Impact of Gender in Renal Cell Carcinoma: The Relationship of FABP7 and BRN2 Expression with Overall Survival

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ABSTRACT

OBJECTIVE: To investigate the relationship between gender differences in fatty acid-binding protein7 (FABP7) and BRN2 (POU class 3 homeobox 2) expression in renal cell carcinoma (RCC) and the prognosis of patients with RCC.

MATERIALS AND METHODS: Immunohistochemical (IHC) staining as well as reverse transcription-polymerase chain reaction (RT-PCR) was performed in renal tissues from 103 patients (83 men, mean age = 63.6 years old; 20 women, mean age = 63.1 years old) underwent radical nephrectomy from January 1, 2001 through December 31, 2010. The probability of overall patient survival was estimated using the Kaplan-Meier method.

RESULTS: FABP7 mRNA expression was more frequent in men ($P = 0.07$) while BRN2 protein expression was significantly more frequent in women ($P = 0.029$). In particular, FABP7 was expressed in 100% of G1 renal cell carcinoma both in mRNA and protein levels. In women, FABP7 (−) and BRN2 (+) groups had a worse prognosis both in mRNA level ($P = 0.038$) and protein level ($P = 0.058$). BRN2 was expressed 100% of papillary RCC both in mRNA and protein levels.

CONCLUSIONS: Our results demonstrated that gender was a key factor in FABP7 and BRN2 expression in RCC, and the combination with FABP7 and BRN2 stratified by gender could be a new potential prognostic factor in patients with RCC.

KEYWORDS: BRN2, FABP7, gender, overall survival, renal cell carcinoma

Introduction

In 2013, a total of 580,350 cancer deaths (306,920 in males and 273,430 in females) are projected to occur in the United States, while in kidney and renal pelvis cancer, 13,680 cancer deaths (8780 in males and 4900 in females) are projected. It is significant that the men to women ratio of patients with projected new occurrence of renal cell carcinoma (RCC) and renal pelvis carcinoma are much higher than carcinoma in general (Pearson chi-square, $P < 0.01$). Similarly, according to the data from National Cancer Center, Japan, the RCC mortality in men is 3 times higher than in women. It is reported that gender independently influenced disease-specific survival (DSS) and overall survival (OS) with a benefit for women. While men often present with high grade tumors and simultaneous metastasis, estrogen receptor beta (ERβ) was more highly expressed in RCC cell lines than in breast cancer cell lines and played a role as a tumor suppressor in RCC cell lines.

It has been demonstrated that the expression level of fatty acid-binding proteins (FABPs) and POU domain-containing family of transcription factors are influenced by gender. FABPs are abundant 14–16 kDa cytoplasmic proteins expressed...
in almost all mammalian tissues involved in the uptake and intracellular trafficking of fatty acids. Fatty acid-binding protein 7 (FABP7), also known as brain-type fatty acid-binding protein (B-FABP), mapped to 6q22–23, is a member of FABPs, which was reported to be expressed in the brain, glia cells, retina, and mammary glands. It is demonstrated that the expression of transcript for FABP7 can be in tumors and/or urine of patients with RCC, although protein expression is not always congruent with mRNA expression in prostate, bladder, and kidney cancer cell lines. Moreover, it was recently shown that FABP7 may regulate the invasiveness of astrocytoma tumors. Also, the POU domain-containing family of transcription factors contains multiple mammalian members divided into 6 classes, which can be expressed broadly or in a cell-specific manner and involved in regulators of cell fate decisions of many different lineages. BRN2, which is encoded by the POU3F2 gene in humans, is expressed predominantly in the central nervous system (CNS) and has been implicated with tumorigenesis in melanoma and lung cancer. What’s more, the Pbx/POU binding site has been demonstrated to be present in the FABP7 promoter region in human RCC cell lines.

The present investigation was conducted to examine the relationship between clinical and pathological differences, especially focused on the gender difference in FABP7 and BRN2 expression in renal cell carcinoma and the prognosis of patients with RCC.

Material and Methods

Subjects. The samples were surgically removed under radical nephrectomy from 103 RCC patients at Hamamatsu University School of Medicine during the period from January 1, 2001 through December 31, 2010. Cases were selected according to tissue availability without any further stratification for clinical or pathological prognostic factors. Staging and histological classification met the 2009 Union for International Cancer Control criteria and World Health Organization criteria, respectively. The pathologic diagnosis was based on the General Rules for Clinical and Pathological Studies on Renal Cell Carcinoma proposed by the Japanese Urological and Pathological Association (Table 1). This study was approved by the medical ethics committee of the Hamamatsu University Medical School.

