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Review Article

SLITRK6 in Cancer Metastasis: Emerging Evidence, Mechanisms and Therapeutic Potential

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ABSTRACT
Cancer metastasis is a complicated biological process where cells from the primary tumour site spread into other organs far from the origin and cause a secondary tumour. The cascade of metastasis includes epithelial to mesenchymal transition (EMT), in which cancerous cells lose the epithelial characters and acquire features of migration and invasion through key signalling pathways as TGF-β, Wnt/β-catenin, and Notch. After EMT, cells can intravasate into the blood or lymphatic vessels, and extravasate into remote tissues, causing secondary tumours. Current cancer therapies are often ineffective against metastatic disease, and therefore, new approaches that target metastasis specifically are needed.
SLIT and NTRK-like family member 6 (SLITRK6) promotes the migration of cancer cells by binding to ROBO receptors and controlling Rho GTPases, which are essential for cytoskeletal dynamics. Moreover, it also impacts the tumour microenvironment by regulating the interactions of immune cells and by promoting the secretion of MMPs, which facilitate tissue invasion. This review discusses the current understanding of SLITRK6's biological functions, especially in the context of cancer, and discusses the molecular pathways through which it influences metastasis. By targeting SLITRK6, it may be possible to disrupt both the migratory behaviour of cancer cells and the supportive microenvironment that facilitates metastasis. Recent studies have identified SLITRK6 as a significant player in cancer metastasis. Its expression is associated with poor prognosis in several cancers. This review aims to provide a comprehensive overview of SLITRK6 in cancer metastasis and its potential as a novel therapeutic target.
Key Words: Cancer metastasis, SLITRK6 gene, Prognostic, Therapeutic target

INTRODUCTION

Overview of Cancer Metastasis

Cancer metastasis is a very complex biological process in which the cancerous cells spread off the primary neoplasm and reach other body organs, thus creating secondary tumors. Such phenomenon is one of the most important predictors of oncological mortality because metastatic disease is often resistant to standard treatment and is difficult to detect at an early diagnostic stage of the disease. Empirical data shows that metastasis is the cause of death in about ninety percent of cancer cases, thus treatment aimed at understanding and reversing this phenomenon have become the focus of researchers. The metastatic cascade progresses via a series of decisive stages beginning with an epithelial-mesenchymal transition (EMT) [1, 2].

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As a result of EMT, cancer cells lose tight cell-cell junctions, apical-basal polarity, and epithelial characteristics. They gain mesenchymal features such as an increased ability to move around, invasiveness, and resistance to apoptosis, which enable tumour cells to detach from the primary tumour and migrate through the tissue surrounding it. The key EMT-promoting signalling pathways include TGF-β, Wnt/β-catenin, and Notch signalling pathway. Through activation of these pathways, tumour cells can enter this new migratory status. EMT transfer endows tumor cells with the ability to enter the vascular or lymphatic system, a process known as intravasation. These EMT cells then migrate into peripheral organs and through extravasation they leave the vasculature and enter resident tissues which leads to the development of secondary tumors [3].
Another mechanism of dissemination of tumor cells is proteolytic dismantling of the extracellular matrix in collaboration with matrix metalloproteinases (MMPs) which increases the motility and invasive power of the cells. It is also essential that a pre-metastatic niche, a

microenvironment created in a separate organ, long before collateral metastatic colonization should establish which provides tumor cells with a favorable soil to grow and live [4].

Importance of Targeting Metastasis in Cancer Therapy

Although current cancer therapies-including surgery, chemotherapy, and radiotherapy-can sometimes be effective in treating the primary tumour, they remain less effective against metastatic disease. Metastasis is still the leading cause of death from cancer: transformed cells can evade conventional treatments through a variety of mechanisms, including genetic mutation, altered drug metabolism, and resistance to apoptosis. Besides, metastatic disease frequently remains asymptomatic in early stages, making detection and intervention more difficult. Under these complications, need to develop new treatment approaches, which directly address the process of metastasis, cannot be disputed as formalized in modern studies [5].

