

2023 HTRS MRA II for Gene Therapy in Hemophilia A



Jonathan J. Morris, PhD

Postdoctoral Fellow

Children's Hospital of
Philadelphia

Project Title

“Elucidating Mechanisms of FVIIIa Regulation to Rationally Engineer Novel FVIII Transgenes”

Mentors

Lindsey A. George, MD, Children's Hospital of Philadelphia, University of Pennsylvania

Dr. John Morris is an NHLBI/NIH T32 trainee in hemostasis and thrombosis at the University of Pennsylvania and a postdoctoral fellow at the Children's Hospital of Philadelphia in Dr. Lindsey George's lab. Dr. Morris received his Ph.D. in biomedical engineering at Rowan University, where his research focused on developing new methodologies for the high-throughput assessment of industrial chemicals for developmental neurotoxicity. His current research focuses on defining the biochemistry of FVIIIa inactivation and elucidating the role of physiologic ligands, FIXa and FX, on FVIIIa inactivation, which has led to the informed design of FVIIIa variants resistant to inactivation with 4-to-12-fold enhanced hemostatic effect. This work sparked an interest in how leveraging the delicate equilibrium of procoagulant and anticoagulant function could lead to new approaches to overcoming clinical limitations of gene transfer. Under the mentorship of Dr. George, Dr. Morris' research for this 2023 MRA Project aims to provide a comprehensive understanding of the mechanisms of FVIIIa regulation and how intermolecular interactions within the intrinsic Xase enzyme complex impact coagulation as well as to exploit this understanding to engineer clotting factors resistant to inactivation to improve translational applications in gene therapies for hemophilia.

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