Introduction

Despite substantial advances in treatment, cancer is the most important public health issue globally and the second principal cause of fatalities in the United States. Between 2007 and 2017, the number of people fatalities from cancer escalated by 25.4% (from 7.62 to 9.56 million). In 2020, the United States nationally estimated that 1,806,590 people were diagnosed with cancer, as well as 606,520 people died from cancer in the United States. Cancer caused fatalities (17%) are far more than those caused by infectious disease, for example, human immunodeficiency virus/acquired immunodeficiency syndrome (1.7%), malaria (1.1%), or tuberculosis (2.1%). Digestive system carcinoma (DSC), which includes esophageal carcinoma (EC), hepatocellular carcinoma (HCC), gastric cancer (GC), colorectal cancer (CRC), as well as pancreatic cancer (PC), undoubtedly serves pivotal roles in the worldwide cause of human fatalities in the 21st century, as well as the greatest impendent to extending life. Worldwide cancer statistics revealed that three of the four cancers that cause cancer death are digestive system tumors. Although some tumor biomarkers, such as HER2, as well as alpha fetoprotein, have been used in the diagnosis and prognosis of DSC, sometimes their clinical utilizations were significantly limited by dismal specificity and tumor diversity. Without timely intervention, deaths caused by DSC will continue to increase. Therefore, it is an urgent need to find effective biomarkers to improve personalized diagnostic and prognostic assessments.
The B7 family is an important costimulatory molecule family, which not only affects T cell proliferation and cytokine release, but also serves a crucial modulatory role in B cell activation and antibody secretion. B7-H3, a new B7 family member, was previously regarded as a modulatory ligand that regulates T cell-mediated immune reaction. In recent years, it was demonstrated to have a close relationship with the occurrence and prognosis of various cancers. Additionally, in different types of tumors, B7-H3 expression had been associated with different prognosis, or even the opposite effect had been observed. Recent studies have shown that B7-H3 has a close correlation with the occurrence and prognosis of DSC. Herein, we reviewed the current studies on B7-H3 in DSC.

B7-H3 in cancer

B7-H3, also referred to as CD276, was in the place cloned from human dendritic cells (DCs)-derived cDNA library by Chapoval in 2001. Among the B7 family members, B7-H3 is the most conserved one with more than 80% amino acid identity between mice and humans. As a novel costimulatory molecule, B7-H3 molecules are widely expressed from teleost fish to mammal and may possess fundamental immunoregulatory roles. B7-H3 expression level is very limited in normal tissues, while is aberrantly expressed in many human malignancies and link to cancer aggressiveness. For instance, positive B7-H3 was reported in more than 80% of lung cancer tissues. Over 90% (28/32) of mesothelioma tissues were expressed B7-H3. In clear cell renal cell carcinoma (ccRCC), 17.4% of tumor cells and 95.1% of tumor vasculature in 743 examined patients expressed B7-H3. High B7-H3 was associate with an increased risk of death from ccRCC. In oral squamous cell carcinoma (OSCC), overexpression of B7-H3 was positively associated with larger tumor size, advanced clinical stage, and low survival rate. Similar to B7-H3 in OSCC, high expression of B7-H3 was linked to poorly differentiated tumors, larger tumor size, lymphovascular infiltration, as well as shorter overall survival of patients with breast cancers. B7-H3 plays a role in regulating immune cells (such as dendritic cells (DCs), monocytes, T cells, B cells, and NK cells) mediated immune responses. In prostate cancer, a median of 80% of cancer cells positive expression of B7-H3, and the high levels of B7-H3 were more prone to increased the risk of disease recurrence, relapse or successive development of hormone-refractory prostate cancer. The foundation of these relationships may be linked to the recognize capacity of B7-H3 to suppress T cell-mediated immunity. In non-small-cell lung cancer (NSCLS), overexpression tumoutal B7-H3 showed correlated with higher numbers of tumor-infiltrating CD45þ immune cells, CD8þ T-cells, NK-cells, and pDCs, moreover, high tumor B7-H3 expression was associated with shorter survival after PD-1 blockade therapy. In RCC, positive B7-H3 was found in both tumor cells and the tumor vasculature, and the expression levels of B7-H3 were associated with FOXP3+ cell number, suggesting that B7-H3 may exert tumor-promoting immunity by interacting with FOXP3+ regulatory T cells in the tumor microenvironment. High B7-H3 expression levels were observed in 73.6% (145/197) of breast cancer samples, and overexpression of B7-H3 was negatively correlated with stromal CD3+ and CD8+ T cell infiltrate density, that is to say, B7-H3 could lead to tumor evasion from immunosurveillance through the suppression of T lymphocyte infiltration, particularly cytotoxic CD8+ T lymphocytes. Additionally, in triple-negative breast cancer, high B7-H3 could promote tumor metastasis and suppress T-cell infiltration by modulating the tumor ECM construction and angiogenesis.