Immunohistochemistry. Slices with 4-µm thickness were used for immunohistochemical (IHC) staining. Slices were deparaffinized in xylene for 15 minutes, rehydrated using graded ethanol, and steamed for 4 minutes at 121 °C in a buffer with (10 mM sodium citrate, pH 6.0, with 1 mM EDTA) in a pressure boiler. Slides were left in the pressure boiler to cool down to 90 °C and then left for 1 hour at room temperature. The detection was done according to the protocol of Ultra Vision LP Detection System HRP Polymer and DAB Plus Chromogen kit (catalog number TL-015-HD, Thermo Scientific, Fremont, CA). For FABP7, slides were incubated overnight with a 1:100 dilution of the polyclonal antibody for the recognition of FABP7.

Table 1. Clinicopathological parameters (percentages in brackets) and mRNA and protein expression of FABP7 and BRN2 in renal cell carcinomas.

|                | FABP7 mRNA | FABP7 Protein | BRN2 mRNA | BRN2 Protein |
|----------------|------------|---------------|------------|--------------|
| All cases      | 103(100)   | 86(83.5)      | 73(70.9)   | 67(65.0)     |
| Age            |            |               |            |              |
| Mean           | 30–87      |               |            |              |
| Gender         |            |               |            |              |
| Male           | 83(80.6)   | 72(86.7)      | 58(69.9)   | 52(62.7)     |
| Female         | 20(19.4)   | 14(70.0)      | 15(75.0)   | 15(75.0)     |
| Histology      |            |               |            |              |
| Clear cell     | 89(86.4)   | 75(84.3)      | 66(74.2)   | 54(60.7)     |
| Papillary      | 6(5.8)     | 6(100)        | 3(50.0)    | 6(100)       |
| Chromophobe    | 8(7.8)     | 5(62.5)       | 4(50.0)    | 7(87.5)      |
| Japan Grading  |            |               |            |              |
| G1             | 9(8.7)     | 9(100)        | 9(100)     | 7(77.8)      |
| G2             | 76(73.8)   | 62(81.6)      | 50(65.8)   | 47(61.8)     |
| G3             | 18(17.5)   | 15(83.3)      | 14(77.8)   | 13(72.2)     |
| Stage          |            |               |            |              |
| I              | 70(70.0)   | 61(87.1)      | 54(77.1)   | 43(61.4)     |
| II             | 9(8.7)     | 6(66.7)       | 5(55.6)    | 7(77.8)      |
| III            | 10(9.7)    | 9(90.0)       | 7(70.0)    | 8(80.0)      |
| IV             | 14(13.8)   | 10(71.4)      | 7(50.0)    | 9(64.3)      |

22 | CLINICAL MEDICINE INSIGHTS: ONCOLOGY 2014:8
FABP7 (catalog number HPA028825, Sigma-Aldrich, Inc, Stockholm, Sweden) in phosphate-buffered saline at 4 °C. For BRN2, slides were incubated overnight with a 1:300 dilution of the polyclonal antibody for BRN2 (catalog number GTX114650, GeneTex, San Antonio, TX) in phosphate-buffered saline at 4 °C. For controls, formalin-fixed, paraffin-embedded sections of neuroglioma served as a positive control for FABP7, while fixed melanoma was used as a control for BRN2 (materials from Department of Dermatology and Neurosurgery, Hamamatsu University School of Medicine). Negative control slides were processed with each slide run and excluded the primary antibody but included all other steps of the procedure.

