NEW INSIGTHS INTO THE TRANSCRIPTIONAL ACTIVITY OF GLUCOCORTICOID RECEPTORS

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Although many mechanisms of action have bee described for glucocorticoids (GC) action, they might be claisfied in two major mechanisms: regulation of gene transcription acting at the level of DNA glucocorticoid responding elements (GREs) or the protein-protein interaction with other transcription factors (TF). We will present new insigths into these mehanisms focused on the regulation of immune-cytokine pahtways by Gcs. There are different levels of interaction between GCs and cytokines with the final outcome of regulation of gene expression. One level of interaction involves the cross-talk between the activated GR and TFs implicated in the regulation of cytokine synthesis and function. This interaction results in the induction or repression of gene transcription, as we will illustrate with the Th1 and Th2 transcription factors Tbet and GATA-3. Also, when cytokine-induced transduction signals cross-talk with the activated GR there may be an enhancement or an inhibition of glucocorticoid response element (GRE) regulated genes. A further level of mutual regulation may be the ubiquitin-proteasome and sumoylation systems, which regulate GR transactivation as will be presented for the SUMO pathway and its enhancer RSUME. The impact on inflammatory pathways as NFkB and regulated cytokines will be discussed.