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Review Summary Fascin protein and tumor

Summarized by :Jafar Abdel-Hadi 1
Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology. No 1095 of Jiefang Road, Wuhan 430032, China

Fascin protein is a member of the actin binding protein Fascin. Initially, Fascin protein was discovered by Bryan J et al. in sea urchin and ocyte in the 70s of the 20th century, and they conducted its separation and purification [1, 2, 3]. In 1993 through the cDNA sequential information of echinoderm's Fascin protein [4], it was revealed that it featured homology with the Drosophila singed protein [5], human 55kD actin binding protein [6] and the orthologues in other vertebrates homology [7, 8, 9], and it was also found that they did not feature homology with other discovered actin binding protein; therefore, they were classified into a new actin binding protein family-Fascin protein family.

The mammalian genome encodes three Fascin genes, i.e. Fascin 1, Fascin 2 and Fascin 3. In humans, the gene that encodes Fascin1 is located at 7p22 of the chromosome, while those of Fascin 2 and Fascin 3 are respectively located at 17q25 and 7q31 [10, 11, 12]. Fascin 10 protein is widely distributed in mesenchymal tissue and the nervous system, while Fascin 2 and Fascin 3 are specially expressed in retina and testis. [8, 13, 14]. Although several kinds of Fascin protein have been found, currently the mostly studies is still human Fascin 1(hereinafter referred to as Fascin), and in this paper, it only conducts a summary of the research progress of this protein in tumors.

1. Fascia Protein

Fascin protein must contain two actin binding sites between it can be bound with the latter. The first site is located at the terminal end of the amino acid, and is between one β- clover folded zone and the residues of 33-47 amino acid; while the other one has been inferred from limited proteolysis, which is located between 277-493residuals. And unlike other actin crosslink proteins, such as protein filamin and α-actinin, Fascin protein is closely bound with F-actin and makes the latter to form a bundle structure that is laid out in parallel, and it also features extraordinary hardness. The use of antibodies to inhibit the binding of the

Fascin and actin can stop the cell migration, but in totally diffused cells, Fascin'sdistribution is diffused, and are not located with F-actin, all these indicated Fascin plays an important role in cell movement and exclusion. And Fascin protein also binds with non-cytoskeletal proteins. Fascin protein in vitro and undamaged ceils is a substrate of PKC [15, 16]. The site of the highly conservative phosphorylation is the 39th serine, and it is located in the first actin binding site, and the phosphorylation of this site inhibits activity of the binding of Fascin protein and actin, and bestow it other activities, i.e. the binding with the regulation zone of active PKCα. The latter interaction has been located at the Zone C1 of PKC [17] The third interaction of a Fascin is the neurotrophin receptor, p75NTR [18]. Such a binding depends on the 3rd and 4th β-clover ruffles zones.

Due to its unique function in cells, Fascin protein possesses extremely important significance in organisms, and regarding this, most profound research has been conducted on the study of Drosophila melanogaster, for example, sign (gen of the same Fascin family) mutation type Drosophila melanogaster had short and thick bristles, and the ocytes are inactive, and are unable to fully develop, thus leading to infertility. Medically, it has been found that Fascin protein is specifically expressed in mature dendritic cells (DC), and now it has become a reliable indicator of mature DC, and can help identify the mutation type DC in the quantitative tissue specimens and groups of culture and differentiation, and can be used in the anti-carcinoma therapy with DC as the targets, and it can also be used for clarifying the pedigree source of diseases' relevant cells, study has shown that in 187cases of Hodgkin's Lymphoma, HL, with the exception of the nodular lymphocyte as the main type, in all types the R-S cells were Fascin protein strongly positive, and only in 15% of the Hodgkin's Lymphoma, HL a small amount of Fascin protein staining could be seen, this may be because a small portion of tumorous cells were weakly positive, were the infiltration dendritic cells, or the staining of vascular endothelial cells, and the results proved that the R-S cells in Hodgkin's Lymphoma, HL originated from dendritic cells. In addition, it ahs been found that changes in Fascin expression

are correlated to some diseases, for example, Fascin protein had up-regulated expression in some tumors of epithelial tissue origin.

2 . Fascin Protein Expression in Normal Mammals

Fascin protein is expressed in the tissues of most vertebrates, especially is highly expressed in brain, ovary and testis. But its expressions in different cell types are not uniformed. In T-cells and several kinds of epithelial cells it had low expression or no expression, while it had high expressions in neurons and glial cell line, skeletal muscle and smooth muscle cell lines, and the epithelial cell line. In the following, we shall respectively introduce the Fascin protein expressions in embryonic development and mature cells.

