Alzheimer’s disease (AD) is an age-related dementia that not only destroys a person’s memory, but also destroys their ability to learn, reason, and execute daily activities. The disease is characterized by a widespread loss of neurons and synaptic connectivity, which is driven by accumulation of toxic β-amyloid peptide. As life expectancy continues to grow, the amount of Americans diagnosed with Alzheimer’s dementia is also expected to grow, tripling in number by 2050. Despite these facts, we still do not have a full understanding of what causes the disease and there continues to be no effective treatments. While it has been well documented that exposure to ambient air pollution can cause respiratory and cardiovascular disease, much less attention has been paid to its effects on neurodegenerative diseases such as Alzheimer’s. Ultrafine particles (UFP) found in air pollution are particularly toxic because of their ability to cross the blood brain barrier and act as a chronic source of neuroinflammation and reactive oxygen species (ROS) production. In our current experiments we utilized AD Model induced pluripotent stem cells (iPSC) to study the neurotoxic effects of UFP matter found in ambient air pollution. These cells have never been used for such a purpose and may be a good alternative to current animal models for studying AD. AD and wildtype (WT) iPSC were treated with H2O control, 2ug/mL UFP or 20ug/mL UFP collected from a high traffic area of Los Angeles. After 4 and 24 hours of treatment the cells were tested for changes in reactive oxygen species (ROS) production, mitochondrial function, cell viability and cell proliferation. From these studies we found that AD iPSC display an increase in ROS formation upon UFP exposure, which may cause the neuroinflammation that leads to Alzheimer Disease progression. We believe that the use of this cell model system may lead to a greater understanding of the underlying molecular events governing AD, which will ultimately lead to a more effective treatment.

Hydrogen sulfide (H2S) is a colorless, neurotoxic gas with a rotten egg odor. Exposure to this gas is an environmental, occupational, and security hazard. H2S has been identified as an environmental pollutant, and is a leading cause of acute death in an occupational setting. Acute effects include eye irritation, seizures, respiratory paralysis and acute death. Neurological sequelae of H2S exposure include auditory impairment and neurodegeneration leading to a vegetative state. Our short-term objective was to develop a mouse model of H2S-induced neurotoxicity using mice. C57 Black mice were exposed to 471 ppm H2S by whole body inhalation for 45 minutes on day 0, followed by 15 minutes/day exposures for 6 consecutive days. Control mice were exposed breathing air. A functional observation battery was used to assess clinical signs of toxicity during H2S exposure and also 2 hours post-exposure. Behavioral and neurochemical changes, and histopathology were additional end-points monitored. Clinical signs noted during exposure included seizures, respiratory depression, and knockdown effect. H2S-exposed mice showed significant impairment in motor activity compared to the controls. In the striatum, dopamine concentration was significantly increased in H2S-exposed animals compared to controls (p<0.05). Also, mice exposed to H2S lost significantly more body weight compared to controls. Histopathology revealed neurodegenerative lesions in the inferior colliculus, the most sensitive brain region. Our study indicates that H2S causes neurotoxicity characterized clinically by seizures and knockdown, impaired motor ability, and histologically the inferior colliculus is the most sensitive brain region, and the striatum to a lesser degree. Ongoing work is examining neurochemical mechanisms in-depth, including oxidative stress.