SIGNIFICANCE STATEMENT

Treatment options for C3 glomerulopathy (C3G, also called dense deposit disease or MPGN II) are limited. Supplement of factor H (FH, a potent complement regulator) in both murine models and patients can ameliorate disease. However, production of sufficient quantities of FH has proved challenging. Recombinant minimal versions of FH (mini-FH) possess improved complement regulatory function and are readily produced in culture but their serum $t_{1/2}$ is approximately 1.5 hours in animal models. By introduction of an FH-related protein dimerization module to mini-FH, the authors have significantly improved complement regulatory function and serum $t_{1/2}$ (approximately 9 hours). This approach represents a practical solution to improving anticomplement drug function and, importantly, could eventually provide a viable treatment for patients with complement-mediated diseases, particularly C3G.