EnM
ENDOCRINOLOGY AND METABOLISM

Letter

Endocrinol Metab 2015;30:231-232
http://dx.doi.org/10.3803/EnM.2015.30.2.231
pISSN 2093-596X · eISSN 2093-5978

# Expression of Glucagon-Like Peptide-1 Receptor in Papillary Thyroid Carcinoma and Its Clinicopathologic Significance
# (*Endocrinol Metab* 2014;29:536-44, Min Jung Jung et al.)

Daeyoon Park, Eun Kyung Lee

Center for Thyroid Cancer, National Cancer Center, Goyang, Korea

Glucagon-like peptide (GLP-1)-based therapy is a method of lowering blood glucose levels [1]. This glycemic control strategy, which increases insulin secretion in a glucose-dependent manner by regulating GLP-1 receptor (GLP-1R) agonist and dipeptidyl peptidase-4 inhibitor levels artificially, induces less hypoglycemia and reduces weight gain (rather than stimulating weight loss) compared with other treatments [2]. Despite such benefits, the mechanism of action of GPL-1 is not understood completely. Interestingly, previous studies have revealed that GLP-1 plays important roles in cellular processes such as proliferation and apoptosis; for example, GLP-1 stimulates the proliferation of pancreatic β-cells [3].

Recently, Jung and Kwon [4] reported that GLP-1R was expressed occasionally in papillary thyroid cancer (PTC) tissues. Furthermore, GLP-1R expression in PTC was associated with less multifocality in PTC tissues. These compelling results highlighted the need to investigate the long-term effects of exogenous GLP-1 on thyroid follicular cells. However, Jung and Kwon [4] did not find a relationship between clinical prognostic markers and GLP-1R expression.

In studies that evaluate the expression of proteins using immunohistochemical staining, a grading system is crucial for definitive studies because pathologist-dependent diagnosis is somewhat subjective. Therefore, the authors described in detail how they graded the intensity of GLP-1R expression in their study: the staining intensity was categorized into three groups of "absent," "weak," and "strong," However, the staining distribution should also be considered.

To compensate for this equivocality, "quickscore," a modified H-score, can be used to quantify protein expression, and it correlated well with immunoassay data in a study by Detre et al. [5]. Briefly summarized, the quickscore categories were based on both the intensity and proportion of brown stained cells: the proportion of positively stained cells was assigned scores from 1 to 6 (1, 0% to 4%; 2, 5% to 19%; 3, 20% to 39%; 4, 40% to 59%; 5, 60% to 79%; and 6, 80% to 100%), and the staining intensity was also rated to produce a multiplicative quickscore. The quickscore categories use two important factors to ensure objective results, compared with simple pathological diagnosis. Therefore, the adoption of this scoring system will produce data that are more categorized to help identify other related factors.

GLP-1R expression in PTC was an unexpected finding, and no studies have reported the clinical significance of GLP-1R expression in PTC or the pathogenic mechanism until now. Fortunately, 18 of 56 cases in this study were sufficient to ascertain

**Received:** 11 February 2015, **Revised:** 16 February 2015,
**Accepted:** 23 February 2015
**Corresponding author:** Eun Kyung Lee
Center for Thyroid Cancer, National Cancer Center, 323 Ilsan-ro, Ilsandong-gu, Goyang 410-769, Korea
**Tel:** +82-31-920-1743, **Fax:** +82-31-920-0846, **E-mail:** waterfol@ncc.re.kr

the expression of GLP-1R in PTC, and the results suggested that GLP-1R was expressed in thyroid follicular cells during inflammation, cellular hyperplasia, or tumorigenesis. Furthermore, the data revealed that GLP-1R expression in PTC was negatively correlated with tumor multifocality. However, more studies are required to demonstrate the actual GLP-1R expression patterns and the association between long-term GLP-1R activation and PTC, as well as other conditions, including the follicular variant of PTC and follicular thyroid cancer.

## CONFLICTS OF INTEREST

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

## REFERENCES

1. American Diabetes Association. Standards of medical care in diabetes: 2014. Diabetes Care 2014;37 Suppl 1:S14-80.
2. Drucker DJ, Nauck MA. The incretin system: glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes. Lancet 2006;368:1696-705.
3. Perfetti R, Zhou J, Doyle ME, Egan JM. Glucagon-like peptide-1 induces cell proliferation and pancreatic-duodenum homeobox-1 expression and increases endocrine cell mass in the pancreas of old, glucose-intolerant rats. Endocrinology 2000;141:4600-5.
4. Jung MJ, Kwon SK. Expression of glucagon-like Peptide-1 receptor in papillary thyroid carcinoma and its clinicopathologic significance. Endocrinol Metab (Seoul) 2014;29:536-44.
5. Detre S, Saclani Jotti G, Dowsett M. A "quickscore" method for immunohistochemical semiquantitation: validation for oestrogen receptor in breast carcinomas. J Clin Pathol 1995;48:876-8.