



Nicholas W Shworak MD, PhD

Nicholas Shworak did his MD (Honors in Medical Research) at the University of Alberta (1981-1985) and then completed a PhD at University of Calgary (1985-1990) studying transcriptional control mechanisms of the metal regulated metallothionein genes. Since then he has focused on the biosynthesis and biology of HS^{AT+}, the best structurally characterized specific heparan sulfate sequence that binds the plasma protein antithrombin (AT). During his postdoctoral studies at Massachusetts Institute of Technology (1990-1993) with Robert Rosenberg, he determined that a unique biochemical pathway is required to synthesize HS^{AT+}. From 1993 to 2001 he was simultaneously appointed at Massachusetts Institute of Technology (Visiting Scientist then Research Associate) and Harvard Medical School (Instructor then Associate Professor of Medicine), where he cloned and identified the rate limiting enzyme that controls HS^{AT+} production (3-OST-1/HS3ST1). With Bob Rosenberg, he also identified the HS3ST1 multigene family and demonstrated the encoded enzymes make two major forms of 3-O-sulfated HS structures. He has been at the Geisel School of Medicine at Dartmouth since 2001, and is presently Associate Professor of Medicine (Cardiology) and Associate Professor of Pharmacology and Toxicology. During this period he generated/characterized *Hs3st1*^{-/-} knockout mice, which provided the unexpected result that vascular HS^{AT+} is not required for normal hemostasis. His presentation will reveal that a major function of HS^{AT+} is to regulate vascular inflammation and that this may provide novel insights into human cardiovascular disease.