During the rats' embryogenesis from E8.0 to E16. 5, Fascin genes transcription was mainly expressed in the nervous system, developing body segments and such other tissues as mesenchymal cells of the mesoderm origin and limbs [19]. During early development, such as E8. 0, Fascin protein was expressed in the neural epithelium of the whole embryonic front — rear axles. Until the later stage of development, Fascin genes had high transcription in some of the regions of the central nervous system, including brain and the spinal cord, and the Dorsal Root Ganglia of peripheral nervous system,. Smooth muscle cells, tissues of mesoderm origin (such as skeletal muscle and tendon) and cranial and dorsal root ganglia) were all locations of Fascin protein high expression, and they were also the locations for the migration and differentiation of developing cells. With the exception of neural epithelium, the developing epithelium had no expression of Fascin protein.

And regarding the Fascin protein's expression in mature cells, it was mainly conducted on human tissue using Immunohistochemistry technique. In vascular endothelial cells, neural cells and fibroblasts expression, the Fascin protein is expressed [20-22]; in lymphoid tissue, Fascin protein is specifically expressed in follicular dendritic cells, FDCs [23]; but it is not expressed in such normal columnar epithelium as bile duct, mammary gland, stomach, colon, ovary, pancreas and stomach expression; in the stratified squamous epithelium of skin and esophagus, Fascin protein had low expression in basal cells, but it is not

expressed in the upper layer of differentiated cells expression.

It was found in the study of Fascin expression in mature mammal tissues using the immunohistochemistry technique that Fascin was expressed in vascular endothelial cells, neural cells and fibroblasts all had expressions [24-26]. In the lymphoid system, the Fascin expression was mainly confined to dendritic cells [27]. And in normal bile duct, mammary gland, colon, ovary, pancreas and the columnar epithelium of stomachs, no Fascin expression was found. But in the basal layer of stratified squamous epithelium of skin and esophagus some hidden low expression could be found, while it was not found in the differentiated cells of the upper layers.

In cells, Fascin protein is located in the actin protein bundle of the filopodium of cytoplasmic stress fibers and the edge of the cell membrane ruffles and the micro-spines [27, 28]. It participates in cell migration, the adhesion between cells and extracellular matrix and the intracellular interaction; but the intracellular microfilament bundle within the cytoplasm participates in the formation of cytoskeleton.

3 . Fascin's Expression in Human Tumors and Its Relation with prognosis

Fascin-1 had no expression in normal tissues or only have low expression, but had different levels of expression in some carcinomaous tissues. Although we have attempted to explain the high expression of Fascin-1 protein with a common mechanism, it is more likely that it has some tissue specificity, because there is a big change in the positive expression rate of Fascin-1 in of tumors with different epithelial origin.

Seen from the existing study achievements, compared with normal tissue, the Fascin expression in tumors is very big. As shown in the table, in the detected tissue tumors, variations Fascinexpression were found among a large portion [29]. Due to the large variations in the proportion of Fascin-positive between different epithelial tumors, the current opinion holds that mechanism that leads to the Fascin expression variations has tissue specificity. For example, over 95% of the malignant pancreatic carcinoma have high Fascin expression [29],andFascin over-expression was found in about 89%

of the early non-small cell lung carcinoma NSCLC) [28]. But in other tumors, the probability of Fascin over-expression was substantially reduced. In gastric carcinoma, about 22.5% of the intramucosal carcinoma had Fascin expression, while the Fascin's positive rate in stage T_4 gastric carcinoma reached 53.3%, indicating the positive rate of Fascin's expression was elevated along with the expansion of the tumor invasion scope [31]. More interestingly, in gastric carcinoma and mammary gland carcinoma, the Fascin staining strength on the lateral tissue was stronger than the staining strength of tumor's center [31, 32]. In partial NSCLC, similar expression modes were also found [27]. Due to the tumor center has the tendency of hypoxia or necrosis, such an expression mode may be correlated to the mechanism of Fascin's over-expression in early tumors. Or due to the excessive Fascin expression by the tumorous cells of the invasive side, these cells have high invasion and can more easily invade into the lymphoid tissue and blood vessels. Since the tissue samples or sections used in the past experiments were unable to completely and accurately assess the scope of the Fascin-positive cells of single tumors, such conclusions call for stricter illustration.

