ISSN: 2690- 912X

Research Article

Journal of Genetic Engineering and Biotechnology Research

Trop2: A Key Player in Oncology - From Research to Clinical Application

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Submitted:2023, July 03; **Accepted:**2023, July 25; **Published:**2023, Aug 30

Citation: Toumi, M., Mathe, I., toth, A., Sztrada, N., Farkas, R et.al. (2023). Trop2: A Key Player in Oncology - From Research to Clinical Application. *J Gene Engg Bio Res, 5*(2), 124-132.

Abstract

This abstract presents an overview of Trop2, a cell surface glycoprotein, and its significance in cancer research. Trop2, also known as tumor-associated calcium signal transducer 2, exhibits minimal expression in healthy tissues but is highly expressed in various malignancies, such as breast, colon, and pancreatic cancer. The level of Trop2 expression directly correlates with the prognosis of these tumors. This glycoprotein plays a pivotal role in tumor cells' self-renewal, proliferation, invasion, and transformation, making it a crucial molecular marker for detecting tumor malignancy and a potential target for tumor therapy. The review comprehensively explores Trop2's structure and physiological functions, shedding light on its association with different types of tumors. Additionally, it delves into the advancements in drug development targeting Trop2, with several promising drugs already undergoing clinical trials. By examining Trop2's role in cancer biology and its potential as a therapeutic point of intervention, this review contributes to the current understanding of Trop2 as a biomarker and a target for innovative cancer treatments.

Keywords: Trop2, Cell Surface Glycoprotein, Malignancies, Proliferation, Invasion, Transformation, Molecular Marker, Tumor Therapy, Drug Development, Clinical Trials.

1. Introduction

Tumor-associated calcium signal transducer 2 (TACST2) is another name for T2 (Tumor-Associated et al. Factor 2). As an alternative, the TACSTD2 gene encodes a member of the TACSTD protein family called the gastrointestinal tumor-associated antigen (GA733-1), a cell surface glycoprotein [1]. Trop2 is crucial in embryonic development and is mainly expressed in epithelial cells [2]. Generally speaking, Trop2 is not present or expressed at low levels in normal tissues but is substantially expressed in several malignant tumors, including prostate cancer ovarian cancer colon cancer pancreatic cancer and gastric cancer [3-7]. According to studies, Trop2 is essential for controlling the self-renewal, proliferation, and transformation of tumor cells [8]. Additionally, the growth and malignancy of different cancers are linked to Trop2 expression. It is a possible target for tumor treatment and a marker for clinically identifying tumor malignancy [9]. Antibody-drug-conjugate drugs (Antibody-drug-conjugate) sacituzumabgovitecan (IMMU-132) can be used to treat a variety of epithelial malignancies, including small cell lung cancer, breast cancer (triple negative breast cancer), and ovarian cancer. In recent years, some progress has been made in the study of TROP2-targeting tumor therapy.

It has now entered the stage of clinical trials [10]. This paper reviewed the structure, physiological function, relationship between Trop2 and tumor and the development of related drugs.

2 Structure and physiological function of Trop2

2.1 Structure of Trop2

The Trop2 protein, encoded by the 1p32.1 locus on the short arm of chromosome 1, is a 323-amino-acid single-transmembrane surface glycoprotein produced by N-terminal glycosylation modification after translation [11,12]. Trop2 has a cytoplasmic tail that contains the highly preserved phosphatidylinositol 4,5-biphosphate, PIP2 binding sequence, tyrosine, and serine phosphorylation sites. Trop2 also has extracellular domains, transmembrane domains, and hydrophobic precursor peptides. Trop2 is anchored to the cell membrane as a result of its unidirectional transmembrane domain (TM), which links the N-terminal ectodomain (EC) with the intracellular peptide (IC) [13]. The thyroglobulin type I domain, a

