DANIEL W. KIPPS, MARY L. PIASKOWSKI, JACOB D. LOGGINS, KAY-CEE K. PATTERSON & NADJA SPITZER. Department of Biological Sciences, Marshall University, Huntington, WV, 25755. Alteration in MAPK/ERK and Akt signaling following exposure to sublethal silver nanoparticles in cultured adult neural stem cells

Silver nanoparticles (AgNPs), an emerging environmental contaminant, have been developed as antimicrobials, biosensors, and for other applications in products ranging from medical devices to consumer goods including toothpaste, socks, and appliances. AgNPs, particularly in consumer goods, can be shed off during use and ingested or inhaled, leading to bioaccumulation in tissues including brain. While they are effectively used for their antimicrobial properties, they also have negative effects on mammalian cells, even at low concentrations of 1μg/mL. We previously found that low-level AgNPs disrupt cytoskeletal function, leading to formation of f-actin inclusions and disrupting neurite dynamics. These effects are partially mediated by interaction with the β-catenin intracellular signaling pathway. Here, we investigate interactions of AgNPs with two other intracellular signaling pathways, MAPK/ERK and Akt, both of which are involved in regulation of neuronal cell differentiation. Specific pharmacological inhibitors of these pathways, in combination with AgNPs, are applied to cultured adult neural stem cells that provide a model for brain cells. Fluorescent labeling and time-lapse microscopy are used to assess disruption of f-actin dynamics and changes in neurite extension. Preliminary data indicate that AgNPs may inhibit both the MAPK/ERK and the Akt intracellular signaling pathways, and thereby induce formation of f-actin inclusions and disrupt neurite dynamics during differentiation. This work will help us to understand chronic effects of low-level AgNP exposure from consumer goods on brain cell function. Our work in neural stem cells is especially applicable to children, whose brains are still developing and therefore depend on neural stem cell function. This material is based upon work supported by NSF Award# 1553667.