Another substantial characteristics is that the Fascin expression in these tumors is correlated to the tumor's malignancy degree and the patients' prognosis. In NSCLC, the quantity and modes of Fascin expression in gastric carcinoma, esophageal carcinoma and mammary glands were correlated to the patients' prognosis and survival rate [26, 31, 32]. But the affection modes were slightly different. The positive rates of Fascin expression in gastric carcinoma and esophageal carcinoma were increased along with the tumor's invasion [31]; however, in mammary gland carcinoma, Fascin expression was correlated to the tumor's clinical staging (P=0. 046), but unrelated to the tumor's size, the metastasis of the lymphoid nodes or distant metastasis [33]. In general, current research results indicted Fascin's high expression is generally correlated to the tumor's malignancy degree.

If we say Fascin is a biomarker of a tumor's malignancy, then the Fascin's positive rate in the metastatic tumor that was formed by the metastasized from the

Fascin-positive tumor should also be rather high. The studies on gastric carcinoma have verified this speculation. Fascin expression was only found in 3% of the metastasized tumors originating from Fascin-negative tumors, while in Fascin-positive metastasized tumors, 72% had Fascin expression [31]. Similarly, since the specimens used in these studies failed to strictly illustrate the correlation between the Fascin over-expression is correlated to the tumor's invasion speed and the possibility of invasion, the verification of this issue calls for large clinical specimens and further illustrations.

4. Mechanism for Fascin over-expression in tumorous cells

Currently, it is still unclear whether the molecular mechanism that leads to Fascin over-expression in tumor occurs in transcription level of post-transcription level. Due to the different status of Fascin expression in different tumors, currently some researchers hold the opinion that the mechanisms for the Fascin over-expression in tumors with different tissue origins might be different.

The over-expression of gene products in tumors is usually resulted from the abnormalities of chromosomes. For example, the encoded product of HER2/neuis a member of the receptor family of epidermal growth factor. The receptor has over-expression in about 30% of mammary gland carcinoma and is also associated with the patient's prognosis. And in mammary gland carcinoma, the over-expression of this protein is closely associated with the amplification of its encoding gene HER2/neu [34]. However, in other types of tumors, the probability variation rate of HER2/neuprotein over-expression is very big and is usually higher that the projected levels, which indicates the existence of other regulation imbalance mechanisms. For Fascin, it is shown by the indexing results of Mitelman's tumor chromosome mutation database (Mitelman Database of Chromosome Aberrations in Carcinoma (2005). Mitelman F, Johansson B and MertensF(Eds.), http:/lcgaP. nci, nih. gov/Chromos- ome}itelman), the amplification in Zone 7P was not the common characteristic of all tumors with Fascin over-expression, and obviously this cannot rule out the correlation Fascin's over-expression with the mutations of the chromosomes; however, current research results indicated a

greater possibility of incidence of regulation irregularity of or/and transcription or/and post-transcription level.

Another method for the comparison of gene transcription level is the detection of genetic expression profile, i.e. DNA chip. This method is being widely used in the studies of tumor studies, and various databases were also formed consequently. One example is the Oncomine database. The database collated some genetic expression data of the corresponding normal tissues of the tumors in some other different databases [35]. Adams et al. collected in the database the mRNA levels of Fascin in various kinds of tumors [29], and the result showed the mRNA levels of Fascin in pancreatic tumor and colon tumor were higher than those in normal tissues, while in such other tumors of the remaining tissue origin as lung carcinoma, mammary gland carcinoma and ovarian carcinoma etc., the mRNA levels of Fascin were higher than those of normal tissues, or the differences had no statistical significance. Using quantitative PCR method, we also detected that the Fascin mRNA level in esophageal carcinoma tissue was higher than the corresponding normal tissues [36]. These results indicated that the up-regulation of transcription levels or the changes in mRNA stability only existed in partial tumors.

