A Novel Animal Model to Study 21-Hydroxylase Deficiency *in vivo*

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**OBJECTIVES**

21-hydroxylase deficiency (21OHD) resulting in imbalances in steroid hormones and a dysregulated hypothalamus pituitary adrenal (HPA) axis is the major cause of the disease congenital adrenal hyperplasia (CAH). Several findings highlight the need for new *in vivo* models to study 21-hydroxylase deficiency:

- In *in vitro* studies on CAH mutations do not always correlate with patient phenotypes
- 21OHD is difficult to study in mice -> mutants are not viable
- Incomplete understanding of systemic consequences of 21OHD

**Aim:** Zebrafish model for 21-hydroxylase deficiency

**METHODS**

Cyp21a2 mutants were generated by TALEN-mediated mutagenesis. The target region contained a BseYI restriction site, used for genotyping. The mutant phenotype was characterised at 120 hpf (hours post fertilisation), when the HPI axis is functional.

**Zebrafish cyp21a2 mutants show hallmarks of 21OHD**

- Cyp21a2 mutants have enlarged interrenal tissue (zebrafish adrenal counterpart)
- Impaired cortisol synthesis and overstimulation of the HPI axis in cyp21a2 mutants
- Reduced expression of glucocorticoid response genes in cyp21a2 mutants

**CONCLUSIONS**

Zebrafish cyp21a2 mutants are a promising model for 21OHD

1. 21-hydroxylase is conserved in zebrafish
2. Zebrafish cyp21a2 mutants have impaired GC signalling
3. Zebrafish cyp21a2 mutants have dysregulated HPI axis

**ACKNOWLEDGEMENTS**

Society for Endocrinology  
Early Career Grant to Andreas Zaucker  
IFCAH  
Project grant to Nils Krone

I declare that I have no potential conflict of interest