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Long Non-Coding RNAs in Kidney Injury: A Comprehensive Review

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Abstract*: *Kidney injury, a global health challenge, necessitates a nuanced understanding of molecular intricacies for effective interventions. Long non-coding RNAs (lncRNAs), once dismissed as transcriptional noise, now emerge as pivotal players in orchestrating renal health. Dysregulation of specific lncRNAs like TUG1, MALAT1, H19, and NEAT1 provides molecular signatures, distinguishing physiological states from pathological conditions. In acute kidney injury (AKI), TUG1 and MALAT1 regulate apoptosis, inflammation, and fibrosis. Chronic kidney disease (CKD) involves lncRNAs like H19 and NEAT1 modulating cell proliferation and apoptosis. Beyond diagnostics, lncRNAs actively shape inflammation, apoptosis, and fibrosis, positioning them as master regulators in the intricate ballet of kidney health. Recent strides in research, coupled with cutting-edge genomics and bioinformatics tools, highlight their roles and therapeutic potential. Challenges in understanding their intricate roles and interactions necessitate the exploration of promising avenues, including single-cell RNA sequencing and artificial intelligence, paving the way for personalized interventions and regenerative medicine in kidney diseases.

Key Words: Long Non-Coding RNAs, Acute Kidney Injury, MALAT1, TUG1, Apoptosis.

1. INTRODUCTION

The increasing global concern regarding kidney damage necessitates a focused exploration of its molecular intricacies for effective treatment strategies [1]. Long non-coding RNAs (lncRNAs), specifically those longer than 200 nucleotides, have emerged as key players in understanding kidney injury. These molecules, once considered transcriptional noise, now play crucial roles in epigenetic modification, chromatin remodeling, and gene regulation, influencing processes like differentiation, apoptosis, and proliferation [4]. Dysregulation of

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lncRNAs, such as TUG1, MALAT1, H19, and NEAT1, has been linked to acute kidney injury (AKI) and chronic kidney disease (CKD), providing potential molecular signatures for diagnosis [5].
Highlighted lncRNAs like TUG1, elevated in AKI, control inflammation and apoptosis, while MALAT1 is implicated in fibrosis [7]. H19 and NEAT1 are involved in CKD, with NEAT1 elevated in inflammation and H19 regulating cell proliferation and apoptosis [8]. Additionally, lncRNAs like HOTAIR and GAS5 are relevant in diabetic nephropathy (DN), influencing apoptosis and fibrosis [9]. These molecules serve as biomarkers differentiating between healthy and pathological states, challenging the notion that they are mere transcriptional noise [10].
The integration of genomics and bioinformatics tools has enhanced our understanding of lncRNA contributions to inflammation, apoptosis, and fibrosis, turning them from passive observers to active conductors in kidney pathophysiology [12-15]. In the complex dance of kidney health and illness, lncRNAs now take center stage as master regulators of gene expression and cellular activities [16]. This review emphasizes the crucial need to identify molecular pathways underlying kidney injury, contributing to the evolving narrative of lncRNAs as conductors in the intricate symphony of kidney health.

2. RELATED WORK

- "Non-Coding RNAs in Kidney Diseases: The Long and Short of Them" by Moreno et al. This paper provides a comprehensive review of the role of lncRNAs in kidney diseases, their molecular mechanisms, and their function as emerging prognostic biomarkers for both acute and chronic kidney diseases [17].
- "Long Non-Coding RNAs in Kidney Disease" by Ignarski et al. This paper provides an overview of the current knowledge on lncRNAs in both glomerular and tubulointerstitial kidney disease [18].
- "Long noncoding RNAs in renal diseases" published in ExRNA. This review summarizes available studies indicating that lncRNAs are heavily involved in kidney development and disease and proposes lncRNAs as novel biomarkers for clinical diagnosis and potential therapeutic targets in renal diseases [19].
- "Non-Coding RNA and Renal Disease" published in Frontiers Research Topic. This paper broadly associates the role of some ncRNAs, such as microRNAs (miRNAs) and long-non-coding-RNAs (lncRNAs), with acute and chronic kidney disease, diabetic nephropathy, fibrosis, and renal cancer [20].
- "The Mission of Long Non-Coding RNAs in Human Adult Renal Stem" by MDPI. This paper discusses the tens of thousands of lncRNA sequences expressed in the kidney and their implications in all phases of renal disorders [21].

3. METHODOLOGY

Literature Search: Conducted a thorough search in PubMed, ScienceDirect, and Google Scholar using keywords like "Long Non-coding RNAs," "Kidney Injury," and "lncRNAs in renal diseases." Identified relevant articles, reviews, and research papers in peer-reviewed journals.

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Selection Criteria: Focused on articles providing in-depth insights into molecular roles of lncRNAs in kidney injury, emphasizing specific ones like TUG1, MALAT1, H19, and NEAT1. Considered studies exploring functional roles of dysregulated lncRNAs in acute and chronic kidney diseases.

Inclusion of Key Studies: Included seminal works like "Non-Coding RNAs in Kidney Diseases" by Moreno et al., "Long Non-Coding RNAs in Kidney Disease" by Ignarski et al., and relevant reviews from ExRNA, Frontiers Research Topic, and MDPI.

