Final Report Summary - XENROID (Xenobiotic-induced thyroid and steroid hormone disruption in wildlife)

The objective of this project is to investigate environmental endocrine-disrupting chemicals posing a threat to wildlife. Thyroid and steroid hormone systems are used to describe endocrine-disruption. The project focused on developing and establishing chemical analysis and gene expression methods enabling assessment of endocrine health in wildlife. We used controlled in-vitro and in-vivo toxicology exposure studies using suspected endocrine disruptors.

During this project we established; highly sensitive mass spectrometry assays to determine a) thyroid hormones and new metabolites, b) corticosteroids, c) selected xenobiotics and metabolites. Gene expression assays quantifying selected genes important for the steroidogenic pathway (CYP17 and CYP19) at mRNA level in amphibians. The amphibian in-vivo model Xenopus laevis was used to study the impact of pesticides on wildlife, and to clarify endocrine-disruption mechanisms and potential cross-talk among biomarkers. A fungicide, named tebuconazole, was found to bioconcentrate in adipose tissue, but also in kidney and brain in the adult male frogs. Importantly, we discovered the fungicide was an endocrine-disrupting chemical by suppressing the action of essential of enzymes important for steroid biosynthesis; resulting in altered androgenic and estrogenic hormone levels.

Establishing new scientific methodologies will assist in deeper mechanistic understanding and, compared to physiological measures, may give earlier warnings of endocrine-disruption in wildlife. Targeting the vital thyroid hormone synthesis, we developed such a methodology to determine 11 different hormones and associated metabolites in amphibian studies. The extensive work resulted in use of novel isotopic-dilution mass spectrometry, and was applied on two frog species; adult Xenopus laevis and tadpole Rana catesbeiana. We found thyroxine as dominant thyroid hormone in adult frogs, however we found previously un-described thyroid hormone metabolites in tadpoles. We are in the process of applying this state-of-the-art scientific tool in a number of studies.

This grant enabled me to establish a sound scientific collaboration and research network with leading researchers, societies and institutions in North America. The expected results from my work and collaboration will impact the research within endocrinology and endocrine-disruption. Continuing work and final results will focus on assessing new endocrine-disruptors and investigate potential cross-talk between thyroid and steroid endocrine axes. Six scientific peer-reviewed journal articles have been published based on this project work.

http://pharmacy.ku.dk/research/section_analytical_biosciences/toxicology_lab/xenobiotic_induced/

Reported by

KOBENHAVNS UNIVERSITET
Denmark

Subjects

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