**Name of Journal:** *World Journal of Clinical Oncology*

**Manuscript NO:** 90642

**Manuscript Type:** EDITORIAL

**TM9SF1 is implicated in promoting the proliferation and invasion of bladder cancer cells**

Zhou SQ *et al*. TM9SF1 promotes bladder growth

Shu-Qing Zhou, Lian-Xiang Luo

**Shu-Qing Zhou,** The First Clinical College, Guangdong Medical University, Zhanjiang 524023, Guangdong Province, China

**Lian-Xiang Luo,** The Marine Biomedical Research Institute, Guangdong Medical University, Zhanjiang 524000, Guangdong Province, China

**Author contributions:** Luo LX conceived and designed the editorial; Zhou SQ wrote the editorial; Luo LX reviewed the paper and provided comments; All authors read and approved the final manuscript.

**Corresponding author: Lian-Xiang Luo, PhD, Associate Professor,** The Marine Biomedical Research Institute, Guangdong Medical University, No. 2 East Wenming Road, Zhanjiang 524000, Guangdong Province, China. luolianxiang321@gdmu.edu.cn

**Received:** December 9, 2023

**Revised:** December 27, 2023

**Accepted:** January 30, 2024

**Published online:** February 24, 2024

**Abstract**

Zhuo *et al* looked into the part of transmembrane 9 superfamily member 1 (TM9SF1) in bladder cancer (BC), and evaluated if it can be used as a therapeutic target. They created a permanent BC cell line and tested the effects of TM9SF1 overexpression and suppression on BC cell growth, movement, invasion, and cell cycle advancement. Their results show that TM9SF1 can boost the growth, movement, and invasion of BC cells and their access into the G2/M stage of the cell cycle. This research gives a novel direction and concept for targeted therapy of BC.

**Key Words:** Bladder cancer; TM9SF1; Cell proliferation; Migration; Invasion; TM9SF1 overexpression; TM9SF1 silencing inhibits

**©The** **Author(s) 2024.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Citation**: Zhou SQ, Luo LX. TM9SF1 is implicated in promoting the proliferation and invasion of bladder cancer cells. *World J Clin Oncol* 2024; 15(2): 175-177

**URL**: https://www.wjgnet.com/2218-4333/full/v15/i2/175.htm

**DOI**: https://dx.doi.org/10.5306/wjco.v15.i2.175

**Core Tip:** The transmembrane 9 superfamily member (TM9SF) TM9SF family's biological function has not been investigated yet. However, some studies have suggested that its expression could be associated with the emergence and progression of tumors. This article used various experimental methods, such as CCK8, wound healing test, transwell test, and flow cytometry, to explore the effect of TM9SF1 on the biological behavior of bladder cancer (BC), in order to offer a novel approach for the treatment of BC.

**INTRODUCTION**

Bladder cancer has a high recurrence rate and is resistant to chemotherapy[1-4]. The most prominent symptom of bladder cancer (BC) is microscopic or visually visible hematuria, and 75% of bladder tumors are uroepithelial carcinomas limited to mucous membranes, *i.e.*, non-muscular aggressive BC (NMIBC)[5-8]. Approximately 80% of bladder cancers are superficial papillary lesions caused by urothelial hyperplasia, which are of low grade and may recur, but rarely invade the bladder wall or metastasize. The remaining 15%-20% are high-grade solid non-papillary BC, which is caused by high-grade intraepithelial urothelial neoplasia, which has a high tendency to spread far. Most bladder cancers (75%-80%) do not involve the bladder muscle wall and are usually treated with transurethral resection of bladder tumor, however, many BC patients have poor prognosis and poor long-term survival[9,10]. So, the treatment of bladder cancer needs to go further.

By establishing an effective prognostic nomogram model for esophageal squamous cell carcinoma, two marker genes were identified that are directly associated with 4-year overall survival of cancer patients, one of which is TM9SF1. The expression value of TM9SF1 gene in cancer patients was found to be significantly higher than that of healthy individuals[11]. ApostolosZaravinos’ study employed enome-wide microarray analysis, classifying samples based on histology and discovering 17 differentially expressed genes, one of which was TM9SF1. This discovery makes it more necessary and possible to investigate the role of TM9SF1 in cancer, as well as its effects and mechanisms on bladder cancer cells[12]. TM9SF1, identified as an estrogen receptor binding fragment-associated antigen 9 (EBAG9) interaction factor, and EBAG9 have been observed to act in harmony to control the migration of prostate cancer cells by influencing genes associated with epithelial-mesenchymal transition. This is in line with the study in this paper that the overexpression of TM9SF1 can promote the migration of BC cells[13]. Zhuo *et al*[14] have discovered that TM9SF1, a transmembrane 9 superfamily member 1, is a functional mRNA target of phosphorylated CTD interaction factor 1 (PCIF1). This gene acts as a tumor suppressor in cancer, with PCIF1 using m6Am to modify the TM9SF1 mRNA, which in turn reduces its translation. It has been found that TM9SF1 can reverse the effect of PCIF1 on the aggressiveness of cancer cells, suggesting different functions and roles in different tumor types. Zhuo *et al*[14] conducted further research to determine the role of TM9SF1 overexpression and silencing in three cell lines (5637, T24, and UMUC-3). Through CCK8, wound healing test, cross-well migration test and separation of high - and low-nutrient protein sets, TM9SF1 was identified as an oncogene in BC. When TM9SF1 was silenced, it suppressed the growth and motility of BC cells *in vitro*. Overexpression of TM9SF1, on the other hand, was found to increase the proliferation of BC cells and enhance their migration and invasion abilities. This opens up the possibility of new treatments for BC.

