Universität Basel

Research Project

Therapeutic Modulation of Adverse Host Defense System Activation on Biomaterial and Cell Surfaces

Third-party funded project

Project title Therapeutic Modulation of Adverse Host Defense System Activation on Biomaterial and Cell Surfaces
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Departement Pharmazeutische Wissenschaften / Molecular Pharmacy (Ricklin)
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Under normal circumstances, the host defense functions of the human complement system help protecting our bodies from microbial threats and accumulating debris. However, the unique ability of complement to swiftly recognize foreign surfaces may suddenly turn into a burden when we are exposed to biomaterials, drug delivery vehicles, and cell or solid organ transplants. Prevention of complement activation directly on such non-self surfaces via protective coating is therefore considered a promising strategy for avoiding inflammatory complications. This proposal aims to design small complement-modulatory entities as a platform technology to be employed either as a surface coating or as a “molecular bridge” that guides physiological complement regulators to tissue, cell or material surfaces facing adverse activation of host defense pathways. The central element of our efforts is the cyclic peptide 5C6, which binds to the major complement regulator in circulation (i.e., Factor H; FH) and recruits it to 5C6-coated surfaces. The first stage of our research plan is focused on elucidating a structure-activity relationship profile of 5C6 to improve binding affinity, stability, and functionalization efficacy. For optimal activity, 5C6 needs to be coated on or tethered to a cell or material surface. The second stage of the proposal therefore aims at identifying promising coupling/targeting entities by focusing on three model systems: 1) liposomal formulations used as drug delivery vehicle; 2) endothelial cells relevant to transplantation; and 3) erythrocytes as a frequent target of erroneous complement attack. Coupling/targeting moieties will be evaluated for their selectivity and suitability to be linked to 5C6. In the third stage, suitable candidate compounds will be evaluated for their ability to prevent complement activation in the respective applications using established models. These targeted, FH-binding peptides are expected to provide attractive options for therapeutic modulation of complement activity on cells and surfaces with broad applicability of this versatile platform technology in transplantation medicine, inflammatory conditions and beyond.

Keywords PNH; Biomaterials; Factor H; Host Defense; Peptide; Transplantation; Erythrocytes; Complement; Immune Modulation
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Add publication

Published results

4486615, Harris, Claire L.; Pouw, Richard B.; Kavanagh, David; Sun, Ruyue; Ricklin, Daniel, Developments in anti-complement therapy; from disease to clinical trial, 0161-5890 ; 1872-9142, Molecular immunology, Publication: JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

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