Mosialos et al. studied the regulating mechanism on the Fascin-1gene transcription level in dendritic cells. Fascin protein is a reliable marker for the maturing of dendritic cells, and the exploration on its expression regulation in DC cells facilitates the unveiling of Fascin over-expression mechanism in tumors. Their research results indicated that Fascin's promoter is located in the 3kb zone of the 5' side of the gene, and the expression is controlled by cis-acting elements. This promoter has very strong in the nerve cell line in which DC Fascin expression were positive, and this promoter's activity was elevated along with the mature status of DC cells. Through progressive 5' loss, within about 20Qbp from the ignition codon, one core promoter zone has been verified, which contained a publicly known GC box, one compound sequence of the CAMP response element/AP-1 binding site and one TATA box. Besides, in an enhancer that is rather far from the initial codon

and has phrasal specific function has a silencer, and in the DC that is maturing and has been subject to immunostimulation, this phrasal specific enhancer can the activity of the promoter, but such an increased activity was not seen in immature DC [37]. How to link these regulatory elements and the Fascin expression in tumors is a current hot research topic.

Previous studies have found that Fascin genes had up-regulated expressions in tumorous cell lines of epithelial origin, such as cervical carcinoma Hela, gastric carcinoma AGS, colorectal carcinoma LIM 1215 and SW480, pancreatic carcinoma BxPC3 and T3H4. Some studies have shown that the up-regulated expression of Intracellular Fascin genes may lead to the increase of cell membrane blebbing, intercellular junctions have dissociation, and meanwhile the cell mobility is accordingly increased by 8-17 times. And in Fascin genes were transected into cell line of SW1222 of colorectal carcinoma with high differentiations and low expression of Fascin genes, the result showed that with the elevation of Fascin genes expression, there would also be such serial changes as increased cell surface projections, and the cell differentiation is rather low, and flourishing cell proliferation, reconstruction of the actin cytoskeleton, and increased cell motility, and in three-dimensional matrix the cells' invasion was increased by 2-5 times, etc.. Zhang Shu, et al. analyzed the expression of Fascin genes mRNA in various ovarian tissues using semi-quantitative RT-PCR method ovary, and the results showed that in normal ovarian tissue there was no expression of Fascin genes, while there was an elevated tendency of Fascin genes expression level in non-metastasis primary ovarian carcinoma, metastasis primary ovarian carcinoma and ovarian carcinoma metastasis, and the deviations among them had substantiality ((P<0.05). Meanwhile, Fascin genes mRNA expression and clinical staging had positive correlation, while it was not associated with histological type of ovarian carcinoma, pathological grading and whether there were ascites or not. Research results have indicated that the high expression of mobility-related Fascin protein is correlated to the metastasis of ovarian carcinoma [38]. RongJu et al. conducted detection and analysis on the differentially expressed

genes that were transformed from immortalized esophageal epithelial cell line SHEE and the esophageal carcinoma cell line that was transformed from SHEE malignancy on the two levels of protein and mRNA, and they analyzed the status of differentiated protein expression between SHEE and SHEEmt using two-dimensional gel electrophoresis, and they conducted assessments on partial points of differentiated expression using MALDI-TOF-MS, and conducted detection on the target genes at mRNA transcription level using RT-PCR, and also conducted sequential detection analysis of RT-PCR products. The results showed in 9 genes of the malignant transformation from SHEE to SHEEmt, there were differentiated expressions, and among them Fascin-1 gene was elevated by 3. 64 times at protein level, and the mRNA level was elevated by 16, 17 times. It can be seen that Fascin-1gene may be correlated to the malignant transformation from SHEE to SHEEmt [39].

It was found in the studies of a series of tumors, tumors with positive expression of Fascin protein usually has higher histological grade or higher invasion, for example, Kempf et al. et al. Through a series of studies of Fascin expressions of the subcutaneous CD30+lymphoproliferative diseases with various malignancy degrees, it was found that with the elevation of malignancy degree, Fascin expression was also elevated [40]. Yoder et al. conducted analysis on the status of Fascin protein expression and of 210 cases of mammary gland infiltration carcinoma and 5-year survival period and the result showed that Fascin was expressed in about 16% of the mammary gland carcinoma, and it had positive correlation with the Bloom-Richardson grading of ER, PR-negative, and was not correlated to HER2 status, tumor staging and metastasis mode. Fascin The average survival rate of patients with positive Fascin protein expression was reduced. Fascin protein high expression in ER, PR-negative mammary gland carcinoma indicated it had more invasive clinical process, Fascin protein may be the new index of molecular therapy of ER-negative mammary gland carcinoma [41]a Pelosi et al. found that in 220 cases of Stage I non-small cell lung carcinoma, Fascin protein was positive in 98% of squamous cell carcinoma, positive in 78%

