PATZ1 acts as a tumor suppressor in thyroid cancer via targeting p53-dependent genes involved in EMT and cell migration.

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Abstract

PATZ1, a POZ-Zinc finger protein, is emerging as an important regulator of development and cancer, but its cancer-related function as oncogene or tumor-suppressor is still debated. Here, we investigated its possible role in thyroid carcinogenesis. We demonstrated PATZ1 is down-regulated in thyroid carcinomas compared to normal thyroid tissues, with an inverse correlation to the degree of cell differentiation. In fact, PATZ1 expression was significantly further down-regulated in poorly differentiated and anaplastic thyroid cancers compared to the papillary histotype, and it resulted increasingly delocalized from the nucleus to the cytoplasm proceeding from differentiated to undifferentiated thyroid carcinomas. Restoration of PATZ1 expression in three thyroid cancer-derived cell lines, all characterized by fully dedifferentiated cells, significantly inhibited their malignant behaviors, including in vitro proliferation, anchorage-independent growth, migration and invasion, as well as in vivo tumor growth. Consistent with recent studies showing a role for PATZ1 in the p53 pathway, we showed that ectopic expression of PATZ1 in thyroid cancer cells activates p53-dependent pathways opposing epithelial-mesenchymal transition and cell migration to prevent invasiveness. These results provide insights into a potential tumor-suppressor role of PATZ1 in thyroid cancer progression, and thus may have potential clinical relevance for the prognosis and therapy of thyroid cancer.

KEYWORDS:

PATZ1; cell migration; epithelial-mesenchymal transition; thyroid cancer