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**Control/Tracking Number:** 2019-S-5243-SfN

**Activity:** Scientific Abstract

**Current Date/Time:** 5/2/2019 4:42:40 PM

**Traffic related air pollution nanosized particulate matter shows batch differences in biological activity in vitro and in vivo**

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**Abstract:**

Air pollution is associated with numerous health disorders including increased risk of Alzheimer disease (Cacciottolo et al 2017, PMID 28140404). Assessment of air pollution toxicity is complicated by inherent variations in composition of air pollutants among sources, locations, seasons, and weather, which may result in variable experimental responses. The current study documents divergent biological responses of nano-sized particulate matters (nPM) collected at different calendar times at the same site near a Los Angeles freeway. A new assay for genomic inflammatory responses was developed using human THP1 monocytes transgenic for a NF- $\kappa$ B reporter. A panel of nPM batches showed up to 10-fold variation in NF- $\kappa$ B activation. These batch variations showed corresponding differences in in-vivo responses of young adult C57BL/6J mice exposed to nPM for 8 weeks (exposure similar to Woodward et al 2017, PMID 28212893). The nPM batch with 2-fold higher NF $\kappa$ B activity in vitro ( $11.7 \pm 0.23$  vs  $5.6 \pm 0.77$ ) caused a 2-fold increases in hippocampal Iba1 and soluble A $\beta$ 42 peptide in cerebral cortex. While the nPM with less NF- $\kappa$ B activity did not alter Iba1 or A $\beta$ 42 peptide levels, it still altered mRNA levels in cerebral cortex. To identify factors contributing to batch differences in biological activities, we compared their endotoxin content, lipid peroxidation, cellular toxicity, total organic compounds (TOC), and inorganic components. Pro-inflammatory activity of nPM batches correlated positively with endotoxin, lipid peroxidation, and TOC, but was negatively correlated with some metals. This in-vitro transcription-based assay for air pollution toxicity may increase the reproducibility of studies by identifying batch differences in air pollution particles. Further studies of fractionated nPM may identify synergies among the components of air pollution that impact neurotoxicity (Forman and Finch 2018, PMID 29407794). This study is funded by NIH grants R01 ES023864 (HJF) and P01 AG055367 (CEF).

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**Presentation Preference (Complete):** Nanosymposium Preferred

**Linking Group (Complete):** CeriseViolet

**Theme and Topic (Complete):** C.07.b. Mechanisms of neurotoxicity ; C.07.h.

Neuroinflammation – Neurodegeneration

**Nanosymposium Information (Complete):**

**Keyword (Complete):** NEURODEGENERATION

**Support (Complete):**

**Support:** Yes

**Grant/Other Support:** : NIH Grant R01 ES023864

**Grant/Other Support:** : NIH Grant P01 AG055367

**Special Requests (Complete):**

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