Results
The FNA samples were obtained from the following histologic lesions: 50 adenomatoid nodules, 10 follicular adenomas, 5 Hürthle-cell adenomas, 23 papillary thyroid carcinomas, 5 follicular variant of papillary thyroid carcinomas, 1 lymphocytic thyroiditis nodule, and 1 Graves’ disease.

In the FNA samples, all 10 genes showed significantly higher odds of being associated with malignancy as compared with benign lesions; the gene, MRC2 (mannose receptor, C type 2) showed the highest discriminating ability. The combination of 3 genes—MRC2+HMGA2 (high mobility group AT-hook 2)+SFN (stratifin)—had a sensitivity of 71%, specificity of 84%, positive predictive value (PPV) of 65%, and negative predictive value (NPV) of 88%. Of the 27 samples that had suspicious or indeterminate FNA results preoperatively, the 3-gene model was 96% specific and 60% sensitive in the prediction of malignancy (PPV, 75%; NPV, 91%). The results of the immunohistochemistry were similar to the PCR data for these 3 genes.

Conclusions
The results suggest that a 3-gene model for the molecular diagnosis of indeterminate thyroid nodules is feasible and promising and that implementation of this as an adjunct to thyroid cytology may significantly impact the clinical management of patients with suspicious or indeterminate thyroid FNA nodules.

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Measuring a Three-Gene Panel May Distinguish Malignant from Benign FNA Samples

Prasad NB, et al.

ANALYSIS AND COMMENTARY

Although a great deal of work went into this study by a very prolific group, the results must still be regarded as preliminary. There were no follicular carcinomas in the FNA group, although there were some follicular and Hürthle-cell carcinomas in the immunohistochemistry group. Since there were no follicular cancers in the FNA samples, the three-gene classifier (MRC2+HMGA2+SFN) is not established for distinguishing follicular adenoma from carcinoma. As the authors state, the method must now be validated by applying it to a test set of samples. A different three-gene biomarker panel was thought to be useful for diagnosis of thyroid cancer, but its diagnostic accuracy was low in a subsequent study (1).

The efficacy of this study must be compared with that of the miRNA studies described in the previous article in this issue (2) and with the use of the more established thyroid cancer biomarkers, BRAF, RET/PTC, RAS, and PAX8/PPARg (3). These biomarkers represent mutations that are understood well with regard to activating pathways of growth. In contrast, the genes up-regulated in the current study do not have well-established roles in oncogenesis, but certainly have potential for contributing to neoplastic growth.

MRC2 is a recycling endocytic receptor that functions in cell motility and remodeling of the extracellular matrix by promoting cell migration and uptake of collagens for intracellular degradation. HMG proteins function as architectural factors and are essential components of the enhancesome. The protein contains structural DNA-binding domains and may act as a transcriptional regulating factor. SFN is an adapter protein that binds to a large number of partners implicated in the regulation of a large spectrum of both general and specialized signaling pathways. I look forward to reading the study that validates these genes as accurate biomarkers for thyroid cancer when applied to FNA in the clinical setting.

— Jerome M. Hershman, MD

References

