MicroRNA Profiling Discriminates Nodular Hyperplasia versus Follicular Adenoma

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INTRODUCTION:

- A variety of benign entities produce thyroid nodular disease, the two most common being nodular hyperplasia (NH) and follicular adenoma (FA).
- NH is non-neoplastic, not requiring surgical excision unless symptomatic.
- FA, considered neoplastic, can justify local resection when viewed as a precursor for progression to cancer.
- Current molecular testing based solely on mutational analysis or RNA classifier does not differentiate between these or other benign states limiting surgery decision-making.
- We show that microRNA (miRNA) profiling can discriminate NH from FA with high accuracy for more informed molecular assessment of cytology indeterminate nodular disease.

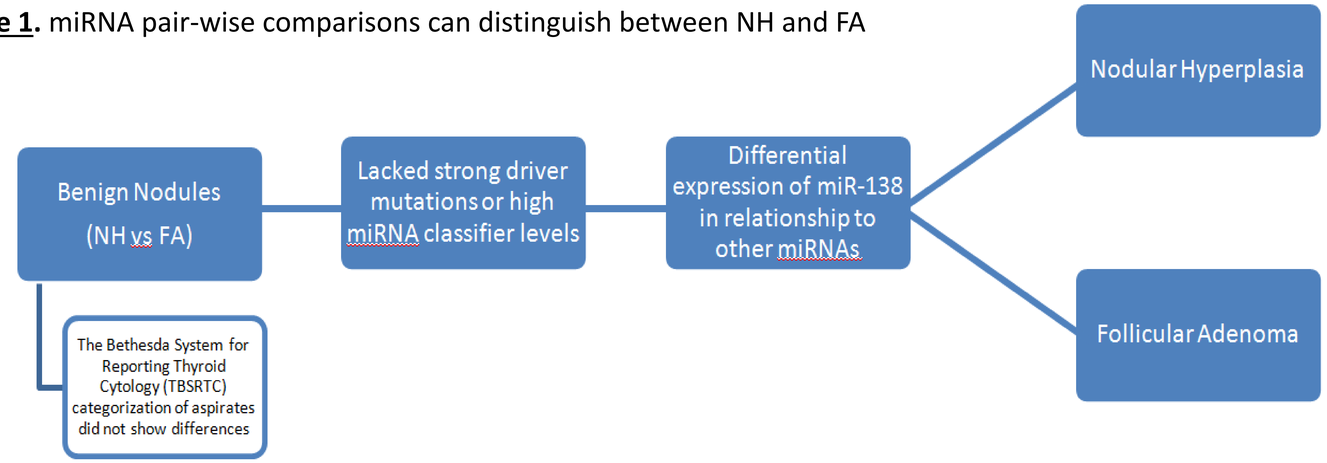
METHODS:

- Cytologically indeterminate thyroid nodules underwent molecular testing (oncogene point mutation/fusion detection [ThyGenX] and miRNA profiling using a 10 marker panel algorithmic classifier determination as well as pair-wise analysis of individual miRNA expression differences [ThyraMIR]), performed either directly on the needle aspirates or via microdissection of cytology slides.
- Histopathology review of combined testing outcome yielded 24 cases of NH and 20 cases of FA.

Table 1. microRNA classifier panel

10 MicroRNA (MiR) Classifier Panel	
Down-regulated	miR-204-5p, miR-139-5p, miR-29b-1-5p, miR-155-5p, miR-138-1-3p
Up-regulated	miR-375, miR-551-b-3p, miR-146b-5p, miR-31-5p, miR-222-3p

Figure 1. miRNA pair-wise comparisons can distinguish between NH and FA



- While the miRNA classifier can discriminate between benign vs malignant states with high accuracy, it cannot differentiate between NH and FA
- Multiple pair-wise differences among specific miRNA panel markers were capable of distinguishing between NH and FA with high accuracy ($p<.0001$)
- Differential expression of miR-138 in relationship to other miRNAs was most discriminating

CONCLUSIONS:

- **A major objective of molecular testing of thyroid nodules is accurate preoperative diagnosis of thyroid nodule states, both benign and malignant.**
- **Benign entities are diverse and cannot be discriminated based solely by lack of detectable mutational change.**
- **We show that the two most common benign lesions are associated with objective miRNA profiling differences enabling the separation of NH and FA preoperatively optimizing individual patient care.**