Journal of the American Society of Cytopathology (2017) xx, 1–9

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jascyto.org/

The role of miRNAs in the evaluation of follicular thyroid neoplasms: an overview of literature

Esther Diana Rossi, MD, PhD, MIAC*, Maurizio Martini, MD, PhD, Sara Capodimonti, BD, PhD, Tonia Cenci, BD, PhD, Luigi Maria Larocca, MD

Division of Anatomic Pathology and Histology, Department of Pathology, Università Cattolica del Sacro Cuore, "Agostino Gemelli" School of Medicine, Rome, Italy

Received 21 December 2016; received in revised form 7 February 2017; accepted 7 February 2017

KEYWORDS
Thyroid FNA;
Thyroid lesions;
Liquid-based cytology;
PTC;
Follicular neoplasms;
DNA analysis;
miRNAs

MicroRNA (miRNA) deregulation has been frequently associated with different human cancers. Not only have miRNAs been involved in almost every cellular function but they have also been linked with a significant number of cancers including thyroid carcinomas. Specifically, thyroid tumors encompass several different miRNA profiles based on the histotypes. Furthermore, thyroid lesions with their broad spectrum of neoplasms (from benign to malignant entities) offer the possibility of studying and recognizing specific subsets of different up-and downregulated miRNAs in each different entity.

To date, the majority of authors completed their evaluation mostly by including histologic samples of thyroid tumors. Nonetheless, in the last years, a few studies are focusing on the role of miRNA expression in thyroid fine-needle aspiration cytology (FNAC) regardless of the cytologic preparation, including liquid-based cytology. This growing interest is driven by the possible role of miRNAs in the malignant risk stratification, especially for the indeterminate categories of follicular neoplasms (FNs). In this review we overview the reliability of analyzing miRNAs on thyroid lesions, including those diagnosed as FNs, to identify whether their profiles are likely to distinguish benign from malignant lesions, providing a predictive molecular diagnosis on FNAC.

All the authors contributed equally.

*Corresponding author: Esther Diana Rossi, MD, PhD, MIAC; Division of Anatomic Pathology and Histology, Department of Pathology, Università Cattolica del Sacro Cuore, "Agostino Gemelli" School of Medicine, Largo Francesco Vito, 1, 00168 Rome, Italy. Tel.: +3906-3015-4433; Fax: +3906-3015-7008.

E-mail address: esther.rossi@rm.unicatt.it (E.D. Rossi).

2213-2945/$36
http://dx.doi.org/10.1016/j.jasc.2017.02.001

Contents

Introduction

Fine-needle aspiration cytology (FNAC) is the first approach in the evaluation of thyroid nodules. Although there is growing evidence of its high diagnostic value, some issues are encountered, particularly in the category of follicular neoplasms (FNs), which represent 25% of all thyroid lesions including different neoplastic entities.[1-6] Although the morphologic diagnosis of either the 70% benign and the 5% to 10% "malignant" thyroid FNACs has been achieved in the majority of cases, the remaining 20% to 25% of them represents the so-called gray zone of FNs, implying vexing issue in both their nature and the consequent management (clinical and/or surgical).[1-15] Thus, several authors have questioned whether the application of ancillary techniques (including immunocytochemistry and molecular tests) would increase the accuracy of cytology in detecting malignant cases among the indeterminate categories, mostly due to the high negative predictive value.[16-35]

Despite the undoubted advantages of the detection of somatic mutations and rearrangements provided by all the different DNA molecular platforms, however, these authors did not supply 100% of the achievements, especially for the diagnosis of FNs.[16-35]

The shortcoming and limits of the DNA approaches in enabling all the indeterminate lesions (mostly the somatic mutation-negative lesions) to be separated into benign and malignant entities has led to the enthusiasm for the cytologic evaluation of microRNAs (miRNAs).[36-41] This analysis placed pressure on the cytology community to recognize the importance of this molecular method, in particular with regard to its clinical implications.[42] In a recent editorial, Beca and Schmitt noted that cytology and ancillary techniques, including evaluation of miRNAs, have also been increasingly used in bedside-to-bench approaches.[42]

Furthermore, miRNA deregulation has been frequently associated with different human cancers.[36-48] Not only have miRNAs been involved in almost every cellular function but also linked with a significant number of cancers through miRNA deregulation. To date, more than 1600 different miRNAs have been identified, mainly as negative (post-transcriptional) regulators of coding gene expression whose deregulation is frequently associated with proliferation, differentiation, and cell death leading to different human cancers.[36-61] On the other hand, a single gene could be a target of many different miRNAs. The application of miRNAs for diagnostically differentiating benign from malignant entities has been based on the growing evidence of miRNAs in cancers. Despite the well-known literature about the diagnostic involvement of miRNAs in several body lesions, however, in the current review we focus our attention on the role of miRNAs in thyroid lesions.[36-70] Since 2005, some authors have been demonstrating that analyzing miRNAs may be a valid diagnostic tool among thyroid lesions.[36-61] The application of miRNA analysis is also encouraged by the documented evidence that miRNA panels have superior advantages over mRNA panels for daily use in cytologic samples.[42] Therefore, despite the fact that identification of some of these miRNAs, alone or as panels, are likely to be carried out in the clinical workflow and management of neoplastic patients, limited data have explored the use of miRNAs on thyroid FNACs as well as their role in the malignant risk stratification, mostly performed as either panels or with other molecular platforms.[36-61]

In fact, according to the literature, thyroid lesions are characterized by different miRNA expression profiles depending on the histologic entities.[51-54] For example, some of them, such as miR-221 and miR-222, have been found in well-differentiated thyroid cancers including both the classical variant of papillary thyroid carcinoma (PTC) and the follicular variant of PTC (FVPC), whereas other miRNAs, such as miR-146 and miR-31 have been reported in PTCs only.[51-54] Nonetheless, their application has been also extended, with specific different profiles, to medullary thyroid cancers (MTCs), poorly differentiated (PDC) and anaplastic (ATC) thyroid cancers.[71,72]

Ultimately, we aimed to review miRNA recognition throughout the literature evaluation on conventional and liquid-based preparations not only in the field of malignant