**Table 2. Primers used for the PCR-amplification.**

| LENGTH | SEQUENCES | CONDITION |
|--------|-----------|-----------|
| FABP7A 339bp | forward: 5’ TGACCAACAGTCAGAACTTT 3’; reverse: 5’ ACATCACCAAAAGTAAGGGT 3’ | 30 seconds at 96 °C, 20 seconds at 54 °C, 20 seconds at 72 °C for 42 cycles |
| FABP7B 294bp | forward: 5’ GTGGGAAATGTGACCAAACC 3’; reverse: 5’ CTCTATGCGGCAACACAGCA 3’ | 30 seconds at 96 °C, 20 seconds at 54 °C, 20 seconds at 72 °C for 35 cycles |
| FABP7C 270bp | forward: 5’ CACGACCTCAAGTACCTT 3’; reverse: 5’ GCCATCCCCATTCTGTATGGT 3’ | 20 seconds at 96 °C, 20 seconds at 54 °C, 1 minute at 72 °C for 35 cycles |
| BRN2 216bp | forward: 5’ GGCGGGATCAAACTGGGATTT 3’; reverse: 5’ TGGCGCTGCGATCTTGTCTAT 3’ | 30 seconds at 94 °C, 30 seconds at 54 °C, 30 seconds at 72 °C for 35 cycles |
| β-actin 353bp | forward: 5’ GCCATCCCCATTCTGTATGGT 3’; reverse: 5’ GCTCGTCGTCGACAACGGCTC 3’ | 30 seconds at 94 °C, 30 seconds at 54 °C, 30 seconds at 72 °C for 35 cycles |

**Note:** A case was considered as FABP7 positive once it showed positive in a random primer among the three pairs of FABP7 primers.

Results

**Reverse transcription-polymerase chain reaction (RT-PCR).** In general, there was no relationship in FABP7 mRNA expression (log-rank test, \( P = 0.55 \)) and BRN2 expression (log-rank test, \( P = 0.19 \)) with overall survival, respectively. There was FABP7 mRNA expression in 100% of G1 RCC.

By gender, FABP7 expression was more frequent in men (Pearson chi-square, \( P = 0.07 \)), while BRN2 mRNA expression had no correlation with gender (Pearson chi-square, \( P = 0.30 \)).
**Figure 1.** FABP7 and BRN2 immunohistochemistry. (A) In normal tissue, FABP7 is preferentially expressed in the proximal tubuli. (B) In carcinomas tissue, FABP7 can be expressed in any part of the cell. (C) In normal tissue, BRN2 is expressed in all parts and can be strongly expressed in a few tubuli. (D) In carcinomas tissue, BRN2 is preferentially expressed in the nucleus.

**FABP7 (−) and BRN2 (+) group in women had a worse prognosis** (log-rank test, \(P = 0.038\)) (Fig. 2A), and there were only 2 women in high stage (stage 3 or 4), and these 2 women were both FABP7 (−) and BRN2 (+) in mRNA level, while in men, there was no relationship (log-rank test, \(P = 0.72\)). In women, 5 were classified as BRN2 (−), and all in low stage (stage 1 or 2), and all have survived until now, while in men, there was no relationship in BRN2 expression with overall survival (log-rank test, \(P = 0.31\)).

In all, 100% of papillary RCC could express FABP7 and BRN2, and clear cell RCC (ccRCC) was more frequently BRN2 (−) compared with the other histology type groups (Pearson chi-square, \(P = 0.019\)).

We had 89 ccRCC patients, and among these, 5 patients (5/89, 5.6%) were FABP7 (−) and BRN2 (−), and all have survived. However, FABP7 and BRN2 were not significantly associated with overall survival (log-rank test, \(P = 0.68\) and \(P = 0.36\), respectively).

**Immunohistochemistry (IHC).** In normal renal tissue, FABP7 showed a weak immunoreactivity in proximal tubuli. Few distal tubuli were also inconsistently positive. No immunoreactivity was observed in glomeruli (Fig. 1A). Among 74 patients with FABP7 expression (71.8%), some carcinoma cells were expressed in the nucleus (57/74, 77.0%), some in the cytoplasmic (53/74, 71.6%), and some in the membrane (48/74, 64.9%) (Fig. 1B).

BRN2 is weakly expressed in the cytoplasmic and membrane of almost all renal tubuli (including proximal tubuli and distal convoluted tubuli), and in the glomeruli, few tubuli can strongly express BRN2 in membrane (3+, intense) in normal tissue (Fig. 1C). Among 72 patients with BRN2 expression (69.9%), some carcinoma cells expressed in nucleus (55/72, 76.4%), some in cytoplasmic (14/72, 19.4%), and some in membrane (15/72, 20.8%) (Fig. 1D).

