A novel antibody against human properdin inhibits the alternative complement system and specifically detects properdin from blood samples.

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Details

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Abstract

The complement system is an essential part of the innate immune system by acting as a first line of defense which is stabilized by properdin, the sole known positive regulator of the alternative complement pathway. Dysregulation of complement can promote a diversity of human inflammatory diseases which are treated by complement inhibitors. Here, we generated a novel blocking monoclonal antibody (mAb) against properdin and devised a new diagnostic assay for this important complement regulator. Mouse mAb 1340 specifically detected native properdin from human samples with high avidity. MAb 1340 inhibited specifically the alternative complement mediated cell lysis within a concentration range of 1-10 µg/mL. Thus, in vitro anti-properdin mAb 1340 was up to fifteen times more efficient in blocking the complement system as compared to anti-C5 or anti-Ba antibodies. Computer-assisted modelling suggested a three-dimensional binding epitope in a properdin-C3(H2O)-clusterin complex to be responsible for the inhibition. Recovery of

properdin in a newly established sandwich ELISA using mAb 1340 was determined at 80-125% for blood sample dilutions above 1:50. Reproducibility assays showed a variation below 25% at dilutions less than 1:1,000. Systemic properdin concentrations of healthy controls and patients with age-related macular degeneration or rheumatic diseases were all in the range of 13-30 µg/mL and did not reveal significant differences. These initial results encourage further investigation into the functional role of properdin in the development, progression and treatment of diseases related to the alternative complement pathway. Thus, mAb 1340 represents a potent properdin inhibitor suitable for further research to understand the exact mechanisms how properdin activates the complement C3-convertase and to determine quantitative levels of properdin in biological samples.

Involved units

Infection Biology Peter F. Zipfel Read more

Leibniz-HKI-Authors



Susanne Ackermann

Details



Christine Skerka

Details



Peter F. Zipfel

Details

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