

**P059** SUMO modification of the ETS-domain transcription factor PEA3 is important for its transcriptional activation properties

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The ETS-domain transcription factor PEA3 is critical for embryogenesis and are relevant to cancer development and metastasis. High levels of PEA3 mRNA exist in cancer cells, especially in metastatic cancer cells. PEA3 is activated by the MAPK signalling pathway and regulates its target genes such as MMPs and COX-2 which are closely related to tumour metastasis. Therefore it is important to know how PEA3 regulates its target genes. Here we have investigated sumoylation of PEA3 and its interplay with the ERK MAP kinase signalling pathway. PEA3 is modified by SUMO *in vitro* and *in vivo* on multiple sites in its N-terminal region. Moreover activation of the ERK MAP kinase pathway promotes sumoylation, in part through acting on an extended PDSM sumoylation motif in PEA3. Importantly, we show that sumoylation of PEA3 is required for maximal activation of target gene promoters, including MMP-1 and COX-2. One key event orchestrated by sumoylation is synergistic promoter activation with CBP. Moreover sumoylation destabilises PEA3, suggesting an important role in recycling PEA3 and hence maintaining maximal PEA3 mediated promoter activation. We also find PEA3 exists in the form of already sumoylated species in colon cancer cell line SW480. Thus sumoylation of PEA3 plays a positive role in PEA3-mediated gene expression and the ERK MAP kinase pathway cooperates with rather than antagonizing this process.