Data Extraction: Extracted key data on lncRNAs' roles in kidney injury, emphasizing inflammation, apoptosis, and fibrosis modulation. Focused on studies using genomics, bioinformatics tools, and molecular biology techniques to elucidate lncRNAs' contributions.

Integration of Findings: Synthesized information from various studies to construct a comprehensive narrative on lncRNAs' involvement in kidney health and pathology. Emphasized molecular mechanisms, crosstalk with other noncoding RNAs, and regulatory roles in inflammation, apoptosis, and fibrosis.

Dysregulated lncRNAs in Kidney Injury

There is a lot of promise for the dysregulated lncRNAs in renal damage as predictive and diagnostic biomarkers [22]. Blood and urine are two biological materials in which their altered expression patterns in kidney injury can be found [23]. Clinicians may be able to detect patients who are at risk of kidney damage or track the course of the illness by evaluating the levels of these lncRNAs [24]. When kidney damage occurs, a number of long non-coding RNAs (lncRNAs) are dysregulated [25]. While HOTAIR, NEAT1, LINC01619, LINC00355, and LINC00511 are upregulated, they also contribute to fibroblast activation, renal fibrosis, and the regulation of pro-inflammatory genes. MALAT1, TUG1, LINC00963, LINC00261, LINC00473, LINC00657, LINC00839, and LINC00908 are upregulated, promoting inflammation and apoptosis in kidney cells. Fibroblast growth is inhibited through downregulation of GAS5. These long noncoding RNAs (lncRNAs) are essential for the complex molecular regulation of kidney health and pathology, and they offer prospective targets for comprehension and manipulation of renal pathophysiology [26]. Table 1 lists the different lncRNAs and their roles in kidney damage.

Sl. No.	lncRNA Name	Upregulation/Downregulation	Role in Kidney Injury	Reference
1	MALAT1	Upregulated	Promotes inflammation and apoptosis in kidney cells	[27]
2	HOTAIR	Upregulated	Promotes activation of fibroblasts and renal fibrosis	[28]
3	NEAT1	Upregulated	Regulates pro-inflammatory genes and promotes apoptosis	[29]

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4	TUG1	Upregulated	Promotes inflammation and apoptosis in kidney cells	[30]
5	GAS5	Downregulated	Inhibits proliferation and activation of fibroblasts	[31]
6	LINC00963	Upregulated	Promotes inflammation and apoptosis in kidney cells	[32]
7	LINC01619	Upregulated	Regulates pro-inflammatory genes and promotes apoptosis	[33]
8	LINC00261	Upregulated	Promotes inflammation and apoptosis in kidney cells	[34]
9	LINC00355	Upregulated	Regulates pro-inflammatory genes and promotes apoptosis	[35]
10	LINC00473	Upregulated	Promotes inflammation and apoptosis in kidney cells	[36]
11	LINC00511	Upregulated	Regulates pro-inflammatory genes and promotes apoptosis	[37]
12	LINC00657	Upregulated	Promotes inflammation and apoptosis in kidney cells	[38]
13	LINC00707	Upregulated	Regulates pro-inflammatory genes and promotes apoptosis	[39]
14	LINC00839	Upregulated	Promotes inflammation and apoptosis in kidney cells	[40]
15	LINC00908	Upregulated	Regulates pro-inflammatory genes and promotes apoptosis	[41]

Table: 1 Upregulation or Downregulation of specific lncRNAs and their roles in kidney injury, providing a clear overview of their involvement in various aspects of renal health and pathology.

Functional Roles oF lncRNAs

Long noncoding RNAs (lncRNAs), once considered "junk" RNA, now emerge as crucial regulators influencing cellular functions and gene expression, especially in contexts like kidney damage [42]. This review explores their functional roles, emphasizing their involvement in fibrosis, apoptosis, inflammation, and interactions with other noncoding RNAs [43].

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Regulation of Inflammation: In kidney injury, lncRNAs play crucial roles in controlling the inflammatory response [30]. For instance, MALAT1 activates the NF-κB signaling pathway in renal tubular epithelial cells, inducing inflammation, while NEAT1 exposure in renal mesangial cells leads to the release of pro-inflammatory cytokines [44,45]. These lncRNAs act as scaffolds, bringing transcription factors and chromatin modifiers together, regulating inflammatory gene expression. Additionally, they can sequester miRNAs, acting as competitive endogenous RNAs (ceRNAs), and modulate signaling pathways linked to inflammation, such as JAK/STAT and NF-κB [46,47].

Modulation of Apoptosis: Apoptosis, a critical process in kidney injury, is regulated by numerous lncRNAs [32]. TUG1 induces mortality in renal tubular epithelial cells by sponging miR-27a, while HOTAIR inhibits renal cell death by interacting with the polycomb repressive complex 2 (PRC2) [48-50]. The intricate regulation of apoptosis involves interactions with essential apoptotic proteins, ceRNA mechanisms, and epigenetic changes affecting gene expression related to apoptosis [51,52].

