Polycyclic aromatic hydrocarbons and environmental lung cancer

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Polycyclic aromatic hydrocarbons (PAH) are products of incomplete combustion of fossil fuels (e.g. coal fired power plants, burning of biomass) and are present in the gaseous and particulate phase of diesel exhaust, and cigarette smoke. The International Agency for Research on Cancer (IARC) has listed air pollution as a Group 1 "known human carcinogen" [1]. The US Environmental Protection Agency monitors 16 priority PAH that determine ambient air quality. Among these benzo[a]pyrene (B[*a*]P) is also listed as Group 1 carcinogen [2]. The World Health Organization estimates that 30% of lung cancer observed in never-smokers is related to the inhalation of polluted air. PAH are absorbed onto fine particulate matter (PM2.5) which can deposit in the deep lung but are inert and require bioactivation to cause their tumorigenic effects. Not everyone exposed to PAH will develop lung cancer suggesting that a significant gene-environment interaction exists. Human susceptibility to these carcinogens is likely to result from intrinsic or acquired phenotypes. Intrinsic phenotypes are related to inherited mutations (single nucleotide polymorphisms) in genes involved in the bioactivation and detoxication of PAH. However, the odds ratios in favor of these mutations are generally modest. By contrast acquired phenotypes related to changes in the transcriptome or "gene batteries" that are induced as a result of an exposure response may be more significant. Using B[*a*]P as a representative PAH, pathways of bioactivation in humans involve the formation of genotoxic species e.g. radical cations, diol-epoxides and *o*-quinones. Gene batteries involved these pathways have been identified and phenotypic underpinning of these genomic changes using intermediate cancer biomarkers is now possible. Identification of this acquired susceptibility to PAH is actionable since individuals with these phenotypes could undergo risk reduction through epigenetic therapy, use of chemopreventive strategies, exposure reduction and/or enter lung cancer surveillance programs. [Supported by National Institutes of Health grant P30-ES013508 to TMP].

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