cysteine-deficient domain, and a tiny disulfide bond-rich domain in Trop2 EC allow Trop2 EC to form a stable dimer [14]. Nuclear magnetic resonance spectroscopy (NMR) to evaluate the structural differences between the phosphorylated and unphosphorylated forms of Trop2 [15]. The findings indicated that phosphorylation of Trop2 IC would result in the recombination of salt Bridges. The conformation of functional areas, notably the C-terminal arrangement, is significantly altered as a result, and these structural characteristics may be required for controlling Trop2 activity. The cytoplasmic tail sequence of human Trop2 protein and mouse Trop2 protein is highly conserved, with only a 3 amino acid difference, and the sequence consistency between the two proteins is 84%. Trop2 has a high structural similarity to epithelial cell adhesion molecule (EpCAM), with 48% sequence homology between Trop2 and EpCAM. At present, the crystal structure of the dimer in the extracellular domain of EpCAM has been analyzed, and based on this, it is speculated that Trop2 can form a similar dimer structure.

2.2 Expression and function of Trop2

Trop2 has low expression in normal tissues such as kidneys, ovaries, and lungs but high expression in various malignant tumors [16]. Indirect immunofluorescence and flow cytometry were used to detect the reactivity of Trop2 monoclonal antibody against multiple target cells. It was found that Trop2 was highly expressed in trophoblast cells during human embryonic development and played an essential role in embryonic development. MadinDaby canine kidney cells (MDCK) stably expressing Trop2 were established using retrovirus vectors and compared with primary cultured ureteral bud cells. The results showed that the expression of Trop2 can inhibit the proliferation and migration of MDCK cells on type I collagen. The high expression of Trop2 is essential for stimulating tumor growth. Analysis of the Trop2 transcription network showed that all transcription factors were closely related, among which HNF4A (hepatocyte nuclear factor 4 alpha) transcription factor was most closely related to all signaling pathways and played an essential role in the growth of stem cells. Most noteworthy is that 20 out of 36 molecules in its transcriptional network are related to tumor and tissue development. For example, wilm tumor gene 1(WT1) is essential in urogenital system development and tumor development [17]. In the study on the expression of receptors on the surface of human prostate cancer cells, Trop2 was found to be distributed in the basal layer and lumen layer of both malignant and benign glands but highly expressed in malignant tumors, indicating that Trop2 could be used as a marker of human prostate cancer stem cellsas shown in figure 1.

