Chimeric Allo-Antigen Receptors (CALLARs) directed to Factor VIII autoantibodies

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Technology description

Market Need

Hemophilia A is an inherited X-linked disease caused by Factor VIII (FVIII) deficiency and is a life-threatening bleeding disorder. The disease is associated with frequent hemarthosis and arthropathy that causes significant morbidity for patients. Factor replacement therapy using recombinant human FVIII (rhFVIII) is the standard of care for patients with hemophilia A. Unfortunately, 10-40% of patients with hemophilia develop antibodies (alloantibodies) to plasma-derived or recombinant human FVIII protein that inhibits the recombinant FVIII function. The consequences of allow antibody formation ranges from needing to increase the concentration of FVIII used to rendering the FVIII therapy useless and placing patients at risk of hemarthrosis and catastrophic intracranial bleeding requiring the use of by-pass agents. Thus, a need exists for strategies to diminish and/or counteract alloantibodies that are formed.

Technology Overview

Our investigators have developed a technology called Chimeric Allo-Antigen Receptors (CALLARS), which harness the power of chimeric T-cell technology and targets these T-cells against the B cells that would potentially form alloantibodies. CALLARS can be introduced to patients T-cells via gene-therapy mediated strategies such as lentiviral vectors. The initial CALLARS express the A2 and C2 domains of human FVIII for targeting the T cell since most inhibitory antibodies bind to epitopes in one of these two domains. CALLARs are activated by and kill B cells and plasma cells expressing surface immunoglobulins that bind to either the A2 or C2 domains for FVIII. The group has in vitro proof of concept data that specific CALLARS secrete IFN✚ specifically in response to anti-A2 or anti-C2 antibodies.

Advantages

- Enhances existing FVIII treatment by targeting inhibitory antibodies
- Gene-therapy mediated delivery ensures longer lasting response

Institution

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