In general, there was no relationship between overall survival and FABP7 protein expression (log-rank test, \(P = 0.99\)) and BRN2 expression (log-rank test, \(P = 0.81\)), respectively. There was FABP7 protein expression in 100% of G1 RCC. Of 12 patients with an FABP7 weighted score ≥9, only 1/12 (8.3%) died of RCC, with the remaining 11 patients still surviving; 5 patients with a BRN2 weighted score ≥9 also survived.

By gender, BRN2 was significantly easier to express in women (Pearson chi-square, \(P = 0.029\)), while FABP7 expression had no correlation with gender (Pearson chi-square, \(P = 0.65\)). Women with FABP7 (−) and BRN2 (+) had a tendency for a worse prognosis (log-rank test, \(P = 0.058\)) (Fig. 2B), while men in this group had no correlation with overall survival (log-rank test, \(P = 0.13\)).

In men, there were 10 patients (10/83, 12.0%) with FABP7 (ws-) and BRN2 (ws+), and all survived (Fig. 3A).
women, there were 8 patients (8/20, 40%) with FABP7 (ws+), and BRN2 (ws+) (Fig. 3B), and all survived.

However, we didn’t find any direct relationship with BRN2 protein expression and FABP7 mRNA expression (Pearson chi-square, $P = 0.52$).

There was no relationship with stage (stages 1 and 2 were recognized as low stages, while stages 3 and 4 were recognized as high stages) and FABP7 mRNA/protein expression (Pearson chi-square, $P = 0.51$ and $P = 0.12$, respectively) and also between stage and BRN2 mRNA/protein expression (Pearson chi-square, $P = 0.50$ and $P = 0.37$, respectively).

In histology, ccRCC had the tendency to be FABP7 (+) more than other histology type groups (Pearson chi-square, $P = 0.064$) and to be BRN2 (−) more than the other histology type groups (Pearson chi-square, $P = 0.044$). However, we still
FABPs, member, FABP3, had mean values that were significantly higher in men than in women when they did serum examination of 2099 normal participants in Takahata, Japan. Furthermore, an analysis of human glial astrocytomas and melanoma found that patient survival was inversely correlated with FABP7 expression level when using gender-mixed data,27-30 while there was a positive correlation in women only with breast cancer from 899 primary operable invasive breast carcinoma cases.6 It is possible that FABPs move into the nucleus and interact with nuclear hormone receptors,10,31 Ilia et al found a POU3 domain transcription factor, Oct-6, had a lower expression level in cortical and cerebellar tissue of male CD1 mice when compared with females and suggested Oct-6 expression takes place in a gender-dependent way. What's more, another POU domain transcription factor, BRN3b can physically interact directly with the estrogen receptor (ER), and enhance its transcriptional effect on an ER element-containing promoter in breast cancer.8,9

Tolle et al11 found RCC with a high tumor Fuhrman grading (grades 3 and 4) showed significantly lower FABP7 mRNA compared with those with a low grading (grades 1 and 2) when quantitative RT-PCR was performed. In our study, using Japan grading, we found FABP7 expression in 100% of G1 RCC in mRNA and protein levels, and among patients with FABP7 weighted score ≥9, 11/12 (91.7%) survived. It was demonstrated that FABP7 is more frequently expressed in lower nuclear gradings, and high weighted score patients will have a better prognosis.

We found female patients with FABP7 (−) and BRN2 (+) had a worse prognosis both in mRNA, protein level, and mRNA clinical data (there were only 2 women in high stage, and both belong to this group in mRNA level). On the other hand, male patients with FABP7 (ws-) and BRN2 (ws+) all survived. It may be that FABP7 (−) and BRN2 (+) can be a potential prognosis factor in patients with RCC stratified by gender, and the system of these 2 proteins is different by gender in patients with RCC.

In the previous study, we found that there was an inverse correlation between FABP7 promoter activity and BRN2 mRNA expression in an RCC cell line,24 while we couldn't find the relationship in the 103 RCC patients or in all 89 ccRCC patients. However, ccRCC is more frequently FABP7 (+) than other histology type groups in protein level and BRN2 (−) in both mRNA and protein levels. Thus, some relationship may exist between FABP7 and BRN2 in ccRCC in clinical data, but it may also be influenced by other factors not examined here.

In our study, FABP7 and BRN2 had no relationship with overall survival both in mRNA and protein levels in all 103 patients with RCC or 89 patients with ccRCC respectively, similar to the result of FABP7 expression in patients with RCC in a previous study.11 However, our study suggests that FABP7 or BRN2 could have a prognostic potential at least in combination with other biomarkers.

