

NRP Endocrine Disruptors

Final Summary

Original project title Prenatal exposure to endocrine disrupting chemicals: effects on the male urogenital system
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Effects of xenoestrogens on male fertility and metabolism

Our goal is a better understanding of the etiology of male infertility and obesity in relation with endocrine disruption. We found through toxicogenomic analysis that Estrogen Receptor alpha is a major contributor in estrogen- or DES-dependant testis dysgenesis and cryptorchidism during in utero exposure. On the contrary, phytoestrogens, a less potent endocrine disruptor, exerts beneficial effects by stimulating fatty oxydation and insulin sensitivity in mice exposed all life long to a soy-rich diet, through the stimulation of the AMP protein activated kinase.

Research questions

Our goal is to investigate the mechanisms by which endocrine disruptors (EDs) exert their effects on fertility and metabolism. For this purpose we focused our attention on two EDs: diethylstilbestrol a classical and potent xenoestrogen and phytoestrogens which are natural compounds with weak estrogenic activities.

DES - Failure of the testes to descent into the scrotum (cryptorchidism) is one of the most common birth defects in humans affecting approximatively 3% of newborns. We investigated the molecular mechanisms leading to estrogen-dependent undescended testes.

Phytoestrogens - Phytoestrogens are natural compounds, mostly found in soy, that can bind to estrogen receptors and thereby imitate the actions of estrogens on target tissues. We investigated the mechanisms mediating dietary phytoestrogens actions on lipid and glucose metabolism.

Results

DES - We have demonstrated using toxicogenomic analysis that the Estrogen Receptor alpha but not the Estrogen Receptor beta mediates the effects of estrogen on testis dysgenesis and cryptorchidism during in utero exposure. These findings may have important implications for the prevention and/or the treatment of sporadic testis dysgenesis and cryptorchidism in humans.

Phytoestrogens - We have been able to show that adult mice fed with a soy-rich diet had reduced body weight, and adiposity. This lean phenotype was associated with an increase in lipid oxidation due to a preferential use of lipids as fuel source and an increase in locomotor activity.

Whether these effects are due exclusively to isoflavones or also associated with soy proteins or other micronutrients remain unclear. The ubiquity of these compounds in human diet emphasizes the importance of further research in this field and warrant further studies for exploiting the preventive or curative potential of soybean compounds for metabolic diseases.

Perspectives

The identification of the mechanisms by which potent xenoestrogens such as DES modulates gene expression through the Estrogen Receptor alpha will have important implications not only in reproductive health, but also in estrogen-mediated diseases such as cancers, obesity and neurological diseases. Concerning phytoestrogens, critical questions remain in our understanding of the role of these compounds in the regulation of the energy balance and obesity. Still, these compounds may well represent an effective natural approach to help prevent the occurrence of the metabolic syndrome in our western societies.