

**Human primordial germ cell formation is diminished by exposure to environmental toxicants acting through the AHR signaling pathway.**

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**Public Summary:**

This manuscript reports on the utility of human embryonic stem cells for assessing environmental exposures and effects on human development, especially the germ line (cells that give rise ultimately to eggs, sperm and the next generation).

**Scientific Abstract:**

Historically, effects of environmental toxicants on human development have been deduced via epidemiological studies because direct experimental analysis has not been possible. However, in recent years, the derivation of human pluripotent stem cells has provided a potential experimental system to directly probe human development. Here, we used human embryonic stem cells (hESCs) to study the effect of environmental toxicants on human germ cell development, with a focus on differentiation of the founding population of primordial germ cells (PGCs), which will go on to form the oocytes of the adult. We demonstrate that human PGC numbers are specifically reduced by exposure to polycyclic aromatic hydrocarbons (PAHs), a group of toxicants common in air pollutants released from gasoline combustion or tobacco smoke. Further, we demonstrate that the adverse effects of PAH exposure are mediated through the aromatic hydrocarbon receptor (AHR) and BAX pathway. This study demonstrates the utility of hESCs as a model system for direct examination of the molecular and genetic pathways of environmental toxicants on human germ cell development.

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