Discussion
Our study is the first to analyze the FABP7 and BRN2 mRNA and protein expression in all 103 patients with RCC and found men more frequently had FABP7 mRNA expression, while in women BRN2 protein expression was significantly frequent. So, we have reason to believe FABP7 and BRN2 expression is affected by gender.

It is reported that hepatic removal of long-chain fatty acids from plasma is nearly twice as fast in women’s livers as in men’s livers.5 And FABPs are involved in the uptake and intracellular trafficking of fatty acids. Niizeki et al4 found 1
It has been demonstrated that there is a method by which FABP7 can be detected in the urine of patients with RCC.12 If there will also be a method to detect BRN2, FABP7/BRN2 can be used to potentially monitor the prognosis of patients with RCC preoperatively and postoperatively in the near future.

Conclusions
Our results demonstrated gender was a key factor in FABP7 and BRN2 expression in patients with RCC, and FABP7 binding with BRN2 stratified by gender could be a new potential survival predictor in patients with RCC. Our study is the first report on both FABP7 and BRN2 mRNA and protein expression in patients with RCC. Further study is warranted with regard to interpreting the relationship between sex hormones with FABP7 and BRN2 in patients with RCC.

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Author Contributions
Conceived and designed the experiments: CT, TT. Analyzed the data: CT. Wrote the first draft of the manuscript: CT. Contributed to the writing of the manuscript: TT, NT, SO. Agree with manuscript results and conclusions: CT, TT, NT, HF, MM, TS, SO. Jointly developed the structure and arguments for the paper: TT, NT, TS. Made critical revisions and approved final version: CT, TT, NT, HF, MM, TS, SO. All authors reviewed and approved of the final manuscript.

DISCLOSURES AND ETHICS
As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICJME authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers received no competing interests.

