Antibody therapeutic candidate reduces immune complexes involved in autoimmune diseases

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A broad variety of autoimmune diseases involve the development of pathogenic immunoglobulin G (IgG) antibodies which can attack cells

and tissues and form immune complexes with the antigen to which they are directed. Immune complexes are particularly problematic as they can deposit in tissues and promote the further development of autoantibodies yet can only be removed or inhibited by invasive methods.

A new study led by investigators at Brigham and Women's Hospital in collaboration with Syntimmune Pharmaceuticals adds to the body of evidence that blocking the neonatal crystallizable fragment receptor (FcRn) has the potential to treat autoimmune diseases by removing not only IgG but also the immune complexes they form. In preclinical studies and a Phase 1 clinical study, the team presents evidence that expands the role of FcRn beyond simply removing IgG antibodies from circulation, showing its potential for treating autoimmune diseases. The team's findings are published in *Science Advances*.

"We anticipate that FcRn antibody therapeutics will be part of an important new class of drugs for the treatment of autoimmune diseases," said corresponding author Richard Blumberg, MD, Vice Chair for Research in the Department of Medicine at Brigham and Women's Hospital. "As these types of drugs move into the clinic, we need to pay attention to their effects on IgG immune complexes as that is something which has not received the attention it deserves."

Previous studies have shown that blocking FcRn can lower levels of IgG in humans, the most common antibody found in the blood. IgG plays a critical role in fighting infection by binding pathogens such as viruses and bacteria but is also tied to autoimmune diseases such as lupus, pemphigus and more. IgG can also form complexes with antigens, which may further promote the autoimmune response, but the effect of blocking FcRn on the immune complexes had not been evaluated until now.

Blumberg and colleagues assessed the effects of SYNT001, an FcRn

blocking monoclonal antibody, on IgG as well as IgG immune complexes in mice, non-human primates and humans. They found that SYNT001 decreased the levels of both IgG and IgG immune complexes in the circulation and inhibited the ability of the immune complexes to activate the immune system. The drug candidate was well tolerated in the Phase 1 study.

"The results of these studies suggest that FcRn blockade using SYNT001 has the potential to treat a variety of inflammatory and autoimmune conditions making it a promising therapeutic agent in reversing the effects of pathogenic IgG and IgG immune complexes," the authors write.

More information: "Blocking FcRn in humans reduces circulating IgG levels and inhibits IgG immune complex–mediated immune responses" *Science Advances* (2019). advances.sciencemag.org/content/5/12/eaax9586

Provided by Brigham and Women's Hospital

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