In addition to membrane B7-H3, B7-H3 also exists in a soluble form, which is released from monocytes, DCs and activated T cells and is detectable in normal human serum, while high levels of soluble form (sB7-H3) have also been elevated in several tumors and correlated with the invasion and metastasis of tumor. For example, in NSCLC, the levels of sH7-B3 were significantly increased. Moreover, sB7-H3 was significantly higher in NSCLC-derived malignant pleural effusions (MPEs) compared with nonneoplastic pleural effusions (NPEs), and the levels of sB7-H3 was correlated with smoking status and TNM stage. In osteosarcoma (OS) patients, sB7-H3 level was significantly higher than that in healthy volunteers, and upregulated serum sB7-H3 in patients with OS were significantly associated with the clinical stage and patients’ poor prognosis. High levels of sB7-H3 were detected in the sera of 47% of patients with non-muscle invasive bladder cancer (NMIBC),
while only 8% in healthy donors. The increase of sB7-H3 significantly determined the rate of recurrence and progression.\textsuperscript{36}

In addition, B7-H3 is closely associated with chemotherapeutic resistance.\textsuperscript{37-40} In Melanoma cells, inhibiting B7-H3 expression could reduce cells growth and glycolytic capacity, and increasing B7-H3 expression led to the cancer eventually decreased sensitivity to multiple chemotherapy.\textsuperscript{37} In acute monocytic leukemia U937 cells, down-regulation of B7-H3 could reduced cells growth, as well as colony-forming potential and remarkably increase the sensitivity of U937 cells to first-line chemotherapy drugs (daunorubicin and cytarabine).\textsuperscript{38} Furthermore, silencing of B7-H3 was also reported to escalate the responsivity of the human pancreatic carcinoma cell line Patu8988 to gemcitabine, thereby enhancing drug-induced apoptosis.\textsuperscript{39} Ectopic B7-H3 expression could reduce the non-small cell lung cancer cellular response to classic chemotherapy drugs (cisplatin).\textsuperscript{41} Therefore, expression of B7-H3 is not only directly linked to tumor proliferation and metastasis, but also related to tumor therapeutic effect. In addition, silencing B7-H3 tends to have a synergistic impact when integrated with chemotherapy or other immune checkpoint repressors.\textsuperscript{42}

**Biological function of B7-H3**

Signal transduction networks, which are the communication line of the cells, allow cells to perceive and relay signals, entailing those from the intracellular and extracellular environment, and transmit them to subsequent targets to properly adapt the cell function to maintain the steady state of the cell, tissue and general homeostasis. The mechanisms of B7-H3 promote tumor biological behavior are extensively studied but still unveiled. Multiple studies have documented that B7-H3 regulates cancer cells migration, infiltration, and adherence via activating downstream signals such as PI3K-Akt and Jak2/Stat3 (Figure 1).

**B7-H3 and PI3K-Akt signaling pathway**

The phosphoinositide 3-kinase (PI3K)–AKT pathway is the most often activated axis in human cancers.\textsuperscript{43} Under physiological status, this pathway can be activated by insulin, cytokines, as well as growth factors, to regulate important metabolic processes, such as glucose metabolism, macromolecular organism synthesis, and redox stability, to maintain systemic metabolic homeostasis and single cell growth and metabolism. Oncogenic activation of the PI3K–AKT axis in cancer cells reprograms

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**Figure 1.** Mechanism of B7-H3. B7-H3 reduces the number of T cells. In addition, B7-H3 can promote the Jak2/Stat3 cascade. B7-H3 upregulates the expression of SREBP-1 cascade and this axis promotes the expression of FASN. Additionally, PI3K/AKT axis is increased by B7-H3, which results in BCL2, mTOR expression. In addition, B7-H3 can promote the TLR4, which active NF-κB pathway. B7-H3 also increases activation of VEGF, MMP2, MMP9, IFA, CDC25A expression.
cellular metabolism by increasing the activity of nutrient transporters and metabolic enzymes, to support the anabolic needs of abnormally growing cells. Excessive PI3K/Akt activation resulted in increased tumor cell proliferation, reduced apoptosis, and stimulate cell growth. Numerous studies demonstrated that PI3K/AKT signaling pathway is a classic downstream signal of diverse cell surface biomolecules in tumor cells, which is closely related to development of cell proliferation, modulation of tumor cells, as well as drugs resistance.

