

Role of the aryl hydrocarbon receptor/cytochrome P4501 (AHR/CYP1)-feedback loop in endocrine signaling and energy homeostasis

The aryl hydrocarbon receptor (AHR), also known as the dioxin receptor, is renowned in toxicology for mediating the adverse effects of environmental pollutants such as dioxins and PCBs. These adverse effects include for example immunotoxicity, reproductive toxicity, endocrine disruption and carcinogenesis.

While the toxicity of AHR signaling has been the focus for the last 40 years within the AHR-field, the focus is more and more shifting to understanding the physiological functions of this receptor. What is known today is that the AHR appears to have critical functions in immune system function, hematopoiesis, cell differentiation processes, hormone secretion and much more. However, how these physiological functions of the AHR are regulated is still unknown.

We previously reported on a critical role of the CYP1 enzyme family in regulating AHR signaling during zebrafish embryo development¹ and gut immunity² in mice. **The aim** of this study is to investigate the role of AHR signaling and CYP1 function in endocrine signaling and energy homeostasis by analyzing related endpoints in tissues or serum samples obtained from mice models with genetic alterations in the AHR or CYP1 pathways.

More specifically, the study aims are: preparing, analyzing and validating RNA sequencing data, performing multiplex protein analysis using ELISA-based methods, analyzing data on steroid hormone levels and finally integrating the results from the different endpoints.

Main methods used include: RNA preparation and cDNA synthesis, gene expression analysis using RNAseq and qRT-PCR, Ingenuity Pathway Analysis and ELISA.

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1. [Wincent, E.](#); Kubota, A.; Timme-Laragy, A.; Jonsson, M. E.; Hahn, M. E.; Stegeman, J. J., Biological effects of 6-formylindolo[3,2-b]carbazole (FICZ) in vivo are enhanced by loss of CYP1A function in an Ahr2-dependent manner. *Biochemical Pharmacology* **2016**, *110*, 117-129.
2. Schiering, C.; [Wincent, E.](#); Metidji, A.; Iseppon, A.; Li, Y.; Potocnik, A. J.; Omenetti, S.; Henderson, C. J.; Wolf, C. R.; Nebert, D. W.; Stockinger, B., Feedback control of AHR signalling regulates intestinal immunity. *Nature* **2017**, *542*, (7640), 242-245.