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Title: Unraveling the glucocorticoid receptor pathway in zebrafish

Issue Date: 2012-06-26

Stellingen

1. Whereas neutrophils respond well to glucocorticoid treatment in 3 day old tail-fin amputated zebrafish larvae, macrophages appear to be resistant to glucocorticoids in this model (Chapter 2 of this thesis).
2. Glucocorticoids have a very general suppressive effect on the transcriptional response to tail fin amputation in zebrafish (Chapter 2 of this thesis).
3. The glucocorticoid receptor α -isoform regulates two clusters of genes: one that contains many cell-cycle related genes and is regulated under basal conditions and one that contains mainly metabolism-related genes and is regulated at high glucocorticoid levels (Chapter 3 of this thesis).
4. The zebrafish glucocorticoid receptor β -isoform does not act as a dominant-negative inhibitor of the transcriptional activity of the α -isoform *in vivo* (Chapter 3 and 4 of this thesis). Hence, the zebrafish should not be used in future research as an *in vivo* model to study the dominant-negative activity of this receptor isoform.
5. An intrinsic transcriptional activity of the zebrafish glucocorticoid receptor β -isoform can still not be ruled out, although it would require high expression levels of this splice variant (Chapter 3 and 4 of this thesis).
6. Glucocorticoids exert both negative and positive effects with a dynamic and bidirectional spectrum of activities on various limbs and components of the immune response (Franchimont 2004, Ann. N.Y. Acad. Sci).
7. The architecture of genomic response elements determines the number of activated glucocorticoid receptors that are required for transcriptional activation of responsive genes (Reddy et al., 2009, Genome Res.; Meijer, 2006, Stress).
8. The occurrence of different transcriptional and translational variants of the human glucocorticoid receptor contributes significantly to the (cell-)specificity of the glucocorticoid response (Oakley & Cidlowski, 2011, J. Biol. Chem.).
9. Systems biology approaches like microarray analysis demonstrate the power of numbers which implies that more input from bioinformaticians will be required for interpreting results.
10. Science is not meant to cure us of mystery, but to reinvent and reinvigorate it (Robert Sapolsky).
11. If you want a scientific question to be answered, there is only one way: do the experiment. (Marcel Schaaf)
12. All I know is that I know nothing (Socrates).