B7-H3 is an imperative modulator of PI3K-Akt signaling pathway in the initial stage. Researches have found that B7-H3 can help activation of PI3K-Akt signaling by facilitating the generation of membrane surface complexes in cancer. Li et al. confirmed that B7-H3 did not affect cell proliferation and apoptosis, while overexpression of B7-H3 via the PI3K/Akt/ signaling pathway enhances the migration and infiltration of human bladder cancer cells, which was also proved by Zhang et al. in non-small cell lung cancer.

Tumor drug resistance development is considered to be the main reason for the failure of clinical chemotherapy in cancer therapy. Studies demonstrated that B7-H3 and PI3K/AKT may act synergistically on cancer cells, leading to the cancer cells sustained growth, as well as acquisition of drug resistance development. For example, Zhou found that B7-H3 via activation of PI3K/AKT signaling axis leading to the enhanced stem-like phenotypes of ovarian cancer cells and finally causing the sustained growth, as well as acquisition of drug resistance. In addition, B7-H3 and PI3K/Akt signaling pathway also resemble synergistic influence on stimulation of oral squamous carcinoma cell lines. These cells secrete the hypoxia-inducible factor 1 alpha (HIF-1α), which is a primary modulator of genes that code for the parts of glycolysis and c-myc oncogene.

B7-H3 and Jak2/Stat3 signaling pathway

The Jak2-Stat3 pathway serves a pivotal role in the biological functions of many human cancer cells such as migration, invasion, and metastasis. Studies have been reported B7-H3 as a crucial modulator of the Jak2-STAT3 signaling pathway. Such as overexpression of B7-H3 could via upregulating Jak2-STAT3 signaling reduced apoptosis of colorectal cancer cell lines. Silencing the B7-H3 expression can inhibit the migration and invasion of HCC cells via the Jak2/Stat3/Slug signaling pathway, which was demonstrated by Kang et al. Moreover, B7-H3 silencing confers to increase the responsivity of breast cancer cells to paclitaxel as a result of increasing drug-triggered apoptosis both in vitro and in vivo, and the mechanism may be associated with B7-H3 interfering with Jak2/Stat3 pathway.

Epithelial-mesenchymal transition (EMT) process involves a series of rapid changes in the cellular phenotype during which epithelial cells go through a molecular transformation from a polarized, epithelial phenotype to a highly active, non-polarized mesenchymal phenotype. EMT is a key event for cancer cells to acquire the ability to migrate and invade, which is frequently observed at the invasive front of advanced tumors and has a closely correlated with metastasis in tumor progression.

JAK2/STAT3 signaling pathway is essential for regulating the cytokine and growth factor-mediated reactions of EMT in cancer. In human salivary adenoid cystic carcinoma (AdCC), researchers characterized B7-H3 expression in AdCC tissue microarrays using immunohistochemical staining, and analyzed potentially related molecules. The results showed that B7-H3 was strongly associated with Slug and p-STAT3, which are key factors in EMT and JAK2/STAT3 signaling pathway. Further mechanism studies indicated that B7-H3 affects the migration, as well as infiltration of AdCC cells by regulating the EMT through JAK2/STAT3 axis components. No doubt, this novel discovery is crucial for studying tumor biological function.

B7-H3 and NF-κB signaling pathway

NF-κB is an extensively studied dimeric transcription factor triggered by various stimuli entailing inflammatory cytokines, lipopolysaccharides, etc. NF-κB activation is moderated by the secretion from the IκB repressive proteins, which maintain NF-κB generally in the cytoplasm. NF-κB activation leads to the induction of various genes that affect cellular proliferation, inflammation, and adhesion. Therefore, the activation and activity of NF-κB are strictly regulated by a series of endogenous mechanisms. In the NF-κB cascade, B7-H3 is a potent positive regulator. Exogenous B7-H3 remarkably escalates the bioactivity of NF-κB, enhances the migration, as well as
invasion of pancreatic cancer cells, and ultimately promotes the expression of IL-8, as well as VEGF.65 On the contrary, knocking down B7-H3 remarkably decreased the phosphorylation level of NF-κB in HCT116 and RKO cells. In addition, rB7-H3 up modulates the expression of VEGFA through the NF-κB pathway-dependent manner to promote tumor angiogenesis.66 In addition, in HSGE cells, B7-H3 can increase the inflammatory response and induce apoptosis through the NF-κB pathway.67

