

P011 Phosphorylation-dependent interaction between c-Jun and TCF4 is required for efficient colon cancer development in a mouse model

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The proto-oncoprotein c-Jun is a component of the AP-1 transcription factor, whose activity is augmented in many tumor types. An important mechanism to stimulate AP-1 function is N-terminal phosphorylation of c-Jun by the c-Jun N-terminal kinases (JNKs). Phosphorylated c-Jun is biologically more active, partially because it acquires the ability to interact with binding partners¹.

Here we show that phosphorylated c-Jun interacts with the HMG-box transcription factor TCF4 to form a ternary complex containing c-Jun, TCF4 and β -catenin. Chromatin immuno-precipitation assays revealed JNK-dependent c-Jun/TCF4 interaction on the c-jun promoter and c-Jun and TCF4 co-operatively activated the c-jun promoter in reporter assays in a β -catenin-dependent manner. Genetic abrogation of c-Jun N-terminal phosphorylation significantly reduced tumor number and size and prolonged life span in the APC Min mouse model of colon cancer. Therefore the phosphorylation-dependent interaction between c-Jun and TCF4 regulates colon cancerogenesis by integrating JNK and APC/ β -catenin, two distinct pathways activated by WNT signalling.

1- A. S. Nateri, L. Riera-Sans, C. Da Costa, A. Behrens, *Science* 303, 1374 (Feb 27, 2004).