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12. Thyroid hormone metabolism

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Disturbed Expression of Type 2 and Type 3 Iodothyronine Deiodinase in Papillary Thyroid Carcinoma

E. L. Souza Meyer [1,*] N. Zennig [1] I. M. Goemann [1] A. L. Bueno [1] S. Wajner [1] A. L. Maia [1]

[1] Thyroid Section - Endocrine Division, HOSPITAL DE CLÍNICAS DE PORTO ALEGRE - RS, Porto Alegre, Brazil

Abstract: Introduction: The deiodinases type 1 (D1) and 2 (D2) activate thyroid hormone. In contrast, the deiodinase type 3 (D3) catalyzes the inactivation of both T4 and T3. All three deiodinases work in concert to maintain intracellular T3 concentration. Previous studies have demonstrated underexpression of D1 and D2 in papillary thyroid carcinoma (PTC), the most common thyroid malignant neoplasia. In an opposite way, D3 overexpression has been described in malignant cell lines and human tumors. Few data is available on D3 expression in thyroid neoplasias. **Objective:** To evaluate D2 and D3 expressions in PTC samples and correlate with pathological and clinical data. **Methods:** Thirty-two samples of PTC and corresponding normal thyroid tissues were obtained from patients undergoing total thyroidectomy at our Hospital. D2 and D3 mRNA expression was measured by Real-Time PCR. D2 activity assays used 1nM unlabeled T4 and ^{125}I-T4 as substrate whereas D3 activity was determined by paper descendent cromatography measuring T2 released after incubation with ^{125}I-T3. Human PTC cell line (K1 cells) was used to study the D3 regulation. **Results:** D2 transcripts and activity were found in all 14 consecutive samples (paired tumor/normal tissue) analyzed. D2 mRNA levels were marked decreased in tumor compared to surrounding normal tissue (0.35±0.34 *vs.* 0.98±0.45 arbitrary units (AU), *P<0.001*, respectively). In contrast, no significant differences were observed in D2 activity (0.34±0.23 *vs.* 0.22±0.14 fmol/min/mg.prot, *P=0.34*, respectively). D3 mRNA expression was present in all tissues (18 paired tumor/normal tissues). D3 mRNA levels were significantly increased in PTC compared with adjacent normal thyroid tissues (~5-fold, *P=0.001*). A higher level of D3 activity was detectable in PTC (0.79±0.51 fmol/min/mg.prot) whereas no activity was found in corresponding normal thyroid tissues. D3 activity was significantly associated with tumor size and tumor stage (*P=0.002 and P=0.003*, respectively). Additional analysis in K1 cells showed that D3 activity was down-regulated by hypothyroidism and enhanced by T3 and cAMP. **Conclusion:** These results indicate that the malignant transformation of thyroid follicular cell promotes opposite changes in D2 and D3 expression by pre-transcriptional mechanisms. The association between increased levels of D3 activity and advanced disease further supports a role for intracellular T3 concentration in the thyroid cell proliferation or/and dedifferentiation.

Disclosure of Interest: None Declared

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