Impact on Fibrosis: Renal fibrosis, a hallmark of chronic kidney disease, is influenced by various lncRNAs. MALAT1 promotes renal fibrosis by activating the TGF-β/Smad signaling pathway, inducing fibrotic gene production [53,54]. The lncRNA H19, through suppression of its target gene COL1A1 and sponging miR-29b, contributes to renal fibrosis. LncRNAs regulate crucial signaling pathways involved in fibrosis, including TGF-β/Smad, Wnt/β-catenin, and Notch, by interacting with key components and regulating gene expression [55,56].

Crosstalk with Other Noncoding RNAs: LncRNAs interact with miRNAs, influencing gene expression and various processes in kidney injury. For instance, GAS5 sequesters miR-21, preventing renal fibrosis. The intricate regulatory mechanisms involve direct base pairing and indirect interactions mediated by RNA-binding proteins [43, 57].

Epigenetic Regulation by lncRNAs: LncRNAs impact epigenetic changes, such as histone modifications and chromatin remodelling, in kidney damage. HOTAIR interacts with PRC2 and LSD1, regulating gene expression in renal cells. ANRIL recruits PRC1 and PRC2, repressing target genes associated with renal fibrosis. The extensive effects of lncRNA-mediated epigenetic regulation span critical processes like fibrosis, apoptosis, and inflammation [52, 58-62].

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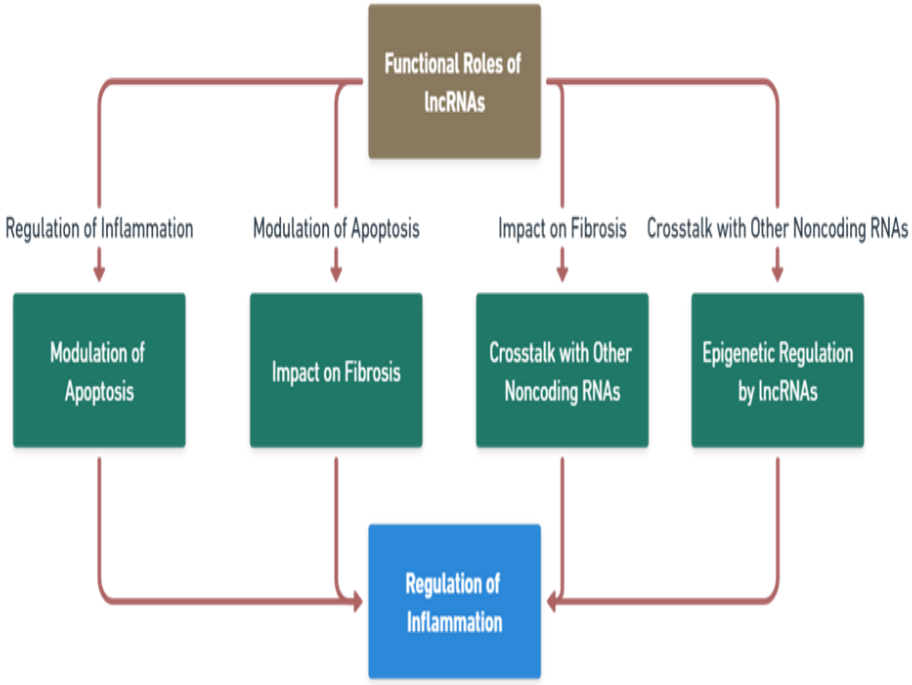

Figure 1: Functional roles of lncRNAs.

Molecular Mechanism oF lncRNAs

Long noncoding RNAs (lncRNAs) have emerged as pivotal regulators of gene expression, intricately intertwined with diverse biological processes, including kidney damage and repair [63,64]. Their profound impact on the cellular and molecular milieu of the kidneys is evident from meticulous investigations into the molecular pathways through which they influence kidney injury. In the realm of acute kidney injury (AKI), various functions of lncRNAs have been spotlighted, with documented evidence of their variable expression and involvement in critical biological processes [65]. Notably, specific lncRNAs play crucial roles in the initiation and progression of AKI, intricately regulating pivotal biochemical pathways. For instance, the lncRNA TUG1 orchestrates ischemia-reperfusion (I/R)-mediated AKI by modulating the miR-494-3p/E-cadherin axis, highlighting their intricate regulatory functions in pivotal biochemical pathways implicated in AKI pathophysiology [66].

The influence of lncRNAs extends to diabetic nephropathy (DN), where ENST0000436340 exacerbates podocyte damage by facilitating the interaction between PTBP1 and RAB3B. The role of lncRNAs in diabetic mesangial cell damage is gaining recognition, offering potential novel therapeutic targets for kidney diseases, including DN [67,68]. Additionally, the dysregulation of Hoxb3os, a lncRNA regulating mTOR signaling, is associated with autosomal dominant polycystic kidney disease [69]. These findings underscore the diverse and context-specific roles of lncRNAs in modulating the pathophysiology of various kidney diseases by interacting with different molecular pathways [70].

These context-dependent roles position lncRNAs as promising targets for innovative therapeutic approaches and potential biomarkers for early detection and prognosis of kidney

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disorders. To comprehensively understand their unique biological roles and intricate mechanisms in kidney damage and healing, further investigation is imperative. This exploration could pave the way for the development of lncRNA-based treatments for a spectrum of renal illnesses, emphasizing the versatility and significance of lncRNAs in kidney injury and repair, as well as their potential role in the development and progression of various kidney diseases [59,71].

