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Aryl hydrocarbon receptor localization and expression after benzo[a]pyrene incubation on human placental models

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Statement of the Problem: Benzo(a)pyrene (BaP) is a persistent environmental pollutant produced by organic combustion from various sources, and is currently classified as highly carcinogenic, mutagenic and reprotoxic substance. Human placenta- an interface between the fetus and the mother plays a critical role as a barrier against many xenobiotics. However, pollutants such as BaP could reach and cross this barrier and thus modify its physiological functions, with significant implications on pregnancy outcome. Within the cell, the main target of BaP is the aryl hydrocarbon receptor (AhR), a cytosolic ligand-activated transcription factor which relocates and triggers the expression of genes involved in xenobiotic metabolism. However, recent data suggest that the AhR is not limited to this process and may assure functions other than detoxification. Our aim was to evaluate the expression, localization and activation of the AhR in several placental models, as well as the impact of BaP exposure toward these parameters.

Methodology & Theoretical Orientation: We characterized, for the first time, the expression profile of the AhR and its activity toward its main target genes in human placental chorionic villi during different periods of pregnancy. Using different methods such as cell fractionation and fluorescence microscopy, we unexpectedly demonstrated a nuclear localization of the AhR in 1) freshly harvested chorionic villi throughout pregnancy, 2) purified term placental primary cells during differentiation into syncytiotrophoblast and 3) BeWo cell line in the absence of any exogenous activator, suggesting an intrinsic activation of the AhR. Furthermore, we studied the impact of BaP exposure toward the localization and activity of this receptor in human trophoblast cells. The expression of AhR, its partner ARNT and its repressor AhRR were unaffected. However, we demonstrated a role of the AhR upon BaP exposure (using RT-qPCR) on the expression of various critical genes involved in different processes such as detoxification, placental function, oxidative stress, inflammation, and epithelial to mesenchymal transition.

Conclusion & Significance: To our knowledge, this is the first study of a global functional cartography of the AhR in human placenta.

Biography

Anaïs Wakx has graduated in Toxicology from the Paris Descartes University, works on the impact of micropollutants, particularly endocrine disruptors and carcinogenic, mutagenic and reprotoxic substances on placenta. She is the recipient of the OPAL Prize awarded by the National Academy of Pharmacy for her work on alternative methods for animal experimentation. Her current work is supported by the French Agency for Food, Environmental and Occupational Health & Safety (ANSES).

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