

NUCLEAR RECEPTOR EXPRESSION IN DIFFERENTIATED THYROID TUMORS

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Background/Purpose: Nuclear receptors (NR) play a key role in endocrine signalling and metabolism and are important therapeutic targets in hormone-dependent malignancies. Studies on the role of NR in thyroid cancer are limited. The objective of the study was to systematically examine the expression of the 48 human NR in a series of benign and malignant thyroid tissues. Within the papillary carcinoma cohort, we sought to determine if NR expression differed significantly by *BRAF* mutation status.

Methods: RNA was isolated from frozen tissue: multinodular goitre (MNG; n = 6), papillary carcinoma (PTC, n=14); follicular carcinoma (FC; n = 5) and Hurthle cell carcinoma (HCC; n = 7). The 48 human NR were profiled in this panel by quantitative RT-PCR using TaqMan Low Density Nuclear Receptor Signature Arrays (Applied Biosystems).

Results: In the PTC there was marked overexpression of RXR- γ and Rev-erbA α compared to MNG; when *BRAF* V600E tumors were compared with wild-type *BRAF*, there was relative upregulation of RXR- γ and Rev-erbA α but downregulation of AR, ERR- γ and ROR- γ . In FC, EAR-2 was overexpressed, while PPAR- α and PPAR- δ were underexpressed compared to MNG. The NR expression profile of HCC was distinct, characterised by significant downregulation of a wide range of NR. We are currently validating expression of selected NR at the protein level by immunohistochemistry.

Discussion & Conclusion: These results represent the first systematic examination of NR expression in thyroid cancer. Our finding of tumor-specific patterns of NR expression as well as significant differences in NR expression between *BRAF* V600E and wild-type *BRAF* PTC provides a basis for further mechanistic studies and highlights potential novel therapeutic targets for this malignancy.