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 ago[1] and is currently again predicted,[2] this would result in the formation of a serologically A-like, *O*-GalNAcα1-Ser/Thr-R, Tn ("T nouvelle") antigenic structure; 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, glyosidic 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, utilizing the phenotype-determining glycotransferases and performing a further (blood group-A-specific (A-allelic) mucin-type) hybrid binding; analogously, the binding to blood group O cells might occur by fucosylation and performance of H- (by fucosyltransferase 1, FUT1) and Le (by fucosyltransferase 2, FUT2) structures.[4, 6] This would not affect the innate and adaptive anti-A isoagglutinin levels (Fig. 1). Apart from a corresponding or

similar observation in a rotavirus infection[7], 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.[8] While this small observation awaits confirmations, blood group O individuals, lacking the blood group-A-determining enzyme, would 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, 9] representing the humoral spearhead of innate immunity and a first line of defense.

References:

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Proposed (virtual) adhesion and/or response

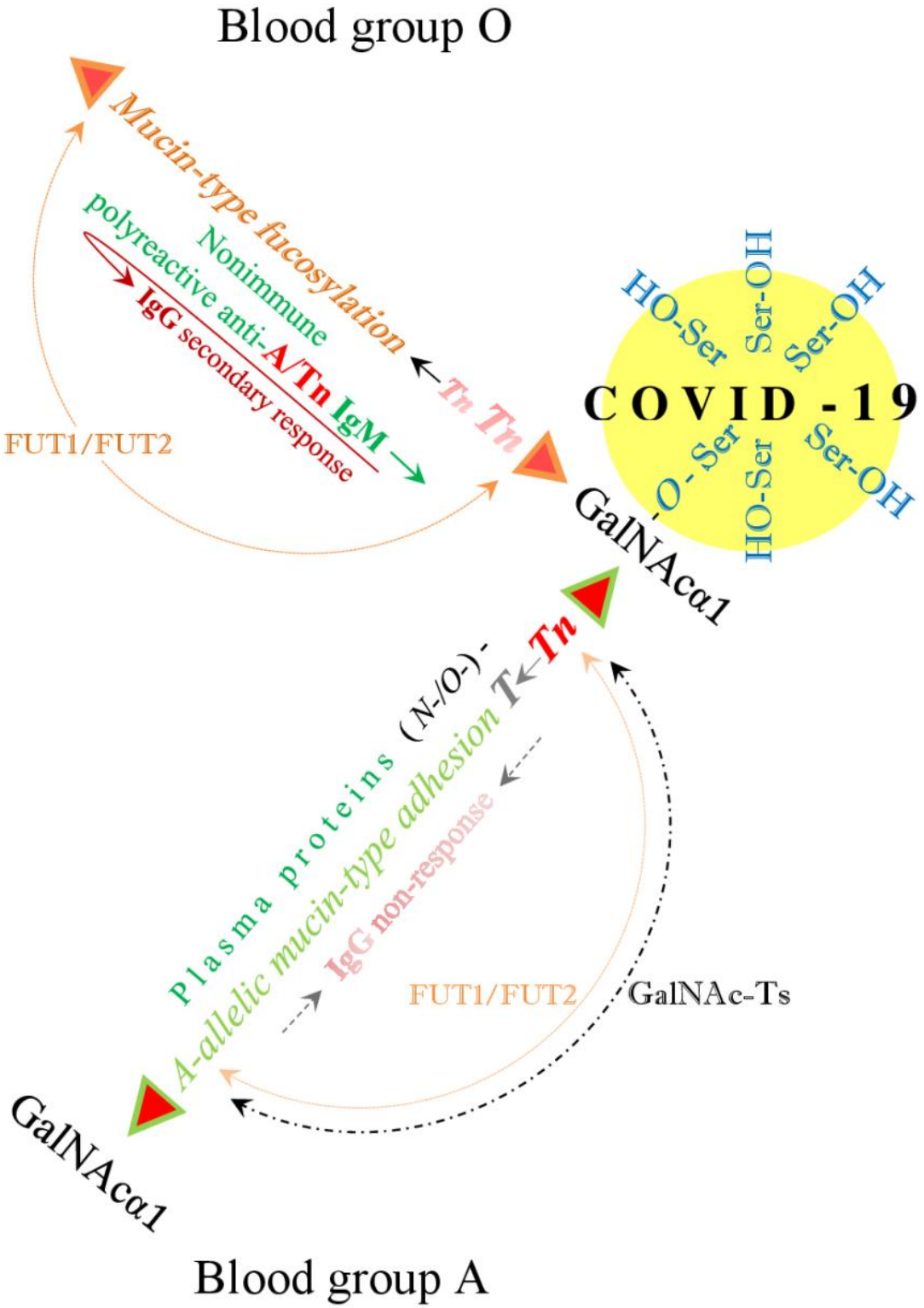

Figure 1. The virus cannot survive outside of its hosts and hypothetically mimicking the ABO phenotype pathways, utilizes the host cell's machinery via hijacking the host's A-like/Tn formation and phenotype-determining enzymes by serine-rich motifs. This figure was constructed according to figure 2 in 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).