of adenocarcinoma, positive in 6 cases of large cell carcinoma 83%, positive in both 2 cases of squamous cell carcinoma. Fascin protein positive expression was closely correlated to tumor histological grade, and in adenocarcinoma, in those with contralateral thoracic or remote metastasis, Fascin was usually diffused positive. Patients with Fascin diffuse positive usually have a shorter survival period, and it was not correlated with other clinicopathological indicators [42]. Domestically, Yu Weixia et al. conducted immunohistochemistry staining of Fascin and Ki-67 on 51 cases of non-small cell lung carcinoma of different histological types and clinical staging, the total Fascin positive rate was 52.9%, among which in 2 cases of highly differentiated mucoepidermoid carcinoma and 4 cases of bronchioloalveolar carcinoma, Fascin expression were both negative, while in 4 cases of large cell carcinoma and 3 cases of pleomorphic carcinoma, the Fascin expression rate was elevated, and in adenocarcinoma, the Fascin positive rate was 43.5%, and in squamous cell carcinoma it was 66.7%. Fascin protein had up-regulated expression in non-small cell lung carcinoma, and it had positive correlation with Ki-67 index. Fascin protein was a marker for the poor differentiation and high malignancy of non-small cell lung carcinoma. And the reason that the lower positive rate was lower than that in the result of Pelosi et al. is not clear, and it may be correlated to antigen retrieval, formation of cases and the differences in the judgment standard. Kabukcuoglu S et al. Immunohistochemistry staining of Fascin protein was conducted on the cervical biopsy specimens of 92 cases, among which the positive rate of 13 cases of chronic cervicitis was 69%, the positive rate of 33 cases of CIN was 94%,and the positive rate of 46 cases of infiltration carcinoma was 67%, the scoring of Fascin protein expression in high CIN was substantially elevated compared with low CIN, chronic cervicitis and infiltration carcinoma; meanwhile, it was found the quantity of microvessels in high CIN was substantially elevated than those in infiltration carcinoma and chronic cervicitis. It indicated that when the cervix has malignancies, Fascin protein expression is also elevated, and similarly, the quantity of microvessels is also elevated [43], A Roma AA et al.

Immunohistochemistry staining of Fascin protein was conducted on 90 cases of multiformeglioblastoma and GBM, and in all cases there were positive expressions, and among 19 cases positive cell number >75%, in 14 cases the positive cell number 50%-75%,in 23cases the positive cell number 25%-50%,in 26 cases the positive cell number was at 5%-25%,in 8cases positive cell number <5%. In the control group, in 11 cases of low-grade astrocytoma, in 9 cases the Fascin positive cell number<50%,10 cases anaplastic astrocytoma, AA in 8 cases the Fascin positive cell number >50%, and all glioma had Fascin protein expressions, and the higher the tumor's malignancy degree, the stronger the Fascin protein staining. In glioblastomamultiforme, there was no correlation between the GBM staining degree and the survival rate, and Fascin may play a role in the infiltration aspects [44]. Xie JJ et al. studied Fascin's role in cell proliferation of esophageal carcinoma and the infiltration aspects, and they sealed the Fascin expression of EC109 of esophageal carcinoma cell line, and the results showed the Fascin's low expression resulted in cell proliferation and the reduction of infiltration. In addition, Fascin may also play roles in the aspects of cell growth regulation. Regarding the aspect of cell infiltration, Fascin was correlated to the activation of metalloproteinase. Xie JJ et al. also found that the reduction of Fascin expression also led to the reduction of C-erbB-2 and β-catenin at protein levels. These results indicated that Fascinmay play a decisive role in regulating the progress of esophageal carcinoma [45]. Adsay NV et al. found that like other malignant processes, the progress of pancreatic carcinoma is a genetic disease that is resulted from a series of genetic carcinoma-related mutations. Fascin protein's high expression and k-ras mutation, HER-2/neu, PSCAabd MUC5 et al. may belong to early changes, while the high expressions of P16 inhibition, MUC1 and cyclin DI belong to mid-term changes, and the high expression of P53 and DPC4inhibiiton, BRCA2 mutation and Ki-67, etc. belong to late-stage changes [46]. Studies by Tong GX et al. found that Fascin protein expression was not found in normal human transitional epithelium, and there were no elevated Fascin protein expressions in cystic bladder dermatitis, glandular flirt

