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Mouse Monoclonal Anti-GATA3: A Useful Nuclear Marker for Breast Carcinoma

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Background:

As an immunohistochemical marker for breast cancer, GATA3 is well known for its particular role in breast luminal cell differentiation.[1] Often associated with hormone-receptor-positive breast carcinomas, GATA3 expression has shown promise in determining favorable prognoses and predicting tumor recurrence.[2] This study examines GATA3 expression across established molecular subtypes of breast carcinoma, including Luminal A, Luminal B, Her2 Type, and Triple Negative Breast Cancer (TNBC).[3]

Design:

Cancerous breast tissue samples from 191 individual cases including 145 invasive ductal carcinoma (IDC), 29 ductal carcinoma *in situ* (DCIS), 9 invasive lobular carcinoma (ILC), and 8 metastatic breast carcinoma (Met-BrCA) subtypes were stained with mouse monoclonal anti-GATA3 by routine immunohistochemistry. Each sample was microscopically evaluated by a pathologist and given a score between 0-4 for anti-GATA3 stain intensity: 0 = negative, 0.5-2.5 = low and 3-4 = high. According to their known estrogen receptor (ER), progesterone receptor (PR), and Her2 status, the cases were then grouped into four distinct cohorts.

Table 1: Morphological Subtype

Subtype	GATA3
IDC	135/145 (90%)
DCIS	29/29 (100%)
ILC	9/9 (100%)
Met-BRCA	7/8 (88%)

Table 2: Molecular Subtype

Subtype	GATA3
Luminal A	75/76 (99%)
Luminal B	44/44 (100%)
Her2 Type	17/19 (89%)
TNBC	40/52 (77%)

cohort 1

76 ER and/or PR + and Her2 + samples, categorized as Luminal A. The 76 Luminal A cases included 54 IDC (54/76, 71%), 15 DCIS (15/76, 20%), 5 ILC (5/76, 6%), and 2 Met-BrCA (2/76, 3%).

cohort 2

44 ER and/or PR + and Her2 – samples, categorized as Luminal B. The 44 Luminal B cases included 31 IDC (31/44, 70%), 12 DCIS (12/44, 27%), and 1 ILC (1/44, 3%).

cohort 3

19 ER and/or PR – and Her2 + samples, categorized as Her2 Type. The 19 Her2 Type cases included 16 IDC (16/19, 84%), 2 DCIS (2/19, 11%), and 1 ILC (1/19, 5%).

cohort 4

52 ER, PR, and Her2 – samples, categorized as TNBC. The 52 TNBC cases included 44 IDC (44/52, 85%), 6 Met-BrCA (6/52, 11%), and 2 ILC (2/52, 4%).

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Results:

As shown in Table 1, GATA3 expression was consistently high among each of the four molecular subtypes. Of the 76 cases in Cohort 1, 67 (67/76, 88%) showed strong diffuse nuclear staining of anti-GATA3 (Figure 1A), while only 8 cases (8/76, 11%) had low expression and 1 case (1/76, 1%) was negative. Similarly, all of the cases in Cohort 2 expressed GATA3 (44/44, 100%), a majority displayed strong immunoreactivity (41/44, 93%), with only 3 cases of low GATA3 expression (3/44, 7%). None of the Luminal B cases were negative for GATA3. Although both Luminal A and Luminal B subtypes share in ER and/or PR positivity (Figure 1B), they differ in Her2 expression with Luminal A classified as Her2– (Figure 1C).

13 of the 19 cases in Cohort 3 revealed strong diffuse nuclear anti-GATA3 staining (13/19, 68%) (Figure 2A), 4 cases (4/19, 21%) showed low GATA3 intensity, and 2 cases (2/19, 11%) were negative for GATA3. Her2 was strongly positive in this cohort, while ER and PR were completely negative (Figures 2B and 2C). Among these three cohorts, those that were ER and/or PR+ had the highest rate of GATA3 expression. Variance in Her2 expression did not correlate with GATA3 expression.

