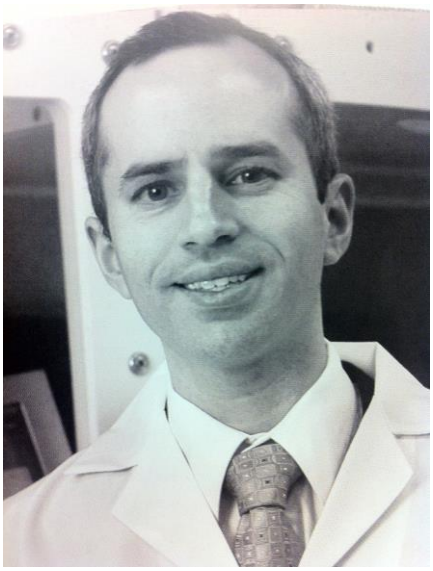
BURKE MEDICAL RESEARCH INSTITUTE | Weill Cornell Medicine

Weekly Colloquium

Tuesday, 5/2/2017, 12:30pm, Billings Building – Rosedale Conference Room

"Mitochondrial Structural and Functional Remodeling in Proinflammatory Microglial Activation"

Brian M. Polster, Ph.D.
Associate Professor
Department of Anesthesiology
University of Maryland School of Medicine
Baltimore, MD



Research Abstract

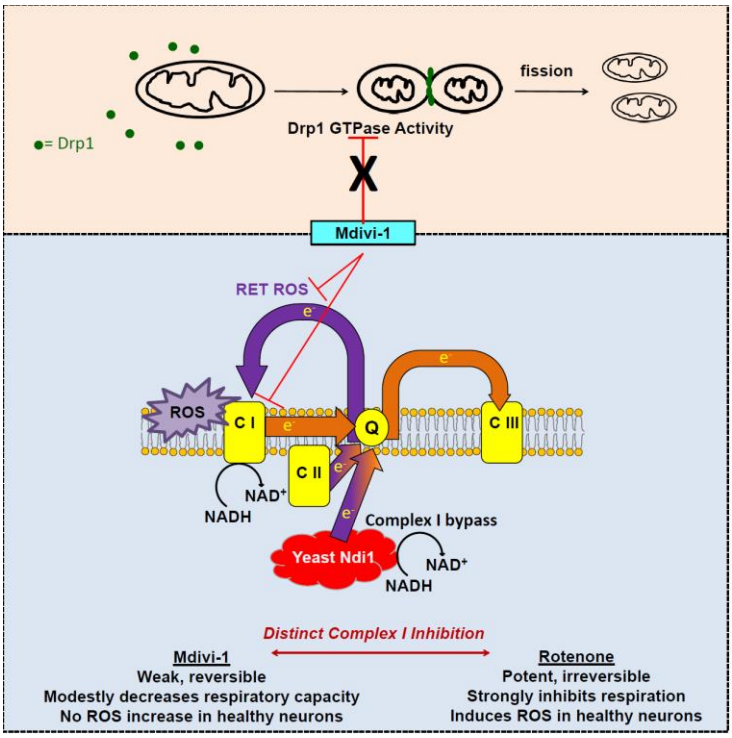
Neuroinflammation is thought to contribute to pathology in most neurodegenerative disorders. Microglia, the innate immune cells of the brain, are activated to proinflammatory states in response to damage-associated molecular pathogens (DAMPs) released by injured cells. During activation, microglia undergo a bioenergetic shift from oxidative phosphorylation to glycolysis. Mitochondrial structural remodeling consistent with the possibility of fission accompanies this functional change. Drp1 is the main GTPase that promotes mitochondrial fission. We hypothesized that proinflammatory microglial activation requires mitochondrial structural and bioenergetic changes that depend on Drp1 activity. Mdivi-1, a drug characterized as a Drp1 inhibitor, suppresses proinflammatory markers of microglial activation *in vitro*. However, surprisingly, it does so without inhibiting mitochondrial structural or functional changes. This talk will describe new targets of mdivi-1 and identify biochemical mechanisms contributing to mitochondrial respiratory suppression during microglial activation.

Recent publications:

Bordt, E.A. and **Polster, B.M.** (2014) NADPH Oxidase- and Mitochondria-derived Reactive Oxygen Species in Proinflammatory Microglial Activation: A Bipartisan Affair? *Free Radic Biol Med* 76: 34-46.

Clerc, P. Ge, S.X., Hwang, H., Waddell, J., Roelofs, B.A., Karbowski, M., Sesaki, H., and **Polster, B.M.** (2014) Drp1 is dispensable for apoptotic cytochrome c release in primed MCF10A and fibroblast cells but affects Bcl-2 antagonist-induced respiratory changes. *Br J Pharmacol* 171: 1988-1999.

Bordt, E.A., Clerc, P., Roelofs, B.A., Saladino, A.J., Tretter, L., Adam-Vizi, V., Cherok, E., Khalil, A., Yadava, N., Ge, S.X., Francis, T.C., Kennedy, N.W., Picton, L.K., Kumar, T., Uppuluri, S., Miller, A.M., Itoh, K., Karbowski, M., Sesaki, H., Hill, R.B., and **Polster, B.M.** (2017) The Putative Drp1 Inhibitor Mdivi-1 is a Reversible Complex I Inhibitor that Modulates Reactive Oxygen Species. *Dev Cell* 40: 583–594.



For more information contact: dwhite@burke.org

Burke Medical Research Institute
Academic Affiliate of Weill Cornell Medicine
785 Mamaroneck Avenue, White Plains, NY 10605 | T. 914.597.2551 | www.burke.org