dermatitis, renal adenoma, inverted papilloma, everted papilloma and adjacent transitional epithelium. In 42% (5/12) of the superficial papillary transitional cell carcinoma, there was weakly positive expression, in 95% (19/20) of the infiltration transitional cell carcinoma, there was strongly positive expression, and in the small infiltration foci, there was also positive expression, but had lighter staining than deep infiltration foci. In addition, in carcinoma in situ, the number of positive cells >50%. These discoveries indicated the increase of Fascin protein expression is correlated to the increase of infiltration of infiltration bladder transitional cell carcinoma of the skin [47]. Xiao T et al. detected the plasma specimens of 628 cases of lung carcinoma using ELISA method and the results showed that the plasma matrix metalloproteinase 1 was substantially elevated in late-stage lung carcinoma, and Fascin protein was detected for the first time using ELISA method [48].

Currently, some literature reported some methods which can reduce the Fascin protein expression, for example Sugihara A et al. Studies have found UVB stimulation can lead to reduction of Fascin protein expression in bone marrow dendritic cells and epidermal Langerhans cells by reducing the rearrangement of cytoskeletal protein [49]. Megiorni F et al. sealed the genes of CREB's binding protein of NT2 precursor cells using RNA interference, and the result showed in the 1. 2K-cDNA hybridization experiment of minor rearrangement, the Fascin protein expression in cells of CBP depletion was reduced than that of the control group [50].

Refrences

[1] Kane R. Actin polymerization and interactions with other proteins in temperature-induced gelation of sea urchin egg extracts. J Cell Biol. 1976,71(3): 704-714.

[2] Bryan J, Kane RE，Separation and interaction of the major components of sea urchin actin gel. J Mol Boil. 2978; 225(2): 207- 224.

[3] Otto JJ, Kane RE, Bryan J. Formation of filopodia in coelomocytes: localization of fascin, a 58,000 dalton actin cross-linking protein. Cell. 1979; 17 (2): 285-93.

[4] Bryan J, Edwards R, Matsudaira P, et al. Fascin, an echinoid actin-bundling

protein, is a homolog of the Drosophila singed gene product. ProcNatlAcadSci USA. 1993; 90(19): 9115-9119.

[5] Paterson 7, O'Hare K. Structure and transcription of the singed locus of Drosophila melanogaster. Genetics. 1991; 129(4): 1073-1084.

[6] Yarnashiro-Matsumura S, Matsumura R Purification and characterization of an bundling 55-kilodalton protein from HeLa cells. J Biol Chem. 1985;5087-5097.

[7]Holthuis JC, Schoonderwoert VT, Martens GJ. A vertebrate homolog of the actin-bundling protein fascin.BiochimBiophysActa. 1994; 1219 (1): 184-188.

[8] Edwards RA, Herrera-Sosa H, Otto J, etaI. Cloning and expression of a murine fascin homolog from mouse brain. J Biol Chem. 1995; 270(18): 10764-10770.

[9] Saishin Y, Shimada S, Morimura H, et al. Isolation of a cDNA encoding a photoreceptor cell-specific actin-bundling protein: retinal fascin. FEBS Lett. 1997;414(2): 381-386.

[10] Tubb BE, Bardien-Kruger S, and Kashork CD. Characterization of human retinal fascin gene (FSCN2) at 17q25: Close physical linkage "of fascin and cytoplasmic actin genes. Genomics.2000: 65: 146-I56.

[11] Tubb BE, Mulholland DJ, Vogl W, Lan ZJ, Neiderberger C, Cooney A, et al.Testisfascin (FSCN3): A novel paralog of the actin-bundling protein fascin expressed specifically in the elongate spermatid head. Experimental Cell Research. 2002; 275:92-109.

[12] Duh FM, Latif F, Weng Y, Geil L, Modi W, StackhouseT, et al. cDNA cloning and .expression of the human homolog of the sea urchin fascin and Drosophila singed genes which encode an actin-bundling protein. DNA and C}11 Biology.1994; 13:821-827.

[13] Edwards R A,&Bryan 7. Fascins, a family of actin bundling proteins. Cell Motility and the Cytoskeleton. 1995; 32: 1-9.

[14] De Arcangelis A, Georges-LabouesseE,&Adams JC. Expression of fascin-1, the gene encoding the actin-bundling protein fascin-1, during mouse embryogenesis.Gene Expression Patterns. 2004; 4: 637-643.