Clinical Implications and Therapeutic Potential of lncRNAs

Long non-coding RNAs (lncRNAs) hold significant clinical implications and therapeutic potential, particularly in cancer, garnering attention for RNA-based medicines such as tiny interfering RNAs (RNAi) and antisense oligonucleotides (ASOs) with multiple FDA approvals highlighting their importance [72-74]. Serving as revolutionary biomarkers, elevated lncRNA H19 expression demonstrates remarkable sensitivity (90%) and specificity (85%) in early hepatocellular carcinoma (HCC) detection [76-78]. LncRNAs like NEAT1 play a crucial role in real-time monitoring of pancreatic ductal adenocarcinoma (PDAC), providing vital information for disease tracking and treatment evaluation [79,80]. Across various cancers, lncRNAs, such as HOTAIR in ovarian cancer, serve as prognostic markers, aiding personalized treatment planning and predicting resistance to platinum-based chemotherapy [81,82]. In colorectal cancer and non-small cell lung cancer (NSCLC), lncRNAs like MALAT1 and SNHG16 function as prognostic markers, indicating poor prognosis, tumor aggressiveness, and disease stage. The correlation between elevated GAS5 levels and a better prognosis in heart failure patients suggests a potential biomarker for predicting outcomes in cardiovascular disorders [83]. Targeting specific lncRNAs shows therapeutic potential in diverse disease domains, such as suppressing HOXA11 in cancer, demonstrating promise in reducing breast cancer cell proliferation and preventing tumor growth [84]. The overexpression of BDNF-AS in neurodegenerative diseases like Alzheimer's presents a potential treatment strategy, while CRISPR/Cas9-mediated removal of ANRIL in cardiovascular research improves heart function and fosters cardiac repair in mice after myocardial infarction [85]. Additionally, NEAT1 knockdown proves beneficial in the metabolic domain, enhancing insulin sensitivity and glucose metabolism in diabetic mice, suggesting a potential treatment target for type 2 diabetes [86].

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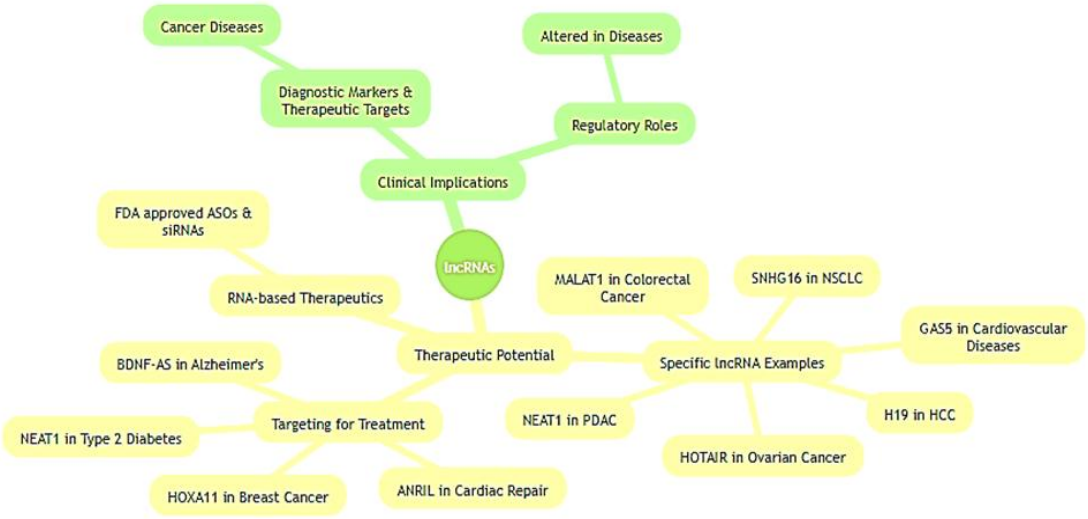

Figure: 2 Clinical implications and therapeutic potential of lncRNAs.

4. RESULT AND DISCUSSION

The evolving landscape of long non-coding RNAs (lncRNAs) in kidney injury presents both exciting possibilities and challenges. The intricate functional diversity of lncRNAs complicates the identification of specific roles in complex processes like kidney damage, hampering targeted therapy options. Understanding their activities across different cell types and their interactions with biomolecules remains a daunting task [83]. The lack of precise knowledge about how lncRNAs impact renal damage limits opportunities for targeted therapy [64]. Identifying reliable kidney injury biomarkers for tailored treatment and early intervention proves challenging, given the difficulty of distinguishing disease-specific lncRNAs from those indicating general stress responses [84].

Recent breakthroughs, notably single-cell RNA sequencing (scRNA-seq), have revolutionized our understanding of lncRNA expression patterns in various kidney cell types [85,86]. ScRNA-seq studies have unveiled novel lncRNAs like lnc-NEAT1, providing insights into their roles in podocyte destruction and chronic kidney disease (CKD) progression. Exploration of circular RNAs (circRNAs) has revealed their potential involvement in renal damage, with circRNA SMARCA5 identified as a regulator of autophagy to counter cisplatin-induced acute kidney injury [64].

The integration of artificial intelligence (AI) to predict lncRNA functions and therapeutic targets represents a significant advancement. AI applications, particularly in forecasting lncRNAs regulating inflammation in acute kidney injury, pave the way for innovative anti-inflammatory treatments, with ongoing development of machine learning techniques [85,86].