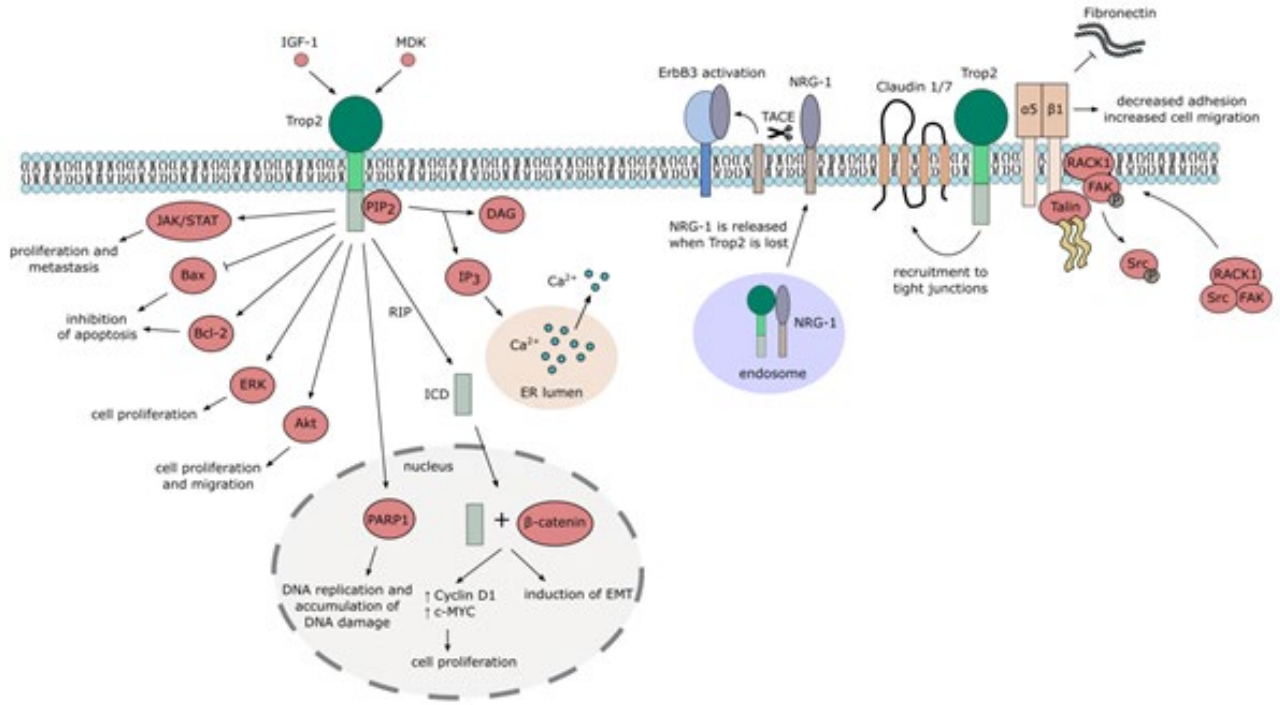

Figure 1: Interactions and signaling of Trop2 with membrane-associated proteins.

2.3 Signal transduction of Trop2

The critical signaling molecules that control the formation of tumors are found on cell surfaces. Some anti-tumor medications are already available that target cell surface receptors, such as PD-1 (programmed death-1), Her2 (human epidermal growth factor receptor 2), and CD33. Recent research has revealed a novel cell surface receptor called Trop2 that plays a role in the genesis and growth of cancers by regulating cell proliferation and apoptosis and mediating various signaling pathways. Trop2 is up regulated in the majority of human malignant tumors.

2.3.1 The expression of Trop2 can mediate the ERK-MAPK signaling pathway

The MAPK pathway's ERK subfamily member is essential for the signaling process that sends information from receptors on the surface to the nucleus [18]. Activator protein 1, or AP-1, is a transcription factor found downstream of the ERK-MAPK signaling pathway. This system regulates extracellular signal-regulated and mitogen-activated protein kinases (MAPK and ERK). Using flow cytometry and genetic tests, the researchers examined 293T cells transfected with a lentiviral vector encoding the secreted alkaline phosphatase (SEAP) reporter gene and the mTrop2 gene. The synthesis of the AP-1 transcription factor was indicated by an increase in SEAP release and a rise in Trop2 expression levels compared to the control group. This data suggests that the MAPK signal can be activated due to Trop2 expression. Through raising the expression of Cyclin D1 and Cyclin E and up-regulating the level of phosphorylated ERK1/2, Trop2 promotes tumor growth and metastasis by controlling the cell cycle process. Additionally, the ERK-MAPK signaling pathway can be activated by the elevated levels of Trop2 in human pancreatic duct epithelium cells and colorectal cancer cells.

In addition, researchers found in cervical cancer cells that the increase of Trop2 expression could not directly promote the increase of ERK1/2 expression but promote the proliferation of tumor cells by up-regulating the phosphorylation of ERK1/2 [19].

