Towards precision medicine in thyroid cancer

With an estimated 567,233 new cases in 2018, thyroid cancer ranks as the ninth most common form of cancer, and accounts for 3.1% of all new cancer cases worldwide (1). The global incidence rate of thyroid cancer is three times higher in women than in men. Thyroid nodules are commonly observed, and the incidence of differentiated thyroid cancer (DTC) rises rapidly in recent decades after the implementation of new diagnostic techniques, such as ultrasonography. To reduce the impacts of overdiagnosis of thyroid cancer, the 2015 American Thyroid Association guidelines updated the risk stratification systems for thyroid nodules and cancer, advocated active surveillance for papillary thyroid microcarcinoma, and recommended performing less extensive surgeries and less radioactive iodine treatment for the management of DTC, especially for the low-risk cancers (2).

Over the past 20 years, significant progress in understanding the genetic and biologic characteristics of the disease have led to the development of molecular targeted therapeutics, and we are entering an era of precision medicine for thyroid cancer management. We are delighted to be the editors for this focused issue of the *Annals of Translational Medicine*, titled "Towards Precision Medicine in Thyroid Cancer". The current special issue provides the latest information on the conceptual, translational, and clinical advances in the field of thyroid cancer research with a focus on precision medicine.

The discovery of the promoter mutations in the telomerase reverse transcriptase (*TERT*) gene is a milestone in the thyroid cancer field. Increasing evidence has demonstrated that the *TERT* promoter mutations are associated with aggressive clinical behaviors and the radioiodine-refractory character of thyroid cancer, while the diagnostic and prognostic values of *TERT* mutations have also been well established (3). In this issue, Yuan *et al.* (4) will provide an astute review of the exciting findings concerning *TERT* promoter mutations in recent thyroid cancer research and further highlight the molecular mechanisms of TERT activation driven by *TERT* mutations and the implication of these mutations in the precision management of thyroid cancer.

With the rapid development of techniques for analyzing circulating cell-free DNA (cfDNA), the clinical significance of cfDNA has been widely evaluated, and cfDNA-based liquid-biopsy diagnostics are now showing great potential in clinical application. For instance, Cao *et al.* (5) screened 50 proto-oncogenes in the search for genetic alterations in cfDNA in malignant thyroid nodules and reported a large difference in the distribution of mutation genes between benign and malignant nodules. Notably, the authors identified that mutations in *PIK3CA* and *EZH2* occur more frequently in papillary thyroid cancer patients than in benign patients.

The current special issue includes three fundamental studies that focus on understanding the molecular pathogenesis of the thyroid cancer. First, the study by Zhao *et al.* (6) shows that β-elemene inhibits the respiratory and glycolytic ability of human DTC cells, thus functioning as a tumor suppressor in DTC. Second, Xu *et al.*'s paper (7) details findings demonstrating that miR-3121-3p promotes the proliferation and metastasis of thyroid cancer cells by inhibiting the expression of Rap1GAP, a tumor suppressor in multiple cancers, through direct binding to the 3' untranslated region of Rap1GAP. Third, Huang *et al.*'s work (8) reports on profiling the long non-coding RNA (lncRNA) expression of anaplastic thyroid cancer (ATC) through whole transcriptome sequencing in ATC and normal thyroid samples, by which mitotically associated log non-coding RNA (MANCR) were identified as a tumor promoter in ATC. These studies will expand our knowledge of thyroid carcinogenesis and provide novel therapeutic targets for thyroid cancer.

A group of studies that mainly focus on the clinical perspective are also included in this issue. Using a national retrospective cohort study, Kim *et al.*'s (9) research explores the effect of radioactive iodine treatment on the incidence of cardiovascular diseases. Next, Liu *et al.*'s prospective observational study of 840 thyroid cancer cases using 3 years of follow-up time (10), clarifies the kinetics of intact parathyroid hormone after central compartment lymph node dissection. Finally, as evaluating the thyroid stimulating hormone (TSH) trend after lobectomy is an essential step for adjusting the dose of thyroid hormone therapy, Wang *et al.* (11) report on the changes in TSH concentration before and after thyroid lobectomy in low risk DTC patients and provide evidence that treatment with 50 μg of levothyroxine (LT4) could be adequate for initial suppression therapy in most patients; they further indicate that a personalized adjustment of the initial dose of LT4 may be needed based on preoperative TSH concentration and the presence of Hashimoto thyroiditis.

We would like to express our appreciation for the contributions of all the authors towards offering our readers a broad-spectrum review of the thyroid cancer field. We believe that the articles presented in this special issue provide insightful perspectives and valuable original data that will accelerate the progress of "bench to bedside" knowledge translation.

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References

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
2. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid 2016;26:1-133.
3. Liu R, Xing M. TERT promoter mutations in thyroid cancer. Endocr Relat Cancer 2016;23:R143-55.
4. Yuan X, Liu T, Xu D. Telomerase reverse transcriptase promoter mutations in thyroid carcinomas: implications in precision oncology- a narrative review. Ann Transl Med 2020;8:1244.
5. Cao S, Yu S, Yin Y, et al. Genetic alterations in cfDNA of benign and malignant thyroid nodules based on amplicon-based next-generation sequencing. Ann Transl Med 2020;8:1225.
6. Zhao L, Wei J, Wang S, et al. Beta-elemene inhibits differentiated thyroid carcinoma metastasis by reducing cellular proliferation, metabolism and invasion ability. Ann Transl Med 2020;8:1232.
7. Xu M, Zhou J, Zhang Q, et al. MiR-3121-3p promotes tumor invasion and metastasis by suppressing Rap1GAP in papillary thyroid cancer in vitro. Ann Transl Med 2020;8:1229.
8. Huang NS, Lei BW, Tan LC, et al. Mitotically associated long non-coding RNA is a tumor promoter in anaplastic thyroid cancer. Ann Transl Med 2020;8:1226.
9. Kim KJ, Song JE, Kim JY, et al. Effects of radioactive iodine treatment on cardiovascular disease in thyroid cancer patients: a nationwide cohort study. Ann Transl Med 2020;8:1235.
10. Liu X, Bian X, Li C, et al. Comparison of iPTH and calcium levels between total thyroidectomy and lobectomy: a prospective study of 840 thyroid cancers with three years of follow-up. Ann Transl Med 2020;8:1243.
11. Wang Z, Angell TE, Sun W, et al. Analysis of the strategy of LT4 prescribing and TSH monitoring for thyroid carcinoma after lobectomy. Ann Transl Med 2020;8:1238.

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Haipeng Xiao

Rengyun Liu

Shuang Yu

Haipeng Xiao[1], MD, PhD
(*Email: xiaohp@mail.sysu.edu.cn*)
Rengyun Liu[2], PhD
(*Email: liury9@mail.sysu.edu.cn*)
Shuang Yu[1], MD, PhD
(Email: yushuang@mail.sysu.edu.cn)
[1]*Department of Endocrinology, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China;*
[2]*Institute of Precision Medicine, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.*
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