Abstract

This study examined if nanosilver (nanoAg) of different sizes and coatings were differentially toxic to oxidative stress-sensitive neurons. N27 rat dopaminergic neurons were exposed (0.5-5ppm) to a set of nanoAg of different sizes (10nm, 75nm) and coatings (PVP, citrate) and their physicochemical, **cellular** and **genomic** response measured. Both coatings retained their manufactured sizes in culture media, however, the zeta potentials of both sizes of PVP-coated nanoAg were significantly less electronegative than those of their citrate-coated counterparts. Markers of oxidative stress, measured at 0.5-5ppm exposure concentrations, indicated that caspase 3/7 activity and glutathione levels were significantly increased by both sizes of PVP-coated nanoAg and by the 75nm citrate-coated nanoAg. Both sizes of PVP-coated nanoAg also increased intra-neuronal nitrite levels and activated ARE/NRF2, a reporter gene for the oxidative stress-protection pathway. Global gene expression on N27 neurons, exposed to 0.5ppm for 8h, indicated a dominant effect by PVP-coated nanoAg over citrate. The 75nm PVP-coated material altered 196 genes that were loosely associated with mitochondrial dysfunction. In contrast, the 10nm PVP-coated nanoAg altered 82 genes that were strongly associated with NRF2 oxidative stress pathways. Less that 20% of the affected genes were shared by both sizes of PVP-coated nanoAg. These **cellular** and **genomic** findings suggest that PVP-coated nanoAg is more bioactive than citrate-coated nanoAg. Although both sizes of PVP-coated nanoAg altered the **genomic** expression of N27 neurons along oxidative stress pathways, exposure to the 75nm nanoAg favored pathways associated with mitochondrial dysfunction, whereas the 10nm PVP-coated nanoAg affected NRF2 neuronal protective pathways.