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GATA binding protein 3 (GATA-3) as a new prognostic marker in breast cancer

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Background: GATA-3 is a transcription factor involved in human cell growth and differentiation and closely associated with clinicopathologic features such as ER (estrogen receptor) expression. It has been suggested that loss of GATA-3 may contribute to tumorigenesis and GATA-3 expression can be a prognostic marker in breast cancer.

Material and Methods: We evaluated GATA-3 expression by immumohistochemical staining and investigated the role of GATA-3 as a prognostic marker in breast cancer. Seventy-four invasive breast cancer tissues were collected from breast cancer patients. Tissues were stained by immunohistochemistry with GATA-3 monoclonal antibody. Evaluation of GATA-3 expression was done by blind method. GATA-3 expression was scored by sum of intensity and percentage staining of nucleus. Patients were followed up and the mean follow up time was 53.1 months.

Results: GATA-3 expression in breast cancer was significantly associated with ER expression ($p = 0.005$), low histologic grade ($p = 0.049$), low nuclear grade ($p = 0.016$), marginally with PR expression ($p = 0.099$), but not with tumor size ($p = 0.466$), lymph node involvement ($p = 1.000$). GATA-3 expression was not significantly associated with recurrence of triple negative (ER/PR/HER-2 negative) breast cancer recurrence ($p = 0.518$). But GATA3 was significantly associated with low recurrence rate in non-triple negative breast cancer ($p = 0.022$) and the significance was more powerful than of ER expression.

Conclusion: GATA-3 expression is associated with known good prognostic markers and it is likely that GATA-3 will be a good prognostic marker in breast cancer, especially in non-triple negative breast cancer.

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Evaluation of serum HER2 extracellular domain levels in patients with metastatic breast cancer and those who underwent preoperative systemic treatment

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Background: Tumor markers can be an easier modality to detect cancer metastasis compared with diagnostic imaging, and its decrease or increase is often correlated with effectiveness of treatment.

Patients and Methods: Serum human epidermal growth factor receptor 2 extracellular domain (HER2-ECD) levels were reviewed in 56 breast cancer patients with metastasis and 21 patients who underwent preoperative systemic therapy (19: chemotherapy, 2: endocrine therapy). Patients were stratified into 2 groups, those with HER2-positive (group I) and negative (group II) breast cancer.

Results: In patients with metastatic disease, median serum HER2-ECD level was 14.6 ng/ml (group I) vs 12.9 ng/ml (group II, $p = 0.14$). furthermore, HER2-ECD levels were assessed in 17 patients at the detection of metastasis. In those, HER2-ECD was significantly higher in patients of group I (median: 17.2 ng/ml) than group II (12.2 ng/ml, $p = 0.03$), and proportion of patients with raised HER2-ECD (>15.3 ng/ml) was 75% (group I) vs 23% (group II, $P = 0.099$). In patients who undergoing preoperative treatment, median HER2-ECD level was 12.8 ng/ml (group I) vs 9.5 ng/ml (group II, $p = 0.28$). Proportion of patients with raised HER2-ECD was significantly higher in group I (60%) than in group II (0%, $p = 0.008$). In those patients, HER2-ECD levels decreased following chemotherapy, and were observed to be less than 15.3 ng/ml in patients who achieved pathological complete response. In 11 patients (85.7%) out of 14 who were evaluated both HER2-ECD levels and imaging diagnosis following systemic therapy, HER2-ECD was successfully associated with tumor response.

Conclusion: Serum HER2-ECD levels were observed to be raised in 75% of HER2-positive breast cancer patients at the time of detection of metastases, and well associated with tumor response in 85.7% of patients.

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MYEOV gene selected by array comparative genomic hybridization is up-regulated in triple negative breast cancer

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Background: We tried to validate the expression level of *MYEOV* selected as a candidate gene for the invasion and metastasis of breast cancer by the analysis of array comparative genomic hybridization (array CGH) and to verify the relationship between *MYEOV* with triple negative breast cancer.

Material and Methods: *MYEOV* gene was selected as the candidate gene for the invasiveness, metastasis of breast cancer by the analysis of previous results of array CGH. (Hwang KT et al. Genomic copy number alterations as predictive markers of systemic recurrence in breast cancer. Int J Cancer 2008;123:1807−15) We performed RT-PCR to validate the expression of *MYEOV* in paired normal and cancer tissues of 20 breast cancer patients, and in 7 breast cell lines including 1 normal breast cell lines (MCF10A) and 6 breast cancer cell lines (MCF7, T47D, MDA-MB453, HCC1954, BT20, MDA-MB231).

Results: The expression of *MYEOV* in cancer tissue is up-regulated in 11 samples (55%), same in 5 samples (25%), and down-regulated only in 4 samples (20%) compared to normal breast tissues. All samples with triple negative breast cancer ($n = 6$, 30%) showed up-regulated expression and 8 (89%) of 9 samples with hormone receptor negative breast cancer showed up-regulated expression. Only MCF10A and MDA-MB453 showed weak expression and all other cell lines showed strong expression. All of 3 cell lines with triple negative phenotype (HCC1954, BT20, MDA-MB231) showed strong expression of *MYEOV.*

Conclusions: The expression level of *MYEOV* in cancer is up-regulated compared to normal breast tissue and this phenomenon is prominent in triple negative breast cancer.

SN	Histology	Age	T stage	N stage	Stage	ER	PR	HER2	NG	HG	Recurrence	RT-PCR
1	IDC	50	3	3	3C	0	0	1	3	3	systemic	down
2	IDC	37	3	3	3C	1	1	1	2	2	0	up
3	IDC	82	4	3	3C	1	1	0	3	3	local	up
4	IDC	64	3	2	3A	1	0	1	3	3	0	ns
5	IDC	62	2	0	2A	0	1	0	3	2	0	ns
6	IDC	83	2	1	2B	1	1	1	3	2	0	up
7	IDC	48	3	3	3C	0	0	1	3	3	systemic	up
8	IDC	50	2	2	3A	1	0	1	2	2	systemic	down
9	IDC	57	3	1	3A	1	1	0	2	?	0	ns
10	IDC	56	2	1	2B	1	0	0	3	3	0	ns
11	DCIS	49	0	0	0	0	0	0	?	?	0	up
12	IDC	60	2	0	2A	0	0	0	3	3	0	up
13	IDC	73	2	2	3A	0	0	0	3	3	systemic	up
14	IDC	45	4	1	3B	0	0	1	3	3	0	up
15	IDC	73	2	1	2B	1	0	1	2	2	0	down
16	IDC	47	3	3	3C	0	0	0	3	3	0	up
17	IDC	47	3	2	3A	1	1	1	3	2	0	down
18	IDC	65	2	0	2A	0	0	0	3	3	0	up
19	IDC	65	2	2	3A	1	0	1	2	3	0	ns
20	IDC	69	2	1	2B	0	0	0	2	2	0	up

SN = serial number; ER = estrogen receptor; PR = progesterone receptor; NG = nuclear grade; HG = histologic grade; IDC = infiltrating ductal carcinoma; DCIS = ductal carcinoma in situ.
ER, PR, HER2: 1 = positive; 0 = negative.
down = downregulated expression of *MYEOV* in cancer tissue; up = upregulated expression of *MYEOV* in cancer tissue; ns = no significantly different expression of *MYEOV* between cancer and normal tissue.