[15] Anllkumar, N.， Parsons, M.， Monk, R.， Ng, T,&Adams J. C. (2003)Interaction of fascin and protein kinase C alpha: A novel intersection in cell adhesion and motility. EMBO Journal, 22,5390-

5402.

[16] Shollukan, T, Bagayogo, I. , McCrea, P. D. , Chao, M. , &Hempstead,B. (2003).Neurotrophin-induced melanoma cell migration is mediated through the actin-bundling protein fascin. Oncogene, 22, 3616-3623.

[17] Goncharuk, V. N.Ross J. S.& Carlson J. A.(2002).Actin-binding Protein fascin expression in skin neoplasia. Journal of CutaneousPathology, 29, 430-438.

[18] Mosialos, G. , Yamashiro, S. , &Baughman, R W. (1994) virus infection induces expression in B lymphocytes.Epstein. BaITof a novel gene encoding an evolutionarily conserved 55-kd actin.bundling protein. Journal of Virology, 68, 7320-7328.

[19] De Arcangelis, A. , Georges-Labouesse, E., &Adams, J. C. (2004). Expression of fascin-1, the gene encoding the actin-bundling protein .

[20] Goncharuk, V. N., Ross, J. S., &Carlson, J. A. (2002).Actin-binding protein fascin expression in skin neoplasia. Journal of Cutaneous Pathology, 29, 430-438.

[21] Mosialos, G. , Yamashiro, S. , &Baughman, R W. (1994).Epstein. BaIT virus infection induces expression in B lymphocytes of a novel gene encoding an evolutionarily conserved 55-kd actin. bundlingprotein.Journal of Virology, 68, 7320-7328.

[22] Jawhari, A. U., Buda, A., Jenkins, M., Shehzad, K., Sarraf, C., Noda,M., et al. (2003). Fascin, an actin-bundling protein, modulatescolonic epithelial cell invasiveness and differentiation in vitro.American Journal of Pathology, 162, 69-80.

[23] Pelosi, G., Pastorino. D, Pasini, E, Maissoneuve, P., Fraggetta,E, lannucci, A., et al.(2003).Independent prognostic value of fascinimmunoreactivity in stageI non-small cell lung cancer.British .Tournal of Cancer, 88, 537-547.

[24] Goncharuk VN, Ross JS, Carlson JA. Actin-binding protein fascin expression in skin neoplasia.Journal of Cutaneous Pathology.2002; 29: 430-438.

[25] Mosialos G, Yamashiro S, Baughman RW. Epstein-Barr virus infection inducesexpression in B lymphocytes of a novel gene encoding an evolutionarilyconserved 55-kd actir}bundling protein. Journal ofV'uology. 1994; 68:7320-7328.

[26]Jawhari AU, Buda A, Jenkins M,

Shehzad 风 Sarraf C, Noda M, et al. Fascin, an actin-bundling protein, modulates colonic epithelial cell invasiveness anddifferentiation in vitro. American Journal of Pathology.2003; 162: 69-80.

[27] Pelosi G, Pastorino U, Pasini F, Maissoneuve P, Fraggetta F, Iannucci .A, et al.Independent prognostic value of fascinimmunoreactivity in stage I non-small celllung cancer. British Journal of Cancer.2003; 88: 537-547.

[28]Adams JC. Formation of stable microspikes containing actin and the 55 kDa actin bundling protein, fascin, is a consequence of cell adhesion to thrombospondin-2:implications for the anti-adhesive activities of thrombospondin-1. J Cell Sci. 1995;108 (Pt 5): 2977-1990.

[29] Hashimoto Y, Skacel M, Adams JC. Roles of fascin in human carcinoma motility and signaling: prospects for a novel biomarker? Tnt J Biochem Cell Biol. 2005 Sep; 37: 1787-804.

[30] Swierczynski SL, Maitra A, Abraham SC, Iacobuzio-Donahue CA, AshfaqR,Cameron et al. Analysis of novel tumor markers pancreatic and biliary carcinomas using tissue microarrays. Human Pathology. 2004: 35, 357-366.

[31] Hashimoto Y, Shimada Y, Kawamura J, Yamasaki S, Imamura M. The prognostic relevance of fascin expression in human gastric carcinoma.Oncology.2004; 67: 262-270.

[32] Grothey A, Hashizume R, Sahin AA, McCrea PD. Fascin, an actin-bundling protein associated with cell motility, is upregulated in hormone receptor negative.

