

## TBX15 as an antiapoptotic factor in cancer cells

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T-box genes regulate development processes, and some of these genes also have a role in cell proliferation and survival. TBX15, as a T-box transcription factor, is required in skeletal development; in fact, the human Cousin syndrome which is characterized by many skeleton malformations is promoted by alterations in the *TBX15* gene. Also, TBX15 has been associated with the differentiation of adipocyte cells. Recently, the methylation of the *TBX15* promoter has been suggested as a marker in prostate cancer, but its function in carcinogenesis is unknown.

Here we investigated the role of TBX15 in carcinogenesis using thyroid cancer cell lines. First, by western blot analysis, we showed that the expression of TBX15 was altered in thyroid cancer cell lines compared to normal thyroid cells. Then, we performed different functional studies including proliferation, cell viability, migration, colony formation and apoptosis assays. These studies were carried out in conditions with ectopical overexpression TBX15 through the transfection of an expression-plasmid in thyroid cancer cells, in the presence or absence of camptothecin as a cytotoxic agent.

Our results proved that TBX15 did not affect the colony formation, cell migration or cell viability; but the TBX15 transcription factor increased cell proliferation after 48 h of transfection ( $P < 0.01$ ). Consistently, apoptosis was reduced in TBX15 transfected cells ( $P < 0.01$ ), both in the presence or absence of camptothecin. A decrease in the proapoptotic Bax regulator and an increase in the antiapoptotic Bcl2 and Bcl-XL regulators was also observed, which indicated the implication of TBX15 in the intrinsic pathway of the cell apoptosis. Additionally, we performed a siRNA shutdown of constitutive TBX15 in the studied cell lines. Compatible with the overexpression experiments, after knocking down TBX15 an increase of apoptotic cells was observed.

Taken together, these results indicate for the first time an antiapoptotic role of TBX15 in cancer cells, suggesting a contribution of TBX15 in carcinogenesis and the potential therapeutic target of TBX15.