Increasing evidence has shown that mammaglobin, GATA-binding protein 3 (GATA3), and epithelial growth factor receptor (EGFR) have unique clinical implications for breast cancer subtyping and classification, as well as for breast cancer targeted therapy. It is particularly important to clarify the correlation between their expression and different molecular breast carcinoma subtypes to better understand the molecular basis of the subtypes and to identify effective therapeutic targets for the disease. This study aimed to evaluate mammaglobin, GATA3, and EGFR expression in different breast cancer subtypes, as well as their clinical significance.

Subjects of the study included 228 patients with breast cancer at The First Affiliated Hospital of University of Science and Technology of China. They were divided into triple negative (TN), Luminal A, Luminal B, and HER-2 positive (HER-2.P) breast cancer groups based on molecular classification. Immunohistochemical methods were used to detect mammaglobin, GATA3, and EGFR expression in cases of different molecular subtypes before determining the correlation between protein expression and subtype. Mammaglobin and GATA3 expression levels were found to significantly vary with respect to histopathological grade, lymph node status, and molecular subtype; EGFR expression was significantly correlated with breast cancer histopathological grade and molecular subtype. For breast cancer, the expression levels of mammaglobin and GATA3, as well as mammaglobin and EGFR, were significantly correlated. In addition, there was a significantly negative correlation between the expression levels of GATA3 and EGFR in breast cancer tissue samples, especially in HER-2.P samples. These findings provide a theoretical basis for assessing breast cancer clinical prognosis based on the cancer subtype, and hence, have significant practical value.

**Key words:** breast cancer; mammaglobin; GATA-binding protein 3; epithelial growth factor receptor; molecular subtype.

**Correspondence:** Chuanying Li, MD, Department of Pathology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai 200025, China. Tel. +86.021.64370045. E-mail: lcy12224@rjh.com.cn

**Contributions:** XK, CL, conceptualization, data curation; XK, QW, methodology; XK, JL, writing-original draft preparation, review and editing; XK, ML, FD, investigation, formal analysis. All authors have read and approved the published version of the manuscript.

**Conflict of interest:** The authors declare no conflict of interest.

**Funding:** This work is supported by the Anhui Natural Science Foundation (1808085MH286) and the Fundamental Research Funds for the Central Universities (WK9110000091).

**Ethical Approval:** Ethical approval for the study was obtained from the Ethical Committee of The First Affiliated Hospital of University of Science and Technology of China (USTC), Hefei, China.

**Availability of data and materials:** The datasets used and/or analysed during the current study are available from the corresponding author.
Introduction

Breast cancer has become one of the most common types of malignant tumours among women worldwide. It has been gaining public attention owing to its association with high morbidity and mortality rates that have become a major public healthcare issue. With rapid advancements in biology and medicine, individualized treatments for different breast cancer molecular subtypes have become the focus in breast cancer research. Studies have shown that mammaglobin, GATA-binding protein 3 (GATA3), and epithelial growth factor receptor (EGFR) are differentially expressed in different tumour types. Mammaglobin is expressed in breast tumours, the endometrium, and sweat and salivary glands, and it might be involved in the regulation of steroid metabolism. Mammaglobin overexpression is associated with breast cancer occurrence and metastasis. The protein GATA3 has also been found to participate in oestriadiol regulation via a transcriptional circuitry that links it to oestrogen receptor α (ERα). Abnormal GATA3 non-expression may cause ERα to not accumulate and induce excessive accumulation of factors critical in epithelial-to-mesenchymal transition and metastasis; this promotes tumour cell metastasis and induces aggressive breast cancer phenotypes and poor prognosis. Several studies have shown that high GATA3 expression is a good prognostic factor for breast cancer. Takaku et al. experimentally demonstrated in vitro that molecular alterations in GATA3 led to the expression of highly aggressive tumour phenotypes. However, GATA3 has not yet been identified as an independent prognostic factor. Voduc et al. found a significant correlation between GATA3 expression and ER in a cohort study involving 3119 breast cancer patients. However, GATA3 has not yet been identified as an independent prognostic factor. The present study explored the sensitivities of mammaglobin, GATA3, and EGFR, and it evaluated the correlation between expression of those proteins and the clinical characteristics of 228 breast cancer patients with different subtypes of the disease, who were treated at The First Affiliated Hospital of University of Science and Technology of China (USTC) in 2019. Furthermore, we explored the application of the proteins as molecular markers for the clinicopathological diagnosis and classification of breast cancer and provided novel strategies for the treatment of the disease.

