

## Expression of cancer stem-like cell markers in papillary thyroid cancer: An immunohistochemical analysis

Hye Min Kim

Yonsei University College of Medicine, South Korea, E-mail: pinkmin15@yuhs.ac

### Abstract

**Purpose:** Cancer stem-like cell markers are reported to be related to the prognosis of various cancers. The aim of this study was to investigate the clinical significance of stem-like cell markers in papillary thyroid carcinoma (PTC). **Methods:** We constructed tissue microarrays with 386 PTC cases. The expression of cancer stem-like cell markers was estimated using immunohistochemical (IHC) staining for CD24, CD15, CD166, CD44, and ALDH1A1. The scores of IHC staining were calculated by multiplying the proportion of stained cells and immunostaining intensity, and were defined as positive when the final score was  $>10$ . Associations between the expression of cancer stem-like cell markers and the clinicopathologic parameters were evaluated. Disease progression was defined as those experiencing recurrence or distant metastasis. **Results:** Among the patients included, a total of 59 patients experienced recurrence or distant metastasis during the follow-up. The proportion of CD15, CD166, CD44, and ALDH1A1 expression was higher in PTC patients with disease progression than without ( $p=0.014$ ,  $<0.001$ ,  $=0.019$ , and  $<0.001$ , respectively). In multivariate Cox-proportional hazard analysis, CD15 positivity, CD166 positivity, and ALDH1A1 positivity were independent factors for shorter progression-free survival (odds ratio: 2.113, 7.413, and 2.574, 95% CI: 1.253-3.564, 4.296-12.791, and 1.014-6.360,  $p = 0.005$ ,  $<0.001$ , and  $=0.041$ , respectively) along with the presence of lymph node metastasis. **Conclusion:** Expression of cancer stem-like cell markers CD15, CD166, CD44, and ALDH1A1 in PTC was associated with shorter progression-free survival. These findings suggest that cancer stem-like cell markers might provide useful information in predicting patient prognosis in PTC. Thyroid cancer is the most common type of endocrine-related cancer, affecting 3.2 million people worldwide in 2015. Among thyroid cancers, papillary thyroid cancer (PTC) accounts for 80–85% of cases. In general, the prognosis of PTC is favorable because of its low biological aggressiveness. However, in cases of disease recurrence or metastasis owing to a poor response or resistance to the standard treatment of thyroidectomy and radioactive iodine-131 therapy, patient death may occur and alternative treatment options should be sought. Therefore, numerous efforts have been made to identify markers of aggressive cancer behaviors. While the cause of aggressiveness in certain patients with PTC is unclear, several lines of evidence suggest an association with a rare subpopulation of tumor cells with stem cell-like features,

also known as cancer stem cells (CSCs). CSCs have important roles in cancer development, growth, recurrence, and metastasis owing to their potential to self-renew and differentiate into various cell lineages. These characteristics may result in the formation of heterogeneous tumor cell masses and the acquisition of resistance to chemotherapy and radiotherapy.

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