TCTP in melanoma malignancy: possibilities of a new therapeutic approach

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Introduction: TCTP is a multifunctional protein overexpressed in several tumor types. Silencing TCTP was shown to be able to induce tumor reversion, the loss of the malignant phenotype. TCTP and p53 present a negative feedback loop with reciprocal repression. Sertraline is an antidepressant, which interacts with TCTP and decreases its cellular levels. **Objective:** Our aim was to evaluate the role of TCTP on melanoma malignancy. **Material and Methods:** We studied the TCTP in a murine melanoma model (B16F10 and B16F1) and human melanoma cell lines (A2058, SK-MEL, Mel-85 and MeWo). Cell viability, proliferation, migration and the clonogenic capacity were evaluated using sertraline or RNAi to decrease TCTP levels. Tumor growth was assessed in vivo (B16F10/C57BL6) using dacarbazine/sertraline. **Results and Discussion:** When B16F10 was compared to B16F1 (less metastatic and tumorigenic) the expression of TCTP mRNA was 1.83-fold higher than in B16-F1. Silencing TCTP by RNAi, reduced cell proliferation (decrease of 25%) and migration (decrease of 75%) when compared to control. Decreased levels of TCTP were confirmed by RT-PCR and immunoblot. TCTP expression is related to phenotypic differences of murine melanoma cell lines. Sertraline was evaluated in vitro and in vivo and the results highlight its effect on inhibiting tumor growth (decrease of ~75%) and on the response to the chemotherapeutic agent dacarbazine, which was highly improved. When human melanoma cells were treated with sertraline and dacarbazine, there was a decrease in viability and in the number of colonies at clonogenic assays. Diminished levels of TCTP were confirmed by immunoblot. **Conclusion:** These results show the use of sertraline as a promising new therapeutic approach for melanoma tumors. Although the results are preliminary, sertraline and the TCTP-p53 axis should be considered a new possibility for the improvement of melanoma treatment.

Keywords: TCTP, Tumor Reversion, Melanoma.

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