Therapeutic challenges linked to metastasis/malignant dissemination are based on heterogeneity of metastatic cells. The presence of molecular diversity between the metastatic clones poses a daunting challenge, because the chemotherapeutic agents which are effective against the primary tumor will have no effect on the metastatic counterparts due to the different genetic background and resistance mechanisms. Besides, metastatic cells are exceptionally adaptive to different microenvironments and possess complex methods of evading immune surveillance, which makes targeted treatment more difficult [6, 7]. Therefore, treatment approaches that rely on targeting metastatic processes instead of focusing on the primary tumor are more promising. Interventions that can hamper EMT, e.g., may prevent malignant cells to obtain migratory and invasive characteristics, may halt the onset of metastasis. A potential novel approach is attacking the pre-metastatic niche by altering the signal transduction pathways involved in niche formation and thus preventing establishment of metastatic colonization of distant organs. Another modern method includes angiogenesis blockage, thus cutting off primary and secondary tumors to the vital vascularized nutrient supplies. These multi-modal approaches have ability to reduce and shield metastatic processes, and hence, improve survival chances of patients with already developed carcinoma [8, 9].

SLITRK6: A Potential Target

The discovery of SLITRK6, which is a part of the SLITRK family of genes, as a critical mediator of cancer metastasis has elicited significant academic attention. Originally involved in the development of neurons, SLITRK6 has been now found to be expressed in a wide range of malignancies, such as breast, lung and pancreatic carcinomas, with expression being associated with poor prognosis and increased metastatic potential. This gene mainly interacts with ROBO receptors to regulate migration and adhesion of cells through Rho GTPases which transduce cytoskeletal reorganization. This mechanism enhances the ability of cancer cells to migrate and invade surrounding tissues, facilitating key metastatic steps such as intravasation into the bloodstream and extravasation into distant organs [10, 11].

In addition to the organization of cell migration, SLITRK6 controls the expression of MMPs which are enzymes that degrade extracellular matrix, thus allowing tumor cells to invade barriers of the tissue and explore new locations. Moreover, there is mounting evidence that SLITRK6 regulates the tumor microenvironment by controlling malignant cells-immune components interaction. This gene could down-regulate the immune cell invasion at metastatic sites, allowing immune evasion, as well as the survival and growth of cancerous cells in the remote organs. Due to its dual action in increasing cellular motility as well as regulating immune dynamics, SLITRK6 is an excellent target for therapeutic interventions to prevent metastasis [12, 13].

Structure and Function of SLITRK6

SLITRK6 belongs to the family of SLITRK genes that is mostly linked to neuronal development, which determines synaptic plasticity and axon guidance. It is found on chromosome 3p21.31 and it encodes a 946-residue protein with a single-pass transmembrane domain and multiple large extracellular leucine-rich repeats that provide protein-protein interactions and cell adhesion. Multiple signaling motifs of SLITRK6 in its cytoplasmic tail are likely to regulate Rho GTPases, which are required in coordinating cellular dynamics of migration and invasion [14].

This dual functionality makes SLITRK6 essential in not only cellular maturation, but also cancer metastasis since it increases the motility of cancerous cells. Its control effect on MMPs also allows tumor cells to violate the tissue boundaries and spread. Recent studies are supportive of the role of SLITRK6 in the tumor microenvironment by modulating tumor-immune interactions, thus, play a role in immune surveillance evasion. Altogether, SLITRK6 is an essential mediator of cellular motility and can be potential therapeutic adverse targets to inhibit the development of metastasis [15, 16].

SLITRK6 Expression Patterns

SLITRK6 is highly and specifically expressed in the central nervous system, particularly in the brain and spinal cord, where it is important in neuronal differentiation, such as axonal pathfinding, synaptic formation, and synaptic plasticity. The protein is

localized to certain regions of the brain including the hippocampus and cerebellum, and it is involved in the development of neuronal circuits that are critical in learning and memory. It is found to have lower expressions in peripheral tissues, such as testis, heart and neuroendocrine organs, implying more regulation in endocrine systems. Recent literature indicates the expression of SLITRK6 in immune cells, and this indicates that it also plays a contributory role in both innate and adaptive immune. Therefore, even though the canonical nature of the gene lies in its existence in neurobiology, its expansive distribution in various tissues is indicative of its existence in other biological roles yet to be fully comprehended [17, 18].

