CRD-BP mediates stabilization of βTrCP1 and c-myc mRNA in response to β-catenin signalling

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Although constitutive activation of β-catenin/Tcf signalling is implicated in the development of human cancers, the mechanisms by which the β-catenin/Tcf pathway promotes tumorigenesis are incompletely understood. Messenger RNA turnover has a major function in regulating gene expression and is responsive to developmental and environmental signals. mRNA decay rates are dictated by *cis*-acting elements within the mRNA and by *trans*-acting factors, such as RNA-binding proteins. Here we show that β-catenin stabilizes the mRNA encoding the F-box protein βTrCP1, and identify the RNA-binding protein CRD-BP (coding region determinant-binding protein) as a previously unknown target of β-catenin/Tcf transcription factor. CRD-BP binds to the coding region of βTrCP1 mRNA. Overexpression of CRD-BP stabilizes βTrCP1 mRNA and elevates βTrCP1 levels (both in cells and in vivo), resulting in the activation of the Skp1-Cullin1-F-box protein ($SCF^{\beta TrCP}$) E3 ubiquitin ligase and in accelerated turnover of its substrates including IκB and β-catenin. CRD-BP is essential for the induction of both βTrCP1 and c-Myc by β-catenin signalling in colorectal cancer cells. High levels of CRD-BP that are found in primary human colorectal tumours exhibiting active β-catenin/Tcf signalling implicates CRD-BP induction in the upregulation of βTrCP1, in the activation of dimeric transcription factor NF-κB and in the suppression of apoptosis in these cancers.

[Reference]

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