

P011 Regulation of the ETS-domain transcription factor PEA3 by SUMOylation

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The ETS-domain transcription factor PEA3 has already been found to be related to tumour development and metastasis. It is downstream of The MAPK pathway and is regulated by MAPK signalling. PEA3 positively regulates cancer metastasis through inducing the expression of relevant molecules such as MMPs, COX-2 and osteopontin etc. However, so far little is known about PEA3 posttranslational modification. By *In vitro* and *in vivo* experiments, PEA3 was found to be able to be SUMOylated. By creating mutations in the consensus $\Psi K \times E$ motif, PEA3 SUMOylation was shown to occur on 3 lysines. Ubc9 was able to remarkably increase PEA3 SUMOylation. Importantly PMA was found to enhance PEA3 SUMOylation significantly, especially at one lysine containing the SUMO consensus $\Psi K \times E \times \times S P$, and this enhancement was blocked by a MEK1 inhibitor U0126. This suggests that MAPK signalling has a positive effect on PEA3 SUMOylation levels. Mutations in SUMOylation sites or SUMOylation inhibitor strongly increase PEA3 transcription effect on a promoter containing reiterated PEA3 response elements. However the same mutations result in a significant reduction of COX-2 promoter activity. Endogenous SUMOylated PEA3 was also found exist in several cancer cell lines such as HCT116, SW480, DU145 and F9. These data suggest that PEA3 modification by SUMO may be related with cancer development and metastasis.