Project Title: Identification of Novel Brain-penetrating Phenoxyalkyl Pyridinium Oxime Countermeasures
Sponsor: NIH U01
Investigators: J.E. Chambers, PI; M.K. Ross, R.W. Wills

This project will establish data on novel chemicals invented to be more effective antidotes to counteract the toxicity induced by nerve agents or highly toxic insecticides. Such poisons could be used by terrorists against civilian populations. Our novel chemistries have the potential to not only save lives but also penetrate the blood-brain barrier and protect the brain from long-term damage caused by these poisons.

Project Title: Identification of Novel Brain-penetrating Oxime Antidotes for Phorate Toxicity
Sponsor: NIH R21
Investigators: J.E. Chambers, PI; M.K. Ross, S.R. Gwaltney

This project will investigate the liver and brain metabolism of the highly toxic organophosphate insecticide phorate to better understand its unusual toxicity profile, and will determine the interaction of phorate metabolites with the target enzyme acetylcholinesterase through computational chemistry.

Project Title: Effects of Organochlorine Pesticide Exposure on Hepatic Lipid Metabolism in Type 2 Diabetes
Sponsor: NIH R15
Investigators: G.E. Howell, III, PI

The current project will examine the effect of exposure to bioaccumulative organochlorine pesticides that are present in the serum of a vast majority of the United States population on the development of type 2 diabetes and associated defects in hepatic lipid metabolism. This research will utilize cultured rat hepatocytes as well as a widely utilized animal model of type 2 diabetes, the high fat fed rodent, to determine if exposure to these compounds promotes abnormal glucose and lipid metabolism. If so, the present study will provide mechanisms through which these compounds promote these defects and will establish exposure to certain organochlorine pesticides as a causative factor for the development of type 2 diabetes and non-alcoholic fatty liver disease.

Project Title: Organochlorine Compound-Induced Alterations in Adipocyte/Macrophage Crosstalk and Effects on Wound Healing
Sponsor: NIH R21
Investigators: G.E. Howell III, Ph.D – PI

The relationship between environmental exposures to the prevalent persistent organic pollutants (POPs) and alterations in the adipose tissue microenvironment with subsequent effects on microbial infection and wound healing has not been explored. Therefore, the goal of the present proposal is to determine the effects of exposure to three of the prevalent organochlorine pesticide based POPs on adipocyte/macrophage cross-talk and resulting alterations in diabetic wound healing. Should POPs

significantly alter the adipose tissue microenvironment and wound healing, these compounds could be used as biomarkers to identify patients which are at increased risk for chronic wounds such as diabetic foot ulcers and other soft tissue infections.

Project Title: TCDD-treated B Cells Modulate T Effector and T Regulatory Function in EAE
Sponsor: NIH R15
Investigators: B.L. Kaplan, PI

The goal of this project is to determine if TCDD-induced regulatory B cells are part of the mechanism by which TCDD suppresses T cell function in a multiple sclerosis model.

Project Title: The Transport of Neurotoxin Antidotes across the Blood-Brain Barrier
Sponsor: DoD/DTRA/Johns Hopkins Institute for Nanobiotechnology
Investigators: J.E. Chambers, Co-PI; P. Searson, PI

The MSU effort involves the synthesis and characterization of select novel oximes that are under patent application. These oximes are acetylcholinesterase reactivators, some of which have been demonstrated to cross the blood-brain barrier and be effective reactivators in the brain from in vivo efficacy tests in rats. Additionally, we will be involved in the synthesis and characterization of two nerve agent surrogates to be supplied to Johns Hopkins University for their tests of blood-brain barrier penetration.