2.3.2 Trop2 mediates the IGF-1R signaling pathway

In lung cancer cells, Trop2 forms a complex with insulin-like growth factor-1 (IFG-1) that activates downstream PIP2 and Ca2+, Regulate the signal of insulin-like growth factor 1 receptor (IGF-1R) and weakens the IGF-1R signaling pathway. In the tumor microenvironment, the thyroglobulin type I domain of the extracellular segment of Trop2 binds to IFG-1 to form a complex, blocks the binding of IFG-1 and IFG-1R, inhibits the activation of β-catenin/slug gene expression mediated by IGF-1R signal, and thus mediates the proliferation and migration of tumor cells [20]. Western blot and human photoreceptor tyrosine kinase array detection showed that the levels of phosphorylated IGF-1R and anaplastic lymphoma kinase (ALK) in HeLa cells of the cervical cancer cell line with Trop2 knockout were up regulated. Utilizing co-immunoprecipitation and protein-protein affinity prediction, it was found that Trop2 protein was in the same protein complex with IGF-1 and midkine (MDK), and the predicted binding free energy between Trop2 and IGF-1 was -10.11 kcal/mol. The predicted binding free energy between Trop2 and MDK is -12.46 kcal/mol, indicating that Trop2 may interact directly with IGF-1 and MDK [21].

2.3.3 Trop2 Promotes Tumor Proliferation through PI3K/AKT Signaling Pathway

AKT's protein kinase B (PKB) signaling pathway is started by upstream activation phosphorylation. Phosphorylation at T308 and S473 is essential for AKT activation and kinase catalytic activity, as well as for apoptosis, the cell cycle, cell proliferation, and cell differentiation. Phosphatidylinositol 3,4,5-trisphosphate (PIP3) is produced when the growth factor binds to receptor tyrosine kinase, which in turn activates phosphatidylinositol 3-kinase catalytic subunit alpha (PIK3CA) and causes its translocation to the cell membrane. The PI3K/AKT signaling pathway is activated when PIP3 binds AKT to the plasma membrane and pyruvate dehydrogenase kinase 1 (PDK1) phosphorylates AKT at T308. In both in vitro and cancer model organisms, Trop2 and AKT expression in human breast cancer are closely synchronized. Trop2 expression can over-phosphorylate glycogen synthase kinase 3 (GSK3) and promote AKT phosphorylation at T308 and S473, which increases Cyclin D1 levels and speeds up the cell cycle.

Additionally, allosteric inhibitors of AKT only slow the growth of tumor cells that express Trop2 in preclinical models; they do not affect tumor cells that do not express Trop2 [22]. High levels of Trop2 expression in ovarian cancer and other malignancies have been shown to stimulate the proliferation and migration of tumor cell lines by activating the PI3K/AKT signaling pathway. Consequently, one of the targets of cancer treatment may be the Trop2/PI3K/AKT signaling pathway.

3 The Role of Trop2 in Tumorigenesis and Development

A prognostic diagnostic for many cancers, high expression of Trop2 is linked to shorter survival and a bad prognosis in patients with multiple tumors. Trop2 is a signal transducer that communicates with cells in various ways, and a complex network of transcription factors controls its transcription. Its increased expression has been shown to accelerate the growth of tumors, and its suppression can slow the proliferation, migration, and invasion of tumor cells, indicating that Trop2 may have a role in the incidence and growth of cancers.

3.1 Trop2 and Breast Cancer

The immunohistochemical examination for Trop2 expression in 288 breast cancer patients revealed a 62.85%(181/288) positive expression rate of Trop2 in breast cancer cells, which was significantly higher than that of benign breast tumors (18.75%, 9/48) and healthy breast tissues (12.5%,6/48). Systematic investigation of the level of Trop2 expression in tumor tissues and the clinicopathological characteristics of the patients revealed a strong correlation between the expression of Trop2 and the clinical

stage, short survival time, and poor prognosis of the patients [23]. Using qRT-PCR and immunohistochemistry methods, Trop2 and epithelial cadherin (vacherin) expression at the mRNA and protein levels was found in cancer tissues and surrounding tissues. The relationship between gene expression levels and the clinicopathological traits of patients was then examined. In breast cancer, Trop2 expression increased, whereas E-cadherin levels dropped. E-cadherin expression was downregulated at a rate of 70.8% (68/96), 51.3% (102/199), and 22.0% (13/59) in triple-negative breast cancer with high Trop2 expression, breast cancer with low TROP2 expression, and nearby tumor tissues, respectively. Furthermore, lymph node status, metastasis, TNM staging, and survival were substantially linked with high Trop2 and low E-cadherin expression. In conclusion, Trop2 may facilitate the down-regulation of E-cadherin expression, preventing cell death and senescence and promoting tumor cell invasion and dissemination, ultimately causing the epithelial-mesenchymal transition (EMT) [24].