Materials and Methods

Tissue samples

In this study, 228 cases of breast cancer, treated in our hospital from December 2018 to December 2019, were selected for the research. According to international consensus, breast cancer can be classified into different molecular subtypes based on expression levels of human epidermal growth factor receptor 2 (HER2), ER, and progesterone receptor (PR) in breast cancer tissues as determined using immunohistochemical methods. Clinicopathological data were obtained from pathology reports. The breast cancer tissues were fixed in 4% paraformaldehyde for 48 h and subsequently embedded in paraffin to prepare them for formalin-fixed paraffin-embedding (FFPE).

Antibodies and immunohistochemistry

The two-step EnVision method was used for immunohistochemical analysis. The positive control was prepared according to the reagent instructions; secondary antibody alone was used as the negative control.

The immunohistochemistry was performed using rabbit anti-human mammaglobin (1:500, clone EP249, Zhongshan Biotechnology, China), mouse anti-human GATA3 (1:100, clone EP368, Zhongshan Biotechnology, China), and mouse anti-human EGFR (1:150, clone EP22, Zhongshan Biotechnology, China) antibodies as the primary antibodies. The FFPE slides were deparaffinized, antigen retrieved, and blocked for endogenous peroxidase (3% H2O2). After pretreatment, the sections were incubated with the primary antibodies overnight at 4°C. Then, the slides were rinsed with PBS and incubated with a secondary antibody (PV600, Zhongshan Biotechnology, China) for 50 min at room temperature. The slides were visualized using an ultra-View Universal DAB detection kit (Ventana Medical Systems, Inc., Tucson, AZ, USA).

The immunohistochemical staining results were determined by a pathologist using a semi-quantitative method, with the percentage of positive or negative cells calculated based on the following criteria: mammaglobin >10% is positive, mammaglobin ≤10% is negative; GATA3 >10% is positive, GATA3 ≤10% is negative; EGFR ≥10% is positive, and EGFR <10% is negative. The magnification of the microscope was 200x, and the yellow-brown area was randomly selected as the observation field. Three areas were selected from each slide for interpretation. Two deputy chief physicians from the pathology department independently evaluated the staining results on two tissue chips, and the average value of the evaluation results of the same case was taken as the result for that case.

Statistical analysis

Data analysis was performed using the SPSS 20.0, Python (version 3.8.2), and Prism (version 8.4.3) software packages. Measurement data were expressed as the number of cases and compared using the t-test, while data involving counts were expressed as percentages (%) and compared using the chi-square (χ2) test. Pearson correlation test was used for correlational analysis and for all comparisons, and p-values <0.05 indicated statistically significant differences. The correlation between mammaglobin, GATA3, and EGFR expression and clinicopathological parameters was determined using the χ2 test.

Results

Correlation of molecular subtypes of breast cancer with clinicopathological characteristics

Table 1 shows the clinicopathological characteristics of breast cancers of four molecular subtypes. In this study, 32 cases of triple negative (TN) breast cancer, 41 cases of Luminal A, 103 cases of Luminal B, and 52 cases of HER-2 positive (HER-2,P) were detected. The average age of the patients was 52.48±12.34 years. Lymph sizes were between 1 and 11 cm, with an average of 5.45±1.25 cm. As for histopathological grades, 55 cases were grade I, while 173 cases were grade II and III. The most common histological type of all the breast cancers was the invasive ductal carcinoma with no special type (range: 80.4%–82.9%). There were 32 cases of TN patients, with an average age of 53.7 years (range: 35–98) and an average tumour size of 17.5 cm3 (1.5–120 cm3). The number of cases in grades I, II, and III were 2 (6.25%), 10 (
had positive axillary lymph nodes. Among the 104 cases of (Figure 1 C,F,I,L) were found to be expressed in the nucleus and A,D,G,J). The proteins GATA3 (Figure 1 B,E,H,K) and EGFR containing patterns of mammaglobin were observed in the breast can-

