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HUMAN SERUM FATTY ACID BINDING PROTEIN AS A PROGNOSTIC FACTOR IN NON-METASTATIC BREAST CANCER PATIENTS: DISAPPOINTING FINDINGS

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Abstract – *Objective:* *Breast cancer is the most common malignancy in women worldwide. It would be of great value to have reliable prognostic factors that could help to find patients with highest risk of recurrence. Fatty acid binding protein (A-FABP) is recognized to affect insulin sensitivity, lipid metabolism, and an inflammatory response associated with atherosclerosis. Circulating A-FABP could be involved in the pathogenesis of breast cancer. In this study, we analyzed serum A-FABP levels in breast cancer patients to evaluate its function as a prognostic factor in breast cancer.*

Patients and Methods: *Seventy-nine breast cancer patients who fulfilled the inclusion criteria enrolled in the study. Before any adjuvant chemotherapy or surgery, peripheral blood samples were collected and serum level of A-FABP was determined by using ELISA kit. The usual breast cancer clinical and pathological variables were also collected. All patients were followed up for 5 years particularly regarding cancer recurrence and patients' survival rate.*

Results: *Forty-two percent of the patients experienced no recurrence after five years. Cumulative risk of recurrence 5 years after the beginning of the study was 0.86. There was no significant correlation between serum level of A-FABP and recurrence rate in 5 years (p=0.925). The mean serum level of A-FABP was not significantly correlated with conventional prognostic factors in breast cancer.*

Conclusions: *According to the results, the serum levels of A-FABP had no role in prognostic role in breast cancer.*

KEYWORDS: *A-FABP, Prognostic factor, Breast cancer.*

INTRODUCTION

Breast cancer is the most prevalent cancer in women all over the world and its rate has increased dramatically from 641,000 cases in 1980 to more than 1.6 million in 2010[1]. Despite improvements in breast cancer screening and therapy, it still kills nearly half-a-million women annually, about 90% of whom die from distant metastases. Therefore, there is great interest in the identification of new cellular and molecular mechanisms that mediate breast cancer growth and metastasis. Even though widely accessible prognostic factors include pathology criteria such as lymph node and estrogen receptor (ER) status, tumor size, and histologic grade, these factors do not predict correctly exact clinical result probably because of heterogeneity of breast cancers[2]. So, more examination of the molecular mechanisms

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underlying the breast tumorigenesis and identification of the potential biomarkers in different types of breast cancers will extremely help clinical diagnosis and facilitate the choice of more effective personalized therapies to augment patient survival[3].

Fatty acid binding proteins (FABPs) consist of a family of cytosolic proteins that coordinate lipid transport and responses[4]. FABP members show tightly adjusted patterns of tissue distribution, such as adipose tissues FABP (A-FABP) and epidermal FABP (E-FABP) in the skin, offering several roles for each type of FABPs in different tissues and cells[5].

Adipose tissue plays a key role in cancer progression not only in obese patients but also in other ones. Understanding its biology in the context of microenvironmental tumour tissue will allow us to identify new therapeutic targets. Adipokines provided by adipose tissue have an important role in cancer initiation and progression. The A-FABP including FABP4 and FABP5 are implicated in tumorigenesis in different cancer types, including glioma and breast, prostate, colorectal, oral, and ovarian cancers.

FABP4 (also known as aP2) is highly expressed by adipocytes, macrophages, and dendritic cells. Although the function of FABP4 in cancer is still uncertain, it has been reported to be highly expressed by human tumors such as ovarian and bladder cancers[6].

A-FABP is recognized to affect insulin sensitivity, lipid metabolism, and an inflammatory response associated with atherosclerosis, and circulating A-FABP could be involved in the pathogenesis of breast cancer.

In this study, we analyzed serum A-FABP levels in breast cancer patients to evaluate its function as a prognostic factor in breast cancer.

PATIENTS AND METHODS

Study population

Patients with diagnosis of breast cancer based on clinical and preclinical data who met the inclusion criteria consisting of age between 25 and 70 years and non-metastatic breast cancer, were enrolled in the study. Patients with autoimmune disease, malignancies other than breast cancer, hypertension, cardiovascular disease, diabetes, liver disease, and cerebral ischemia were excluded.