Dysregulated Expression in Cancers

It has been demonstrated that SLITRK6 is frequently dysregulated in several different types of cancer with overexpression (Table 1) observed in a variety of cancers such as breast, non-small cell lung, and gastric tumors. High levels of SLITRK6 are associated with unfavorable clinical prognoses and high metastatic capacity, because this protein facilitates cell migration, invasion and adhesion between tumors and cells, each of which is a key mediator of metastatic spread. Elevated levels of SLITRK6 are associated with increased MMPs, which degrade the extracellular matrix and facilitate cancer cell invasion. Furthermore, SLITRK6 may also play a role in the generation of a pro-metastatic microenvironment by remodelling the extracellular matrix and facilitating the formation of pre-metastatic niches in distant organs. In breast cancer, SLITRK6 overexpression has been shown to enhance the migratory and invasive potential of tumour cells, whereas in pancreatic cancer, it is associated with poor survival and increased distant metastasis. SLITRK6 is an indicator of poor prognosis and a key in the metastatic process. Therefore, it is a good candidate for a therapeutic target [10, 15, 16, 19-21].

Table 1: SLITRK6 expression and metastasis related findings across various cancer types

Cancer Type	Expression Pattern	Metastasis related findings	References
Breast	Overexpressed in cell lines	N/A	(15)
Lung (NSCLC/LUAD)	Overexpressed	Promotes progression via PI3K/AKT/mTOR; invasion in assays	(19)
Urothelial/Bladder	High (54-90% cases; predominant expression); higher in UTUC vs UBUC	Biomarker for ADCs (ASG-15ME); poor prognosis; earliest reported cancer expression	(15, 16)
Colorectal	Heterogeneous; downregulated in LN/liver mets	CSC heterogeneity; not pro-metastatic	(20)
Hepatocellular (HCC)	Downregulated in tumours; mutations common	Biomarker via bioinformatics; survival impact	(10)
Brain Tumours (GBM, Medulloblastoma)	Detected in multiple types (astrocytoma, oligodendroglioma, GBM, medulloblastoma, PNET)	Expression profile unique among SLITRK family; role unclear	(21)

SLITRK6 in Neuronal and Non-Neuronal Cells

SLITRK6 plays a vital role in the development of nervous system where it regulates neuronal migration, axon guidance, and synaptogenesis. It plays an important role in the formation of neuronal networks in the developing brain, which guarantees proper connectivity and regulates the synaptic plasticity. Signaling during development of the interaction with ROBO receptors on growing neurons aids in axon pathfinding and correct positioning of neurons. SLITRK6 perturbation leads to aberrant neurodevelopment, and has been associated with neurodevelopmental disorders, such as autism spectrum disorders. Incidences of mutations or deletions in SLITRK6 impair synaptic connectivity, highlighting its two-fold functions in neural development and maintenance of functional neural circuits [22, 23].

Recent studies have indicated that SLITRK6, which was long known for its role in the nervous system, has significant functions outside of neural tissues, primarily in immune and epithelial cells. In immune cells, SLITRK6 seems to be involved in regulating T cell function and may even influence the movement of immune cells, which are important in various autoimmune diseases and cancer metastasis. SLITRK6 is crucial in the regulation of cell adhesion and migration, critical processes that epithelial integrity depends on and wound healing. In the process of

EMT, SLITRK6 expression increases, which helps the cells lose adhesion and enables them to present migratory and invasive characteristics of cancerous cells. This would imply that SLITRK6 plays a key role in the metastasis of tumours by modulating both the immune responses and the invasive behaviour of cancer cells through its influence on epithelial plasticity [24-26].