3.2 Trop2 and Pancreatic Cancer

Immunohistochemical analysis of 199 paraffin-embedded primary tumor specimens of pancreatic cancer patients showed that Trop2 was highly expressed in about 55% of the patients. The expression of Trop2 significantly affected the clinicopathological characteristics of patients. The median survival time (MST) of pancreatic cancer patients with high expression of Trop2 and those without high expression of TROP2 was 8 months and 14 months, respectively. Meanwhile, the high expression of Trop2 accelerated the progression of pancreatic cancer, and 27% of patients could not receive surgical treatment due to the high degree of malignancy of the tumor. In patients treated with surgery, overall survival (OS) and progression-free survival (PFS) were significantly reduced in patients with high Trop2 expression. This evidence indicates that high expression of Trop2 is related to the occurrence and malignancy of pancreatic cancer, can significantly shorten the survival of patients and lead to poor prognosis, and maybe a new prognostic biomarker. Trop2 could be a potential target protein of photo immunotherapy (PIT) through immunohistochemical studies. Subsequently, the researchers prepared a new photosensitizer-coupled humanized antioxidant IR700 (Trop2-IR700) for photo immunotherapy [25]. In vitro cultured pancreatic cancer cells, it can be observed that Trop2-IR700 can specifically target tumor cells and kill cells after irradiation with near-infrared light. When this monoclonal antibody was injected intravenously into mice, TROP2-IR700 significantly inhibited tumor growth in mice, demonstrating the effectiveness of targeted Trop2 in treating pancreatic cancer.

3.3 Trop2 and Non-Small Cell Lung Cancer

Trop2 is either not expressed at all or substantially expressed in lung cancer tissues compared to normal lung tissues. 164 non-small cell lung malignancies, comprising 64 lung squamous cell carcinomas and 100 lung adenocarcinomas, were examined using immunohistochemistry on tissue chips, and it was discovered that Trop2 was strongly expressed in 64.1% (41/64) of the lung squamous cell carcinomas and 23% (23/108) of the lung adenocarcinomas. The high expression of Trop2 is highly connected with the pathological T stage in lung squamous cell carcinoma, and it tends to increase patients' OS. The high expression of Trop2 in adenocarcinoma of the lung tissues is solely associated with tumor differentiation and has no relation to lymph node metastasis, pathological T stage, or TNM stage. Moreover, the high expression of Trop2 has a positive effect on OS and PFS in lung adenocarcinoma patients, especially in stage II and III patients. This indicates that Trop2 may be involved in cell-cell adhesion in lung cancer tissues, and its loss will promote the shedding of tumor cells.

Pathogenic grade and patient survival increased, and Trop2 expression is associated with [26]. High Trop2 expression can encourage cell proliferation, migration, and invasion in the lung cancer cell line A549. Contrarily, high levels of Trop2 expression in PC-9 cells can prevent cell death and obliterate cell proliferation, migration, and invasion, indicating that Trop2 could be used as a target for future tumor therapies [27].