The correlation between mammaglobin, GATA-3, and EGFR expression with clinicopathological characteristics

The correlation between mammaglobin, GATA3, and EGFR expression and clinicopathological parameters was analysed using SPSS20.0. We found the expression levels of these proteins to be significantly correlated with histopathological grade, ER status, PR status, and breast cancer molecular subtype (p<0.05). Mammaglobin expression was detected in 132 (57.9%) samples and was significantly correlated with lymph node status, HER2 status, and Ki-67 expression levels (p<0.01). Expression of GATA3 was detected in 193 (84.6%) samples and was significantly correlated with lymph node status and HER2 status (p<0.01); however, there was no correlation between its expression levels and those of Ki-67 (p=0.054). Expression of EGFR was detected in 31 (13.6%) samples and was significantly correlated with Ki-67 expression levels (p<0.001) but was not correlated with lymph node status (p=0.069) or HER2 status (p=0.349). Of all the tissue samples, 84.6% (193/228) were GATA-3-positive, and this was significantly higher than the proportion of mammaglobin-positive (57.9%) and EGFR-positive (13.6%) samples. These data are presented in detail in Table 2.

Table 1. Clinical and pathological characteristics of breast cancer tissues analysed in this study.

| Total cases | TN (%) | Luminal A (%) | Luminal B (%) | HER-2.P (%) |
|-------------|--------|---------------|---------------|-------------|
| 32          | 32     | 104           | 51            |
| Median age (y) | 53.7 | 51.9          | 49.7          | 48.9        |
| Minimum     | 35     | 27            | 31            | 22          |
| Maximum     | 98     | 84            | 81            | 75          |
| Median tumor size (mm) | 17.50 | 16.53         | 15.25         | 20.67       |
| Minimum     | 15     | 2.04          | 0.36          | 0.64        |
| Maximum     | 120    | 102           | 230           | 117.6       |
| Grade       |        |               |               |             |
| I           | 2 (6.25) | 2 (4.88)     | 2 (1.92)     | 1 (1.96)    |
| II          | 10 (31.25) | 18 (48.90)   | 55 (52.88)   | 23 (45.16)  |
| III         | 10 (31.25) | 4 (12.20)    | 12 (25.0)    | 11 (21.57)  |
| Unknown     | 11 (34.38) | 17 (41.46)   | 30 (77.0)    | 16 (31.37)  |
| Histological type |       |               |               |             |
| Invasive ductal carcinoma | 26 (81.3) | 34 (82.9)    | 84 (80.6)    | 41 (80.4)   |
| Intraductal carcinoma | 1 (3.1) | 1 (2.4)      | 8 (7.7)      | 5 (9.8)     |
| Poorly differentiated carcinoma | 0 (0.0) | 0 (0.0)      | 6 (5.8)      | 3 (5.9)     |
| Secretory carcinoma | 0 (0.0) | 1 (2.4)      | 3 (2.9)      | 1 (2.0)     |
| Mucinous adenocarcinoma | 0 (0.0) | 5 (12.2)     | 0 (0.0)      | 0 (0.0)     |
| Papillary carcinoma | 1 (3.1) | 0 (0.0)      | 1 (1.0)      | 1 (2.0)     |
| Invasive lobular carcinoma | 0 (0.0) | 0 (0.0)      | 1 (1.0)      | 0 (0.0)     |
| Medullary carcinoma | 1 (3.1) | 0 (0.0)      | 0 (0.0)      | 0 (0.0)     |
| Apocrine carcinoma | 1 (3.1) | 0 (0.0)      | 0 (0.0)      | 0 (0.0)     |
| Other        | 2 (6.3) | 0 (0.0)      | 1 (1.0)      | 0 (0.0)     |
| Hormonal receptor and Her2 status |       |               |               |             |
| ER negative | 32 (100.0) | 0 (0.0)      | 18 (17.3)    | 45 (88.2)   |
| PR negative | 32 (100.0) | 0 (0.0)      | 2 (1.9)      | 44 (86.2)   |
| HER2 negative | 32 (100.0) | 41 (100.0)   | 27 (26.0)    | 0 (0.0)     |
| Lymph node status |       |               |               |             |
| Positive    | 8 (25.0) | 15 (38.6)    | 35 (33.7)    | 15 (29.4)   |
| Negative    | 11 (34.4) | 16 (39.0)    | 20 (19.2)    | 16 (31.4)   |
| Unknown     | 14 (43.8) | 19 (44.4)    | 47 (45.2)    | 20 (39.2)   |
Correlation of mammaglobin, GATA3, and EGFR expression in different breast cancer molecular subtypes

