

EVALUATION OF TYPE 1 GROWTH FACTOR RECEPTOR FAMILY EXPRESSION IN 205 THYROID LESIONS REVEALS DIAGNOSTIC UTILITY AND TARGETED THERAPEUTIC POTENTIAL FOR HER1, HER3, AND HER4

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Objectives: The aim of this study was to evaluate the diagnostic and prognostic utility of the type 1 growth factor receptor (T1GFR) family (HER1, HER2, HER3, HER4) in the management of differentiated thyroid cancer (DTC). A secondary objective was to evaluate the proportion of DTC expressing T1GFR family members.

Methodology: Tissue microarrays (TMAs) consisting of 100 benign thyroid lesions and 105 malignant thyroid lesions were stained for HER1, HER2, HER3, and HER4. Correlation of clinicopathologic characteristics with expression of each of the markers was assessed with contingency table tests (χ^2 or Fisher's Exact where appropriate) for categorical variables and the Mann-Whitney U-test for continuous variables. A *p* value of less than 0.05 was considered statistically significant.

Results: HER1, HER2, HER3, and HER4 were expressed in 76%, 2%, 57%, and 73% of DTC cases respectively. HER1 and HER3 showed significantly increased expression in DTC compared to benign thyroid lesions (76.3% vs. 59.6%, *p*=0.022 and 56.5% vs. 34.3%, *p*=0.013, respectively). HER4 showed significantly decreased expression in DTCs compared to benign thyroid lesions (72.7% vs. 85.9%, *p*=0.032). For HER2 there was no significant difference in expression between benign and DTC lesions. The expression of HER3 correlated with the presence of lymph node metastasis (*p*=0.012), tumor type (only follicular carcinoma stained negative) (*p*=0.013), and higher N stage (*p*=0.022); the expression of HER4 correlated with lower T stage (*p*=0.037). A classifier targeting benign versus malignant status with all four markers as potential predictors displayed an accuracy, sensitivity and specificity of 67.2%, 60.4%, and 74.0% , respectively.

Conclusions: Expression of the T1GFR family helps distinguish DTCs from benign thyroid lesions and the high proportion of cancers which expressed HER1, HER3, and HER4 suggests that investigation of currently utilized anticancer agents, which target one or more of these family members, warrants further clinical study in individuals diagnosed with DTC.