Ethics

This is a clinical study conducted from April 2005 to July 2014 at the Cancer Institute, Omid Hospital and Oncology Department of Ghaem Hospital affiliated to Mashhad University of Medical Sciences (Iran). The study protocol was confirmed by the local Ethics Committee of Mashhad University of Medical Sciences (code: 85169). All participants signed written consent forms.

Study protocol

A questionnaire containing demographic data and patients' characteristics (including age, weight, height, family history of cancer, age at first pregnancy), pathological findings (including histologic grade, lymph node involvement, and metastasis) and cytology (including steroid receptor, HER2, P53and Ki67 status) was completed for all patients.

Ten milliliters of peripheral blood were collected from all patients and centrifuged at 10000 rpm for 10 minutes. The plasma fraction was separated and stored at -70°C until required for analysis. Patients were evaluated for recurrence every 6 months by clinical oncologist for 5 years and at each follow-up session physical examination and, if necessary, mammography or ultrasound and CT scan and also laboratory tests were performed.

Determination of human A-FABP serum concentration

Serum level of human A-FABP was measured with an enzyme-linked immunosorbent assay (ELISA) kit (BioVendor, Tokyo, Japan); each assay was calibrated using A-FABP standard curve following the manufacturer's instructions. The kit was kept at a temperature of 2-8°C before its application.

Sample size

Based on available data from the previous pilot study which is reported σ (risk rate) 1.5593, assuming α error of 5%, and study power of 80% (β = 0.20), the calculated sample size was 80 according to the following formula:

$$N = 2(z1-\alpha/2+z1-\beta)2/(\mathrm{Ln}\ \sigma)2$$

Statistical Analysis

Statistical analysis was carried out by SPSS16 (SPSS Inc., Chicago, IL, USA). Kaplan-Meier method was used to estimate patients' survival and hazard estimation. Moreover, for investigation of the relationship between breast cancer risk factors and

serum biomarkers, Cox regression model was used. It should be noted that in all analysis $p<0.05$ was considered statistically significant.

RESULTS

Characteristics of the study Population

Seventy-nine eligible patients according to the inclusion criteria completed the study. All patients admitted in this study were diagnosed with nonmetastatic breast cancer and invasive ductal carcinoma (IDC) was the most common type of malignancy in patients. About half of patients was diagnosed with histologic stage 2 of breast cancer. The most common chemotherapy regimen administered to patients was "Adriamycin, Cyclophosphamide-Paclitaxel" (AC-Taxol) (44.3%). The mean age of patients admitted to the study was 46.47±9.39 years old and all patients were females. Demographic characteristics, risk factors for breast cancer and prognostic factors related to breast cancer are summarized in Tables 1 and 2.

Evaluation of survival and hazard function

By using Kaplan-Meier method, it can be estimated that 42% of the patients experienced no recurrence after five years. Figure 1 shows five-year survival and annual recurrence rate for study population. Cumulative risk of recurrence 5 years after diagnosis of breast cancer was 0.86 (Figure 2).

Evaluation of the correlation between recurrence and five-year survival with breast cancer risk factors and serum A-FABP in study population

After performing collinearity test, affecting factors in Cox regression model were identified and entered in a Cox regression model. These include factors such as age, BMI, family history, stage of breast cancer, estrogen receptor-positive, age at first pregnancy, number of pregnancies and HER2 and Ki67 and P53 status. General appropriateness of the model was evaluated based on Enter method, which was statistically significant (p=0.037).

TABLE 1. Demographic data, characteristics and risk factors of study population.

Demographic characteristics		
Gender (female) (%)	100	
Height (cm)	153.98±6.451 (138-173)[2]	
Weight (kg)	68.12±13.051 (42-104)[2]	
Age (years)	46.47±9.391 (27-70)[2]	
BMI1 (kg/m^2)	28.83±5.801 (14-46.5)[2]	
A-FABP (pg/mL)	18.82±6.99	
Risk factors		
BMI>30 (%)	48.1	
Family history of breast cancer (%)	19	
Age at first pregnancy (years)	20.67±5.341 (15-37)[2]	
Type of Breast Cancer (%)	IDC[2]	89.3
	Others	10.7
Type of chemotherapy (%)	AC-Taxol[3]	44.3
	CAF[4]	32.9
	CSF[5]	21.5
	None	1.3
Number of chemotherapy sessions (N)	5c (0-8)	
Radiation dose (Gy)	5267±457a (4600-6400)[b]	
Co-treatment with radiotherapy (%)	84.8	
Trastuzumab administration (%) 8.9		

Abbreviations: [1]BMI: body mass index; [2]IDC: invasive ductal carcinoma; [3]AC-taxol: adriamycin, cyclophosphamide, paclitaxel; [4]CAF: cyclophosphamide, adriamycin, fluorouracil; [5]CSF: cytarabine, aclarubicin, g-csf. a) Mean±SD; b) Range; c) Median.