Figure 2 shows the proportions of positive mammaglobin, GATA3, and EGFR expression in different breast cancer molecular subtypes. The percentages of mammaglobin-positive samples in the TN, Luminal A, Luminal B, and Her2.P groups were 9.4%, 56.1%, 71.2%, and 62.7%, respectively, there was no correlation between mammaglobin expression in the different groups (results not shown). The percentages of GATA-3-positive samples in the TN, Luminal A, Luminal B, and Her2.P groups were 43.8%, 100%, 97.1%, and 72.5%, respectively, indicating that GATA3 was highly expressed in luminal cancers. The percentages of EGFR-positive samples in the TN, Luminal A, Luminal B, and Her2.P groups were 50%, 0%, 5.8%, and 17.6%, respectively, suggesting the possibility of a correlation between EGFR expression and breast cancer molecular subtype. To verify our findings, the RNA-seq data for 117 breast cancer samples were collected and analysed on the cBioPortal website (https://www.cbioportal.org/datasets), which was developed based on the work of Krug et al.[22] We found GATA3 expression to be significantly associated with breast cancer subtype (p<0.001, Figure 3A); similar results were obtained for EGFR expression (p<0.001, Figure 3B). These findings support the differential expression of GATA3 and EGFR with respect to breast cancer tissue subtype.

Correlation between GATA3 and EGFR expression in breast cancer tissues

We analysed the correlation between mammaglobin, GATA3, and EGFR expression in breast cancer tissues and found that there was a significant correlation between mammaglobin and GATA3 expression in breast cancer tissues (p=0.002, Table 3); similar results were obtained for GATA3 and EGFR (p=0.0001, Table 3). We used the GEPIA database (http://gepia.cancer-pku.cn/) to evaluate the correlation between the gene expression levels of mammaglobin, GATA3, and EGFR in breast cancer tissues. As shown in Figure 4A, there was a significant negative correlation between GATA3 and EGFR gene expression levels in breast cancer samples (p<0.0002). The correlation between mammaglobin and GATA3 gene expression levels were not significant; thus, the results are not shown.

Previous studies have shown that GATA3 and EGFR expression significantly vary with breast cancer subtype. There was a sig-

### Table 2. Mammaglobin, GATA3, and EGFR expression levels and their correlation with clinicopathological parameters, biomarker expression levels, and primary tumour molecular subtypes.

