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Association of Serum Progranulin Levels with Progression of Papillary Thyroid Cancer

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Recent epidemiological studies have reported a strong association between obesity and thyroid cancer, especially papillary thyroid carcinoma (PTC) [1,2]. Data from a recent meta-analysis of 22 prospective studies suggested that overweight and obese individuals have 25% and 55% higher risks of thyroid cancer, respectively, than their normal-weight counterparts [2]. Some evidence exists regarding a potential association of overweight and obesity with more aggressive clinical and pathological characteristics in patients with thyroid cancer [3]. These findings underscore the need to study potential mechanisms implicated in the effects of obesity on the process of thyroid carcinogenesis and cancer progression. Various molecular pathways may explain the underlying mechanism of obesity-induced carcinogenesis and cancer progression because obesity can cause complex and diverse metabolic changes. Insulin resistance, augmented insulin-like growth factor 1 signaling, increased oxidative stress, increased levels of free fatty acids and other macromolecules, and changes in cytokine and adipokine levels may contribute to the carcinogenesis, progression, and metastasis of thyroid cancer [3]. In obesity, decreased levels of anti-inflammatory adipokines, such as adiponectin, and increased levels of pro-inflammatory adipokines, such as leptin and resistin, can stimulate or suppress several signaling pathways associated with thyroid carcinogenesis [4].

In this issue of *Endocrinology and Metabolism*, Kwon et al. [5] evaluated the serum levels of two important adipokines, adiponectin and progranulin, in patients with PTC. They included 131 patients with PTC and 26 patients with confirmed benign thyroid nodules after thyroid surgery. The median level of serum adiponectin was 5.4 and 6.3 μg/mL in the PTC group and the benign nodule group, respectively. However, this difference was not statistically significant. In patients with PTC, serum adiponectin levels were not associated with clinicopathological parameters, including primary tumor size, cervical lymph node metastasis, extrathyroidal extension, and multifocality. These results on serum adiponectin levels in PTC patients are consistent with those of a previous study that evaluated serum adiponectin levels and the expression of its receptor in patients with PTC [6]. That study suggested that adiponectin receptor expression in tumor tissue, but not serum adiponectin levels, played an important role. A significant negative correlation was found between adiponectin receptor expression in tumor tissue and poorer pathological parameters, including multifocality, extrathyroidal extension, and advanced tumor-node-metastasis (TNM) staging [7]. These findings suggest that serum adiponectin levels *per se* are not an important factor explaining the potential mechanism through which obesity influences the carcinogenesis of PTC.

Kwon et al. [5] also evaluated the serum levels of progranulin, an adipokine implicated in diverse biological processes in embryogenesis, inflammation, insulin resistance, and carcinogenesis [8]. This is the first study to report a potential role of progranulin in thyroid carcinogenesis. The median serum progranulin

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level was 106.1 and 101.5 ng/mL in the PTC group and benign nodule group, respectively. The median progranulin level was significantly higher in patients with PTC greater than 1 cm than in those with micro-PTC. The proportion of patients with microscopic and gross extrathyroidal extension significantly increased with serum progranulin quartiles. These findings suggested that progranulin, a cysteine-rich secretory protein, may be a potential biomarker and therapeutic target of PTC. Progranulin is known to be as a growth factor implicated in tumorigenesis and a poor prognostic marker in breast cancer, non-small cell lung cancer, astrocytoma, glioblastoma, cervical cancer, and biliary tract cancers [8]. However, the mechanism of action through which progranulin contributes to carcinogenesis is unclear because the signaling receptor is still elusive. Recently, several candidate receptors such as sortilin, tumor necrosis factor receptor, and ephrin type-A receptor have emerged as potential links involved in the action of progranulin [9,10]. The potential association of progranulin upregulation with poorer pathological parameters of PTC might facilitate further research into the possible value of progranulin as a biomarker and therapeutic target.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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