Human Tip41 is a novel regulator of the transcription factor MafB

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Tip41 is a conserved protein that is likely to be involved in different signaling pathways, although its functional role was poorly characterized. Tip41 was initially identified in yeast as an inhibitor of the TOR signaling pathway, which controls cell growth in response to nutrients via different effectors. Strikingly, its human counterpart (TipRL) was isolated as a potential MAPK activator. In this study, we have searched for TipRL interacting partners using a yeast two-hybrid screen in order to clarify its function. We have identified MafB, a bZIP transcription factor of the Maf family, as such a partner. Maf proteins are important transcriptional regulators of cellular differentiation and morphogenesis, along several distinct developmental pathways such as hematopoiesis, lens differentiation and segmentation of hindbrain. MafB interacts with TipRL through its bZIP domain. The interaction has been confirmed by *in vitro* binding assays as well as by analyses showing that the endogenous TipRL binds to the recombinant bZIP domain of MafB. In addition, MafB co-localizes with TipRL to the nucleus in human embryonic kidney cells. Furthermore, the bZIP domain of Mafs is involved in the recognition of its DNA target sequences and TipRL disrupts MafB-DNA binding. Therefore, TipRL may be involved in mechanisms of transcriptional control through the regulation of MafB activity.

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