

P014 Interplay of JNK and SUMO pathways in the regulation of glucocorticoid receptor activity

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Phosphorylation of the glucocorticoid receptor (GR) is mediated by two families of kinases, cyclin-dependent kinases (CDKs) and mitogen activated protein (MAP) kinases. Phosphorylation of GR by CDKs is associated with stimulation whereas phosphorylation by JNK is associated with inhibition of GR transcriptional activity. Here we demonstrate that the JNK family of proteins phosphorylates GR at serine 246 (S246) in a rapid and transient manner. We have observed that endogenous GR is phosphorylated at S246 in cells where JNK is activated by MLK3 or UV treatment using an antibody that specifically recognises the phosphorylated S246 GR isoform. Furthermore, we provide evidence that JNK dependent phosphorylation of GR modulates other post-translational modifications of the receptor such as addition of the small ubiquitin related modifier (SUMOylation). Our results indicate that JNK activation correlates with upregulation of GR SUMOylation and consequently abrogation of its function and suggest molecular mechanism that could explain effects of signalling pathways on the GR dependent activities observed in our and other laboratories in UV and hormone treated cells.