Function of coregulators in the glucocorticoid receptor mediated regulation of the HPA axis activity: colocalisation studies

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Corticotrophin Releasing Hormone (CRH) and Proopiomelanocortin (POMC) expression, in the paraventricular nucleus (PVN) of the hypothalamus and in the pituitary respectively, are considered to be markers for the activity of the hypothalamic-pituitary-adrenal (HPA) axis. The expression of these signalling neuropeptides is directly regulated by the Glucocorticoid Receptor (GR). The GR is a ligand-dependent transcription factor which, upon binding of its cognate ligand in the cytoplasm of the cell, translocates to the nucleus and modulates expression of target genes by recruiting coregulators to the promoter region of these genes. Known coregulators are Steroid Receptor Coactivators (SRCs), Silencing Mediator of Retinoid and Thyroid hormone receptor (SMRT) and Nuclear receptor Corepressor (NCoR). The recruitment of these coregulators by ligand-activated GR has been extensively investigated *in vitro* and is proposed to determine transrepression or transinduction of target genes. Therefore we hypothesise that the intracellular ratio of expressed coregulator proteins (coactivators and corepressors) in the cells of the PVN and the pituitary directs the nature and the magnitude of the ligand-activated GR transcriptional effects.
Determining whether co-expression of CRH and POMC mRNA with GR and coregulator proteins occurs in single cells of the PVN and the pituitary is being tested on rat tissue by combining non radioactive riboprobe *in situ* hybridisation with immunohistochemistry. We demonstrate that in the corticotrophs of the anterior lobe of the pituitary POMC mRNA is co-expressed with SRC1 proteins. This suggests that SRC1 may contribute to the GR-mediated transcriptional responses to glucocorticoids in the pituitary corticotrophs.

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