

Novel method for in vitro diagnosis of a thyroid tumour and related kit.

KEYWORDS

- ❑ THYROID NODULES
- ❑ INDETERMINATE CYTOLOGY
- ❑ THYROID CANCER
- ❑ BIOMARKERS
- ❑ NEXT-GENERATION SEQUENCING
- ❑ MUTATIONS
- ❑ DIGITALPCR
- ❑ MICRORNA EXPRESSION

AREA

- ❑ BIOMEDICAL

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Priority Number

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Patent Type

Patent for invention.

Ownership

Sapienza Università di Roma 100%.

Inventors

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Industrial & Commercial Reference

Biomedical companies that offer kits based on molecular biology techniques.

Time to Market

Carried out analytical validation on different cytological samples and clinical validation. Ready for placement on the reference market - TRL4.

Availability

Licensing, Research, Develop-ment, Experimentation and Collaboration.

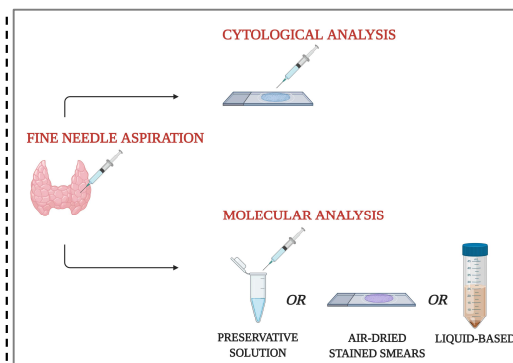


Fig. 1 Molecular analysis of thyroid nodule aspirates.

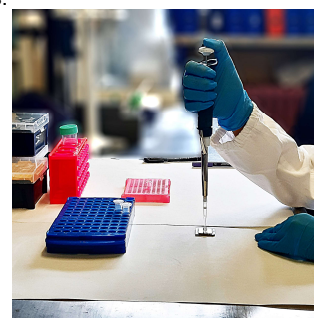


Fig. 2 Chip loading for NGS analysis.



Fig. 3 NGS system set-up.

Abstract

Thyroid nodules are being identified with increasing frequency in clinical practice, but very few of the lesions are malignant (7–15%). Fine-needle aspiration cytology is the most reliable method for identifying these lesions preoperatively, but up to 30% of thyroid FNA samples yield indeterminate results. A high proportion of these patients are subjected to diagnostic surgery, but only a minority of resected indeterminate thyroid nodules are histologically diagnosed

The present invention relates to a new method and relative kit for the diagnosis of a thyroid tumor able to overcome the intrinsic diagnostic limits of cytology and personalize treatment of thyroid cancer patients.

Pubblicazioni

❖ Sponziello M, Brunelli C, Verrienti A, Grani G, Pecce V, Abballe L, Ramundo V, Damante G, Russo D, Lombardi CP, Durante C, Rossi ED, Straccia P, Fadda G, Filetti S. Performance of a dual-component molecular assay in cytologically indeterminate thyroid nodules. *Endocrine*. 2020 May;68(2):458-465. doi: 10.1007/s12020-020-02271-y. PMID: 32232767.



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Technical Description

The novel test is based on a combined molecular approach that involves next-generation sequencing (NGS)-based detection of thyroid cancer drivers (point mutations and indels in 19 genes and 204 gene fusions involving 7 known thyroid cancer driver genes) and digital polymerase chain reaction (PCR) evaluation of the expression levels of an microRNA strongly associated with thyroid cancer.

Samples with single-assay positivity (mutation detection or miRNA expression above the calculated cut-off value) or combined-assay positivity (mutation detection and miRNA expression) in the molecular assay were considered positive for thyroid malignancy; those with negative findings in both assays were classified as negative for thyroid malignancy.

Technologies & Advantages

The described procedure allows to perform a molecular diagnosis of the cytological samples tested quickly and reliably. The comparison with other molecular platforms available on the market shows some advantages, including i) a relatively low number of molecular markers, which translates into lower overall testing costs; ii) our test can be also carried out on the same material used for the cytologic diagnosis, avoiding the patient to be subject to a second dedicated sampling; iii) moreover, it employs high-sensitivity methods for both mutation detection (NGS) and assessment of miRNA expression levels (dPCR), ensuring reliable results as well as the detection of low-frequency, multiple, or unknown variants, and precise quantification of miRNA levels. And last but not least, iv) it offers high performance, with sensitivity and NPV higher than those of the currently available tests.

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Applications

The main application is the preoperative molecular diagnosis in cytologically indeterminate thyroid nodules with the main aim of identifying those benign and decreasing the number of unnecessary diagnostic surgeries.

In addition, this molecular approach allows for identification of predictive factors, useful for choosing an optimal clinical management strategy. Indeed, the use of the molecular platform provides simultaneous testing for multiple alterations, allowing the identification of the most aggressive carcinomas thanks to the presence of multiple mutations in the preoperative material (eg *TERT* and *BRAF* or *TERT* and *RAS*). It also provides to determine eligibility for specific clinical trials, given the presence of actionable genes in the panel.

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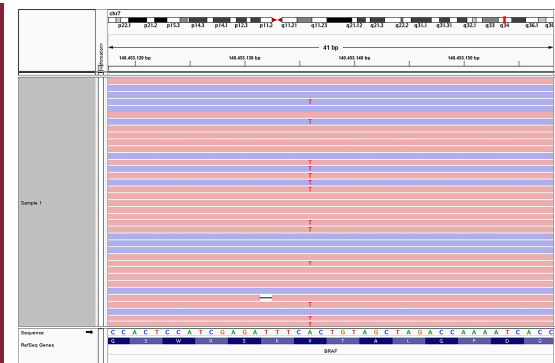


Fig. 4 NGS data analysis.

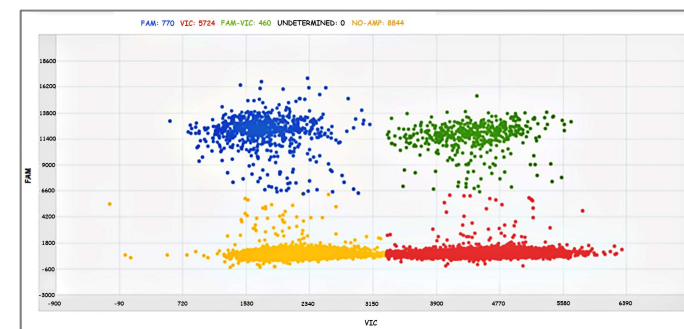


Fig.5 dPCR data analysis.



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