TABLE 2. Prognostic factor in study population.

Prognostic factor in study population		
Stage of the disease (%)	Stage 1	17.1
	Stage 2	55.7
	Stage3	26.6
ER1 negative (%)		30.4%
PR2 negative (%)		35.4%
HER23 negative (%)		82.9%
Ki67 positive (%)		75.8%
P53 positive (%)		61.9%
The largest mean tumor size (cm)		3.28±1.57a (1-8)[b]

Abbreviations: [1]ER: Estrogen receptor; [2]PR: Progesterone receptor; [3]HER2: Human epidermal growth factor 2 receptor. a) Mean±SD; b) Range.

Table 3 shows the result of the Wald test. Age, BMI, positive family history, and number of pregnancies were effective on survival rate and other variables such as serum A-FABP level had no role in regression equation (p=0.925) and there was no correlation between these factors and recurrence rate or five-year survival.

DISCUSSION

FABP4, also known as aFABP and aP2, is a low-molecular-weight protein that transports long-chain fatty acids (LCFAs) and other hydrophobic ligands. FABP4 was first described in adipocytes and macrophages, but it is also expressed in other cell types and tumors. FABP4 is known as a metabolic and vascular risk biomarker. FABP4 can exert its metabolic action in a paracrine or exocrine manner. In fact, high blood levels of FABP4 are connected with metabolic diseases, including obesity, metabolic syndrome, type 2 diabetes, and atherosclerosis[7].

FABP4 has an important role in tumor initiation and progression. It is involved in lipid transfer between adipocytes and tumor cells, inducing the fatty acid oxidation pathway to fuel tumor growth.

In this study, the A-FABP blood concentration of 79 patients suffering breast cancer was determined and its correlation with risk of a second relapse has been evaluated every 6 months for 4 years follow-up. Based on our findings, there was not any connection between serum concentration of A-FABP and

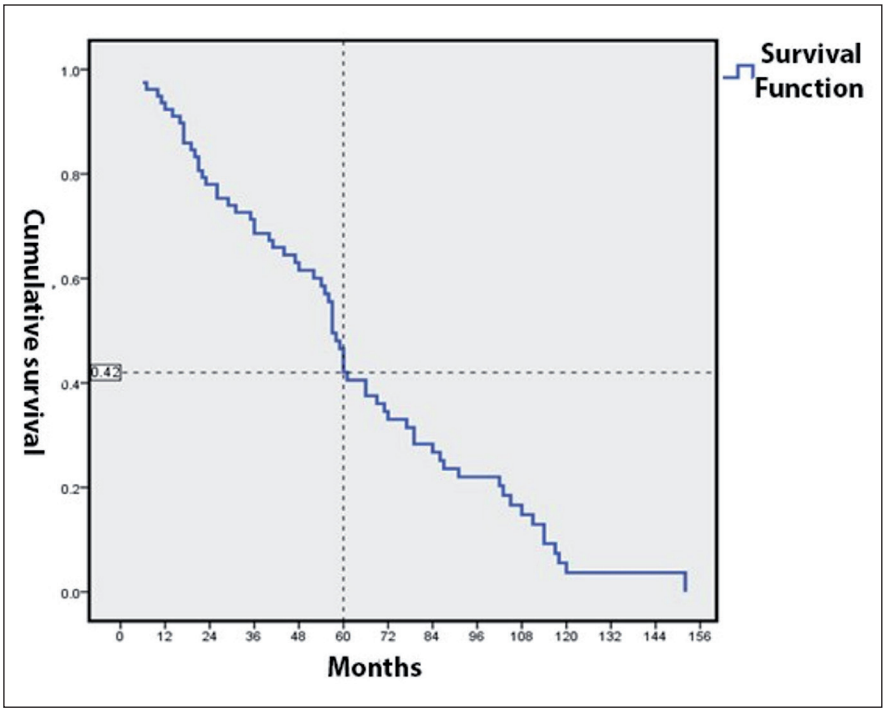

Fig. 1. Kaplan-Meier estimates of disease-free survival in primary breast cancer patients (n=79).

