## **GSA Abstract 2019**

Title: Cardiac antioxidant response to air pollution in mice is altered by ApoE alleles and sex

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## **Abstract**

ApoE4 is a risk factor for heart disease by increasing levels of low-density lipoproteins causing arterial plaque formation and increased oxidative damage [1]. Furthermore, air pollution is associated with cardiovascular disease, together with inflammation and oxidant generation [2]. Anti-oxidant defenses are induced by air pollution in experimental models. Nuclear factor erythriod-2- related factor 2 (Nrf2), initiates gene expression of a wide array of antioxidants, e.g. peroxiredoxin 6 (Prdx6) that detoxifies hydrogen peroxide and oxidized lipids. We hypothesized that Nrf2 translocation and antioxidant response would be diminished in ApoE4 mice exposed to air pollution. This hypothesis was tested with mice carrying transgenes for human ApoE alleles and exposed to nano-sized particulate matter (nPM) collected from an urban freeway corridor [3]. Myocardia of 7month-old mice were collected after exposure to nPM or filtered air for 15 weeks and showed allele and sex differences in response. Nuclear accumulation of Nrf2 was decreased 45% in ApoE3 females compared to male ApoE3. Prdx6 levels also were 50% lower in ApoE4 females than normal ApoE4 females. These data suggest that antioxidant response differ by sex, ApoE status, and that exposure to nPM negatively impacts Nrf2 related antioxidant gene expression.

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## References

- R.W. Mahley, Apolipoprotein E: from cardiovascular disease to neurodegenerative disorders, J. Mol. Med. Berl. Ger. 94 (2016) 739–746. doi:10.1007/s00109-016-1427-y.
- [2] B.-J. Lee, B. Kim, K. Lee, Air Pollution Exposure and Cardiovascular Disease, Toxicol. Res. 30 (2014) 71–75. doi:10.5487/TR.2014.30.2.071.
- [3] N.C. Woodward, M.C. Levine, A. Haghani, F. Shirmohammadi, A. Saffari, C. Sioutas, T.E. Morgan, C.E. Finch, Toll-like receptor 4 in glial inflammatory responses to air pollution in vitro and in vivo, J. Neuroinflammation. 14 (2017) 84. doi:10.1186/s12974-017-0858-x.