Role of SLITRK6 in Cancer Cell Behaviour
Impact on Cell Adhesion, Migration, Invasion
SLITRK6 is implicated in regulating critical cellular behaviour for the metastatic spread of cancer cells including cell adhesion, migration, and invasion. In normal tissues, the proteins involved in maintaining adhesion between the cells and the extracellular matrix. However, due to the modified molecular machinery of adhesion molecules and signalling pathways in cancer, tumour cells detach from the primary site and migrate towards distant sites. SLITRK6 is known to facilitate cell migration and invasion by interaction with Rho GTPases, which are regulators of actin cytoskeleton dynamics that is essential for cell movement. The interaction of ROBO receptors with SLITRK6 increases motility of cells and further facilitates cellular reorganization, which is essential in cellular migration. SLITRK6 has been reported to be overexpressed in a range of malignancies including breast carcinoma, pancreatic carcinoma and non-small cell lung carcinoma (NSCLC), where it significantly enhances the migratory and invasive abilities of malignant cells. This up-regulation is linked to an increase in secretion of MMPs which breakdown the extracellular matrix (ECM) and consequently permits tumoral invasion of adjacent tissues and the formation of secondary lesions. Together, SLITRK6 is also important in the process of metastasis by means such as intravasation and extravasation [19, 27].

SLITRK6 Influence on EMT and Metastasis
EMT is a key metastasis process, in which epithelial cells lose tight junction integrity and polarity, acquiring mesenchymal characteristics to enable them to be more motile and invasive. SLITRK6 has been indicated to stimulate EMT through suppression of epithelial markers like E-cadherin and up-regulation of mesenchymal markers like N-cadherin and vimentin. It also affects canonical EMT-related signaling (TGF-β, Wnt/ β-catenin, and Notch signaling) necessary to EMT process. Incidentally, up-regulation of SLITRK6 in cancer including breast and pancreatic carcinoma increases the strength of EMT, which improves the metastatic capacity of tumor cells by enhancing the capability of tumor cell movement via the ECM and vascular compartments. EMT mediated by SLITRK6 is also involved in the development of chemoresistance and in this way, tumor cells become less susceptible to traditional treatments. Therefore, SLITRK6 does not only plays a role in metastatic spread, but also on resistance to treatment, thereby making it a central figure in cancer pathophysiology [10, 11].

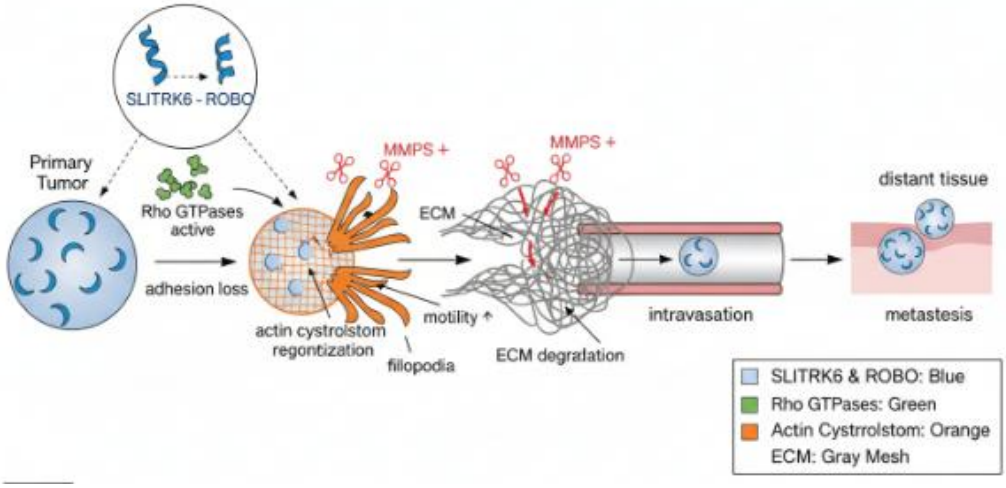

Figure 1: Schematic (left-to-right) showing a primary tumor cell expressing SLITRK6, the downstream signaling events that increase motility and extracellular matrix (ECM) breakdown, and the subsequent intravasation and extravasation steps that lead to distant metastasis. Image created via visily.ai

SLITRK6 in Tumour Microenvironment
Interaction with Stromal Cells
SLITRK6 is involved in TME by its interaction with stromal cells, mainly fibroblasts and endothelial cells. It is overexpressed in both cancer and stromal cells, in which, it encourages tumour cell invasion by stimulating the activity of fibroblasts. Overexpression of SLITRK6 in cancer cells results in the release of growth factors and cytokines that induce fibroblasts to secrete collagen and other extracellular matrix components, thus making tumours more invasive. SLITRK6 also impacts endothelial cells, which are vital

for angiogenesis, the process of new blood vessel formation, which is critical for tumour growth and metastasis. SLITRK6 could modulate VEGF to promote endothelial cell behaviour and support the formation of blood vessels, thus aiding both primary tumours and metastatic sites [16].

