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**Complement depletion with humanized cobra venom factor reduces tissue damage  
in a mouse model for age-related macular degeneration.**

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There are several lines of evidence, including both genetic and immunological, that inappropriate complement activation is associated with age-related macular degeneration (AMD), the main cause of vision loss in people 55 and older. HC3-1496 is a humanized cobra venom factor (CVF) in which the 168 C-terminal amino acids of the  $\alpha$ -chain of human C3 were replaced with homologous CVF sequences. Previous studies have shown that, like CVF, HC3-1496 is effective in depleting serum complement, both *in vitro* and *in vivo*. However, unlike CVF, treatment with HC3-1496 does not activate C5, thereby preventing the generation of the pro-inflammatory C5a anaphylatoxin. In this study, we have tested the ability of complement depletion with HC3-1496 to reduce tissue damage in a laser-induced choroidal neovascularization model (used as a model for AMD) in mice. Mice were injected i.p. daily with either PBS (- control) or a very low dose (25  $\mu$ g/kg body weight) of HC3-1496. Approximately two hours after the first injection, laser coagulation surgery was performed. Lesions were measured directly following laser surgery, and on days 8 and 28. The laser-caused damage was less in HC3-1496-treated mice than in the control mice, as measured by mean lesion volume and mean lesion area. Similar results were obtained in CVF transgenic mice which constitutively express CVF and exhibit low serum complement levels. These data suggest that complement depletion with humanized CVF may be a useful treatment for slowing the damage in AMD.

