Functionally Selective Ligands for Study and Inhibition of Inflammation

Tech ID: 25919 / UC Case 2016-024-2

The complement system is part of innate immunity and is activated through the classical, lectin, and alternative pathways. The end-result of complement activation on pathogen surfaces is opsonisation (by C3b) for phagocytosis, formation of pore-making membrane attack complexes (MAC) for cell lysis, and initiation of inflammatory responses (by C3a and C5a). Complement activation on host cells is prevented by regulators (Factors I and H, MCP, DAF, CR1), but when regulation is compromised complement contributes to inflammatory and autoimmune diseases. Inflammation is mediated by C3a and C5a, which bind on leukocyte receptors. Design of selective exogenous ligands for C3a and C5a receptors provides the basis for assay development for mechanistic studies and a platform for drug design to combat complement mediated inflammatory diseases.

BRIEF DESCRIPTION

Background:

Due to the complexity of the complement system cascade, biological roles of many signaling receptors are unknown. Additionally, biased ligand binding to cell-bound receptors may lead to selective intracellular effector binding and ligand-specific pathway activation and function. Mechanistic knowledge forms the basis for assay development to explore pharmacology against complement-mediated inflammatory diseases.

Brief Description:

A multidisciplinary team of researchers from UCR, Texas A&M, Sheffield, and Queensland have discovered the first functionally selective peptide ligands for a complement system receptor that is involved in inflammation. The peptides are functionally selective ligands of C5aR2 but not C5aR1 or C3aR, and they have been characterized in vitro and in vivo. These peptides are novel tools that can modulate the activity of the receptor in vitro and in vivo, and interrogate the function of the receptor and its implication in inflammatory diseases.
ADVANTAGES
▶ Investigate selective ligand activity and the molecular origins of disease
▶ Develop agonists or antagonists with therapeutic potential as treatments for inflammatory disease

APPLICATIONS
▶ Biopharmaceutical industry – pharmacology
▶ Assay development for in vitro & in vivo mechanistic studies
▶ Drug discovery

RELATED MATERIALS