Future directions in lncRNA research suggest promising avenues, including the development of focused kidney damage treatments and non-invasive diagnostic tools through the identification of disease-specific lncRNAs [82]. Research on lncRNA-based regenerative medicine explores the potential use of lncRNAs to promote kidney regeneration and healing post-injury. The concept of personalized treatment based on lncRNA expression patterns for specific kidney injury types and underlying genetic factors is intriguing [83]. As research

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progresses, close attention to ethical concerns related to the use of lncRNA-based therapies and the evaluation of benefits and drawbacks remains imperative.

5. CONCLUSION

Dysregulated long non-coding RNAs (lncRNAs) like MALAT1 and TUG1 serve as molecular indicators for detecting renal illness, playing a significant role as regulators in kidney damage. These lncRNAs directly impact complex biological processes, including inflammation, fibrosis, and apoptosis. Beyond diagnostics, lncRNAs such as H19 and NEAT1 intricately interact with miRNAs, influencing the aetiology of renal diseases. With RNA-based therapeutics gaining prominence, lncRNAs emerge as potential therapeutic targets and diagnostic indicators in clinical settings, aided by recent advancements in single-cell RNA sequencing and artificial intelligence for a deeper understanding and treatment of kidney injury.

6. REFERENCES

1. N Perico, G Remuzzi et al. Chronic kidney disease: a research and public health priority. Nephrol Dial Transplant. 2012;27(suppl_3):iii19-26.
2. EL Bamgboye. The challenges of ESRD care in developing economies: sub-Saharan African opportunities for significant improvement. Clin Nephrol. 2016;86(13):18-22.
3. R Tripathi, P Chakraborty, PK Varadwaj. Unraveling long non-coding RNAs through analysis of high-throughput RNA-sequencing data. Non-coding RNA Res. 2017;2(2):111-8.
4. N Qu, T Luan, N Liu, C Kong, L Xu, H Yu et al. Hepatocyte nuclear factor 4α (HNF4α): A perspective in cancer. Biomed Pharmacother. 2023;169:115923.
5. NH Navise, GG Mokwatsi, LF Gafane-Matemane, J Fabian, L Lammertyn et al. Kidney dysfunction: prevalence and associated risk factors in a community-based study from the North West Province of South Africa. BMC Nephrol. 2023;24(1):1-8.
6. GS Shields, WG Moons, GM Slavich et al. Inflammation, self-regulation, and health: An immunologic model of self-regulatory failure. Perspect Psychol Sci. 2017;12(4):588-612.
7. Y Cai, Y Zhou, Z Li, P Xia, X ChenFu, A Shi, J Zhang, P Yu et al. Non-coding RNAs in necroptosis, pyroptosis, and ferroptosis in cardiovascular diseases. Front Cardiovasc Med. 2022;9:909716.
8. Q Wu, F Huang. LncRNA H19: a novel player in the regulation of diabetic kidney disease. Front Endocrinol. 2023;14:1238981.
9. Y Zhao, G Yan, J Mi, G Wang, M Yu, D Jin et al. The impact of lncRNA on diabetic kidney disease: systematic review and in silico analyses. Comput Intell Neurosci. 2022;2022:8400106.
10. K Schlosser, J Hanson, PJ Villeneuve, J Dimitroulakos, L McIntyre, L Pilote, DJ Stewart et al. Assessment of circulating LncRNAs under physiologic and pathologic conditions in humans reveals potential limitations as biomarkers. Sci Rep. 2016;6(1):36596.