3.4 Trop2 and Prostate Cancer

Immunohistochemical analysis of the expression of Trop2 from mRNA and protein levels showed that Trop2 was highly expressed in human prostate cancer tissues and was mainly expressed in the basal layer of prostate epithelial cells. In mouse models, high expression of Trop2 can stimulate the growth of tumor cells, leading to shortened survival and poor prognosis of patients [28]. It was found that Trop2 can induce phosphorylation of focal adhesion kinase (FAK) and promote the accumulation of receptors for activated c-kinase 1(RACK1) on the cell membrane. Resulting in beta (1) integrin-Rack1-faK-src (integrin beta 1-receptor for activated c-kinase 1-focal adhesion kin-src) tyrosine kinases (tyrosine kinases) signaling pathways are activated, thereby inhibiting the adhesion of prostate cancer cells to fibrin and promoting tumor metastasis [29]. DNA methylation-specific qRT-PCR analysis of 19 prostatic intraepithelial neoplasia (PIN) and 35 prostate tumor tissue samples showed that Trop2 methylation was not found in 19 PIN tissue samples. Trop2 hypermethylation was observed in 6 out of 35 prostate tumor tissue samples. Because Trop2 is highly methylated in prostate tumors and not in PIN, Trop2 is expected to become a potential target for emerging methylation-based prostate cancer detection or diagnosis [30].

3.5 Trop2 and Other Tumors

Trop2 is highly expressed in common malignant tumors such as cervical, gastric, colon, and ovarian cancers. It is related to histological grade, prognosis, proliferation, migration and invasion of tumor cells. The high expression of Trop2 in cervical cancer cells increases the expression of Cyclin D1, CyclinE, CDK2 (cyclin-dependent kinase 2) and CDK4, activates the ERK1/2 signaling pathway, and decreases the expression of p27 and E-cadherin. Thus promoting tumor cell growth, invasion and metastasis [25].

In ovarian cancer, after the decrease of Trop2 expression, the expression of BCL-2(B-cell lymphoma) is down-regulated, and the expression of BCL2-associated X (Bcl2-associated X) is up-regulated, suggesting that Trop2 may be involved in the occurrence and development of tumors by disrupting the balance of Bax/BCL-2. The molecular mechanism of Trop2 promoting EMT in gastric cancer cells through in vivo and in vitro experiments and found that inhibiting the expression of Trop2 in gastric cancer tissues could prevent the migration and invasion of gastric cancer cells in vivo.

4 Anti-tumor drugs targeting Trop2

Currently, the research direction of anti-tumor drugs targeting Trop2 mainly includes antibodies and ADC drugs targeting Trop2. As of January 2020, 6 anti-tumor drugs targeting Trop2 have entered the clinical trial research stage, and these 6 drugs are introduced in Table 1. The only one to reach Phase III is sacituzumab govitecan (IMMU-132), developed by Immunomedics, which treats triple-negative breast cancer.

Sacituzumab govitecan	Phase I/II/III	Targeted binding of Trop2 and internal ization of active metabolite SN-38 of irinotecan into tumor cells for killing	Urinary reproductive system cancer, prostate cancer, breast cancer, endometrial carcinoma, etc.	Humanized Trop2 monoclonal antibody hRS7 IgG1Kcoupling of SN-38
111In-IMP-288	Phase I/II	Combined with bispecific antibody TF12, it can quickly target tumors and kill them	Metastatic colorectal cancer	IMP-288 peptide containing DOTA bound to 111In was radiolabelled
SKB-264	Phase I/II	Combined with Trop2 extracellular segment, toxic small molecules were located in tumor cells for cell killing	Ovarian epithelial carcinoma, gastric adenocarcinoma, pancreatic adenocarcinoma, triple negative breast cancer, bladder cancer	Trop2 monoclonal antibody coupled with toxic small molecules
BAT8003	Phase I	Maytansine was localized to tumor cells in combination with the extracellular segment of Trop2 for cell killing	Trop2 positive advanced epithelial carcinoma, such as breast cancer, gastric cancer, non-small cell lung cancer, etc.	Recombinant humanized Trop2 monoclonal antibody is conjugated with metropin
DS-1062	Phase I	Topoisomerase I inhibitors were targeted to tumor cells to kill tumor cells by affecting DNA replication	Non-small cell lung cancer	Trop2 humanized monoclonal antibody coupled with DXd (topoisomerase I inhibitor)
DAC-002	Clinical application was accepted	Antitubulysin B analogues are targeted to tumor cells in combination with Trop2 extracellular segments to kill tumor cells through microtubule depolymerization	Triple negative breast cancer, small cell lung cancer, non small cell lung cancer, pancreatic cancer	Recombinant humanized Trop2 monoclonal antibody coupled with antitubulysin B analogue Tub196

