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Immunity to Glycan Alpha-Gal and COVID-19: Possibilities for Disease Control and Prevention

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ABSTRACT

The coronavirus disease 19 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has affected millions of people worldwide. The characterization of the immunological mechanisms involved in disease symptomatology and protective response is important to advance in disease control and prevention. Humans evolved by losing the capacity to synthesize the glycan Galα1-3Galβ1-(3)4GlcNAc-R (alpha-Gal), which resulted in the alpha-Gal syndrome associated with tick salivary glycoproteins with alpha-Gal modifications that after tick bite can induce in some individuals the production of high levels of anti-alpha-Gal IgE antibodies that mediate delayed anaphylaxis to mammalian meat and immediate anaphylaxis to tick bites. In contrast, humans can develop of a protective response against pathogens containing this modification on membrane proteins mediated by anti-alpha-Gal IgM/IgG antibodies naturally produced in response to bacterial microbiota. In addition to anti-alpha-Gal antibody-mediated pathogen opsonization, this glycan induces various immune mechanisms such as B-cell maturation, macrophage response, activation of the complement system, innate immune pathway and TLR-mediated anti-inflammatory responses that have shown protection in animal models against infectious diseases. Based on these results, we hypothesized that the immune response to alpha-Gal may contribute to the control of COVID-19. To address this hypothesis, we characterized the antibody response to alpha-Gal in patients at different stages of COVID-19 and healthy control individuals. The results showed that while the inflammatory response and the anti-SARS-CoV-2 IgG antibody titers increased, reduction in anti-alpha-Gal IgE, IgM and IgG antibody titers and alteration of anti-alpha-Gal antibody isotype composition correlated with COVID-19 severity. These results suggested that the inhibition of the alpha-Gal-induced immune response may translate into more aggressive viremia and severe disease inflammatory symptoms. These results support our proposal of developing interventions such as probiotics/postbiotics based on commensal bacteria with alpha-Gal epitopes to modify the microbiota and increase the alpha-Gal-induced protective immune response and reduce the severity of COVID-19.

Keywords: Coronavirus, Microbiota, Immune pathway, Inflammatory response

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