|                      | Mammaglobin               | GATA3                  | EGFR                   |
|----------------------|---------------------------|------------------------|------------------------|
|                      | Positive (57.9%)          | Negative (42.1%)       | Positive (84.6%)       | Negative (15.4%)       | Positive (13.6%)       | Negative (86.4%)       |
|                      | p-value                   | p-value                | p-value                | p-value                | p-value                | p-value                |
| Total cases          | 132                       | 96                     | 193                    | 35                     | 31                     | 197                    |
| Lymph node status    |                           |                        |                        |                        |                        |                        |
|                      | Positive                  | Negative               | Positive               | Negative               | Positive               | Negative               |
|                      | 52                        | 21                     | 0.009                  | 69                     | 4                      | 0.008                  | 12                     | 61                     | 0.069                  |
|                      | 31                        | 32                     |                        | 50                     | 13                     |                        | 4                      | 59                     |
| Grade                |                           |                        |                        |                        |                        |                        |
|                      | I-II                      | III                    |                        |                        |                        |                        |
|                      | 69                        | 44                     | 0.033                  | 100                    | 13                     | 0.028                  | 13                     | 100                    | 0.028                  |
|                      | 16                        | 22                     |                        | 28                     | 10                     |                        | 10                     | 28                     |
| ER                   |                           |                        |                        |                        |                        |                        |
|                      | Positive                  | Negative               | Positive               | Negative               | Positive               | Negative               |
|                      | 99                        | 50                     | <0.0001                | 147                    | 2                      | <0.0001                | 6                      | 143                    | <0.0001                |
|                      | 33                        | 46                     |                        | 46                     | 33                     |                        | 25                     | 54                     |
| PR                   |                           |                        |                        |                        |                        |                        |
|                      | Positive                  | Negative               | Positive               | Negative               | Positive               | Negative               |
|                      | 90                        | 44                     | <0.0001                | 130                    | 4                      | <0.0001                | 6                      | 128                    | <0.0001                |
|                      | 42                        | 32                     |                        | 63                     | 31                     |                        | 25                     | 69                     |
| Her2                 |                           |                        |                        |                        |                        |                        |
|                      | Positive                  | Negative               | Positive               | Negative               | Positive               | Negative               |
|                      | 93                        | 35                     | <0.0001                | 117                    | 11                     | 0.002                  | 15                     | 113                    | 0.349                  |
|                      | 39                        | 61                     |                        | 76                     | 24                     |                        | 16                     | 84                     |
| Ki-67                |                           |                        |                        |                        |                        |                        |
|                      | High                      | Low                    |                        |                        |                        |                        |
|                      | 73                        | 26                     | <0.0001                | 89                     | 10                     | 0.054                  | 30                     | 69                     | <0.0001                |
|                      | 59                        | 70                     |                        | 104                    | 25                     |                        | 1                      | 128                    |
| Subtype              |                           |                        |                        |                        |                        |                        |
|                      | TN                        | Luminal A               | Luminal B               | HER-2.P                 |                        |                        |
|                      | 3                         | 23                     | 32                     | 14                     | 18                     | <0.0001                | 16                     | 16                     | <0.0001                |
|                      | 73                        | 41                     | 41                     | 0                      | 0                      |                        | 6                      | 41                     |
|                      | 101                       | 3                      | 6                      | 98                     |

### Table 3. Correlation between mammaglobin, GATA3, and EGFR expression in breast cancer tissues.

|                      | Mammaglobin               | GATA3                  | EGFR                   |
|----------------------|---------------------------|------------------------|------------------------|
|                      | Positive (57.9%)          | Negative (42.1%)       | Positive (84.6%)       | Negative (15.4%)       |
|                      | p-value                   | p-value                | p-value                | p-value                |
| GATA3                |                           |                        |                        |                        |
|                      | Positive                  | Negative               | Positive               | Negative               |
|                      | 120                       | 73                     | 0.002                  | 18                     | 175                    | 0.052                  |
|                      | 12                        | 23                     |
| EGFR                 |                           |                        |                        |                        |
|                      | Positive                  | Negative               | Positive               | Negative               |
|                      | 13                        | 18                     | <0.0001                | 13                     | 22                     |
|                      | 119                       | 78                     |

[European Journal of Histochemistry 2022; 66:3315]
significantly negative correlation between GATA3 and EGFR expression in breast cancer tissues. Thus, we analysed the correlation between their expression levels in the different breast cancer subtypes. Our findings showed that GATA3 and EGFR exhibited significantly different expression levels in the TN, Luminal A, Luminal B, and HER-2.P breast cancers subtypes (Table 4, p<0.0001). The RNA data described above were used to perform linear regression analyses on GATA3 and EGFR expression levels.

Figure 1. Immunohistochemical analysis of mammaglobin, GATA3, and EGFR expression in four breast cancer subtypes. A-C) Expression of the three markers in the TN subtype. D-F) Expression of the three markers in the Luminal A subtype. G-I) Expression of the three markers in the Luminal B subtype. J-L) Expression of the three markers in the HER-2.P subtype. The white arrow indicates the cytoplasmic pattern of mammaglobin expression (A). The black arrow indicates the membranous pattern of mammaglobin expression (D). The green arrow indicates the nuclear pattern of GATA3 expression (H). The blue arrow indicates the cytoplasmic pattern of EGFR expression (C). The red arrow indicates negative EGFR staining in tumour cells (F). Magnification: 10×; scale bar: 200 μm.
in the four breast cancer subtypes. Expression of the proteins was found to be significantly negatively correlated only in the HER-2.P breast cancer subtype (p=0.0001, Figure 4B).