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http://journal.hmjournals.com/index.php/JPDMHD
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11. AA Fachel, AC Tahira, SA Vilella-Arias, V Maracaja-Coutinho, ER Gimba, GM Vignal, ... et al. Expression analysis and in silico characterization of intronic long noncoding RNAs in renal cell carcinoma: emerging functional associations. Mol Cancer. 2013;12:1-23.
12. F Lausecker, R Lennon, MJ Randles et al. The kidney matrisome in health, aging, and disease. Kidney Int. 2022;102(5):1000-12.
13. C Domingues, A Santos, C Alvarez-Lorenzo, A Concheiro, I Jarak, F Veiga, ... et al. Where is nano today and where is it headed? A review of nanomedicine and the dilemma of nanotoxicology. ACS Nano. 2022;16(7):9994-10041.
14. C Ekhator, H Grezenko, Z Haider, UA Cheema, H Haider, SN Mohsin, ... et al. Beneath the Layers: Deciphering the Molecular Pathways, Therapeutic Avenues, and Neurological Connections of Soft Tissue Sarcomas. Cureus. 2023;15(9).
15. F Leti, E Morrison, JK DiStefano. Long noncoding RNAs in the pathogenesis of diabetic kidney disease: implications for novel therapeutic strategies. Pers Med. 2017;14(3):271-8.
16. J Ouyang, Q Wang. Spotlight on iron and ferroptosis: research progress in diabetic retinopathy. Front Endocrinol. 2023;14:1234824.
17. Moreno JA, Hamza E, Guerrero-Hue M, Rayego-Mateos S, García-Caballero C, Vallejo-Mudarra M, et al. Non-coding RNAs in kidney diseases: The long and short of them. Int J Mol Sci. 2021;22(11):6077.
18. Ignarski M, Islam R, Müller RU. Long non-coding RNAs in kidney disease. Int J Mol Sci. 2019 Jul 3;20(13):3276.
19. Liu M, Ren J. Long noncoding RNAs in renal diseases. ExRNA. 2019;1(1):1-9.
20. Kato M, Chen Z, Das S, Wu X, Wang J, Li A, et al. Long non-coding RNA lncMGC mediates the expression of TGF-β-induced genes in renal cells via nucleosome remodelers. Front Mol Biosci. 2023;10:1204124.
21. Giannuzzi F, Maiullari S, Gesualdo L, Sallustio F. The Mission of Long Non-Coding RNAs in Human Adult Renal Stem/Progenitor Cells and Renal Diseases. Cells. 2023;12(8):1115.
22. T Ma, H Jia, P Ji, Y He, L Chen. Identification of the candidate lncRNA biomarkers for acute kidney injury: a systematic review and meta-analysis. Expert Rev Mol Diagn. 2021;21(1):77-89.
23. ED Siew, LB Ware, TA Ikizler. Biological markers of acute kidney injury. J Am Soc Nephrol. 2011;22(5):810-20.
24. LJ Zhou, DW Yang, LN Ou, XR Guo, BL Wu. Circulating expression level of LncRNA Malat1 in diabetic kidney disease patients and its clinical significance. J Diabetes Res. 2020;2020.
25. M Kato. Noncoding RNAs as therapeutic targets in early stage diabetic kidney disease. Kidney Res Clin Pract. 2018;37(3):197.
26. H Tian, M Wu, P Zhou, C Huang, C Ye, L Wang. The long non-coding RNA MALAT1 is increased in renal ischemia-reperfusion injury and inhibits hypoxia-induced inflammation. Ren Fail. 2018;40(1):527-33.
27. H Zhou, L Gao, ZH Yu, SJ Hong, ZW Zhang, ZZ Qiu. LncRNA HOTAIR promotes renal interstitial fibrosis by regulating Notch1 pathway via the modulation of miR-124. Nephrology. 2019;24(4):472-80.

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http://journal.hmjournals.com/index.php/JPDMHD
DOI: https://doi.org/10.55529/jpdmhd.42.39.52

28. J Ma, N Zhao, L Du, Y Wang. Downregulation of lncRNA NEAT1 inhibits mouse mesangial cell proliferation, fibrosis, and inflammation but promotes apoptosis in diabetic nephropathy. Int J Clin Exp Pathol. 2019;12(4):1174.
29. Y Xu, Y Niu, H Li, G Pan. Downregulation of lncRNA TUG1 attenuates inflammation and apoptosis of renal tubular epithelial cell induced by ischemia-reperfusion by sponging miR-449b-5p via targeting HMGB1 and MMP2. Inflammation. 2020;43:1362-74.
30. R Tang, YC Wang, X Mei, N Shi, C Sun, R Ran et al. LncRNA GAS5 attenuates fibroblast activation through inhibiting Smad3 signaling. Am J Physiol Cell Physiol. 2020;319(1):C105-C115.
31. W Chen, ZQ Zhou, YQ Ren, L Zhang, LN Sun, YL Man, ... et al. Effects of long non-coding RNA LINC00667 on renal tubular epithelial cell proliferation, apoptosis, and renal fibrosis via the miR-19b-3p/LINC00667/CTGF signaling pathway in chronic renal failure. Cell Signal. 2019;54:102-14.
32. Y Zhong, CL Ashley, M Steain, SF Ataide. Assessing the suitability of long non-coding RNAs as therapeutic targets and biomarkers in SARS-CoV-2 infection. Front Mol Biosci. 2022;9:975322.
33. X Li, J Li, P Lu, M Li. LINC00261 relieves the progression of sepsis-induced acute kidney injury by inhibiting NF-κB activation through targeting the miR-654-5p/SOCS3 axis. J Bioenerg Biomembr. 2021;53:129-37.
34. A Arunima, EJ van Schaik, JE Samuel. The emerging roles of long non-coding RNA in host immune response and intracellular bacterial infections. Front Cell Infect Microbiol. 2023;13:456.
35. G Fan, J Liu, Y Zhang, X Guan. LINC00473 exacerbates osteoarthritis development by promoting chondrocyte apoptosis and proinflammatory cytokine production through the miR 424-5p/LY6E axis. Exp Ther Med. 2021;22(5):1-3.
36. Dolcino M, Tinazzi E, Vitali C, Del Papa N, Puccetti A, Lunardi C. Long non-coding RNAs modulate Sjögren's syndrome associated gene expression and are involved in the pathogenesis of the disease. J Clin Med. 2019;8(9):1349.
37. Liang Y, Xu XD, Xu X, Cai YB, Zhu ZX, Zhu L, et al. Linc00657 promoted pyroptosis in THP-1-derived macrophages and exacerbated atherosclerosis via the miR-106b-5p/TXNIP/NLRP3 axis. Int J Biol Macromol. 2023;253:126953.
38. Wu Z, Huang X, Cai M, Huang P. Potential biomarkers for predicting the overall survival outcome of kidney renal papillary cell carcinoma: an analysis of ferroptosis-related lncRNAs. BMC Urology. 2022 Dec;22(1):1-2.
39. Xiao X, Cai W, Ding Z, Mao Z, Shi Y, Zhang Q. LincRNA00612 inhibits apoptosis and inflammation in LPS-induced BEAS-2B cells via enhancing interaction between p-STAT3 and A2M promoter. PeerJ. 2023 Mar 2;11:e14986.
40. Deniz E, Erman B. Long noncoding RNA (lincRNA), a new paradigm in gene expression control. Funct Integr Genomics. 2017;17:135-43.
41. Moreno JA, Hamza E, Guerrero-Hue M, Rayego-Mateos S, García-Caballero C, Vallejo-Mudarra M, Metzinger L, Metzinger-Le Meuth V. Non-coding RNAs in kidney diseases: The long and short of them. Int J Mol Sci. 2021;22(11):6077.

