Exploring the interplay of lncRNA, senescence and urinary tumors: opportunities and challenges

De-Chao Feng1,*, Rui-Cheng Wu2, Zhou-Ting Tuo3, Jie Wang1, Xing Ye4, Deng-Xiong Li1*

1Department of Urology, Institute of Urology, West China Hospital, Sichuan University, Chengdu 610041, China. 2Department of Rehabilitation, the Affiliated Hospital of Southwest Medical University, Luzhou 646000, China. 3Department of Urology, the Second Affiliated Hospital of Anhui Medical University, Hefei 230601, China. *Samuel Oschin Comprehensive Cancer Institute, Department of Medicine, Department of Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, CA 90048, USA.

*These authors contributed equally to this work and are co-first authors.

Corresponding to: De-Chao Feng and Deng-Xiong Li, Department of Urology, Institute of Urology, West China Hospital, Sichuan University, No. 37 Guoxue Alley, Wuhou District, Chengdu 610041, China. E-mail: dfcfenix@stu.scu.edu.cn; lidengxiongwch@stu.scu.edu.cn.

Introduction

About 72% of human genome is transcribed to non-coding RNAs, which have captivated researchers a lot for shedding light on their pivotal roles in regulating the initiation and progression of various diseases, including cancers [1]. Among these, long non-coding RNAs (lncRNAs) have emerged as key players in the complex landscape of gene regulation. LncRNAs perform a variety of roles, including scaffolding to encourage the interaction of related proteins, decoys to thwart transcriptional factors from the target gene’s promoter, sponges of linked miRNA to prevent target gene destruction, and guide molecules to recruit components for chromatin remodeling [1]. Many cancers are closely related to age [2–5] and such patients are expected be increased gradually as almost 20% of the world’s population will be 65 or older by 2030 [6] and those over the age of 65 have an 11-fold higher incidence of cancer than people under that age [7]. As one of the typical hallmarks of aging [8], cellular senescence is Cellular senescence is induced by stressful insults and certain physiological processes and is characterized by a prolonged and essentially irreversible cell-cycle arrest with secretory features, macromolecular damage, and altered metabolism [9]. Here, we aim to provide insights of the intersection between lncRNAs, cellular senescence, and urinary tumors, unraveling the potential implications and therapeutic avenues within this multifaceted network.

Senescence: guardian and culprit

Cellular senescence is responsible for a dual role in pathophysiological processes of cancers. Among these processes, senescence-associated secretory phenotype (SASP) is supposed to be a key factor in mediating many of their pathophysiological effects. SASP refers to a myriad of secretomes like pro-inflammatory cytokines and chemokines, growth modulators, angiogenic factors, and matrix metalloproteinases, secreted by senescent cells [9]. On the one hand, senescent tumor cells can contribute to the growth of tumor by attracting immune cells to the tumor microenvironment through SASP [10]. On the other hand, the SASP can attract immature myeloid cells that inhibit the immune system to tumors in the liver and prostate and can promote the growth of new cancers by promoting angiogenesis and metastasis [9]. Thus, striking a balance between the pro-tumorigenic and anti-tumorigenic aspects of senescence is crucial for unlocking its therapeutic potential.

The dance of lncRNAs and senescence

The dysregulation of lncRNAs is increasingly evident in urinary tumors. These molecules, such as NEAT1 [11], H19 [12], LNMAT2 [13], PTENP1 [14] and UCA1 [15], exert influence on crucial signaling pathways associated with tumor initiation, progression, and response to therapy. A comprehensive understanding of lncRNA expression patterns in urinary tumors provides valuable insights into their diagnostic and prognostic potential. Recent studies have uncovered a complex interplay between lncRNAs and senescence. These molecules actively participate in modulating key senescence-associated pathways, influencing cellular fate and the potential for malignant transformation. Chen et al. [16] found that obesity-induced insulin resistance is encouraged by the hepatic endothelium’s cellular senescence, which is strictly controlled by lncRNA Meg3 expression. Another study revealed that by stabilizing the HSF1 protein level, downregulation of the lncRNA MAGI2-AS3 reduced the H2O2 content and postponed cell senescence, suggesting a possible antiaging use [17]. In addition, Marta et al. [18] demonstrated that lncRNA MIR31HG played a dual role in senescence depending on its localization and pointed to the lncRNA as a potential therapeutic target in the treatment of senescence-related pathologies. In terms of cancers, Xiang et al. [19] found that lncRNA PINTS7aa was significantly increased in the hydrogen peroxide-induced hepatocellular carcinoma cell senescence model and its overexpression could induce growth inhibition, cellular senescence, and decreased mitophagy in vitro and in vivo. Furthermore, it has been demonstrated that lncRNA SENEBLOC has a role in both replicative and oncogenic senescence, and that lncRNA SENEBLOC expression is necessary for rapamycin’s antagonistic effects on senescence [20]. Exploring these interactions holds promise for identifying novel biomarkers and therapeutic targets.

Therapeutic prospects and future avenues

Currently, there is a relative paucity of quantitative studies investigating the interplay between lncRNAs and senescence on cancer initiation, progression and drug resistance, especially in the realm of urinary cancers despite the fact that some senescence-related lncRNAs have been reported in these cancers [6]. Unraveling the intricate network of lncRNA-mediated senescence in urinary tumors is of paramount importance. The elucidation of the lncRNA-senescence axis in urinary tumors offers promising therapeutic implications. Targeting specific lncRNAs or manipulating senescence-associated pathways may present innovative strategies for treating or preventing urinary tumors. Delving into these regulatory networks opens avenues for the development of targeted interventions to modulate senescence in urinary tumors. However, challenges such as off-target effects and the need for precise delivery systems must be addressed to translate these findings into clinically viable applications.

Conclusion

The convergence of lncRNAs, senescence, and urinary tumors represents a captivating frontier in cancer research. With a deeper comprehension of the complex molecular mechanisms underlying these processes, novel approaches to diagnosis and treatment become possible. Utilizing lncRNAs’ regulatory ability to modify senescence in bladder cancers has enormous potential for individualized medicine, giving patients new hope and fundamentally altering the way that cancer treatment is delivered.

References

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Author contributions

DCF and RCW proposed the project, conducted data analysis, interpreted the data, and wrote the manuscript; DCF and DXL supervised the project, and interpreted the data. All authors reviewed and edited the manuscript.

Competing interests

The authors declare no conflicts of interest.

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Abbreviations

lncRNAs, long non-coding RNAs; SASP, senescence-associated secretory phenotype.

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