

PERSISTENT ORGANIC POLLUTANTS AND THE Ah (DIOXIN) RECEPTOR: MOLECULAR MECHANISMS OF ACTION AND BIOASSAY DEVELOPMENT

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Halogenated aromatic hydrocarbons (HAHs), such as polychlorinated dibenzo-p-dioxins, dibenzofurans and biphenyls, represent a large group of ubiquitous and highly toxic persistent organic pollutants present in food, environmental and wildlife and human tissue samples. Exposure to dioxin-like HAHs and related chemicals can produce diverse toxic and biological effects, the majority of which are mediated by the aryl hydrocarbon receptor (AhR), an intracellular protein that binds these chemicals with high affinity. While the AhR signaling pathway is activated by structurally diverse chemicals, only metabolically persistent dioxin-like HAHs produce AhR dependent toxicity. Taking advantage of key aspects of the AhR-dependent molecular mechanism of dioxin action led to the development, validation, application and regulatory approval of recombinant cell lines (such as CALUX) as simple, rapid and inexpensive screening bioassays for detection and relative quantitation of dioxin-like HAHs in diverse matrices. Recent progress on AhR mechanisms of action and cell bioassay development will be described.