Discussion

Breast cancer is a commonly encountered malignant tumour in clinical practice.24 Because of its high degree of heterogeneity, its disease progression and treatment options significantly differ for different molecular subtypes. This heterogeneity also affects disease prognosis in patients, affecting the physical and mental health, life, and property safety of most patients. Therefore, pathological diagnosis at the molecular level is important for early breast cancer detection, and it is particularly critical in developing more accurate detection methods and identifying effective indicators for diagnostic and prognostic purposes.

Mammaglobin is a well-known specific marker for breast cancer, and the high expression of mammaglobin is associated with tumour stage,9 histological grading,3,6 lymph node metastasis,3,19 and endocrine state.5,6 In this study, we found mammaglobin expression to be significantly associated with lymph node status, histopathological grade, and Ki-67 expression, despite its low sensitivity. These findings agree with those reported by previous studies, in which mammaglobin overexpression was found to be correlated with lymph node metastasis and was identified as a potential protein metastasis marker in breast cancer patients.5,19

As a member of the GATA transcription factor family, GATA3 plays a key role in the regulation of breast tissue growth and promotes differentiation.10,25,26 In addition, GATA3 is an emerging diagnostic molecular marker for breast cancer27 and is more sensitive than traditional tumour markers, such as mammaglobin and GCDFP15.18 Previous studies have demonstrated the value of GATA3 as an early diagnostic and prognostic marker for breast cancer;12,28,29 however, its differential expression in breast cancer molecular subtypes is unclear. This study demonstrated that GATA3 expression is significantly associated with prognostic

![Figure 2. Percentages of mammaglobin GATA3 and EGFR-positive expression in four breast cancer subtypes.](image)

![Figure 3. RNA expression of GATA3 and EGFR in four breast cancer subtypes. A: GATA3 RNA expression in four breast cancer subtypes. B: EGFR RNA expression in four breast cancer subtypes. The RNA-seq data used for analysis were obtained from 29 TN samples, 57 Luminal A samples, 17 Luminal B samples, and 14 HER-2.P samples. The p-values for differences in gene expression between the four breast cancer groups were determined using one-way ANOVA, and p<0.05 was considered statistically significant.](image)

| GATA3 positive | GATA3 negative |
|----------------|----------------|
| EGFR positive  | EGFR negative  |
| TN             | 6              | 8              | 10             | 8              |
| Luminal A      | 0              | 41             | 0              | 0              |
| Luminal B      | 6              | 95             | 0              | 3              |
| HER-2.P        | 6              | 31             | 3              | 11             |
| p-value        | <0.0001        |

Table 4. Correlation between GATA3 and EGFR expression in different breast cancer molecular subtypes.
markers, such as lymph node metastasis and histopathological grade. This further demonstrated the importance of GATA3 expression in the identification of different breast cancer subtypes. Our findings showed a significant difference in GATA3 expression between the TN, Luminal A, Luminal B, and HER-2.P breast cancer subtypes, suggesting that GATA3 expression may be related to breast cancer subtype.

The protein EGFR is highly expressed in a variety of tumours and plays an important role in tumour occurrence and progression. It promotes tumour cell proliferation, adhesion, and metastasis, and it induces angiogenesis, inhibits apoptosis, and promotes tumour progression. Nicholson et al. found that when compared to tumour patients with low EGFR expression, those with high EGFR expression were more prone to tumour metastasis and had a shorter tumour recurrence time, a higher tumour recurrence rate, and a shorter survival period. In breast cancer patients, high EGFR expression is often accompanied by poor prognosis and rapid disease development, as evidenced by our findings, which showed EGFR expression to be significantly correlated with histopathological grade and Ki-67 expression; however, only a few studies have reported EGFR expression to be related to breast cancer subtype. Our study demonstrated a significant difference in EGFR expression between the TN, Luminal A, Luminal B, and HER-2.P breast cancer subtypes. Through the correlation analysis conducted on the three biomarkers, we found a significant correlation between GATA3 and EGFR expression in breast cancer patients. This result was confirmed using the "OLS" function in the "stats models" package in Python, and p<0.05 was considered statistically significant.

