Docket #: S20-208

MEASUREMENT OF AFUCOSYLATED IgG Fc GLYCANS TO PREDICT RISK OF SEVERE COVID-19 DISEASE

Researchers at Stanford have developed a method for identifying a subject that is at risk of progression to clinically significant COVID-19 infection or disease.

A minority of individuals infected with SARS-CoV-2 mount an extreme inflammatory response that is implicated in the disease's pathogenesis. Mechanisms contributing to this response are not well understood. Antibodies formed early during infection can bind virus particles, forming immune complexes that neutralize or mediate clearance of virus. However, immune complexes can also promote inflammation and exacerbate symptoms of disease via interactions between antibody Fc domains and Fc gamma receptors, particularly on myeloid cells, which are central regulators of the inflammatory response. How antibodies within immune complexes modulate infection depends, in part, on their Fc domain structure. IgG is the dominant antibody isotype in systemic antiviral immunity. The inventors and others have found that a high abundance of afucosylated IgG antibodies is linked to severe COVID-19, however whether afucosylated IgG production is a consequence of, or an antecedent to, the development of more severe COVID-19 remained unclear.

Stage of Development
Research –

in vitro

Stage of Research
Two independent cohorts were assessed during an initial period of mild COVID-19 and it was found that the absence of neutralizing antibodies and an increased abundance of afucosylated IgG was associated with a rapid progression to more severe disease. Elevated frequencies of monocytes expressing the receptor for

afucosylated IgG, CD16a, were also associated with more severe outcomes. Immune complexes formed from SARS-CoV-2 mRNA vaccine-elicited IgG did not trigger the robust immune activation that was associated with afucosylated IgG in vivo. The researchers have therefore established a method for determining that a subject is symptomatic or prone to present one or more symptoms of COVID-19 and at risk of progression to clinically significant COVID-19 infection.

Technology Reference
CZB-169S-PC, S20-208

Applications

- Elevated production of afucosylated IgG was found to precede onset of severe disease symptoms, and stayed high over time.
- Combining searches for early non-neutralizing titers and afucosylated anti-spike IgG could separate progressors from non-progressors towards severe disease with higher accuracy than either attribute alone.
- mRNA vaccination elicits the production of neutralizing IgG with glycoforms that are distinct from those elicited by infection

Advantages

- The development of prognostic biomarkers and clarification in the mechanisms underlying the distinct trajectories in COVID-19 may help halt disease progression to severe COVID-19.
- A method to identify subjects who are prone to progress to severe COVID-19 disease.

Publications

- Chakraborty, S., Gonzalez, J.C., Tan, G.S., Wang, T.T., et al. "Early non-neutralizing, afucosylated antibody responses are associated with COVID-19 severity." 2022. Science Translational Medicine. 14(635), eabm7853.

Patents

- Published Application: WO2021231304
- Published Application: 20230176068

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