

Wednesday, February 19, 2020

LSC 3 | 1:00 - 2:00PM



Dr. Timothy Nichols

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“Novel Preclinical Approaches to Hemophilia A Complicated by Inhibitors”

Hemophilia A is a genetic bleeding disorder caused by mutations in the F8 gene encoding clotting factor VIII (FVIII), and occurs at a frequency of 1 in 5000 male births. Severe hemophilia A, defined as having less than 1% functional FVIII in the circulation, can be treated with either recombinant or plasma-derived FVIII replacement therapy for prophylaxis or for treating bleeding episodes. Unfortunately, up to 1/3 of hemophilia A patients who receive FVIII infusions develop inhibitory antibodies to functional domains of FVIII (commonly called “inhibitors”).

Currently, the standard clinical approach to hemophilia A patients with low inhibitor titers (<10 BU/ml) is a process called Immune Tolerance Induction (ITI) that consists of repeated high-dose FVIII infusion for months or even years. While ITI is the only clinically proven strategy for induction of FVIII-specific immune tolerance, it is not only a lengthy procedure but also of extremely high cost (> \$1M per year per patient), and 20% to 40% of patients fail ITI therapy or “break” tolerance once achieved. For patients with inhibitor titers persistently higher than 10 Bethesda Units (BU, high responders), ITI is difficult to achieve. While other strategies to treat or prevent bleeding in inhibitor patients are in use including the paradigm-changing emicizumab, none of these therapies achieve tolerance.

A major focus of our research is to develop and test novel strategies for preventing inhibitor formation, eradicating inhibitors once formed to achieve tolerance, and circumventing and bypassing inhibitors in models of hemophilia A. This work will be reviewed and future directions discussed.

Live Online Seminar Viewing:
<https://tinyurl.com/CBR-Seminar-2020>



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