Differential expression profile of CXCR3 splicing variants is associated with thyroid neoplasia. Potential role in papillary thyroid carcinoma oncogenesis?

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Papillary thyroid cancer (PTC) is the most prevalent endocrine neoplasia. The increased incidence of PTC in patients with thyroiditis and the frequent immune infiltrate found in PTC suggest that inflammation might be a risk factor for PTC development. The CXCR3-ligand system is involved in thyroid inflammation and CXCR3 has been found upregulated in many tumors, suggesting its pro-tumorigenic role under the inflammatory microenvironment. CXCR3 ligands (CXCL4, CXCL9, CXCL10 and CXCL11) trigger antagonistic responses partly due to the presence of two splice variants, CXCR3A and CXCR3B. Whereas CXCR3A promotes cell proliferation, CXCR3B induces

apoptosis. However, the relation between CXCR3 variant expression with chronic inflammation and PTC development remains unknown. Here, we characterized the expression pattern of CXCR3 variants and their ligands in benign tumors and PTC. We found that CXCR3A and CXCL10 mRNA levels were increased in non-metastatic PTC when compared to non-neoplastic tissue. This increment was also observed in a PTC epithelial cell line (TPC-1). Although elevated protein levels of both isoforms were detected in benign and malignant tumors, the CXCR3A expression remained greater than CXCR3B and promoted proliferation in Nthy-ori-3-1 cells. In non-metastatic PTC, inflammation was conditioning for the CXCR3 ligands increased availability. Consistently, CXCL10 was strongly induced by interferon gamma in normal and tumor thyrocytes. Our results suggest that persistent inflammation upregulates CXCL10 expression favoring tumor development via enhanced CXCR3A-CXCL10 signaling. These findings may help to further understand the contribution of inflammation as a risk factor in PTC development and set the basis for potential therapeutic studies.

Chemokine receptors

CXCL10

CXCR3

Inflammation

Papillary thyroid cancer

chemokine receptor CXCR3

chemokine receptor CXCR3A

chemokine receptor CXCR3B

gamma interferon

gamma interferon inducible protein 10

messenger RNA

unclassified drug

adult

Article

carcinogenesis

cell proliferation

clinical article

controlled study

female

human

human tissue

inflammation

lymph node metastasis

male

Nthy-ori 3-1 cell line

protein expression

thyroid follicular cell

thyroid papillary carcinoma

thyroiditis

TPC-1 cell line