Universität Basel

Research Project

Chemicals Disrupting Adrenal Steroidogenesis and/or Peripheral Steroid Action

Third-party funded project

Project title Chemicals Disrupting Adrenal Steroidogenesis and/or Peripheral Steroid Action
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0.0.1 Rationale for the research area

An increasing number of chemicals have been suspected of mimicking hormonal effects and altering steroid hormone regulation. Endocrine-disrupting chemicals (EDCs) may contribute to the development and progression of major diseases, including developmental disorders, immune diseases, various forms of cancer and cardio-metabolic diseases such as diabetes, but the mechanisms underlying chemical-induced disruption of endocrine functions are often unknown. Thus, there is a great demand to identify key events of disrupted steroid homeostasis, as well as to develop suitable tools – in vitro and in silico – for early detection of chemical-induced disturbances of steroid homeostasis.

0.0.2 Objectives

The aim is to generate experimental data that can serve as a basis to improve regulatory test systems for the characterisation of EDCs affecting steroidogenesis and peripheral steroid action. Current regulatory tests for EDCs focus on effects on oestrogen, androgen, and thyroid receptor signalling and on sex steroid production, but do not adequately assess mineralocorticoids, glucocorticoids and adrenal androgens. The proposed project aims to refine the use of the established regulatory cell-based test system (the human adrenal cancer cell line H295R) to characterise effects on these other steroids. Furthermore, effects of EDCs on peripheral steroid action will be investigated by employing computer-based models, biological testing systems and using targeted and untargeted steroid profiling and gene expression analyses.

0.0.3 Regulatory Significance

Regulatory authorities are participating in large-scale projects on chemical safety, focusing on substances that disrupt endocrine functions; however, the currently available methods and potential targets under investigation are still highly limited, and additional testing strategies are required. The tools to be developed in this project should help in the identification of potentially hazardous chemicals, and the steroidomic profiling should facilitate the investigation of their modes of action and thus risk assessment in humans.

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