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## Novel Human C3 Derivatives for Therapeutic Complement Depletion

The complement system is part of the immune system and is important in both innate and adaptive immunity. However, the complement system can also be a pathogenetic factor in many diseases including, rheumatoid arthritis, reperfusion injury, myasthenia gravis, and more. Complement has also been shown to be important for the development of antibodies to biological therapeutics such as human Factor VIII in hemophilia A.

The development of agents to interfere with or modulate the complement cascade has been an area of intense interest for the past two decades. Furthermore, the FDA recently issued a guidance for the adoption of a risk-based approach to evaluating and mitigating immunogenicity associated with therapeutic proteins.

### Technology:

Dr. Carl-Wilhelm Vogel, a respected expert on the human complement system, and his colleagues have developed a novel therapeutic approach to complement pathogenesis: complement depletion. This approach came out of years of research with cobra venom factor (CVF), a C3 analog known to be able to deplete complement. Utilizing the knowledge of the structure and function of CVF and the C3 component of complement, Dr. Vogel and his colleagues created derivatives of human C3 (which they called humanized CVF or hCVF) which display CVF-like activity in depleting complement without displaying toxicity.

These hCVF C3 derivatives were tested for therapeutic complement depletion in multiple preclinical models of diseases with complement pathology, including reperfusion injury, age-related macular degeneration (AMD), paroxysmal nocturnal hemoglobinuria (PNH), and immunogenicity to Factor VIII in hemophilia A and consistently showed therapeutic efficacy. Chinese hamster ovary (CHO) cell lines have been developed for gram quantity production of the hCVF C3 derivatives.

These C3 derivatives induce complement depletion without toxicity, even after intra-arterial injection into the pulmonary artery of primates. No immunogenicity, to date, has been observed. As such, these derivatives would be excellent candidates for clinical applications requiring short-term complement depletion, even on a repeated basis.

### Applications:

- Treatment of chronic diseases with complement involvement
  - Rheumatoid Arthritis
  - Age-related Macular Degeneration
  - Myasthenia Gravis

- Paroxysmal Nocturnal Hemoglobinuria
- Atypical Hemolytic-Uremic Syndrome
- Acute treatments with complement involvement
  - Reperfusion injury
  - Ventilator-induced lung Injury
  - Angioplasty
  - mAb therapy of lymphoma
- Immunogenicity from biologic therapeutics
  - Hemophilia A
  - Other orphan diseases

Additional Information:

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