



miRNA Expression Pattern in Predicting BRCA Mutation Status in Invasive Breast Carcinoma



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Introduction:

- BRCA-mutated breast carcinomas are seen in younger patients and have a more aggressive clinical course.
- Dysregulation of miRNAs (short, non-coding RNAs involved in post-transcriptional gene regulation) and their cognate targets is increasingly implicated in many cancers.
- Three miRNAs have been associated with breast tumorigenesis: miR-17, miR-21, and let-7a.
- It is unknown whether these miRNAs correlate with mutation status in breast carcinoma.

Aim:

- To evaluate the expression of miR-17, miR-21, and let-7a in BRCA-mutated invasive breast carcinoma.

Material and Methods:

- 13 cases of invasive ductal carcinoma were selected (6 BRCA-mutated and 7 wild type).
- Cases were subjected to in situ hybridization (ISH) using FAM-labeled miRNA probes (BioGenex) for miR-17, miR-21, and let-7a followed by super sensitive ISH Detection Kit (BioGenex, DF400-YAX).
- miRNA staining was evaluated in tumor nuclei and benign epithelium as weak, moderate, or strong; percent positivity was estimated as focal (<50%) or diffuse (>50%).

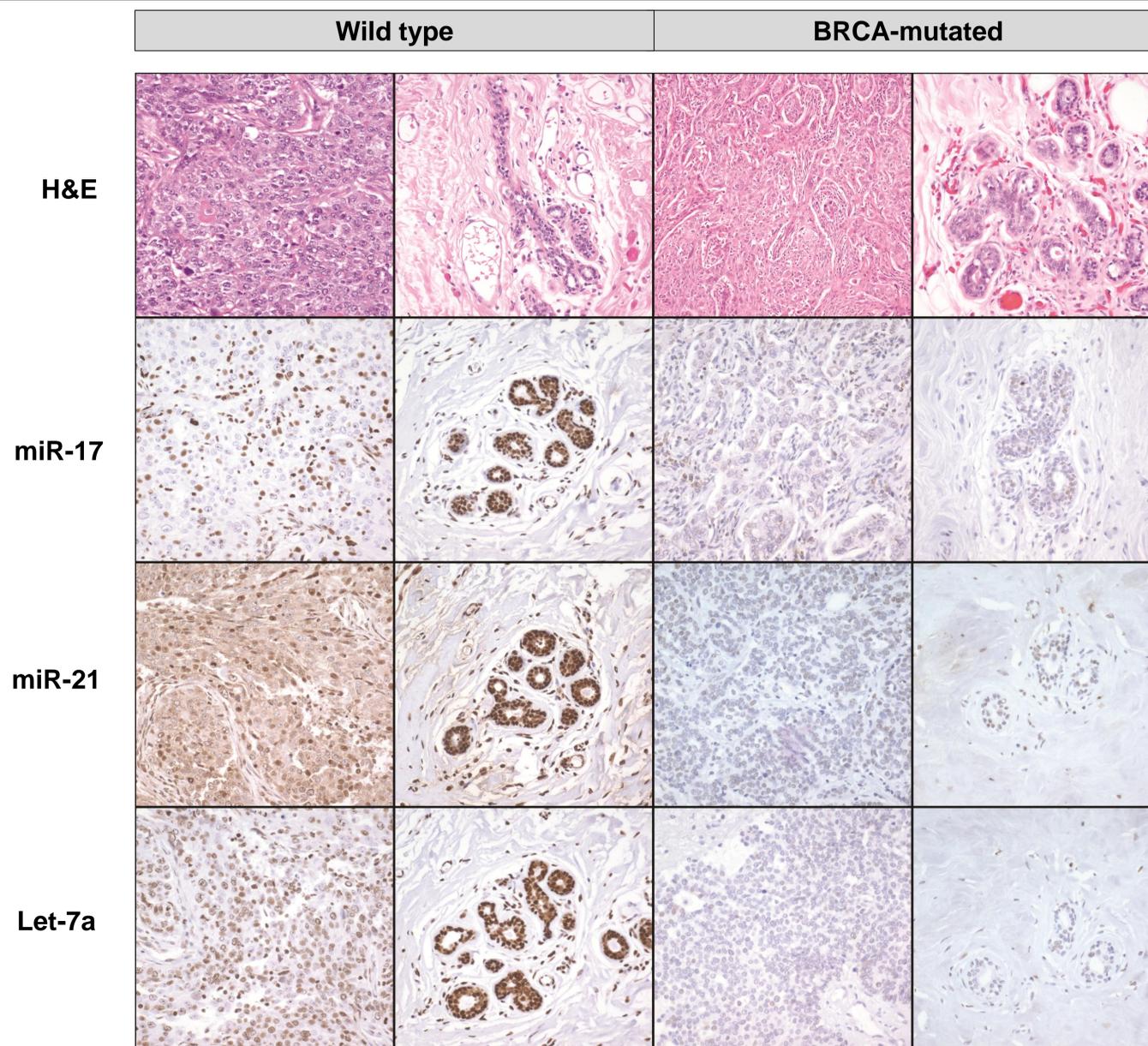


Table 1.

Tumor Category	Total Cases	miR-17 +	miR-21 +	let-7a +	Molecular subtype
Wild type	7	7 (100%)	7 (100%)	7 (100%)	Basal: 2 Luminal: 5
BRCA mutated	6	1 (17%)	1 (17%)	3 (50%)	Basal: 1 Luminal: 5

Results:

- All results are summarized in Table 1.
- All cases of wild type breast carcinoma show strong and diffuse nuclear positivity for miR-17, miR-21, and let-7a miRNAs in both benign epithelium and tumor nuclei.
- BRCA-mutated carcinomas show minimal nuclear positivity in benign epithelium and tumor nuclei, with 17% of cases staining for miR-17 and miR-21 and 50% staining positive for let-7a.

Conclusions:

- Expression of miR-17, miR-21, and let-7a is down-regulated in BRCA-mutated breast carcinoma compared to wild-type breast carcinoma.
- Expression of specific miRNAs in breast carcinoma may serve as biomarkers that may be useful to predict BRCA mutation status.
- The ability to predict mutation status may help more accurately determine patients suitable for BRCA genetic testing, which is both costly and time consuming.
- The relationship of these miRNA's to BRCA associated pathways in breast carcinoma requires further investigation.