

C5 Genetic Variants Affect the Stability of the C5-Eculizumab Complex

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The monoclonal antibody eculizumab targets complement protein C5. It is a treatment for disorders involving complement system dysregulation, such as the rare disease Paroxysmal Nocturnal Hemoglobinuria (PNH). PNH is an acquired condition affecting hematopoietic stem cells, leading to abnormal red blood cell destruction, chronic hemolytic anemia, and increased risk of thrombosis^{1,2}. This study applies molecular dynamics simulations to explore the molecular interactions between C5 and eculizumab. It focuses on how specific single-nucleotide polymorphisms in the C5 gene - particularly the Arg⁸⁸⁵His and Arg⁸⁸⁵Cys variants - may alter the protein's structure and compromise its binding with the antibody^{3,4}.

The findings indicate that these mutations cause conformational changes at key interaction sites, reducing the stability of the C5-eculizumab complex. These insights help explain reduced treatment responses in patients carrying these mutations and may support the development of improved therapeutic strategies⁵.

Keywords: Computational simulation; eculizumab; complement C5; genetic polymorphisms; structural analysis

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