REFERENCES
1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin. 2013;63:3–30.
2. May M, Aziz A, Zieguner R, et al. Members of the CORONA project the Young Academic Urologists Renal Cancer Group. Gender differences in clinicopathological features and survival in surgically treated patients with renal cell carcinoma: an analysis of the multicenter CORONA database. World J Urol. 2013;31(5):1073–80.
3. Yu CP, Ho JY, Huang YT, et al. Estrogen inhibits renal cell carcinoma cell progression through estrogen receptor-beta activation. PLoS One. 2013;8:e56667.
4. Niiizeti T, Takeishi Y, Takahatake N, et al. Circulating levels of heart-type fatty acid-binding protein in a general Japanese population: effects of age, gender, and physiologic characteristics. Circ J. 2007;71:1452–7.
5. Hayge TA, Christensen E, Greun M, Christophersen BO. Regulation of the metabolism of polyunsaturated fatty acids. Sand J Clin Lab Invest Suppl. 1988;191:33–46.
6. Zhang H, Rakha EA, Ball GR, et al. The proteins FABP7 and OATP2A are associated with the basal phenotype and patient outcome in human breast cancer. Breast Cancer Res Treat. 2010;121:41–51.
7. Ilia M, Sugiyama Y, Price J. Gender and age related expression of Oct-6—a Pou III domain transcription factor, in the adult mouse brain. Neurosci Lett. 2003;344:138–40.
8. Dennis JH, Budhram-Mahadeo V, Latchman DS. The Brn-3b POU family transcription factor regulates the cellular growth, proliferation, and anchorage dependence of MCF7 human breast cancer cells. Oncogene. 2001;20:4961–71.
9. Loo SA, Ndisang D, Patel C, et al. Expression of the Brn-3b transcription factor correlates with expression of HSP-27 in breast cancer biopsies and is required for maximal activation of the HSP-27 promoter. Cancer Res. 2005;65:3072–80.
10. Furushashi M, Hotamisligil GS. Fatty acid-binding proteins: role in metabolic diseases and potential as drug targets. Nut Rev Drug Discov. 2008;7:489–503.
11. Tolle A, Jung M, Lein M, et al. Brain-type and liver-type fatty acid-binding proteins: new tumor markers for renal cancer? BMC Cancer. 2009;9:248.
12. Teratani T, Domoto T, Kuriki K, et al. Detection of transcript for brain-type fatty Acid-binding protein in tumor and urine of patients with renal cell carcinoma. Urology. 2007;69:236–40.
13. Domoto T, Miyama Y, Suenoki H, et al. Evaluation of SH0A10, annnexin II and B-FABP expression as markers for renal cell carcinoma. Cancer Sci. 2007;98:57–82.
14. Tolle A, Suhail S, Jung M, Jung K, Stephan C. Fatty acid binding proteins (FABPs) in prostate, bladder and kidney cancer cell lines and the use of IL-FABP as survival predictor in patients with renal cell carcinoma. BMC Cancer. 2011;11:302.
15. Tolle A, Krause H, Miller K, Jung K, Stephan C. Importance of brain-type fatty acid binding protein for cell-biological processes in human renal carcinoma cells. Oncol Rep. 2011;25:107–12.
16. Mita R, Colon JE, Globeschi DD, Sung R, Sun X, Godbout RB. B-FABP-expressing radial glial cells: the malignant glioma cell of origin? Neoplasia. 2007;9:344–44.
17. Schreiber E, Tobler A, Malipiero U, Schaffner W, Fontana A. cDNA cloning of human N-Oct3, a nervous-system specific POU domain transcription factor binding to the octamer DNA motif. Nucleic Acids Res. 1993;21:253–8.
18. Goodall J, Martinotti S, Dröger TJ, et al. Brn-2 expression controls melanoma proliferation and is directly regulated by beta-catenin. Mol Cell Biol. 2004;24:2915–22.
19. Thomson JA, Murphy K, Baker E, et al. The brn-2 gene regulates the melanocyte phenotype and tumorigenic potential of human melanoma cells. Oncogene. 1996;13:691–700.
20. Eisen T, Easry DJ, Bennett DC, Goding CR. The POU domain transcription factor Brn-2: elevated expression in malignant melanoma and regulation of melanocyte-specific gene expression. Oncogene. 1995;11:2157–64.
21. Schreiber E, Himmelmann A, Malipiero U, Tobler A, Stahel R, Fontana A. Human small cell lung cancer expresses the octamer DNA-binding and nervous system-specific transcription factor N-Oct 3 (brain-3). Cancer Res. 1992;52:6121–4.
22. Ishii J, Sato H, Sakada M, et al. POU domain transcription factor BRN2 is crucial for expression of ASCL1, NDI and neuroendocrine marker molecules and cell growth in small cell lung cancer. Pathol Int. 2013;63:158–68.
23. Sanchez-Font MF, Bosch-Comas A, Gonzalez-Duarte R, Marfany G. Overexpression of FABP7 in Down syndrome fetal brains is associated with PKNOX1 gene–dosage imbalance. Nucleic Acids Res. 2003;31:2769–77.
24. Takaoka N, Takayama T, Teratani T, Sugiyama T, Mugiya S, Osumi S. Analysis of the regulation of fatty acid binding protein 7 expression in human renal carcinoma cell lines. BMC Med Biol. 2011;12:31.
25. The Japanese Urological Association, The Japanese Society of Pathology, Japan Radiological Society. General Rules for Clinical and Pathological Studies on Renal Cell Carcinoma. 4th ed. Tokyo, Japan: Kanehara; 2011.
26. Sinicropo FA, Ruan SB, Clary KR, Stephens LC, Lee JJ, Levin B. bcl-2 and p53 oncprotein expression during colorectal tumorigenesis. Cancer Res. 1995;55:237–41.
27. Goto T, Koyanagi K, Narita N, et al. Alberant fatty acid-binding protein-7 gene expression in cutaneous malignant melanoma. J Invest Dermatol. 2010;130:221–9.
28. Kaloshi G, Mokhtari K, Carpenter C, et al. FABP7 expression in glioblastomas: relation to prognosis, invasion and EGFR status. J Neurooncol. 2007;84:245–8.
29. Goto Y, Matsuzaki Y, Kurihara S, et al. A new melanoma antigen fatty acid-binding protein 7, a pore involved in proliferation and invasion, is a potential target for immunotherapy and molecular target therapy. Cancer Res. 2006;66:4443–9.
30. Liang Y, Bollen AW, Aldape KD, Gupta N. Nuclear FABP7 immunoreactivity is preferentially expressed in infiltrative glioma and is associated with poor prognosis in EGFRvIII-expressing glioblastoma. BMC Cancer. 2006;6:97.