[33] Yoder BJ, Tso E, SkacelM,Pettay J, Tarr S, Budd T, et al. The expression of fascin,an actin-bundling motility protein, correlates with hormone receptor-negative breast cancer and a more aggressive clinical course. Clinical Cancer Research.2005; 11:186-192.

[34] Slamon DJ, Clark GM, Wong SG, Levin WJ, Ullrich A, McGuire WL. Human breast cancer: Correlation of relapse and survival with amplification of the HER-2/nenoncogene.Science. 1987; 235: 177-182.

[35] Rhodes DR, Yu J, Shanker 风 Deshpande N, Varambally R, Ghosh D, et al Oncomine: A cancer microarray database and integrated data-mining platform.Neoplasia. 2004; 6: 1-6..

[36] Zhang H, Xu L, Xiao D, Xie J, Zeng H, Cai W, Niu Y, Yang Z, Shen Z,

Li E. Fascin is a' potential biomarker for early-stage esophageal squamous cell carcinoma. J ClinPathol. 2006 Mar 8; [Epub ahead of print]

[37] Ross R, Ross XL, Schwing J, Langin T, Reske-Kunz AB. The actin-bundling protein fascin is involved in the formation of dendritic process in maturing epidermal Langerhans cells. Journal of Immunology.1998; 160: 3776-3782.

[38] 张殊、林其德、狄文。BRMS1 和 Fascin,基因在卵巢上皮癌中的表达及其意义。现代妇产科进展 2003 年 5 月第 12 卷第 3 期。

[39] 荣举、许丽艳、蔡唯佳等。Fascin-1 基因在永生化食管上皮细胞癌变中的表达。(癌症)2004 23(3):243-248。

[40]Kempf W, Levi E, Kamarashev J, et a1.Fascin expression in CD30-positive cutaneous lymphoproliferative disorders. J CutanPathol. 2002 May;29(5):295-300.

[41] Yoder BJ, Tso E, Skacel M, et a1.The expression of fascin, an actin-bundling motility protein, correlates with hormone receptor-negative breast cancer and a more aggressive clinical Clin Cancer Res. 2005 Jan 1;11(1):186-92.

[42] Pelosi G, Pastorino U, Pasini F, et al. Independent prognostic value of fascinimmunoreactivity in stage I nonsmall cell lung cancer. Br J Cancer. 2003 Feb 24;88(4):537-47.

[43] Kabukcuoglu S, Ozalp SS, Oner U, et al. Fascin, an actin-bundling protein expression in cervical neoplasms.Eur J GynaecolOncol. 2005;26(6):636-41.

[44] Roma AA, PraysonRA.Fascin expression in 90 patients with glioblastomamultiforme.AnnDiagnPathol. 2005 Dec;9(6):307-11.

[45] Xie JJ, Xu LY, Zhang HH, et a1.Role of fascin in the proliferation and invasiveness of esophageal carcinoma cells. BiochemBiophys Res Commun. 2005 Nov 11;337(1):355-62.

[46] Adsay NV, Basturk O, Cheng JD, et al.Ductalneoplasia of the pancreas: nosologic,clinicopathologic, and biologic aspects. SeminRadiatOncol. 2005 Oct; l S(4):254-64.

[47] Tong GX, Yee H, Chiriboga L, et al.Fascin-1 expression in papillary and invasive urothelial carcinomas of the urinary bladder. Hum Pathol. 2005 Ju1;36(7):741-6.

[48] Xiao T, Ying W, Li L, et a1.An approach to studying lung cancer-related proteins in cancer-related proteins in human blood. Mol Cell proteomics.2005

Oct;4(10):1480-6. Epub 2005 Jun 20.

[49] Sugihara A, Okamoto H, HorioT.Effects of UVB onfascin expression in dendritic cells and Langerhans cells. J Dermatol Sci. 2005 Dec;40(3):177-85. Epub 2005 Jul 1.

[50] Megiorni F, Indovina P, Mora B, et a1.Minor expression of fascin-I gene (FSCNI)in NTera2 cells depleted of CREB-binding protein. NeurosciLett. 2005 Jun 10-17;3 81(1-2):169-74.

[51] Menard S, Casalini P, Campiglio M, Pupa SM, Tagliabue E. Role of HER2/neuinprogression and therapy. Cellular and Molecular Life Science.2004; 61:2965-2978.