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THYROID NODULES

The genetic characteristics of benign thyroid nodules

BACKGROUND

Thyroid nodules are common, occurring in 1/3rd to ½ of individuals that have imaging studies of the neck. The vast majority of thyroid nodules are not cancerous (benign). Thyroid nodules are typically evaluated by neck ultrasound, and depending on the imaging features, thyroid biopsy. Testing of biopsy specimens for molecular markers is sometimes considered, especially if the biopsy is indeterminate (unable to make a diagnosis based on cytology alone). The genetic mutations in the most common type of thyroid cancer, papillary thyroid cancer, have been well-characterized and, if present in a biopsy specimen, usually leads thyroid surgery. However, the genetic characteristics of benign thyroid nodules are not well understood. The aim of this study was to define the genetic characteristics of benign thyroid nodules, in contrast to papillary thyroid cancer.

THE FULL ARTICLE TITLE

Ye L et al The genetic landscape of benign thyroid nodules revealed by whole exome and transcriptome sequencing. Nature Commun 2017;8:15533.

SUMMARY OF THE STUDY

The authors analyzed DNA and RNA from thyroid tissue samples from thyroid surgery specimens from 21 individuals who had both papillary thyroid cancer and benign thyroid nodule(s) as well as 8 individuals who had benign thyroid nodule(s) without papillary thyroid cancer. Thyroid tissue samples were matched for each individual. The genetic mutations identified in this study were evaluated in 328 fresh-frozen benign thyroid nodule tissues from 259 patients.

Using a laboratory technique of whole-exome sequencing and/or transcriptome sequencing techniques, the authors detected the following mutations, according to diagnosis: papillary thyroid cancer - BRAF (22/32 papillary thyroid cancer specimens but no benign nodule specimens), benign nodules - mutations in SPOP (4/38 benign nodules but not papillary thyroid cancer), ZNF148 (6/38 benign nodules but not papillary thyroid cancer) and EZH1 (3/38 benign nodules but not papillary thyroid cancer). In a separate study group including 328 benign thyroid nodules from 259 patients, the authors identified mutually exclusive SPOPP94R, EZH1Q571R and ZNF148 mutations in 24.3% of specimens.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that there were distinct genetic expression patterns in benign thyroid nodules compared to papillary thyroid cancer and they suggested that papillary thyroid cancer evolved independently from matched benign nodules within the same patients. Although larger confirmatory studies are needed, these data are important to inform our understanding of the molecular profile of benign thyroid nodules.

— Anna M. Sawka, MD, PhD, FRCPC

ATA THYROID BROCHURE LINKS

Thyroid Nodules: https://www.thyroid.org/thyroid-nodules/

Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/

ABBREVIATIONS & DEFINITIONS

Thyroid nodule: an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5% are cancerous.

Thyroid Ultrasound: a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses soundwaves to create a picture of the structure of the thyroid gland and accurately identify and

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characterize nodules within the thyroid. Ultrasound is also frequently used to guide the needle into a nodule during a thyroid nodule biopsy.

Thyroid biopsy: a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

Indeterminate thyroid biopsy: this happens a few atypical cells are seen but not enough to be abnormal (atypia of unknown significance (AUS) or follicular lesion of unknown significance (FLUS)) or when the diagnosis is a follicular or hurthle cell lesion. Follicular and hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurthle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

Mutation: A permanent change in one of the genes.

Genes: a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

Papillary thyroid cancer: the most common type of thyroid cancer.

Molecular markers: genes and microRNAs that are expressed in benign or cancerous cells. Molecular markers can be used in thyroid biopsy specimens to either to diagnose cancer or to determine that the nodule is benign. The two most common molecular marker tests are the AfirmaTM Gene Expression Classifier and ThyroseqTM

Cancer-associated genes: these are genes that are normally expressed in cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these genes cause the cancer or are just associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC, TERT and RAS.