

Micro- and Nanoplastics Exposure Exacerbates Alzheimer's Disease Pathology in APP/PSEN1 Mice

Mackenzie Pavlik^{*ab}, Lauren Gaspar^{ab}, Thomas Kelly^{ab}, Hannah Tobias-Wallingford^{ab}, Giuseppe Coppotelli^{ab}, Jaime M. Ross^{ab}

(a) Department of Biomedical and Pharmaceutical Sciences, College of Pharmacy, University of Rhode Island Kingston, RI USA

(b) George and Anne Ryan Institute for Neuroscience, University of Rhode Island Kingston, RI USA

Alzheimer's disease and related dementias (AD/ADRD) are among the most prevalent cognitive disorders, affecting more than 6 million Americans over the age of 65. While the exact cause remains unknown, risk factors include genetics, lifestyle, and environmental toxins. In recent years, micro- and nanoplastics (MNPs) (1 μm – 5 mm and $\leq 1 \mu\text{m}$ in size, respectively) have emerged as pervasive environmental pollutants. Studies have shown that MNPs can accumulate in peripheral tissues throughout the body of both humans and animals, raising concerns about their potential health impacts, as evidence suggests they may induce inflammation, oxidative stress, and disruption of metabolic and endocrine functions. Furthermore, MNPs have been demonstrated to cross the blood-brain barrier and accumulate throughout the brain, resulting in alterations in cognitive behavior and immune markers consistent with neurological disease. In line with this, we have previously demonstrated that exposure to MNPs impairs cognitive function and increases inflammation in both young and aged mice, as well as in mice carrying the APOE4 allele, the strongest genetic risk factor for sporadic Alzheimer's disease, in a sex-dependent manner. In the present study, we investigated the effects of chronic MNPs exposure in a transgenic mouse model of Alzheimer's disease pathology (APP/PSEN1). Following chronic 3-month exposure to pristine polystyrene MNPs, APP/PSEN1 mice exhibited a significant increase in amyloid- β plaque burden. This was accompanied by exacerbated cognitive impairment, reduced synaptic integrity, impaired lysosomal function, and increased microglial abundance, collectively suggesting that MNPs exposure may accelerate key neuropathological processes associated with Alzheimer's disease progression.