**B7-H3 and other signaling pathway**

In addition to the PI3K-Akt, Jak2/Stat3, and NF-κB signaling pathways, B7-H3 can impact pathological and physiological processes by interacting with other signaling pathways. B7-H3 can influence pathological and physiological processes by contacting with other signaling pathways. Fang showed that B7-H3 is involved in monocyte/macrophage-mediated inflammatory responses by enlarging p65, LPS, and MAPK p38 signaling.68 Qing et al., have demonstrated that B7-H3 could promote myeloma cells survival and proliferation via a ROS-dependent signaling pathway.69 B7-H3 has also been shown to increase the contents of reactive oxygen species (ROS) and HIF-1α to promote glycolysis in melanoma.70 In addition, B7-H3 overexpression in lung cancer leads to aberrant lipid metabolism through SREBP-1/FASN signaling cascade.71 Furthermore, B7-H3 could affect the metastasis of tumor cells through connection with signaling pathway. VEGF is a key angiogenic factor in various human cancers that plays a critical role in the metastasis of solid tumors.72–74 Strong intensity of B7-H3 could remarkably lead to low expression of VEGF, as well as MVD in breast carcinoma cells. On the contrary, knocking down B7-H3 increased the mRNA and protein secretion of VEGF secretion.7 Therefore, B7-H3 serves an important role in a wide range cancers, and its biological function could be strongly connected with different signaling pathways. The molecular mechanism of B7-H3 needs further investigation.

**B7-H3 in DSC**

Numerous studies have been performed on the expression and role of B7-H3 in DSC (Table 1). Lots of tissue microarray, as well as immunohistochemical data indicated that B7-H3 is strongly expressed in EC, HCC, GC, PC, as well as CRC. Moreover, B7-H3 is also highly expressed in the serum of HCC and CRC patients.19,74 Therefore, B7-H3 might be a potential specific biosignature and prognostic factor for DSC.

**EC**

EC is the eighth most often occurring cancer and the sixth extensive cause of cancer-related fatalities.75 Studies have shown that B7-H3 plays a key role in esophageal cancer growth and metastasis. Wang found that B7-H3 expressed in 90.6% of esophageal squamous cell carcinoma (ESCC) samples.8 Silencing B7-H3 can effectively suppress the migration and invasion of ESCC cell. Moreover, a study by Chen group showed the strong intensity of B7-H3 in ESCC tissues was closely connected with strong tumor cells invasion, and knocking down of B7-H3 could suppress the proliferation, colony formation, migration and invasion of ESCC cell lines.9 In addition, higher B7-H3 expression was remarkably linked to poorer survival outcomes of ESCC.9,76 B7-H3 and B7-H4 combined expression was directly and remarkably linked to the tumor infiltration depth, TNM stage, and recurrence rate of postoperative, which can be used as a potential prognostic marker in ESCC.76 These result show the useful diagnosis and prognostic indicators role of B7-H3 in ESCC.

