formation of hybrid, serologically A-like, *O*-GalNAc α 1-Ser/Thr-R, Tn (“T nouvelle”) antigenic structures; the virus cannot survive outside of its hosts and hypothetically utilizes the host cell’s machinery via hijacking its A-like/Tn formation by serine-rich motifs. Similar suggestions are subject of the recent review, published by Watanabe et al. (2019).³ The adhesion of the virus to host cells would primarily occur independent of the ABO blood group through the genetically undefined intermediate, A-like/Tn evolutionary/developmental structure, which is common to all metazoan growth processes and apparently acts as a host-pathogen functional bridge in different, unrelated infectious diseases.^{4, 5} However, while susceptibility to an infection and its severity depend on many factors, individuals with blood group A could not respond with either acquired or innate antibodies to the synthesis of hybrid A-like structures due to clonal selection and phenotypic, glycosidic accommodation of plasma proteins.⁶ Thus, blood group A individuals would become a preferred target for the virus, which hypothetically mimicks the ABO phenotype pathways: while serine residues, preserved on the viral spike protein, become available through the host’s transmembrane serine protease TMPRSS2,⁷ the angiotensin converting enzyme (ACE) receptor protein is codetermined by the ABO phenotype,^{8, 9, 10} and via an as yet undefined process might mediate the ABO glycan transferring enzyme activity, which performs a further (blood group-A-specific (A-allelic) mucin-type) hybrid binding. Analogously, the binding to

blood group O cells might occur by mucin-type fucosylation via fucosyltransferases 1 and 2 (FUT1/FUT2) and performance of a hybrid H antigen,^{4, 5} which would not affect the innate and adaptive anti-A isoagglutinin levels (Fig. 1). Apart from a corresponding or similar observation in a rotavirus infection,¹¹ a first statistical study indicates that people with blood group A have a significantly higher risk for acquiring COVID-19, whereas people with blood group O have a significantly lower risk for the infection compared with non-O blood groups.¹² While this small observation awaits confirmations, Chile, where 85% of people have blood group O, appears to have the lowest COVID 19 cases and death rates per 1 million inhabitants. Blood group O individuals, lacking the blood group-A-determining enzyme, may develop the least molecular contact with the pathogen and maintain the anti-A/Tn cross-reactive, complement-dependent isoagglutinin activity, which is exerted by the polyreactive, nonimmune immunoglobulin M (IgM),^{4, 5, 13} representing the humoral spearhead of innate immunity and a first line of defense.

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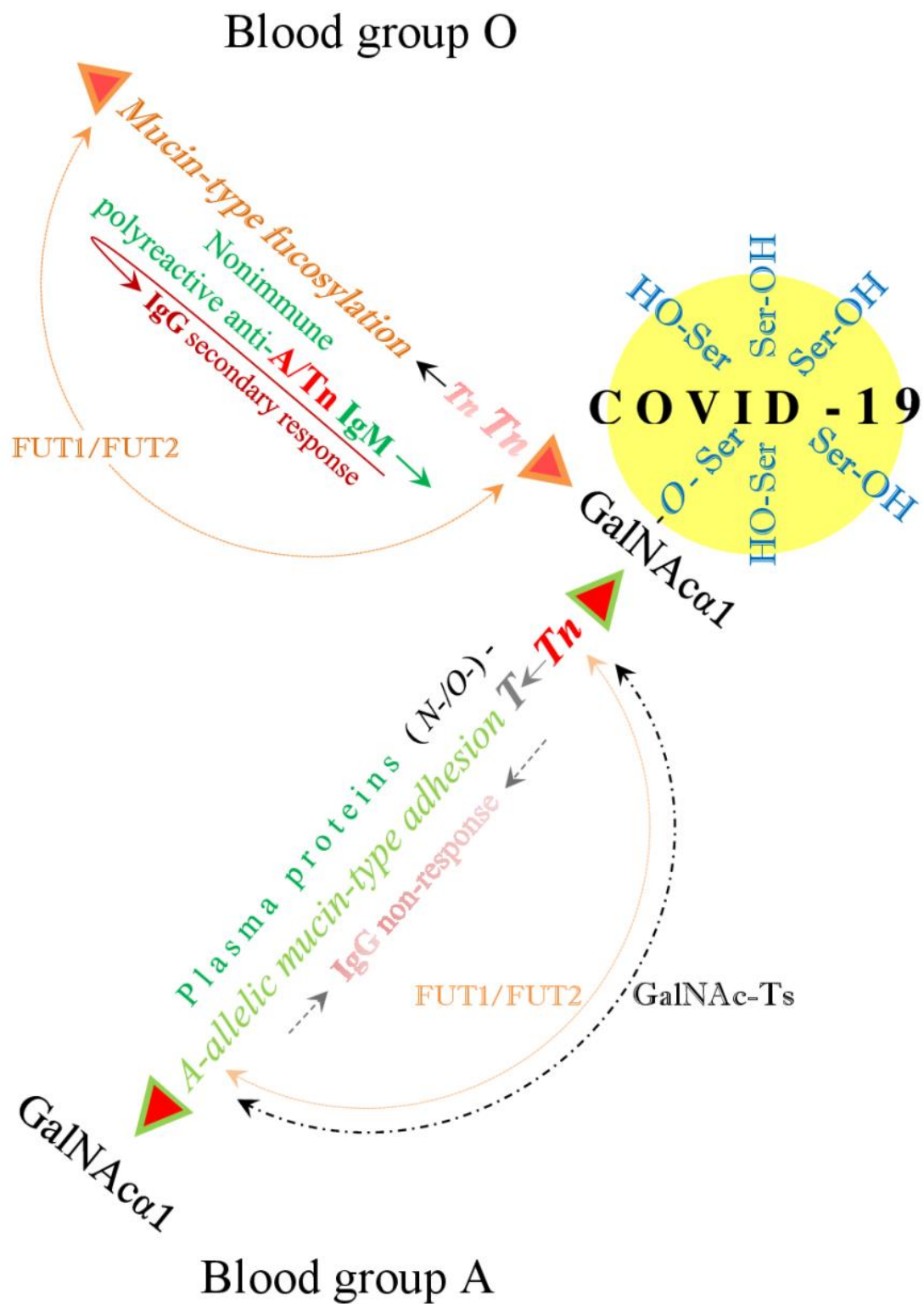


Figure 1. The virus cannot survive outside of its hosts and hypothetically mimicking the ABO phenotype pathways, utilizes the host cell's machinery via hijacking the host's A-like/Tn formation and phenotype-determining enzymes by serine-rich motifs. This figure was constructed according to figure 2 in a previous article, in which this mechanism may be similarly utilized by a non-viral pathogen, such as the protozoan parasite *Plasmodium falciparum* (See references 4 and 5).