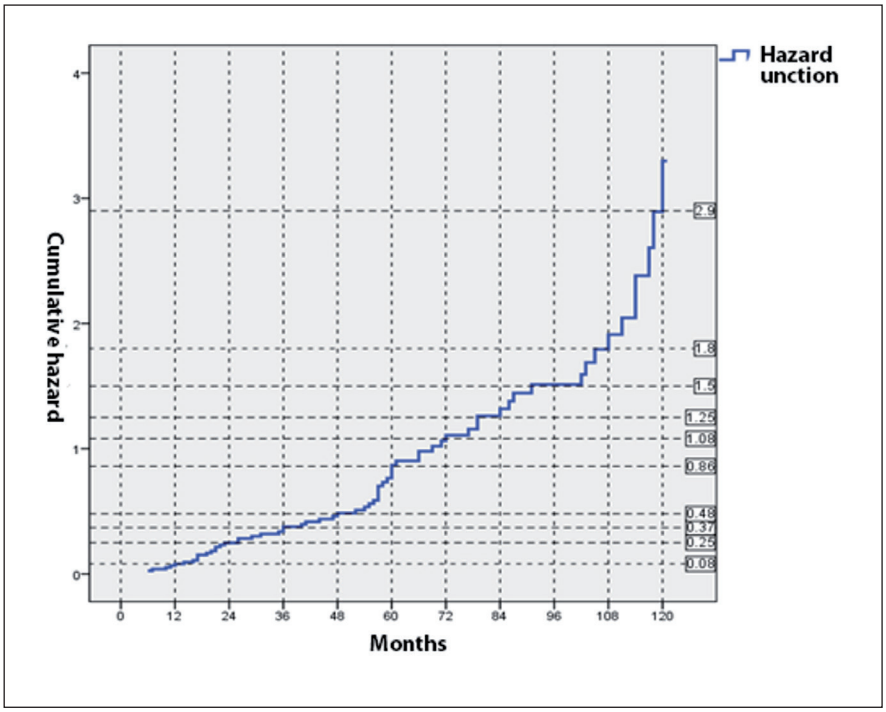

Fig. 2. Kaplan-Meier estimates of recurrence in primary breast cancer patients (n=79).

the second relapse during four years follow-up. To the best of our knowledge, no clinical studies have considered the relation between A-FABP blood concentration and patients' relapse and survival. Moreover, the results of other previous studies were controversy. One reason for controversy findings of previous studies is ignoring the confounding factors which are effective on A-FABP serum level. The patients suffering diabetes, hypertension and ischemic heart disease were removed from this study because these aforementioned diseases are confounding factors and can affect the serum concentration of A-FABP. Previous studies revealed that diabetes type 2 (T2DM) intensifies serum concentration of A-FABP. Xu et al[8] demonstrated that higher A-FABP levels in overweight/obese people were significantly associated with insulin resistance, adiposity, dyslipidemia, and glucose intolerance[9]. A 10-year cohort study in China also found that serum A-FABP levels were associated with glucose dysregulation and could predict the development of T2DM[9].

There is also a relation between serum level of A-FABP and heart ischemia. Serum level of A-FABP in ischemic patients is significantly higher in comparison with healthy people. Several studies have examined the connection between the circulating A-FABP concentration and future cardiovascular events.

TABLE 3. Correlation between recurrence rate and five-year survival with breast cancer risk factors.

Variable	*p-value*[1]	*Degree of freedom*	*Standard error*	β	*Wald statistic*
Age	0.001*	1	0.64	0.21	10.72
BMI	0.02*	1	0.18	0.41	5.42
Family History	0.06	1	1.16	-2.15	3.41
Stage of breast cancer	0.66	1	0.49	-0.22	0.19
ER positive	0.32	1	0.63	0.64	1.03
Age at first pregnancy	0.25	1	0.06	-0.07	1.30
Number of pregnancies	0.002*	1	0.22	-0.65	9.18
P53	0.18	1	0.69	0.93	1.83
HER2	0.63	1	0.54	-0.26	0.23
Ki67	0.11	1	1.16	1.84	2.56
A-FABP	0.643	1	0.005	-0.002	0.208

Abbreviations: BMI: body mass index; ER: estrogen receptor; HER2: Human epidermal growth factor 2 receptor. [1]Wald test.

