TBX2: A TRANSCRIPTIONAL REGULATOR WITH A ROLE IN MITOSIS?

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The T-box family of transcription factors plays a crucial role in development[1] and accumulating evidence suggests that over-expression of some T-box factors may be a feature of cellular transformation and cancer. For example, Tbx2 can suppress senescence through repressing p19 and p21 gene expression[2−4] and has been reported to be over-expressed in breast tumours[5,6] and 50% of pancreatic cancer cell lines[7]. These results suggest that Tbx2 may contribute to cell cycle control but its precise role is poorly defined.

Here we show that Tbx2 may play a role in mitosis. FACS analysis shows that a subpopulation of cells ectopically expressing Tbx2 undergoes aneuploidy, suggesting that they are blocked at some point of the cell cycle prior to separation of their daughter cells. Immunofluorescent analysis of asynchronous COS cells transfected with Tbx2 show that the protein binds mitotic chromatin. In keeping with a role for Tbx2 in mitosis, western blot analysis of cell lines that can be induced to express Tbx2, reveal that its protein levels accumulate during mitosis. Using coimmunoprecipitation assays and GST-pulldown experiments, we show that Tbx2 is able to interact with the mitotic cyclin B1, and that this interaction is dependent on the DNA binding domain of Tbx2. Furthermore, we show that Tbx2 is a substrate for the cyclin B1-cdc2 kinase and that the identified target sites are phosphorylated both in vitro and in vivo. Lastly, we show that Tbx2 mutants, which inhibit phosphorylation by the cdc2-kinase affects the stability of the protein in vivo.

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