**GC**

GC, one kind of GI cancer, is responsible for about 8.6% of newly diagnosed cancer cases globally and is the third highest cause of cancer fatalities.3 There are a total of three studies on B7-H3 expressions in GC.10,11,77 Wu firstly reported in 2006 that B7-H3 expression in gastric carcinoma tissue,10 58.8% of GC patients in a series of 102 patients were reported to express B7-H3 in the cell membrane and cytoplasm. Studies by Dai et al, found that B7-H3 account for 84.3% (27/32) of gastric carcinoma samples, while the B7-H3 expression in normal GC samples was very low.77 The expression of B7-H3 was also directly linked to metastasis, survival time and invasion depth of gastric carcinoma.11 Dai et al. conducted a wound scrape assay to assess cell motility, a transwell invasion assay to test cell invasiveness of gastric cancer cell line SGC-7901, the results indicated that B7-H3
| Cancer type | Number of patients | % Positive | Expression isoform | Clinical significance | Bad/Good | Ref |
|-------------|--------------------|------------|-------------------|----------------------|----------|-----|
| ESCC        | 66                 | 90.6       | Membrane          | Higher tumor B7-H3 associated with advanced TNM stage and lymph node metastasis | Bad      | Fan et al.61 |
| GC          | 102                | 58.8       | Membrane and cytoplasm | Postive B7-H3 expression correlates with better survival time of patients, infiltration depth and histology type of tumor | Good     | Perkins 64 |
| GC          | 32                 | 84.3       | Membrane          | B7-H3 promotes cancer cell migration and invasiveness via non-immunomechanisms | Bad      | Xie et al.65 |
| HCC         | 149                | 76.5       | Souble isoform    | Serum sB7-H3 levels can be considered an index for the differential diagnosis of cirrhotic patients with and without ESHCC | Bad      | Wu et al.60 |
| HCC         | 225                | 93.8       | Membrane and cytoplasm | B7-H3 serves as an independent prognostic factor for recurrence | Bad      | Arigami et al.11 |
| HCC         | 70                 | 88.57      | Membrane and cytoplasm | Positive B7-H3 promote cancer cell growth, adhesion, migration, and invasion | Bad      | Li et al.67 |
| PC          | 59                 | 93.2       | membrane and cytoplasm | B7-H3 expression was significantly more intense in cases with lymph node metastasis and advanced pathological stage. | Bad      | Fang et al.68 |
| PC          | 26                 | 65.38      | Membrane and cytoplasm | B7-H3 may regulate tumor progression by promoting cell migration and invasiveness via non-immunomechanisms | Bad      | Lin et al.69 |
| PC          | 150                | 66         | Membrane          | High B7-H3 expression is independently associated with poor survival in patients and that this association is stronger in tumors with p-stage I–II than in those with p-stage III–IV. | Bad      | Lim et al.70 |
| PC          | 68                 | 88.2       | membrane and cytoplasm | Patients with high tumor B7-H3 levels had a significantly better postoperative prognosis, and B7-H3 expression significantly correlated with the number of tumor-infiltrating CD8+ T cells | Good     | Luo et al.71 |
| CRC         | 102                | 54.3       | Membrane and cytoplasm and souble isoform | B7-H3 expression was significantly correlated to patient’s tumor grade and negatively associated with the intensity of infiltrating T lymphocytes both in tumor nest and in tumor stroma | Bad      | Dvorak et al.74 |
| CRC         | 275                | 72         | Membrane and cytoplasm and nuclear | Nuclear of B7-H3 was strongly and independently associated with reduced metastasis-free, disease-specific and overall survival in colon cancer patient | Good     | Chen et al.76 |
| CRC         | 223                | 70.4       | Membrane and cytoplasm | High expression of B7-H3 was identified as a significant independent predictor of poor overall survival | Bad      | Dai et al.77 |
plays a crucial role in tumor migration and invasion. The results were also confirmed in orthotopic transplantation GC mouse model. In addition, bioinformatics research found that the content of B7-H3 mRNA in blood samples of GC patients was significantly higher than that of healthy volunteers without cancer, and the 5-year survival rate of individuals with high expression of B7-H3 was remarkable lower than that of patients with low expression. Collectively, these data provide new insights into the function of B7-H3 in GC and may have putatively significant implications for future gastric cancer immunotherapy.

**HCC**

HCC is the 5th most frequent cancer globally, making it the second principal cause of cancer-linked fatalities. Although the HCC therapy tends to be diverse and comprehensive, it is challenging to achieve further advancements in the long-term survival of HCC patients in the last 10 years. Wang et al. research indicated that B7-H3 is abnormally high expressed in HCC tissues and cells, and its aberrantly expression is significantly linked to the poor clinical prognosis. Similar conclusions were drawn by Sun group. The team found that 17 of 24 (70.8%) HCC tissues had B7-H3 upregulation, and it was remarkably correlated with the risk of relapse and severe clinicopathologic characteristics in a cohort of 240 HCC individuals undergoing curative resection. The data were further verified in an independent cohort of 206 HCC patients. Zhao showed that sB7-H3 was very low in the serum of healthy donors, as well as hepatitis patients, while cirrhotic patients with HCC had abundantly increased in the level of sB7-H3. In addition, the sB7-H3 in serum can be an attractive biosignature for non-invasive diagnostic of HCC. In early-stage hepatocellular carcinoma (ESHCC), the significance of circulating sB7-H3 as a diagnostic biosignature was studied in parallel with other tumor biosignatures, including AFP, CA199, as well as CA125, and the result showed that serum sB7-H3 sensitivity and specificity are better than the other options for distinguishing between patients with and without ESHCC. Numerous studies are required to compare the performance and specificity of different tumor markers, and to establish which marker is most appropriate for clinical diagnosis.

