

Editorial

## Landscape of Circular Ribonucleic Acids in Urological Cancers

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### HIGHLIGHTS

- Circular RNAs (circRNAs) regulate numerous pathways related to carcinogenesis.
- Recently, several circRNAs have been determined to implicate in urological cancers.
- Further studies are required to ascertain the role of circRNAs in urological tumors.

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### ABSTRACT

The urological malignancies are among the most important neoplastic diseases imposing a significant burden on health care systems globally. The current therapeutic measures for these cancers have unsatisfactory results, and comprehensive knowledge of pathways involved in carcinogenesis and progression of these cancers is of utmost importance. Circular Ribonucleic Acids (circRNAs) are a class of non-coding RNAs characterized by their single-stranded covalently closed loops, exert their regulatory effects mainly by sponging the microRNAs (miRNAs) associated with the regulation of gene expression. In the past few years, several circRNAs have been identified to be implicated in the malignancies of the urinary system. A number of these circRNAs are involved in the common carcinogenic pathways, such as MAPK/ERK, TGF- $\beta$ , and PI3K-Akt pathways. However, further studies are required to ascertain the exact mechanism of numerous circRNAs in urological cancers and determine their diagnostic, prognostic, and therapeutic roles in patients with these cancers.

**Keywords:** Circular Ribonucleic Acids; Urologic Neoplasms; Prostate Neoplasms; Urinary Bladder Neoplasms; Kidney Neoplasms

**Editorial:** The urological malignancies are among the most important neoplastic disease imposing a significant burden on health care systems globally. As estimated in 2018, three main types of urological tumors, including prostate, bladder, and renal cancers, reached a total worldwide incidence of 2.2 million new cases contributing to the death of more than 730,000 patients (1). The current therapeutic measures for these cancers have unsatisfactory results, given their high recurrence rates, metastatic behavior, and progression to drug-resistant states (2, 3). Thus, comprehensive knowledge of pathways involved in carcinogenesis and progression of these cancers and the determination of new targets for the treatment of these neoplasms are of utmost importance. Circular RNAs (circRNAs) are a class of non-coding RNAs characterized by their single-stranded covalently

closed loops without 5' and 3' ends. As a result of their high stability and tissue-specific expression, circRNAs play pivotal roles in various biological functions and the regulation of numerous pathways from cellular proliferation to apoptosis or angiogenesis (3). CircRNAs exert their regulatory effects by several key mechanisms: 1. Sponging the microRNAs (miRNAs) associated with regulation of gene expression, 2. Providing a reservoir for miRNAs to elevate their availability, leading to increased regulation of target messenger RNAs (mRNAs), consequently their corresponding genes, and 3. Binding directly to the proteins and mediating their actions (3, 4). Therefore, alteration in the expression of different circRNAs may act as oncogenic or tumor suppressor factors depending on the circRNA-miRNA-mRNA interaction networks. Moreover, circRNAs

may exit from the cells and be utilized as diagnostic, prognostic, or therapeutic biomarkers.

In the past few years, several circRNAs have been identified to be implicated in the malignancies of the urinary system. In fact, a recent review described over 58 circRNAs involved in the carcinogenesis of three major urological cancers, including prostate, bladder, and renal cancer (3). A number of these circRNAs interact with the common carcinogenic pathways, such as MAPK/ERK, TGF- $\beta$ , and PI3K-Akt pathways (3, 5). In addition to the roles of circRNAs in the development and progression of urological cancers, several circRNAs have been ascertained as diagnostic and prognostic biomarkers. For instance, circEGLN3 reached an accuracy of 97% to distinguish between renal cancer and normal tissue (6). Given the abundant existence of circRNAs in body fluids, these circRNAs can be served as liquid biopsy factors for the cancers of the urinary system. Regarding prognostic endpoints, the dysregulated expression of numerous circRNAs has been demonstrated to associate with the survival of patients with urological tumors (3, 7). As the evidence emerges, different circRNAs are introduced in various aspects of urinary system tumors, expanding the knowledge concerning the tumorigenesis and management of these cancers.

### Conclusions

CircRNAs exert crucial functions related to the development and progression of neoplastic diseases by mainly interacting with miRNAs. Recently, several circRNAs have been identified in urological cancers, among which some of them are involved in common carcinogenic pathways, such as MAPK/ERK, TGF- $\beta$ , and PI3K-Akt pathways. Further studies are required to ascertain the exact mechanism of numerous circRNAs in urological cancers and determine their diagnostic, prognostic, and therapeutic roles in patients with these cancers.

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### Abbreviations

CIRC RNA	Circular RNA
MIRNA	Micro RNA
MRNA	Messenger RNA

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