Table 1: Trop2-Targeting Drug Entering the Clinic

4.1 Sacituzumab govitecan (IMMU-132)

The innovative ADC medication sacituzumab govitecan (IMMU-132), also known as sacituzumab, is made up of a humanized anti-TROP2 antibody (hRS7) that targets Trop2 and the active irinotecan SN-38 metabolite. Sacituzumab is an epithelial cancer drug that is effective in treating a wide range of epithelial tumors, including triple-negative breast cancer, cancer of the gastric tract, non-small cell lung cancer, pancreas cancer and prostate cancer [31-35]. The FDA approved sacituzumab's marketing application on December 26, 2019; its indication is triple-negative breast cancer. Currently, sacituzumab clinical studies for treating different solid tumors are in phases I, II, and III. The objective response rate (ORR) for sacituzumab in 110 patients with triple-negative breast cancer was 34% (37/110), according to clinical data published by Immunomedics. Three experienced complete remission (CR), and 34 experienced partial remission (PR). The clinical benefit rate, or CBR, was 46% (defined as CR+PR+SD (stable disease)>6 months). PFS was 5.5 months, OS was 12.7 months, and the median response duration (mDOR) was 7.6 months. Of these, 11 patients had longer PFS and superior treatment results, ranging from 12 to 30 months [36-39].

Panitumumab combined with three PARP (poly ADP-ribose polymerase) inhibitors (olaparib, olaparib or talazoparib) could effectively inhibit tumor growth [40-44]. In a mouse model of breast cancer, panitumumab combined with olaparib or talazoparib significantly enhanced the anti-tumor ability. It delayed the time of tumor progression in mice compared with monotherapy. At the same time, the total number of white blood cells, lymphocytes, and other blood parameters were not significantly changed by the detection of blood concentration of the combined drug, indicating that the combined drug had no blood toxicity. Studies

of sacituzumab in combination with PARP inhibitors have also entered Phase I/II.

4.2 TF12 is combined with 111In-IMP-288

TF12 is a double-specific antibody that can be used to target various malignancies. It comprises two anti-TROP2 Fab segments and one anti-histamine-Succinyl-Glycine (HSG) Fab fragment. Tetraazacyclododecane-1,4,7,10-tetracarboxylic acid is the source of 111In-IMP-288. It is a radiolabelled hapten peptide with the structural formula DOTA-D-Tyr-DLys (HSG)-D-Glu-DLys(HSG)-NH2, typically employed with TF12. The effects of different doses and administration intervals of TF12 and 111In-IMP-288 on drug intake were analyzed in a mouse prostate cancer model. The results showed that when the injection dose of TF12 was ≥ 2.5nmol and the injection dose of 111In-IMP-288 was ≤ 0.1nmol, Tumors had the highest drug intake, and the optimal interval of administration of TF12 and 111In-IMP-288 was 16 h. pre-targeted radioimmunotherapy (PRIT) was used to analyze the combination therapy and monotherapy, and it was found that the combination therapy could significantly prolong the survival of patients compared with monotherapy. Experiments have shown that under certain optimized conditions, TF12 and 111In-IMP-288 can still make the radiolabeled hapten peptide rapidly and efficiently accumulate in the tumor after 1 h of drug injection. At the same time, the detection of blood concentration showed that 111In-IMP-288 could be rapidly absorbed into bone marrow without blood toxicity, which indicates that the combination of TF12 and 111In-IMP-288 May be applied to prostate treatment in the future [45-49]. In addition, the combination of TF12 and 111In-IMP-288 for treating metastatic colorectal cancer has entered the clinical phase I/II study.