Chow et al[10] reported that the serum concentration of A-FABP predicted the progress of cardiovascular disease in a community-based cohort[10].

Eynatten et al[11] found a connection between the circulating A-FABP concentration and long-term prognosis in patients with coronary heart disease. In their study, many participants were patients with an old myocardial infarction undergoing coronary artery bypass grafting, PCI, or non-invasive treatment. It is also possible to see a correlation between A-FABP serum level and blood pressure.

Ota et al[12] found that in a group of 30 normotensive patients, those with a positive family history of hypertension had higher levels of A-FABP than those with negative family history. However, it is unknown whether elevated circulating A-FABP is directly effective on insulin resistance and hypertension and that determination of serum A-FABP might be a novel approach for identifying individuals at risk of hypertension and atherosclerotic events[12].

A-FABP can be a meaningful parameter in metabolic syndrome. The increase of A-FABP can lead to the rise of resistance to insulin which itself is a predisposing factor for arteriosclerosis and dyslipidemia. Some previous studies demonstrated that circulating A-FABP is not only a biomarker, but it also plays an important role in the progression of obesity, metabolic syndrome, and cardiovascular disease. Other groups reported the usefulness of the circulating A-FABP concentration as a prognostic biomarker in patients with acute coronary syndrome as well as in those with end-stage renal disease. Therefore, by eliminating these confounding factors, we could achieve a more reliable result. In some studies, the level of A-FABP mRNA expression has been compared between normal and cancer cells that have reported paradoxical results.

According to Hao et al[13], the expression of A-FABP in tumor-associated macrophages, promotes breast cancer progression. Although upregulation of A-FABP was inversely related to breast cancer survival, deficiency of A-FABP significantly decreased mammary tumor growth and metastasis[13]. Yet, the important point is that A-FABP is expressed in fat tissue and then is secreted to the blood circulation. So, the level of mRNA may be different from the blood level of A-FABP. The next difference of our study with other ones is that they have just considered the serum level of A-FABP in a specific group of breast cancer patients.

Hancke et al[14] have studied 200 post-menopause women, 159 patients with breast cancer and 41 people with benign breast lesions. The concentration of A-FABP was higher in women suffering from breast cancer with BMI higher than 25 kg/m^2. This study demonstrated a relationship between obesity and

TABLE 4. Mean serum A-FABP levels in the groups of conventional prognostic factors.

Prognostic factors		*Mean lipocalin (ng/ml^{-1})*	*p-value*	*Mean A-FABP (ng/ml^{-1})*	*p-value*
Tumor size (T)	1 (n=17) 2-4 (n=62)	62.35±61.14 43.24±29.46	0.08	18.06±6.09 19.03±7.25	0.58
Nodal status (N)	0 (n=41) 1-3 (n=32)	50.96±46.67 43.37±27.86	0.391	19.8±8.24 17.71±5.12	0.185
Histologic grade	1-2 (n=63) 3 (n=16)	48±42.01 44.34±19.58	0.627	18.99±6.84 18.14±7.76	0.691
ER expression	Positive (n=54) Negative (n=25)	46.86±32.6 48.43±51.51	0.895	18.38±6.56 19.84±7.95	0.434
PR expression	Positive (n=50) Negative (n=29)	47.89±32.38 46.25±49.25	0.879	18.58±6.35 19.25±8.15	0.708
Ki-67	Positive (n=60) Negative (n=19)	51.55±52.28 36.91±18.99	0.255	21.07±7.87 16.94±3.78	0.056
Her-2	Positive (n=3) Negative (n=76)	21±8.2 47.44±40.92	0.042*	14±4.01 19.43±7.43	0.642
P 53	Positive (n=52) Negative (n=27)	47.89±31.27 54.39±62.03	0.709	20.2±7.1 17.11±7.19	0.185
Histology	Ductal (n=72) Others (n=7)	47.52±39.05 44.98±38.14	0.881	18.92±7.09 17.58±6.07	0.626
HRT use	Received (n=57) Not received (n=22)	46.76±31.7 48.97±55.61	0.871	18.18±6.46 20.58±8.2	0.237
Age	Pre-menopause (n=63) Post-menopause (n=16)	46.42±41.57 50.93±25.06	0.595	18.32±6.19 20.8±9.52	0.207

