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Development of a Large-Scale Antibody-Depleted Human Complement for Neisseria sp. Vaccine Immunogenicity Testing

Author(s)

Chris Lyle, PhD MBA

Chief Technology Officer

Pel-Freez Biologicals

Robert Natuk, PhD

Director of Strategic Partnerships

Pel-Freez Biologicals

Ashley Willis, BS

R&D Supervisor

Pel-Freez Biologicals

McKinzie Fruchtl, PhD

R&D Engineer

Pel-Freez Biologicals

Tre Donson, BS

R&D Lab Technician

Pel-Freez Biologicals

Brian Bonk, PhD

President and CEO

Pel-Freez Biologicals

Background

Immunogenicity assays used in vaccine development for Gram-negative bacteria such as Neisseria sp. and Gram-positive bacteria such as Streptococcus sp. vaccines rely on exogenous complement from humans and baby rabbits, respectively. Screening for seronegative human donors is a lengthy and expensive process that yields small quantities of usable serum. Repeated serum screening, pooling, bridging, and qualification is necessary to maintain an adequate amount of human complement to perform serum bactericidal assays (hSBA). Pel-Freez Biologicals has supplied baby rabbit complement to vaccine developers for decades, but until recently, human complement compatible with immunogenicity assays was not commercially available. Pel-Freez Biologicals introduced IgG/IgM-depleted human complement in 2018 and has since worked to expand commercial production to large-scale lots (>5 L) and to develop an IgA removal step. Using its proprietary antibody depletion process, Pel-Freez Biologicals has also developed negative matrix serum

useful for assay, equipment, and technician qualification, as well as dilutional linearity, proficiency panel and quality control serum production.

Aim/Methods

The aim of this project is to develop and characterize a large-scale source of antibody-depleted human complement to assist vaccine developers in immunogenicity testing and reduce reliance on seronegative donors. Pel-Freez uses proprietary methods to remove IgG and IgM antibodies and is currently scaling up IgA removal. Following antibody depletion, human serum is tested for residual antibodies and complement activity. Mass spectrometry analysis of human serum pools prior to and following antibody depletion has also been performed to gain insight into the effect of depletion on non-immunoglobulin serum proteins.

Results

IgG and IgM are consistently depleted to less than 3.5% residual antibodies as measured by HPLC. Human complement hemolytic titer at 50% dilution (CH50) and mass spectrometry demonstrate functionally active complement and preservation of key complement proteins following antibody depletion.

Conclusions

A large-scale (> 5L) antibody-depleted human complement reagent has been developed by Pel-Freez Biologicals that has been used successfully in a variety of Neisseria sp. vaccine programs from assay development stage through advancing clinical trials. Additional iterations of this product (varied concentrations, IgA-removal, etc.) are likely to prove useful to the Neisseria sp. vaccine research community.

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Supplemental Document Upload

PFB ADHC vs. MnC Qual Complement