

Study links mitochondrial variation with air pollution exposure response

By Eddy Ball

In what the authors believe is the first epidemiological evidence of its kind, a new [study](http://www.ncbi.nlm.nih.gov/pubmed/23717615) (<http://www.ncbi.nlm.nih.gov/pubmed/23717615>) links mitochondrial DNA with susceptibility to air pollution. Published May 23 in the journal PLOS ONE, the study examined associations between elderly individuals' inflammatory response to components of traffic-related air pollution and their mitochondrial DNA haplogroup — the unique pattern of single-nucleotide polymorphisms (SNPs) that make up their cells' energy-production DNA, which is independent of the nuclear DNA that encodes most of the rest of the genome.

The research team was led by two NIEHS-funded scientists, M.D./Ph.D. fellow and first author [Sharine Wittkopp](http://mstp.uci.edu/Sharine/), (<http://mstp.uci.edu/Sharine/>) and professor and lead author [Ralph Delfino, M.D., Ph.D.](http://www.epi.uci.edu/features/delfino_aqmd.asp), (http://www.epi.uci.edu/features/delfino_aqmd.asp) from the University of California, Irvine (UCI). They found that people with haplogroup H, in contrast to those with haplogroup U, showed adverse modification of the effects of air pollution on the production of inflammatory cytokines, specifically interleukin 6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha). A number of scientific studies have associated IL-6 and TNF-alpha with the initiation and progression of cardiovascular and other diseases.

“This finding is relevant to advancing the field of personalized medicine,” the team concluded, “since such studies indicate there is potential value in tailoring interventions based on mitochondrial haplogroup. For example, antioxidant treatment in those with greater intrinsic oxidative stress may help ameliorate the proinflammatory effects of environmental pro-oxidant chemicals, such as those in traffic-related air pollution.”

Epidemiology, biomarker measurement, genotyping, and exposure analysis

The team began with an established cohort of 60 elderly residents with coronary artery disease, at four retirement communities in the Los Angeles air basin, where air pollution levels are generally higher than in other urban areas in the U.S. To control for exposure, only residents with no outside employment were accepted. Genotyping resulted in identifying 27 subjects belonging to haplogroup H, and nine to haplogroup U, while the remainder had mitochondria from other haplogroups.

Biomarkers measured include IL-6, TNF-alpha, C-reactive protein, IL-6 soluble receptor, and TNF-alpha soluble receptor II. Air pollutants included nitrogen oxides (NO₂), carbon monoxide (CO), black carbon, (BC), and other markers of fossil fuel combustion, and three sizes of particulate matter (PM). Over the 47-week period, the team also analyzed PM for polycyclic aromatic hydrocarbons (PAH); hopanes, which are found in lubricant oils of diesel and gasoline vehicles; and *in vitro* oxidative potential (ROS) of aqueous particle extracts.

Outcomes

For many of the measured traffic-related air pollution components, the team found elevated levels of IL-6 and TNF-alpha in participants with haplogroup H, and in most cases the differences between responses by people in the different haplogroups were dramatic (see graphs).

As earlier research has found in relation to epilepsy, Parkinson's, and other diseases, people in this study with the mitochondrial DNA haplogroup U enjoyed greater protection from traffic pollution-related cardiovascular disease, because of their lower mitochondrial production of ROS. Exposures among those with haplogroup H were associated with greater increases in systemic inflammation and, thus, susceptibility to the adverse effects of air pollution.

“These results support the hypothesis that relatively small differences in mitochondrial coupling efficiency, which alter the cellular oxidative burden, may alter responses to exogenous inducers of oxidative stress, such as traffic-related air pollution,” the researchers concluded. “This potentially important genetic risk factor has not been previously assessed in environmental epidemiological studies.”

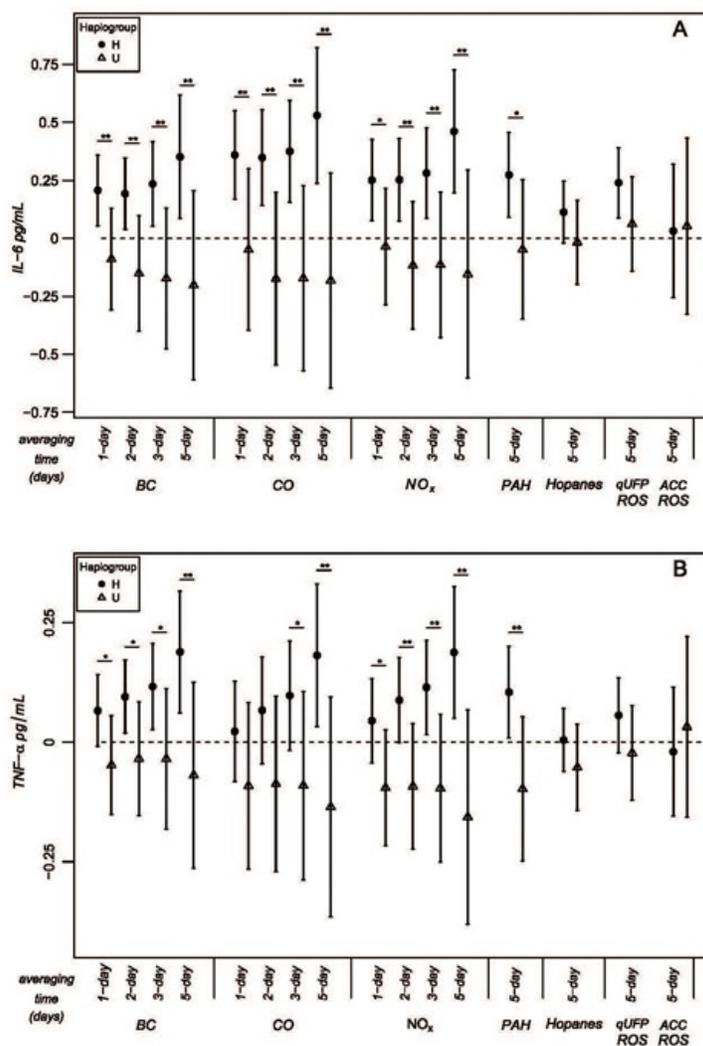


Wittkopp is an NIEHS-funded fellow in the UCI Medical Scientist Training Program. She was honored with the 2013 Women in Medicine Student Scholarship and selected as the TEDxUCIrvine Salon Speaker in February. (Photo courtesy of Sharine Wittkopp)



Delfino is a professor and vice-chair for graduate education and research in the Department of Epidemiology at the UCI School of Medicine. (Photo courtesy of UCI)

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Published in PLOS ONE as part of the study, these graphs show marked differences in the inflammatory responses of H and U haplogroups to traffic-related air pollution exposure. (Photo courtesy of Sharine Wittkopp)

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