SLITRK6 changes TME through regulating the activity of immune cells, especially T lymphocytes and myeloid-derived suppressor cells (MDSCs). It has been indicated that SLITRK6 facilitates an immune-repressed environment which supports metastasis and increased tumor growth. Indicatively, direct migration of T cells toward the tumor site could be improved by ectopic expression of SLITRK6 in T cell, which would promote immune evasion and augment tumor-associated immune responses. Also, SLITRK6 seems to mediate recruitment and activation of tumor-associated macrophages (TAMs) that produce pro-inflammatory cytokines that enhance tumorigenic mechanisms. SLITRK6 modulates immune composition of the TME, which leads to the creation of a niche that supports malignant progression and immune escape, and eventually metastatic proliferation [10].

SLITRK6 and Cancer Stem Cells

Cancer stem cells (CSCs) are the tumor initiating cell type which expresses properties of the stem cell, i.e. self-renewal, multilineage differentiation and have the ability to maintain tumorigenesis. These cells play an important role in metastasis and recurrence, because they can endure extreme microenvironment conditions, they are resistant to traditional treatments, and they seed new metastatic lesions. Recent studies indicate that SLITRK6 might have a regulatory effect on CSC properties that are prerequisites of tumorigenesis, metastasis and recurrence. The upregulation of the SLITRK6 in CSCs of various cancer types, such as breast, pancreatic, and glioblastoma, is associated with an increase in stemness, cell growth, and survival. This up-regulation has the potential to regulate key signaling pathways, including Notch and Wnt/ 2 -catenin, which are essential in sustaining CSC phenotypes. The regulation of these pathways' aids CSC self-renewal and differentiation, which enhance tumor development and invasion [11, 28, 29].

Molecular Mechanisms of SLITRK6 in Metastasis. Inhibition of Metastatic Signalling Pathways

SLITRK6 has been shown to influence several key signalling pathways that regulate cancer cell behaviour, particularly those involved in metastasis. These pathways include Rho GTPases, PI3K/Akt, and MAPK/ERK, all of which are central to controlling cell movement, survival, and invasion. SLITRK6 engages RhoA, RhoC, and Rac1-GTPases and is indispensable to regulate actin cytoskeletal remodeling for optimal cell motility and invasive potency required in the process of metastasis. Moreover, the ROBO1's function can also be modulated indirectly by activating its SLITRK6 counterpart and hence influencing downstream GTPases [21, 28]. Activation of the PI3K/Akt pathway has been proposed for SLITRK6, since it interacts with ROBO receptors, promoting survival and migration, a two-step metastatic process. Activation of Akt can upregulate MMPs, thereby degrading ECM and facilitating cancer cell invasion [19, 30]. SLITRK6 acts as a regulator of the MAPK/ERK pathway that affects the migratory and invasive properties of cancer cells. The phosphorylation of ERK enhances the activation of downstream targets that mediate cell cycle progression and metastatic behavior [26].

Another aspect where SLITRK6 plays a very vital role is in initiating EMT, that is, by imparting epithelial cancer cells the loss of their tight junctions and the acquisition of mesenchymal-like properties, thus a more movable and invasive trait. Expression of mesenchymal markers, for example, N-cadherin, vimentin and repression of epithelial markers, for example, E-cadherin, enhance the metastatic potential [28, 31].

