

Based on preliminary studies that suggested that nitrogen oxides (NO_x) contribute to sickle cell pulmonary disease, Dr. Harrison Farber and associates planned to define the role of NO in vascular responses in a sickle cell transgenic mouse by correlating functional assays, lung histology, and animal mortality with changes in NO metabolism at baseline and during induced crisis. The specific aims of this project were to: define the role of NO in vascular responses and vaso-occlusive events in a sickle cell transgenic mouse by correlating functional assays, lung histology and animal mortality with changes in NO metabolism at baseline and during crisis induced by hypoxia; define the effect of pharmacological manipulation of ACS-like crisis in a sickle cell transgenic mouse using a) NOS substrate (arginine), NOS cofactors (BH₄), NOS inhibitors and inhaled NO; or b) antioxidants (glutathione, OTC, EUK-8) and examining functional assays, lung histology and animal mortality at baseline and during crisis induced by hypoxia; define the importance of NO metabolism and oxidative stress in a sickle cell transgenic mouse by interbreeding it with: a) a NOS3 (or NOS2) deficient mouse; b) a glutathione peroxidase (GPx-1) deficient mouse; or c) a glucose-6-phosphate dehydrogenase (G6PD) mutant mouse and examining functional assays, lung histology and animal mortality at baseline and during induced crisis.