**PC**

PC, a highly fatal disease and remains the lowest of 5-year relative survival rate for all cancers, is commonly diagnosed at an advanced stage and there is almost little effective treatment. Numerous studies have found that tumor-linked B7-H3 expression was enriched in most human PC tissues, which was low or no in healthy tissue or normal pancreas. For example, the B7-H3 expression in 59 PC tissues was detected by immunohistochemistry, and the results showed that 55 patients (93.2%) had positive staining on the cell membrane, as well as in the cytoplasm of cancer cells, while only four patients (6.8%) did not have B7-H3 staining. Zhao showed that more than 50% (17/26) of PC specimens were positively stained for B7-H3 expression, while no B7-H3 was detected in normal pancreas specimens. In addition, published data showed that B7-H3 expression is linked to survival in patients with PC and can be as a speculative stimulator of antitumor response in PC. Loos et al. found that high expression of B7-H3 had a better postoperative prognosis relative to patients with low levels of B7-H3. Kentaro et al. demonstrated that B7-H3-positive tumors were correlated with lower DFS and lower overall survival in PC, and that this relationship is stronger in tumors with p-stages I and II relative to those with p-stages III–IV. B7-H3 expression could be a useful potential stimulator of antitumor response and prognostic biosignature for identifying early-stage PC.

Besides, CAR T cells targeting B7-H3 have been found to be effectively control the growth of pancreatic ductal adenocarcinoma (PDAC). Du group showed that B7-H3 CAR-T particularly recognized tumor cells and promoted tumor cell apoptosis in five human PDAC cell lines that express B7-H3, and similar conclusions were drawn in PDAC xenograft mice models and PDAC patient-derived xenograft (PDAC-PDX) tumor models. This provides a new direction for immunotherapy of pancreatic cancer.

**CRC**

CRC ranks third regarding incidence and second in terms of fatalities malignant tumor. There were more than 1.8 million new CRC patients and 881,000 deaths in 2018. Although the diagnosis
and therapeutic strategies for CRC have been improved, 5-year survival rate is still poor. Therefore, it is imperative to identify novel markers and explore new treatment strategies for CRC to improve diagnosis and prolong survival. Sun et al. indicated that the level of B7-H3 in 102 pathological samples of colorectal cancer patients increased significantly relative to the control group, and the B7-H3 expression was inversely linked to the strength of invading T lymphocytes both in tumor nest and in tumor stroma. Moreover, the content of B7-H3 was associated with the prognosis of CRC. Ingebrigtsen reported the B7-H3 expression in tumor-associated vasculature and fibroblasts in the majority of samples, and nuclear B7-H3 expression was independently and remarkably correlated with diminished metastasis-free, disease-distinct and overall survival. The same conclusion was confirmed by Zhang et al. All the findings reveal that B7-H3 might participate in the progression and metastasis of colon cancer, B7-H3 may be a useful prognostic biosignature in colon cancer. Of course, large-scale experiments are needed to verify this conclusion.

Conclusion

Since the B7-H3 was discovered, the field of exploring its impact on DSC has been extremely active and rapidly advancing. The differential expression of B7-H3 in DSC and normal tissues makes targeting of B7-H3 particularly attractive. The levels of B7-H3 are strongly related to the aggressive and metastasis of tumor cells. This makes, B7-H3 expression could predict therapy outcome, inhibition or reduction of B7-H3 protein expression in tumors cells could decrease proliferation. In addition, B7-H3 plays an important role in the coinhibitory and costimulatory T cells, indicating the potential usage of this pathway for cancer immunotherapy.

Previous studies have shown that construction of CAR modified immune cells targeting B7-H3 seems to be an attractive therapeutic strategy, but it still faces many challenges, such as the suppressive of solid tumor microenvironment and lack of persistence of CAR-T cells within the body. These obstacles may inhibit T cells trying to move into the tumor cells and influence the dampen the functionality of this method. Therefore, research on B7-H3 from laboratory to clinical still has many technical bottlenecks, and the mechanism of B7-H3 in the process of DSC has not been thoroughly explained and more studies are needed.

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