Cohort 4 had the lowest GATA3 sensitivity with more negative cases than any other cohort (12/52, 23%). 24 cases were low expressing (24/52, 46%) compared to just 16 cases that showed strong immunoreactivity (16/52, 31%) (Figure 3A). ER, PR, and Her2 were negative for all cases in this cohort (Figures 3B and 3C).

As shown in Table 2, anti-GATA3 stained 94% (179/191) of morphological subtypes contained within Cohorts 1-4, demonstrating consistent nuclear sensitivity among all four morphological subtypes.

References:

1. Cimino-Mathews A, et al. GATA3 expression in breast carcinoma: utility in triple-negative, sarcomatoid, and metastatic carcinomas. Human Pathology. 2012; 44:1341-1349.
2. Mehra R, et al. Identification of GATA3 as a Breast Cancer Prognostic Marker by Global Gene Expression Meta-analysis. American Association for Cancer Research. 2005; 65:11259-11264.
3. Haque R, et al. Impact of Breast Cancer Subtypes and Treatment on Survival: An Analysis Spanning Two Decades. Cancer Epidemiology Biomarkers & Prevention. 2012; 21:1848-55.

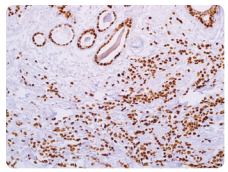

Figure 1A: Strong diffuse nuclear stain of anti-GATA3 on ILC (200x)

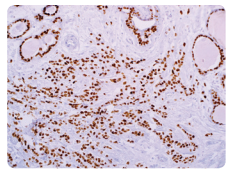

Figure 1B: ILC tumor cells are highly positive for ER expression (200x)

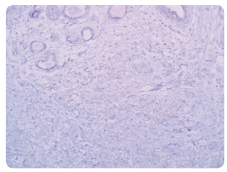

Figure 1C: Her2 antibody reveals no immunoreactivity of ILC tumor cells (200x)

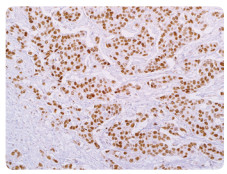

Figure 2A: Strong diffuse nuclear stain of anti-GATA3 on IDC (200x)

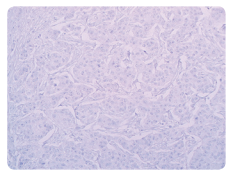

Figure 2B: IDC tumor cells do not express ER protein (200x)

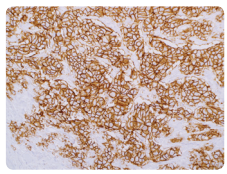

Figure 2C: IDC tumor cells demonstrate strong immunoreactivity of Her2 antibody (200x)

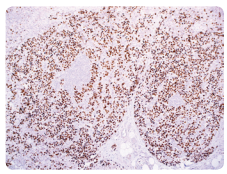

Figure 3A: Strong diffuse nuclear stain of anti-GATA3 on Met-BrCA (100x)

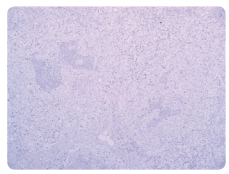

Figure 3B: Met-BrCA tumor cells show no expression of ER protein (100x)

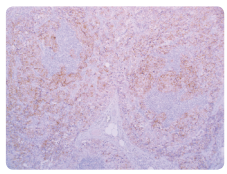

Figure 3C: Tumor cells of Met-BrCA are negative for Her2 expression (100x)

Conclusion:

The hormone-receptor-positive Luminal A and Luminal B subgroups displayed the highest percentages of GATA3 expression, followed by Her2 Type and TNBC. Compared to the variability of ER, PR, and Her2 expression, GATA3 offers consistent nuclear sensitivity in morphological and molecular subtypes of breast carcinoma. Although GATA3 is not a specific marker for breast carcinoma, due to its high sensitivity it has the potential to be useful beyond breast luminal cell differentiation.

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