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http://journal.hmjournals.com/index.php/JPDMHD
DOI: https://doi.org/10.55529/jpdmhd.42.39.52

42. Zhan JF, Huang HW, Huang C, Hu LL, Xu WW. Long non-coding RNA NEAT1 regulates pyroptosis in diabetic nephropathy via mediating the miR-34c/NLRP3 axis. Kidney Blood Press Res. 2020;45(4):589-602.
43. Lin J, Jiang Z, Liu C, Zhou D, Song J, Liao Y, Chen J. Emerging roles of long non-coding RNAs in renal fibrosis. Life. 2020;10(8):131.
44. Kartha RV, Subramanian S. Competing endogenous RNAs (ceRNAs): new entrants to the intricacies of gene regulation. Front Genet. 2014 30;5:8.
45. Liu P, Zhang BO, Chen Z, He Y, Du Y, Liu Y, Chen X. m6A-induced lncRNA MALAT1 aggravates renal fibrogenesis in obstructive nephropathy through the miR-145/FAK pathway. Aging (Albany NY). 2020;12(6):5280.
46. Kota SK, Kota SB. Noncoding RNA and epigenetic gene regulation in renal diseases. Drug Discov Today. 2017 Jul 1;22(7):1112-22.
47. Meng XM, Nikolic-Paterson DJ, Lan HY. TGF-β: the master regulator of fibrosis. Nat Rev Nephrol. 2016;12(6):325-38.
48. Yoon JH, Abdelmohsen K, Gorospe M. Functional interactions among microRNAs and long noncoding RNAs. Semin Cell Dev Biol. 2014;34:9-14.
49. Sacco LD, Masotti A. Recent insights and novel bioinformatics tools to understand the role of microRNAs binding to 5'untranslated region. Int J Mol Sci. 2013;14(1):480-95.
50. Liu J, Li H, Zheng B, Sun L, Yuan Y, Xing C. Competitive endogenous RNA (ceRNA) regulation network of lncRNA–miRNA–mRNA in colorectal carcinogenesis. Dig Dis Sci. 2019;64:1868-77.
51. Rottach A, Leonhardt H, Spada F. DNA methylation-mediated epigenetic control. J Cell Biochem. 2009;108(1):43-51.
52. Guo C, Dong G, Liang X, Dong Z. Epigenetic regulation in AKI and kidney repair: mechanisms and therapeutic implications. Nat Rev Nephrol. 2019;15(4):220-39.
53. Lorenzen JM, Thum T. Long noncoding RNAs in kidney and cardiovascular diseases. Nat Rev Nephrol. 2016;12(6):360-73.
54. Fernandes JC, Acuña SM, Aoki JI, Floeter-Winter LM, Muxel SM. Long non-coding RNAs in the regulation of gene expression: physiology and disease. Noncoding RNA. 2019;5(1):17.
55. Brandenburger T, Somoza AS, Devaux Y, Lorenzen JM. Noncoding RNAs in acute kidney injury. Kidney Int. 2018;94(5):870-81.Ren GL, Zhu J, Li J, Meng XM. Noncoding RNAs in acute kidney injury. J Cell Physiol. 2019;234(3):2266-76.
56. Chen L, Xu JY, Tan HB. LncRNA TUG1 regulates the development of ischemia-reperfusion mediated acute kidney injury through miR-494-3p/E-cadherin axis. J Inflamm. 2021;18(1):1-10.
57. Jiao H, Xie D, Qiao Y. LncRNA PRINS is involved in the development of nephropathy in patients with diabetes via interaction with Smad7. Exp Ther Med. 2019;17(4):3203-8.
58. Stampone E, Caldarelli I, Zullo A, Bencivenga D, Mancini FP, Della Ragione F, et al. Genetic and epigenetic control of CDKN1C expression: importance in cell commitment and differentiation, tissue homeostasis and human diseases. Int J Mol Sci. 2018;19(4):1055.

