## LAY ABSTRACT

TITLE: Is breast cancer a result of epigenetic responses to traffic-related air pollution? A review of the latest evidence.

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Environmental toxicants can cause health problems through a process referred to as epigenetic regulation. This is the process whereby environmental toxicants chemically modify DNA constituents, or alter the way DNA is arranged, thereby affecting the function of important genes. For example, one of these processes involves adding or subtracting a methyl group to DNA, which in turn may inactivate or activate a gene. We conducted a review of studies assessing traffic-related air pollution (TRAP) exposure and breast cancer (BC) risk, and whether epigenetic regulation may be involved. We found that 14 human studies that took epidemiological population science approaches to answer this question demonstrated associations between TRAP exposure and BC risk. Epidemiology is a branch of medicine which deals with the incidence, distribution, and control of diseases. A total of 26 comparisons were assessed in all the 14 studies. 11 of these comparisons reported a positive association, whereas 15 comparisons were negative. 5 publications linked TRAP exposure to epigenetic alterations in genes whose function seems related to BC risk. 1 animal study provided experimental evidence that TRAP-treatment may cause tumors in mammary glands. In conclusion, associations

between specific TRAP components that are products of combustion, such as polycyclic aromatic hydrocarbons (PAH), and nitrogen dioxide (NO2) gasses, were consistently found with BC risk. In addition, reporting of comparisons that are not statistically significant may not indicate there is no relation between TRAP and breast cancer risk, but rather, differences related to methodological approaches, including the various time windows of susceptibility examined. Future studies with measures of environmental pollution and epigenetic regulation are needed to interrogate the relationship between TRAP and BC risk. Determining the causes and mechanisms of health problems allows for more targeted interventions to reduce risk of breast cancer and other air pollution-related diseases.