



# Transgelin in bladder cancer: A potential biomarker and therapeutic target



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Bladder cancer is one of the most common and expensive cancers to treat in the world [1,2]. Although radical surgery can usually be archived, disease progression and tumour metastasis occur frequently. Currently, there are limited clinicopathological factors that can effectively predict bladder cancer [2]. Cisplatin-based systemic chemotherapy or immunotherapy has been empirically adapted in combination with radical surgery, to improve the prognosis in invasive bladder cancer, but not always achieve a successful outcome [2]. Comprehensive genomic characterisation of bladder cancer tissues shows a high tumour heterogeneity, suggesting a presence of distinct cancer molecular subtypes [3,4]. Therefore, it is critical to identify novel targets in bladder cancer, not only for prognostic purposes but also for therapeutic intervention.

The actin cytoskeleton plays crucial roles for tumorigenesis and cancer metastasis [5]. Transgelin is a well-characterized actin-binding protein that induces actin gelation and regulates the actin cytoskeleton [5]. Therefore, transgelin may be a potential oncogenic factor that is involved in tumour development and progression. In a study published in *EBioMedicine*, Chen and colleagues integrated bioinformatics analysis, clinical samples and a series of functional assays to explore the molecular function of transgelin in bladder cancer [6]. Firstly, they demonstrated that high transgelin expression is significantly associated with aggressive pathological features, such as a high probability of cancer metastasis and poor prognosis in bladder cancer cohorts (TCGA, GSE13507, and PKU).

These results suggest a potential link between transgelin and bladder cancer progression. In line with this, another group compared tissue proteomics from laser microdissected tumour tissue and adjacent non-tumourous tissue to discover candidate biomarkers for bladder cancer [7]. They found that transgelin is significantly over-expressed in bladder cancer tissues and urine specimens, suggesting its potential as a biomarker for non-invasive bladder cancer screening.

Secondly, in distinct bladder cancer-derived cell lines, changes in transgelin levels altered the cell colony formation, cell invasion, and migration capacity through invadopodia formation and the induction of epithelial-mesenchymal transition.

The xenograft metastatic mouse model showed that targeting transgelin by genetic silencing significantly suppressed tumour growth. Finally, they verified that transgelin is essential for transforming growth factor beta (TGF- $\beta$ )-induced metastasis in bladder cancer. In the clinical tissues and cell lines, TGF- $\beta$  and transgelin were significantly correlated with advanced or metastatic bladder cancer. The transgelin and mesenchymal marker/transcription factor expression levels were upregulated by TGF- $\beta$  stimulation. The stimulatory effect of TGF- $\beta$  was attenuated by transgelin inhibition. TGF- $\beta$  as an activator, mainly promotes tumour growth, invasion, and metastasis and thus induces escape from immune surveillance [8]. Its role in regulating transgelin may contribute to a critical mechanism that links transgelin to both immune and oncogenic pathways. Recent studies show that transgelin expression can be inhibited by microRNAs (miRNAs). miR-133b and miR-145-5p bind to bases 215–221 and 211–217 in 3'-untranslated

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regions (UTRs) of mRNA to inhibit transgelin transcription in human bladder cancer tissues [9,10]. These miRNAs reduce cancer cell proliferation, migration, invasion, and angiogenesis by suppressing transgelin expression, further demonstrating a potential role of transgelin in tumour progression.

Validation in clinical samples, a xenograft mouse model, and *in vitro* studies suggest that transgelin may serve as a prognostic biomarker and a potential druggable target for treating bladder cancer metastasis [6]. Since transgelin is a widely expressed structural protein, potential toxic side effects should be noted. In the future, new drugs that specifically target transgelin should be tested with appropriate drug delivery systems to confirm the therapeutic efficacy.

## Disclosure

The authors declared no conflicts of interest.

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