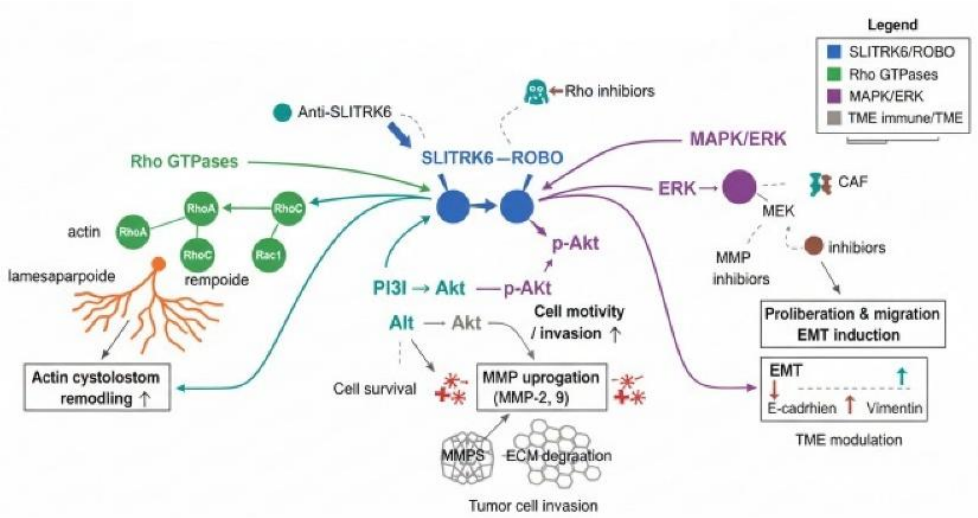

Figure 2: Molecular mechanisms of SLITRK6 in metastasis

Recent Findings on SLITRK6 in Cancer Metastasis

Recent research on SLITRK6 has uncovered important insights into its role in cancer metastasis, with studies spanning from preclinical findings to clinical applications. Below is a detailed discussion of the most relevant and recent findings regarding SLITRK6's involvement in cancer metastasis and its potential as a biomarker for prognosis and treatment response. SLITRK6 was shown to dramatically enhance the cell migration and invasion in many different cancer cell lines. For example, overexpression of SLITRK6 enhances the cell's ability to migrate through the Matrigel assay in the MDA-MB-231 breast cancer cell lines, among others. The likely mechanism by which this effect is achieved is through Rho GTPase activation, as these are important regulators of the cytoskeleton that reorganizes in preparation for cell movement [11, 32]. Similarly, overexpression of SLITRK6 has been reported to correlate with poor prognostic factors in urothelial carcinoma, indicating that this protein might be a biomarker of aggressive disease and treatment resistance towards new immunotherapies [33].

SLITRK6 as a Biomarker for Cancer Prognosis

The diagnostic potential of SLITRK6 is in the detection of early metastatic spread at various stages of the progression of cancers. SLITRK6 may be a useful molecular marker for metastatic disease within CTCs and tumor biopsies. Non-invasive diagnostic methods involving liquid biopsies may make use of the expression of SLITRK6 for determining patients with higher risk of developing metastasis and progression of disease [10]. The expression of SLITRK6 was detected in circulatory tumor cells (CTCs) isolated from peripheral blood of patients with cancer in several studies. This is found more commonly in metastatic cancers. The detection of SLITRK6 positive CTCs in blood might be an indicator of disseminated disease and thereby identify the group of patients with risk to develop distant metastases [16]. Samples of metastatic cancer patients are often found to have increased levels of SLITRK6. Therefore, this is a very useful biomarker in assessing the metastatic potential of primary tumors. Pathological examination of tumor tissue for the expression of SLITRK6 can complement the traditional staging systems and help identify high-risk patients [15].

Challenges and Limitations in Using SLITRK6 as a Biomarker

While the potential for SLITRK6 to serve as a biomarker for cancer metastasis is promising, there are several challenges that need to be addressed. SLITRK6 expression varies between different types of cancers and even within different stages of the same cancer, making it not very useful as a universal biomarker for metastasis. For example, SLITRK6 was shown to be downregulated in lymph node metastases of colorectal cancer, which suggests heterogeneity in its expression associated with cancer progression and metastasis [28]. Since the expression of SLITRK6 has not been standardized using techniques such as immunohistochemistry, qPCR, and Western blotting across multiple tissues, it is another deficiency. Reliable and reproducible methods for the measurement of SLITRK6 expression need to be well established for its application in the clinical setting [15]. Because SLITRK6 is expressed in neural tissues and a variety of cancers, its specificity as a cancer-specific biomarker could be an issue. Further studies are required to assess the specificity of SLITRK6 expression in relation to normal tissue versus metastatic disease [11].

