

Abstract: Fine particulate matter (PM2.5) contributes to respiratory and cardiovascular disease exacerbations associated with increased susceptibility to respiratory infection. Our previous research showed that wildfire PM2.5 exposure altered NK cell cytokine production and diminished COVID-19 vaccine immunity and that chronic traffic-related air pollution (TRAP) exposure led to diminished metabolic activity in splenic immune cells cultured ex vivo. A growing body of evidence further shows that PM2.5 induces mitochondrial injury, including excess mitochondrial reactive oxygen species (mtROS), altered ATP production, disrupted mitochondrial ultrastructure, and dysregulated mitochondrial dynamics in the respiratory tract. Additionally, we found a positive correlation between markers of NK cell activation and mitochondrial energy production and antioxidant genes as well as markers of mitochondrial fusion and mitophagy, all potential indicators of stress. As proper mitochondrial function is essential for immune-cell activation, survival, cytokine production, and cytotoxic effector function, it is critical to determine the mechanistic link between mitochondrial dysfunction, NK cell dysfunction, and impaired immune response to infection after direct exposure to PM2.5. My central hypothesis states that chronic TRAP and/or wildfire PM2.5 exposure results in mitochondrial dysfunction which impairs cytotoxic function and alters cytokine responses in NK cells leading to loss of antiviral defense.