The findings of this study showed that GATA3 and EGFR expression levels were significantly different in different breast cancer subtypes and were negatively correlated in the HER-2.P subtype. In subsequent studies, we will further explore the specific signalling pathways involved in GATA3 and EGFR expression in breast cancer tissues.

Acknowledgments
The authors would like to thank Editage (www.editage.cn) for English language editing.

References
1. Austin CD, De Mazière AM, Piscacane PI, van Dijk SM, Eigenbrot C, Sliwkowski MX, et al. Endocytosis and sorting of ErbB2 and the site of action of cancer therapeutics trastuzumab and geldanamycin. Mol Biol Cell 2004;15:5268-82.
2. Li J, Zhang P, Xia Y. Aberrant expression of CCDC69 in breast cancer and its clinicopathologic significance. Eur J Histochem 2021;65:3207.
3. Monsalve-Lancheros A, Ibanez-Pinilla M, Ramirez-Clavijo S. Detection of mammaglobin by RT-PCR as a biomarker for lymph node metastasis in breast cancer patients: A systematic review and meta-analysis. PLoS One 2019;14:e0216989.
4. Galvis-Jimenez JM, Curtidor H, Patarroyo MA, Monterrey P, Ramirez-Clavijo SR. Mammaglobin peptide as a novel biomarker for breast cancer detection. Cancer Biol Ther 2013;14:327-32.
5. Babaer D, Amara S, McAdory BS, Johnson O, Myles EL, Zent R, et al. Oligodeoxynucleotides ODN 2006 and M362 exert potent adjuvant effect through TLR-9/-6 synergy to exaggerate mammaglobin-A peptide specific cytotoxic CD8+T lymphocyte responses against breast cancer cells. Cancers (Basel) 2019;11:672.
6. Ghasemi-Dehkordi P, Doosti A, Jamis MS. The concurrent
effects of azurin and Mammaglobin-A genes in inhibition of breast cancer progression and immune system stimulation in cancerous BALB/c mice. 3 Biotech 2019;9:271.

7. Takaku M, Grimm SA, Wade PA. GATA3 in breast cancer: Tumor Suppressor or oncogene? Gene Express 2015;16:163-8.

8. Ordoñez NG. Value of GATA3 immunostaining in the diagnosis of parathyroid tumors. Appl Immunohistochem Mol Morphol 2014;22:756-61.

9. Kandalaft PL, Simon RA, Isacson C, Gown AM. Comparative sensitivities and specificities of antibodies to markers GCDFP-15, mammaglobin A, and different clones of antibodies to GATA-3: A study of 338 tumors using whole sections. Appl Immunohistochem Mol Morphol 2016;24:609-14.

10. Voduc D, Cheang M, Nielsen T. GATA-3 expression in breast cancer has a strong association with estrogen receptor but lacks independent prognostic value. Cancer Epidemiol Biomarkers Prev 2008;17:365-73.

11. Mehra R, Varambally S, Ding L, Shen R, Sabel MS, Ghosh D, et al. Identification of GATA3 as a breast cancer prognostic marker by global gene expression meta-analysis. Cancer Res 2005;65:11259-64.

12. Takaku M, Grimm SA, De Kumar B, Bennett BD, Wade PA. Cancer-specific mutation of GATA3 disrupts the transcriptional regulatory network governed by estrogen receptor alpha, FOXA1 and GATA3. Nucleic Acids Res 2020;48:4756-68.

13. Warrick JI, Walter V, Yamashita H, Chung E, Shuman L, Amponsa VO, et al. FOXA1, GATA3 and PPARγ cooperate to drive luminal subtype in bladder cancer: A molecular analysis of established human cell lines. Sci Rep 2016;6:38531.

