Degree project in environmental toxicology 2018/2019: Effects of endocrine disrupting compounds (EDCs) in a chicken embryo model

Would you like to help us to learn more about how chemicals found in the environment and in blood in pregnant women can affect the developing embryo? Here are some proposals for a degree project in Environmental Toxicology.

Background

The continuous exposure of humans and wildlife to mixtures of a wide variety of chemicals that may disrupt endocrine functions is of growing societal concern. During the latest decades increasing trends of disorders related to the hormone systems have been observed in humans and wildlife. Epidemiological studies associate such effects to exposure to endocrine disrupting compounds (EDCs) but cause-effect relationships are often not clear. Laboratory studies of animals have shown that developmental exposure to potent EDCs can result for instance in reduced reproductive capacity, altered levels of thyroid hormones and metabolic changes. Certain EDCs, e.g. androgen disrupting compounds, may also affect development of the immune organ Bursa of Fabricius in birds.

We participate in an EU project called EDC-MixRisk which aims to improve our understanding of health effects of EDCs. In EDC-MixRisk, three different mixtures of common chemicals have been identified in blood from pregnant women in Sweden and associated with risk for adverse effects in their children (http://edcmixrisk.ki.se/). Two of these mixtures were associated to altered growth (mixture G1) and sexual development (mixture S1).

Bisphenol A (BPA) is one of the most highly produced chemicals worldwide with a very wide range of applications. BPA has been found in the majority of the tissue and plasma samples taken from humans, and it is present in surface waters, sediment and wildlife. BPA is classified as an endocrine disruptor and a reproductive toxicant [7]. Due to concerns relating to human and environmental health effects of exposure, BPA is increasingly replaced by alternative bisphenols, for instance bisphenol AD (BPAF). However, the majority of the replacement bisphenols are either poorly studied or have similar toxic properties as BPA (e.g. estrogenic).

Projects

We use the chicken embryo as a model to investigate how early-life exposure to EDCs, as single compounds or as mixtures, may affect endpoints related metabolism and sexual development.

Project 1: Does mixture S1 affect development of the reproductive organs and the bursa (immune organ) in the chicken embryo?

Project 2: Does mixture G1 affect metabolism, growth, fat deposition, and the thyroid gland in chicken embryos?

Project 3: Does bisphenol AF (BPAF) affect development of the reproductive organs in the chicken embryo?

Experimental design and methods

Chicken embryos have been exposed to the EDC-MixRisk mixtures G1 and S1 with exposure starting at embryonic day 4. The embryos were dissected and sampled on day 16 (G1) and 19 (S1).

Project 1: The morphology of the reproductive organs has been analyzed. We will also study the histology of the bursa using certain staining techniques followed by image analysis. The gonads will be analyzed regarding expression of genes involved in sex differentiation. A bisphenolA metabolite (MBP) is included as a positive control.

Project 2: We have collected data on body weight and amount of fat tissue in the embryo. Fat tissue and liver will be analyzed regarding expression of genes involved in adipogenesis and thyroid hormone signaling. We will also analyze accumulation of fat in liver using histological sections and analyze histological sections of the thyroid gland. This will be done by staining followed by quantitative image analysis. Allantoic fluid and liver will be analyzed regarding content of metabolites, fatty acids and lipids (performed at Swedish Metabolomics Center). Tributyltin (TBT) is used as a positive control.

Project 3: We have done initial dose-finding studies with BPAF and identified doses that cause testicular feminization in male embryos. We plan to perform a full-scale experiment with BPAF and more thoroughly assess responses related disrupted estrogen signaling in both female and male embryos. Investigated endpoints include gross morphology and histology of ovaries and testicles, development of the embryonic oviduct, and expression of estrogen-regulated genes.

In the proposed degree projects, one or more laboratory techniques may be used, for instance staining, evaluation and quantitative analysis of histological tissue sections or real-time PCR gene expression analysis. The project outline will be determined together with the student.

The project will include participation in planning of work and choice of methods, laboratory work, analysis and evaluation of results, literature studies and participation in department meetings, seminars, and group discussions.

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