Research reveals how pollutants affect early embryo development

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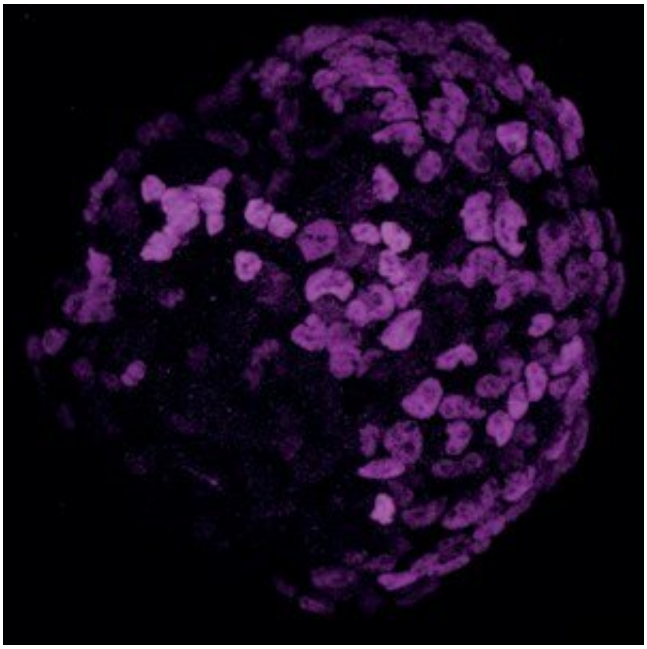

Credit: The Francis Crick Institute

Chemicals found in cigarette smoke, factories and incinerators can interfere with the crucial early stages of embryo development, suggests new research from the Francis Crick Institute.

The study, published in *Stem Cell Reports*, investigated the effects of chemicals that activate the aryl hydrocarbon receptor in mouse stem cells and embryos. This receptor is normally switched on and off by natural processes in the body, but aryl hydrocarbons produced by incomplete

combustion or industrial processes can keep it switched on. When pregnant mice were exposed to synthetic aryl hydrocarbons, the development of their embryos was affected at very early stages.

Problems in embryo development typically lead to miscarriage or stillbirth, while it has been previously shown that embryos that develop after aryl hydrocarbon exposure often have developmental problems including cleft palate. Until now, however, the molecular mechanism by which such chemicals affect development was not known.

The new study has now revealed that aryl hydrocarbons affect the fundamental network that tells cells in developing embryos which cell type to become.

"Cells in the early embryo all begin as 'totipotent' cells, meaning they can become any cell type in the body or placenta," explains Dr Manolis Gialitakis of the Francis Crick Institute, first author of the paper. "The earliest choice that a cell makes is whether to become an embryonic stem cell, or a cell type that will eventually form part of the placenta. Embryonic stem cells subsequently face the choice of whether to become cells that will form the yolk sac or those that give rise to the embryo.

"By analysing embryonic stem cells and embryos at different stages of development, we found that aryl hydrocarbons affect both of these fundamental decisions. This as well as other disruptions led to a substantial proportion of embryos failing to develop at all, highlighting the crucial nature of these early differentiation decisions. Embryo development is incredibly complex, so the timing of every cell decision is key to successful development. We identified a wide range of proteins that interact with the aryl hydrocarbon receptor, which allowed us to map out the different processes that are affected when it is abnormally activated."

The aryl hydrocarbon receptor (AhR) plays an important role in human health, and low levels of aryl hydrocarbons are all around us naturally. However, there are many sources of synthetic aryl hydrocarbons such as dioxins that are not metabolized and can stay in the human body for a long time, causing serious damage.

"It's striking to see how fundamentally these chemicals can alter embryo development," says Dr Gialitakis. "As they are found in tobacco smoke, this could help to explain how smoking can lead to birth defects and lower fertility rates. As these chemicals can stay in the body for a long time, smokers who want to have children should consider quitting several months before trying to conceive."

Dr Brigitta Stockinger, senior author of the paper from the Francis Crick Institute, says: "We already know that AhR acts as a vital control centre to maintain our immune defences, particularly in our intestines, lungs and skin. This latest study builds on our knowledge and shows that exposure of stem cells to AhR activation, particularly if prolonged and non-physiological, plays a detrimental role in the earliest days of embryo development. We are now looking at the consequences of transient AhR activation by physiological ligands compared with prolonged activation by chemicals that are difficult to metabolise."

More information: Manolis Gialitakis et al. Activation of the Aryl Hydrocarbon Receptor Interferes with Early Embryonic Development, *Stem Cell Reports* (2017). DOI: 10.1016/j.stemcr.2017.09.025

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https://phys.org/news/2017-10-reveals-pollutants-affect-early-embryo.html