

# THE MECHANISM FOR PARAQUAT TOXICITY INVOLVES OXIDATIVE STRESS AND INFLAMMATION: A MODEL FOR PARKINSON'S DISEASE

Rebecca Louise Miller

Dr. Albert Y. Sun, Dissertation Supervisor

## ABSTRACT

Parkinson's disease (PD) is a neurodegenerative disorder known to affect the dopaminergic neurons in the substantia nigra. Epidemiological studies have shown an increased risk of developing PD with exposure to paraquat. In this study, we examined the source of reactive oxygen species (ROS) and the underlying signaling pathway for paraquat-induced cytotoxicity to BV-2 microglial cells. Paraquat-induced ROS production was attenuated by inhibitors for NADPH oxidase, protein kinase C and extracellular signal-regulated kinases 1/2. Under inflammatory conditions, microglial cells respond to cytokines by induction of inducible nitric oxide synthase which produces nitric oxide (NO). Our results show that paraquat inhibited cytokine-induced NO production but only moderately enhanced ROS production in microglial cells. We wanted to determine the role of NADPH oxidase in neuronal cells. Paraquat induced the upregulation of the p67<sub>phox</sub> subunit protein and NOX2 mRNA of NADPH oxidase in differentiated SH-SY5Y cells. In conclusion, our data suggest that NADPH oxidase plays a significant role in the toxicity of paraquat.