Gene Therapy Targeting Vascular Function in Cardiovascular Disease: Are We There Yet?

This past decade has witnessed a renaissance in gene therapies for a broad array of human diseases. Dr. Fisher’s talk will focus on mRNA splice variants as targets for gene therapies that by shifting the expression of naturally occurring protein isoforms may have therapeutic benefit. The specific focus is the smooth muscle myosin phosphatase (MP) enzyme, the end effector of vasodilation and key end target of signaling pathways regulating vessel tone and thus blood flow and blood pressure. Our data supports a model in which a splice variant of the MP regulatory subunit Mypt1 sets vascular sensitivity to NO, ANP, and ROS vasodilator signaling. After reviewing this data, Dr. Fisher will present his recent experiments testing the alternative gene therapy approaches of Crispr/Cas9 gene editing and splice-blocking anti-sense oligonucleotides targeting Mypt1 E24. These are potential novel therapies for hypertension and its sequelae HFpEF, the #1 preventable cause of early mortality world-wide.