4.3 Other anti-tumor drugs

DS-1062 is a novel ADC drug with a human monoclonal conjugate topoisomerase I inhibitor (Dxd) against Trop2. In published Phase I clinical data, 12 of 40 patients with advanced non-small cell, carcinoma (after repeated treatment including EGFR, ALK inhibitors, and immune checkpoint inhibitors) achieved a partial response, of which 10 have been confirmed, and 2 require further confirmation of efficacy [50-52]. At the same time, DS-1062 and Trop2 monoclonal antibodies were similar in plasma, indicating that DS-1062 has good stability in circulation and is a new hope for patients with advanced non-small cell carcinoma. Clinical trials of this drug have been listed on ClinicalTrials.gov (NCT03401385). SKB-264 is a new injectable ADC drug targeting Trop2 developed by Sichuan Kelun Pharmaceutical. Non-clinical study data show that SKB-264 for injection has significant anti-tumor activity, good safety and tolerability in animal models of triple-negative breast, stomach, lung and colorectal cancer and was filed for clinical trials in 2019. (Rap)2-E1-(Rap)2 is a novel antibody-coupling drug that pairs humanized monoclonal antibodies against Trop2 with amphibious ribonuclease (Rap). In mouse non-small cell lung cancer transplant tumor models, When the maximum tolerated dose of (Rap) 2-E1-(Rap) 2 is administered, survival is significantly improved. Other TROP2-targeting drugs, such as monoclonal antibodies and chimeric Trop2 virus-like particles, are under development [53-55].

5. Conclusions

TROP2, as a highly expressed biomarker in various malignant tumors, has emerged as a promising target for both diagnosis and treatment in the realm of cancer research. Its involvement in tumor formation and development, along with its association with reduced survival rates and unfavorable prognoses in cancer patients, emphasizes its significance as a potential therapeutic target. Nevertheless, the underlying molecular mechanisms responsible for TROP2-mediated tumor cell proliferation and migration still require thorough elucidation, calling for further research to strengthen our understanding. Encouragingly, significant progress has been made in developing drugs that specifically target TROP2. These innovative treatments encompass a range of modalities, such as monoclonal antibodies, bispecific antibodies, virus-like particles, and ADC drugs. Notably, six of these TROP2-targeting drugs have advanced to clinical trials, demonstrating the substantial interest and investment in this field. Sacituzumabgovitecan, the pioneering drug in this category, has entered Phase III clinical trials and even filed for marketing approval in 2019, signaling an impending breakthrough as the first commercially available ADC drug targeting TROP2. Additionally, other drugs in clinical testing have also shown promising results, raising hope for more effective therapeutic options in the clinic.

As the research on TROP2 continues to progress, the prospect of harnessing its potential as a robust biomarker and therapeutic target becomes increasingly promising. With the advent of new TROP2-targeted therapeutics, we envision a future where cancer patients can access more tailored and effective treatment regimens, ultimately leading to improved outcomes and enhanced quality of life. This optimism stems from the expectation that ongoing studies and clinical trials will unveil novel insights into the intricate mechanisms that govern TROP2's influence on cancer biology.

In conclusion, the journey towards fully exploiting the potential of TROP2 as a cancer biomarker and therapeutic target is well underway, with encouraging advancements in drug development and promising clinical results. The ongoing commitment to unraveling the intricate molecular pathways will pave the way for future breakthroughs, expanding the arsenal of treatment options for cancer patients and elevating their chances of successful treatment and survival. The collective efforts of researchers, clinicians, and pharmaceutical developers instill hope for a future where TROP2-targeted therapies play a central role in the fight against cancer, benefiting an ever-increasing number of patients worldwide.

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