**CONCLUSION**

This editorial has demonstrated that TM9SF1, a member of the transmembrane 9 superfamily, could be used as a biomarker for bladder cancer treatment, thus offering a fresh approach to treating the condition.

**REFERENCES**

1 **Matuszczak M**, Kiljańczyk A, Salagierski M. A Liquid Biopsy in Bladder Cancer-The Current Landscape in Urinary Biomarkers. *Int J Mol Sci* 2022; **23** [PMID: 35955727 DOI: 10.3390/ijms23158597]

2 **Chang CH**, Lin BJ, Chen CH, Nguyen NL, Hsieh TH, Su JH, Chen MC. Stellettin B Induces Cell Death in Bladder Cancer Via Activating the Autophagy/DAPK2/Apoptosis Signaling Cascade. *Mar Drugs* 2023; **21** [PMID: 36827114 DOI: 10.3390/md21020073]

3 **Sung H**, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021; **71**: 209-249 [PMID: 33538338 DOI: 10.3322/caac.21660]

4 **Afonso J**, Santos LL, Longatto-Filho A, Baltazar F. Competitive glucose metabolism as a target to boost bladder cancer immunotherapy. *Nat Rev Urol* 2020; **17**: 77-106 [PMID: 31953517 DOI: 10.1038/s41585-019-0263-6]

5 **Tran L**, Xiao JF, Agarwal N, Duex JE, Theodorescu D. Advances in bladder cancer biology and therapy. *Nat Rev Cancer* 2021; **21**: 104-121 [PMID: 33268841 DOI: 10.1038/s41568-020-00313-1]

6 **Zhu S**, Yu W, Yang X, Wu C, Cheng F. Traditional Classification and Novel Subtyping Systems for Bladder Cancer. *Front Oncol* 2020; **10**: 102 [PMID: 32117752 DOI: 10.3389/fonc.2020.00102]

7 **Berdik C**. Unlocking bladder cancer. *Nature* 2017; **551**: S34-S35 [PMID: 29117159 DOI: 10.1038/551S34a]

8 **Funt SA**, Rosenberg JE. Systemic, perioperative management of muscle-invasive bladder cancer and future horizons. *Nat Rev Clin Oncol* 2017; **14**: 221-234 [PMID: 27874062 DOI: 10.1038/nrclinonc.2016.188]

9 . Bladder cancer: diagnosis and management of bladder cancer: © NICE (2015) Bladder cancer: diagnosis and management of bladder cancer. *BJU Int* 2017; **120**: 755-765 [PMID: 29168333 DOI: 10.1111/bju.14045]

10 **Charlton ME**, Adamo MP, Sun L, Deorah S. Bladder cancer collaborative stage variables and their data quality, usage, and clinical implications: a review of SEER data, 2004-2010. *Cancer* 2014; **120 Suppl 23**: 3815-3825 [PMID: 25412393 DOI: 10.1002/cncr.29047]

11 **Liu K**, Jiao YL, Shen LQ, Chen P, Zhao Y, Li MX, Gu BL, Lan ZJ, Ruan HJ, Liu QW, Xu FB, Yuan X, Qi YJ, Gao SG. A Prognostic Model Based on mRNA Expression Analysis of Esophageal Squamous Cell Carcinoma. *Front Bioeng Biotechnol* 2022; **10**: 823619 [PMID: 35299644 DOI: 10.3389/fbioe.2022.823619]

12 **Zaravinos A**, Lambrou GI, Boulalas I, Delakas D, Spandidos DA. Identification of common differentially expressed genes in urinary bladder cancer. *PLoS One* 2011; **6**: e18135 [PMID: 21483740 DOI: 10.1371/journal.pone.0018135]

13 **Miyazaki T**, Ikeda K, Sato W, Horie-Inoue K, Inoue S. Extracellular vesicle-mediated EBAG9 transfer from cancer cells to tumor microenvironment promotes immune escape and tumor progression. *Oncogenesis* 2018; **7**: 7 [PMID: 29362448 DOI: 10.1038/s41389-017-0022-6]

14 **Zhuo W**, Sun M, Wang K, Zhang L, Li K, Yi D, Li M, Sun Q, Ma X, Liu W, Teng L, Yi C, Zhou T. m(6)Am methyltransferase PCIF1 is essential for aggressiveness of gastric cancer cells by inhibiting TM9SF1 mRNA translation. *Cell Discov* 2022; **8**: 48 [PMID: 35597784 DOI: 10.1038/s41421-022-00395-1]

**Footnotes**

**Conflict-of-interest statement:** All the authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** December 9, 2023

**First decision:** December 18, 2023

**Article in press:** January 30, 2024

**Specialty type:** Cell biology

**Country/Territory of origin:** China

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): 0

Grade D (Fair): D

Grade E (Poor): 0

**P-Reviewer:** Chen BH, Taiwan **S-Editor:** Liu JH **L-Editor:** A **P-Editor:** Zhang XD



Published by **Baishideng Publishing Group Inc**

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** office@baishideng.com

**Help Desk:** https://www.f6publishing.com/helpdesk

https://www.wjgnet.com



**© 2024 Baishideng Publishing Group Inc. All rights reserved.**