Abbreviations: ER=oestrogen receptor; PR=progesterone receptor.

the risk of breast cancer. Based on this study, breast cancer patients with a higher serum concentration of A-FABP have a worse prognosis in comparison to the others. Moreover, the serum levels of A-FABP appear to be significantly higher in postmenopausal breast cancer patients, but subgroup analysis should be cautiously interpreted because of the smaller sample size[14].

A new research conducted by Li et al[13] indicated that increased levels of A-FABP are associated with an increased risk of breast cancer.

To investigate the link between A-FABP and increased risk of breast cancer, authors collected serum samples from 285 women with breast lesions before they underwent diagnostic biopsies. Importantly, they found that circulating levels of A-FABP were just elevated in women with obesity who were diagnosed with breast cancer.

Given the complexity of breast cancer and the breath of obesity/cancer associations, circulating A-FABP is unlikely to be the sole unifying ''one fits all'' mechanism underlying obesity-associated cancers. There are several potential caveats of the study. For example, circulating A-FABP levels may be affected by other factors, including concomitant medication use (e.g., statins) for other comorbidities (e.g., cardiovascular diseases), but these factors have not been considered in the current study due to the lack of the information.

In Guaita-Esteruelas et al[15] study, 294 women with a positive family history of breast cancer had been selected. Among them, 198 people were suffering from cancer and the remaining 96 ones were healthy. They analyzed the association of FABP4 and FABP5 with breast cancer, while adjusting for demographic, anthropometric, and biochemical parameters. Blood concentration of FABP4 and FABP5 were significantly higher in breast cancer patients (24.8% ($p<.0001$) and 11.4% ($p<.05$) for FABP4 and FABP5, respectively). However, different confounding factors like age, BMI, very-low-density lipoprotein cholesterol (VLDLc), non-high-density lipoprotein cholesterol (non-HDLc), Apolipoprotein B 100 (ApoB100), triglycerides, glycerol, glucose, and hsCRP were affective on FABP4 and 5 serum level. The positive association of FABP4 with breast cancer was remained after adjusting for these covariates, in contrast to FABP5 correlation[15].

Also, in Kim et al[16] study, tumour samples obtained from 476 breast cancer patients were used to construct tissue microarrays. Considering tumor subtype, FABP4 positivity was associated with significantly shorter disease-free survival ($p = 0.005$) and overall survival ($p = 0.041$) in triple negative breast cancer. Moreover, the expression of FABP4 was highest in HER2 tumors and lowest in luminal A tumors. These results are upheld by the observations that serum FABP levels are significantly higher in breast cancer patients than in healthy patients, and high serum levels of FABP are connected with adverse tumor characteristics, like large tumor size and lymph node metastasis. Similar relationships have also been found in bladder and prostate cancer[16].

LIMITATIONS

This study has several limitations. First, a small number of patients was enrolled. Second, in this study we did not consider dyslipidemia and its effect on A-FABP concentration. Moreover, we just had one serum sample from patients which was collected at the beginning of treatment course. It could be better to collect serum sample before and after treatment course and compare the levels of AFABP between them. It is possible that there was a correlation between serum level of AFABP after chemotherapy course with recurrence and survival rate. Another limitation is the follow-up period which could be longer in future studies.

CONCLUSIONS

Based on our findings, serum concentrations of A-FABP may not have any role in breast cancer prognosis prediction including patients' recurrence and survival rate. Further studies should be performed to investigate the correlation between pre- and post-chemotherapy A-FABP serum level and breast cancer prognosis in larger populations.

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Conflict of Interest:

None

REFERENCES

1. Hao J, Yan F, Zhang Y, Triplett A, Zhang Y, Schultz DA, Sun Y, Zeng J, Siverstein KAT, Zheng Q, Bernlohr DA, Cleary MP, Eglimez NK, Sauter E, Liu S, Suttles J, Li B. Expression of adipocyte/macrophage fatty acid binding protein in tumor associated macrophages promotes breast cancer progression. Cancer Res 2018; 78: 2343-2355.
2. Lee S-A, Sung H, Han W, Noh D-Y, Ahn S-H, Kang D. Serum adiponectin but not leptin at diagnosis as a predictor of breast cancer survival. Asian Pac J Cancer Prev 2014; 15: 6137-6143.
3. Leng X, Wu Y, Arlinghaus RB. Relationships of lipocalin 2 with breast tumorigenesis and metastasis. J Cell Physiol 2011; 226: 309-314.

