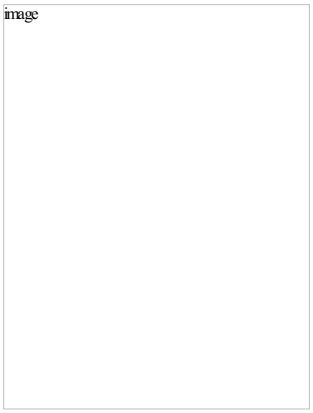

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www.elsevier.com/locate/bios

PII: S0037-1963(18)30005-2
DOI: https://doi.org/10.1053/j.seminhematol.2018.02.003
Reference: YSHEM50938

To appear in: *Seminars in Hematology*

Cite this article as: Ronald P. Taylor and Margaret A. Lindorfer, Mechanisms of complement-mediated damage in hematological disorders, *Seminars in Hematology,* doi:10.1053/j.seminhematol.2018.02.003

Mechanisms of complement-mediated damage in hematological disorders

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Declarations of interest: none

Abstract

The complement cascade is an ancient defense system that destroys and eliminates threats to normal homeostasis in the bloodstream and tissues. Although multiple controls keep complement in check to minimize innocent bystander injury to normal cells and tissues, defects in complement regulation due to mutations in, or autoantibodies to, complement control proteins underlie the pathogenesis of several hemolytic diseases including paroxysmal nocturnal hemoglobinuria, and atypical hemolytic uremic syndrome. In autoimmune hemolytic anemias complement plays an important role in erythrocyte destruction mediated by anti-erythrocyte antibodies. The pathogenic mechanisms of these hemolytic diseases are discussed, with an emphasis on pivotal steps in complement activation.

Abbreviations: aHUS, atypical hemolytic uremic syndrome; AIHA, autoimmune hemolytic anemia; AP, alternative pathway of complement; CAD, cold agglutinin disease; C1s*, C1r*, activated forms of C1s and C1r respectively; CFHR proteins, complement factor H related proteins; CLL, chronic lymphocytic leukemia; CP, classical pathway of complement; DAF, decay accelerating factor, CD55; IC, immune complex; MAC, membrane attack complex; MBL, mannan binding lectin pathway of complement; MCP, membrane co-factor protein, CD46; MIRL, membrane inhibitor of reactive lysis, CD59; PNH, paroxysmal nocturnal hemoglobinuria; THBD, thrombomodulin.