

# Nitropolycyclic aromatic hydrocarbons, a potential human cancer hazard in diesel exhaust and urban air pollution

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Humans are rarely environmentally exposed to single toxic substances but more commonly to complex mixtures. In order to evaluate the health risks posed by these mixtures of chemicals understanding their mode(s) of action is critical for accurate risk assessment. Exposure to diesel exhaust material is linked to the development of lung cancer and the International Agency for Research on Cancer (IARC) recently classified diesel engine exhaust as carcinogenic to humans (Group 1) [1]. A US study in non-metal miners included a cohort study and a nested case-control analysis adjusted for tobacco smoking. Both showed positive trends in lung cancer with increasing exposure to diesel exhaust, a 2-3 fold increased risk in the highest categories of cumulative or average exposure. However, the mechanisms of diesel exhaust carcinogenesis and the precise identity of the critical carcinogenic components of diesel exhaust are still not fully understood, as is the magnitude of the carcinogenic risk from environmental exposure. The particulate phase of diesel exhaust contains carcinogenic polycyclic aromatic hydrocarbons (PAHs), nitro-PAHs and metals. Although environmental levels of nitro-PAHs are lower compared to unsubstituted PAHs, it has become clear that certain nitro-PAHs (e.g. 1-nitropyrene, 3-nitrobenzanthrone, 6-nitrochrysene, 1,8-dinitropyrene) are highly genotoxic. However, the biological activity of nitro-PAHs depends mostly on reactive intermediates generated in the course of metabolic activation. Nitro-PAHs can be reduced by nitroreductases to hydroxylamino and amino metabolites, and the hydroxylamino intermediates have been shown to bind to DNA to form pre-mutagenic DNA adducts. There is strong evidence that the ability of diesel exhaust to induce cancer in humans is through genotoxicity including those induced by nitro-PAHs. Considering that exposure to diesel emissions is at least partly unavoidable, it is crucial to understand the host factors that are involved in mediating the carcinogenic response. For targeted hazard/risk assessment of nitro-PAHs a broader monitoring of environmental levels of nitro-PAHs is required.

[1] IARC (2013) *IARC Monogr. Eval. Carcinog. Risk. Hum.* **105**.