4. Furuhashi M, Hotamisligil GS. Fatty acid-binding proteins: role in metabolic diseases and potential as drug targets. Nat Rev Drug Discov 2008; 7: 489-503.
5. Storch J, Mcdermott L. Structural and functional analysis of fatty acid-binding proteins. J Lipid Res 2009; 50: S126-S131.
6. Lee D, Wada K, Taniguchi Y, Al-Shareef H, Masuda T, Usami Y, Aikawa T, Okura M, Kamisaki Y, Kogo M. Expression of fatty acid binding protein 4 is involved in the cell growth of oral squamous cell carcinoma. Oncol Rep 2014; 31: 1116-1120.
7. Girona J, Rosales R, Plana N, Saavedra P, Masana L, Vallvé JC. Correction: FABP4 Induces Vascular Smooth Muscle Cell Proliferation and Migration through a MAPK-Dependent Pathway. PLoS One 2016; 11: e0146632.
8. Xu A, Wang Y, Xu JY, Stejskal D, Tam S, Zhang J, Wat NMS, Wong WK, Lam KSL. Adipocyte fatty acid–binding protein is a plasma biomarker closely associated with obesity and metabolic syndrome. Clin Chem 2006; 52: 405-413.
9. Tso AW, Xu A, Sham PC, Wat NMS, Wang Y, Fong CHY, Cheung BMY, Janus ED, Lam KSL. Serum adipocyte fatty acid binding protein as a new biomarker predicting the development of type 2 diabetes-a 10-year prospective study in Chinese. Diabetes Care 2007; 30: 2667-2672.
10. Chow WS, Tso AWK, Xu A, Yuen MMA, Fong CHY, Lam TH, Lo SV, Tse HF, Woo YC, Yeung CY, Cheung BMY, Lam KSL. Elevated circulating adipocyte-fatty acid binding protein levels predict incident cardiovascular events in a community-based cohort: a 12-year prospective study. J Am Heart Assoc 2013; 2: e004176.
11. Eynatten MV, Breitling LP, Roos M, Baumann M, Rothenbacher D, Brenner H. Circulating adipocyte fatty acid-binding protein levels and cardiovascular morbidity and mortality in patients with coronary heart disease: a 10-year prospective study. Arterioscler Thromb Vasc Biol 2012; 32: 2327-2335.
12. Ota H, Furuhashi M, Ishimura S, Koyama M, Okazaki Y, Mita T, Fuseya T, Yamashita T, Tanaka M, Yoshida H, Shimamoto K, Miura T. Elevation of fatty acid-binding protein 4 is predisposed by family history of hypertension and contributes to blood pressure elevation. Am J Hypertens 2012; 25: 1124-1130.
13. Hao J, Zhang Y, Yan X, Yan F, Sun Y, Zeng J, Waigel S, Yin Y, Fraig MM, Egilmez NK, Suttles J, Kong M, Liu S, Cleary MP, Sauter E, Li B. Circulating Adipose Fatty Acid Binding Protein Is a New Link Underlying Obesity-Associated Breast/Mammary Tumor Development. Cell Metab 2018; 28: 689-705. e685.
14. Hancke K, Grubeck D, Hauser N, Kreienberg R, Weiss J. Adipocyte fatty acid-binding protein as a novel prognostic factor in obese breast cancer patients. Breast Cancer Res Treat 2010; 119: 367-377.
15. Guaita-Esteruelas S, Saavedra-García P, Bosquet A, Borras J, Girona J, Amiliano K, Rodriguez-Balada M, Heras M, Masana L, Guma J. Adipose-derived fatty acid-binding proteins plasma concentrations are increased in breast cancer patients. Oncologist 2017; 22: 1309-1315.
16. Kim S, Lee Y, Koo JS. Differential expression of lipid metabolism-related proteins in different breast cancer subtypes. PLoS One 2015; 10: e0119473.