14. Voduc D, Cheang M, Nielsen T. GATA-3 expression in breast cancer has a strong association with estrogen receptor but lacks independent prognostic value. Cancer Epidemiol Biomarkers Prev 2008;17:365-73.

15. Gonzalez-Conchas GA, Rodriguez-Romo L, Hernandez-Barajas D, Gonzalez-Guerrero JF, Rodriguez-Fernandez IA, Verdines-Perez A, et al. Epidermal growth factor receptor overexpression and outcomes in early breast cancer: A systematic review and a meta-analysis. Cancer Treat Rev 2018;62:1-8.

16. Burness ML, Grushko TA, Olopade OI. Epidermal growth factor receptor in triple-negative and basal-like breast cancer: promising clinical target or only a marker? Cancer J 2010;16:23-32.

17. Jackisch C, Harbeck N, Huober J, von Minckwitz G, Gerber B, Kreipe HH, et al. 14th St. Gallen International Breast Cancer Conference 2015: Evidence, Controversies, Consensus - Primary therapy of early breast cancer: Opinions expressed by German experts. Breast Care 2015;10:211-9.

18. Krings G, Nyström M, Meldi I, Vohra P, Chen YY. Diagnostic utility and sensitivities of GATA3 antibodies in triple-negative breast cancer. Hum Pathol 2014;45:2225-32.

19. Li C, Zhang T. Human mammaglobin: A specific marker for breast cancer prognosis. J BUON 2016;21:35-41.

20. Shiva JW, Papadimos DJ, Walsh MD. GATA3: a promising marker for metastatic breast carcinoma in serous effusion specimens. Cancer Cytopathol 2014;122:307-12.

21. Masuda H, Zhang D, Bartholomeusz C, Doihara H, Hortobagyi GN, Ueno NT. Role of epidermal growth factor receptor in breast cancer. Breast Cancer Res Treat 2012;136:331-45.

22. Cerami E, Gao J, Drgusoez U, Gross BE, Sumer SO, Aksoy BA, et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. Cancer Discov 2012; 2:401-4.

23. Gyorffy B, Lángczyk A, Szállási Z. Implementing an online tool for genome-wide validation of survival-associated biomarkers in ovarian-cancer using microarray data from 1287 patients. Endocr Relat Cancer 2012;19:197-208.

24. Anastasiad Z, Lianos GD, Ignatiadou E, Harissi-HV, Mitsis M. Breast cancer in young women: an overview. Updates Surg 2017;69:313-7.

25. Shiva JW, Papadimos DJ, Walsh MD. GATA3: a promising marker for metastatic breast carcinoma in serous effusion specimens. Cancer Cytopathol 2014;122:307-12.

26. Zeng W, Yang Y, Lu S, Zhu W. Sensitivity analysis on the novel marker GATA3 expression in different surrogate molecular subtypes of breast carcinoma. J Mol Imaging 2018;41:493-8.

27. Miettinen M, Cao PAM, Sarlomo-Rikala M, Rys J, Czapiewski P, Wazny K, et al. GATA3: a multispecific but potentially useful marker in surgical pathology: a systematic analysis of 2500 epithelial and nonepithelial tumors. Am J Surg Pathol 2014;38:13-22.

28. Asselin-Labat ML, Sutherland KD, Barker H, Thomas R, Shackleton M, Forrest NC, et al. GATA-3 is an essential regulator of mammary-gland morphogenesis and luminal-cell differentiation. Nat Cell Biol 2007;9:201-9.

29. Xie Y, Shi J, Li X, Sui J, Yi H, et al. Expression of GATA3 in breast cancer tissues and its relationship with ER expression. Nat Cell Biol 2007;9:201-9.

30. Aksoy BA, et al. The cBio cancer genomics portal: an open platform for genome-wide validation of survival-associated biomarkers in ovarian-cancer using microarray data from 1287 patients. Cancer Cytopathol 2014;122:307-12.

31. Nicholson RI, Gee JMW, Harper ME. EGFR and cancer prognosis. Eur J Cancer 2001;37:S9-S15.

32. Li C, Zhang T. Human mammaglobin: A specific marker for breast cancer prognosis. J BUON 2016;21:35-41.