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Titel des Beitrags: The Zyxin-related protein thyroid receptor interacting protein 6 (TRIP6) is overexpressed in Ewing's sarcoma and promotes migration, invasion and cell growth.

Abstract: Ewing's sarcoma (ES) is the second most common bone-associated malignancy in children and is driven by the fusion oncogene EWS/FLI1 and characterised by rapid growth and early metastasis. Here, we explored the role of the Zyxin-related protein thyroid receptor interacting protein 6 (TRIP6) in ES. The Zyxin family comprises seven homologous proteins involved in migration and proliferation of many cell types of which Zyxin has been described as a tumour suppressor in ES. By interrogation of published microarray data (n = 1254), we observed that of all Zyxin proteins, only TRIP6 is highly overexpressed in primary ES compared with normal tissues. Re-analysis of published EWS/FLI1 gain- and loss-of-function microarray experiments as well as chromatin-immunoprecipitation assays revealed that TRIP6 overexpression is not mediated by EWS/FLI1. Microarray and subsequent gene-set enrichment analyses of ES cells with and without RNA interference-mediated TRIP6 knockdown demonstrated that TRIP6 expression confers a pro-proliferative and pro-invasive transcriptional signature to ES cells. While short-term proliferation was not considerably affected by TRIP6 knockdown, silencing of the protein significantly
reduced migration, invasion, long-term proliferation and clonogenicity of ES cells in vitro as well as tumourigenicity in vivo. Taken together, our data indicate that TRIP6 acts, in contrast to Zyxin, as an oncogene that partially accounts for the autonomous migratory, invasive and proliferative properties of ES cells independent of EWS/FLI1.

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