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Benzene Exposure During Pregnancy Affects Later-Life Metabolic Health

Prenatal exposure to the air pollutant benzene may lead to a higher risk of metabolic diseases later in life, according to a study in mice partially funded by the NIEHS Superfund Research Program (SRP). Benzene affects neurodevelopment, predisposing offspring to harmful metabolic effects, according to a research team led by Marianna Sadagurski, Ph.D., of the Wayne State University SRP Center.

Benzene is one of the 20 most widely used chemicals in the U.S. People can be exposed to it from industrial emissions, gasoline fumes, tobacco smoke, and when using some consumer products such as glues, solvents, paints, and detergents. Researchers have linked benzene exposure to many adverse health effects, including metabolic disorders and type 2 diabetes. More recently, studies suggest that exposure to benzene before birth can harm the offspring's metabolic health.

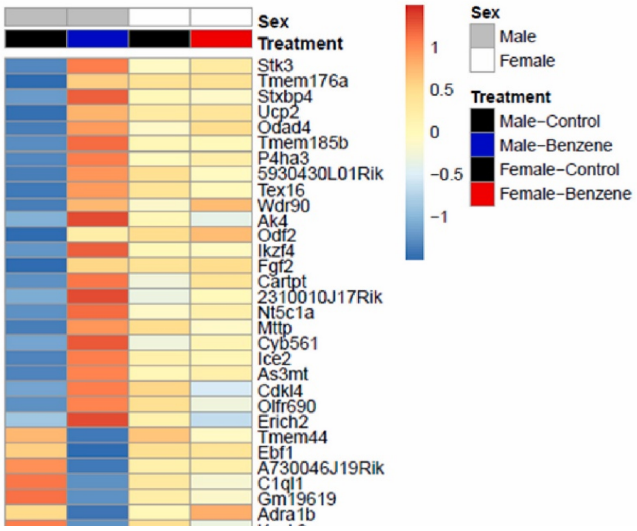
The underlying mechanisms by which benzene exposure impairs metabolic health was of interest. In particular, the scientists wanted to study effects on the hypothalamus, an area of the brain that regulates several metabolic processes, including the production of hormones that suppress or stimulate appetite.

Pinpointing Genetic Changes

They exposed female mice to benzene during pregnancy. After birth, some mice continued benzene exposure during lactation. When the pups were 21 days old, the researchers used transcriptomic analyses — a technique that identifies which genes are expressed or suppressed — to evaluate changes to the hypothalamus.

Finally, the team conducted studies in mice to test the ability of a drug called BVD-523, an ERK inhibitor that is currently in clinical trials as a cancer treatment, to protect against lung damage. BVD-523 blocked ERK activation and subsequent PPAR-gamma degradation. Mice treated with BVD-523 did not exhibit the characteristic increase in TNF-alpha and interleukin-6 or decreased interleukin-10 following cadmium exposure or S. pneumoniae infection. More importantly, they were protected from lung injury and had better survival than mice not treated with BVD-523.

According to the authors, targeting regulation of PPAR-gamma in monocyte-derived macrophages via ERK could be a novel target to reduce the severity of lung injury following exposure to air pollution and respiratory infections.



Transcriptomic analyses revealed 66 changed genes in male offspring (not all displayed), but no significant changes for female (Image courtesy of Koshko et al., 2023)

Fighting Stressors in Adulthood

The research team followed a group of offspring into adulthood who were additionally fed a high-fat diet for five months. They observed that, compared to mice that were not exposed to benzene prenatally, both male and female benzene-exposed mice exhibited decreased glucose tolerance and increased inflammation in the hypothalamus.

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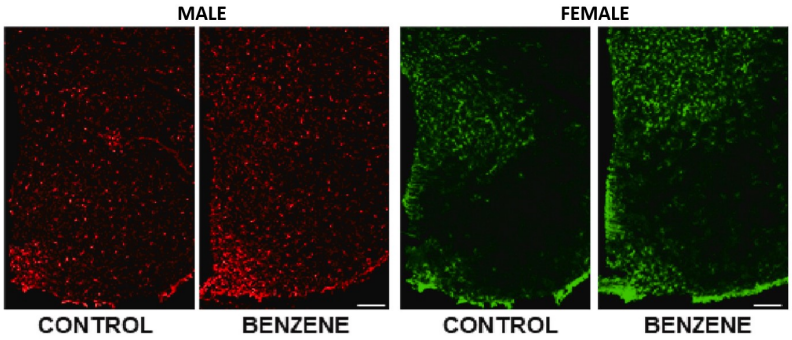

Mice treated with BVD-523 were protected from the characteristic decrease in survival following S. pneumoniae infection. (Image adapted from Larson-Casey et al., 2023)

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To learn more about this research, please refer to the following source:

Koshko L, Scofield S, Debarba L, Stilgenbauer L, Fakhoury P, Jayarathne H, Perez-Mojica JE, Griggs E, Lempradl A and Sadagurski M. (2023). Prenatal benzene exposure in mice alters offspring hypothalamic development predisposing to metabolic disease in later life. Chemosphere 330, 138738. doi:10.1016/j.chemosphere.2023.138738 PMID:37084897