Co-targeting SLITRK6 with Metastasis-Related Molecules

Integrins are cell surface receptors that mediate cell adhesion and migration. Integrins are known to play a well-established role in cancer metastasis. Co-targeting SLITRK6 with integrin inhibitors could synergistically reduce tumour cell adhesion and migration, thereby limiting metastatic spread. For instance, experiments have indicated that the silencing of SLITRK6 combined with inhibitors of integrin αvβ3 in models of melanoma and breast carcinoma has resulted in the decreased adhesion of tumour cells to the extracellular matrix and decreased lung and liver colonization with metastases. This two-way approach can also improve therapy efficiency by affecting various pathways in the process of metastasis at once [14].

MMPs are enzymes responsible for the degradation of the ECM. Cancer cell invasion and metastasis significantly depend on MMP. Since SLITRK6 stimulates MMP, its inhibition together with MMP inhibition can be more potent in inhibiting metastasis. In the preclinical model, it was proven that tumour invasiveness is reduced when the MMP inhibitor was combined with a targeted therapy to SLITRK6 and subsequent metastatic spread. This dual targeting approach could potentially improve the effectiveness of treatment regimens by attacking both cellular adhesion and ECM degradation processes that are involved in metastasis [16].

Integrating SLITRK6 targeted therapy with established ones such as chemotherapy, immunotherapy, and radiotherapy will create new avenues towards the achievement of synergistic and therapeutic effects in treatments. Simultaneous co-targeting with metastasis related molecules such as integrins, and MMP's would provide complete approaches to metastasis preventor while developing improved treatment efficacy strategies.

Challenges in Therapeutic Targeting of SLITRK6

A major issue in the therapeutic targeting of SLITRK6 is specificity. SLITRK6 is not only expressed in the tumour cells but also in the neurons and other normal tissues. The therapies that target SLITRK6 have a high possibility of off-target effect with toxicities in normal cells. SLITRK6 expression in the brain is a concern with possible neurological side effects in patients being treated with SLITRK6-targeting therapies. Achieving tumour-specific targeting is crucial for reducing side effects and ensuring the safety of SLITRK6-based therapies. Tumour-specific targeted therapies with the ability to selectively target cancer cells without affecting normal neuronal tissues will demand careful screening as well as development of tumour-specific delivery systems such as nanoparticles and antibody-drug conjugates [15, 16, 34].

Table 2: SLITRK6-Targated therapeutics and Challenges

Approach	Agent/Example	Cancer Focus	Evidence Stage	Limitations/ Challenges	References
Antibody-Drug Conjugate	ASG-15ME	Urothelial/Bladder	Phase I trials	Neurological off target (brain expr.)	(15, 35)
RNAi/Silencing	siRNA in cell lines	Breast, Lung	Preclinical (in vitro)	Delivery, specificity	(19)
ADC (novel)	PRO1106 (Susten)	Urothelial	Preclinical	Tissue heterogeneity	(14)

CONCLUSION and FUTURE DIRECTIONS

Altogether, the review highlight role of SLITRK6 in cancer metastasis and it makes this gene a future therapeutic target. Metastasis is the leading cause of oncological mortality, and it is often resistant to traditional therapy, so it is urgent to understand how SLITRK6 regulates the migration and invasion of tumor cells. The given data reveals that SLITRK6 does not only promote invasive and migratory properties in the context of reacting to ROBO receptors and Rho GTPases but regulates immune microenvironmental interaction and extracellular matrix remodeling. The dual nature of SLITRK6 as both stimulator of cellular motility and promotor of a favorable metastatic habitat makes it an interesting target in anti-metastatic targeted therapy.

The direction of future research should be to clarify the specific molecular mechanisms that are behind SLITRK6-mediated processes and ways on how its activity can be effectively inhibited. By attacking SLITRK6, it is possible to impair the major cascade steps of metastasis, thus enhancing patient outcomes and survival rates in metastatic cancer. The review finally recommends the need to conduct more studies on the role of SLITRK6 in metastasis, hence its significance in designing novel therapeutic interventions to counter overwhelming development of cancer.

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