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59. Lei H, Gao Y, Xu X. LncRNA TUG1 influences papillary thyroid cancer cell proliferation, migration and EMT formation through targeting miR-145. Acta Biochim Biophys Sin. 2017;49(7):588-97.
60. Hussain MS, Majami AA, Ali H, Kumar G, Almalki WH, et al. The complex role of MEG3: An emerging long non-coding RNA in breast cancer. Pathol Res Pract. 2023:154850.
61. Wang YN, Yang CE, Zhang DD, Chen YY, Yu XY, Zhao YY, et al. Long non-coding RNAs: A double-edged sword in aging kidney and renal disease. Chemico-Biol Interact. 2021;337:109396.
62. Qian Y, Shi L, Luo Z. Long non-coding RNAs in cancer: implications for diagnosis, prognosis, and therapy. Front Med (China). 2020 Nov 30;7:902.
63. Tian X, Sun D, Zhao S, Xiong H, Fang J. Screening of potential diagnostic markers and therapeutic targets against colorectal cancer. Oncotarget. 2015:1691-9.
64. Garbo S, Maione R, Tripodi M, Battistelli C. Next RNA therapeutics: the mine of non-coding. Int J Mol Sci. 2022;23(13):7471.
65. Bhan A, Mandal SS. Long noncoding RNAs: emerging stars in gene regulation, epigenetics and human disease. ChemMedChem. 2014;9(9):1932-56.
66. Fatima R, Akhade VS, Pal D, Rao SM. Long noncoding RNAs in development and cancer: potential biomarkers and therapeutic targets. Mol Cell Ther. 2015;3:1-9.
67. Chen T. Circulating non-coding RNAs as potential diagnostic biomarkers in hepatocellular carcinoma. J Hepatocell Carcinoma. 2022;9:1029-40.
68. Wazir H, Abid M, Essani B, Saeed H, Khan MA, Nasrullah FN, et al. Diagnosis and Treatment of Liver Disease: Current Trends and Future Directions. Cureus. 2023;15(12).
69. Wang S, Sun ST, Zhang XY, Ding HR, Yuan Y, He JJ, et al. The Evolution of Single-Cell RNA Sequencing Technology and Application: Progress and Perspectives. Int J Mol Sci. 2023;24(3):2943.
70. Shakhpazyan NK, Mikhaleva LM, Bedzhanyan AL, Sadykhov NK, Midiber KY, Konyukova AK, et al. Long Non-Coding RNAs in Colorectal Cancer: Navigating the Intersections of Immunity, Intercellular Communication, and Therapeutic Potential. Biomedicines. 2023;11(9):2411.
71. Chen Y, Zitello E, Guo R, Deng Y. The function of LncRNAs and their role in the prediction, diagnosis, and prognosis of lung cancer. Clin Transl Med. 2021;11(4):e367.
72. Guo C, Song C, Zhang J, Gao Y, Qi Y, Zhao Z, et al. Revisiting chemoresistance in ovarian cancer: Mechanism, biomarkers, and precision medicine. Genes Dis. 2022;9(3):668-81.
73. Kumarswamy R, Bauters C, Volkmann I, Maury F, Fetisch J, Holzmann A, et al. Circulating long noncoding RNA, LIPCAR, predicts survival in patients with heart failure. Circ Res. 2014;114(10):1569-75.
74. Saltarella I, Apollonio B, Lamanuzzi A, Desantis V, Mariggiò MA, Desaphy JF, et al. The Landscape of lncRNAs in Multiple Myeloma: Implications in the "Hallmarks of Cancer", Clinical Perspectives and Therapeutic Opportunities. Cancers. 2022;14(8):1963.
75. [70] Das S, Shah R, Dimmeler S, Freedman JE, Holley C, Lee JM, Moore K, et al. Noncoding RNAs in cardiovascular disease: current knowledge, tools and technologies

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DOI: https://doi.org/10.55529/jpdmhd.42.39.52

for investigation, and future directions: a scientific statement from the American Heart Association. Circ Genom Precis Med. 2020;13(4):e000062.
76. Durr AJ. Amelioration of Mitochondrial Bioenergetic Dysfunction in Diabetes Mellitus: Delving into Specialized and Non-specific Therapeutics for the Ailing Heart. West Virginia University; 2022.
77. Jiang N, Li W, Jiang S, Xie M, Liu R. Acetylation in pathogenesis: Revealing emerging mechanisms and therapeutic prospects. Biomed Pharmacother. 2023;167:115519.
78. Han JD. Understanding biological functions through molecular networks. Cell Res. 2008;18(2):224-37.
79. Nguyen MT, Devarajan P. Biomarkers for the early detection of acute kidney injury. Pediatr Nephrol. 2008;23(12):2151-7.
80. Iatrou A, Clark EM, Wang Y. Nuclear dynamics and stress responses in Alzheimer's disease. Mol Neurodegener. 2021;16(1):1-5.
81. Graves PR, Haystead TA. Molecular biologist's guide to proteomics. Microbiol Mol Biol Rev. 2002 Mar;66(1):39-63.
82. Hun M, Wen H, Wen M, Tian Q, Wang Z, Han P, et al. The Recent Evolution of the Application of Single-Cell Analysis in Kidney Diseases: A bibliometric analysis. 2023:1-78.
83. Chao MU, Xiao-Lu WA, Ying RU, Jia-Jia SU, Xin-Rong HU, Cheng Y. Recent advances in the contribution of circRNAs to cisplatin chemotherapy resistance in cancers. Neoplasma. 2021;68(6):885-93.
84. Tu J, Hu L, Mohammed KJ, Le BN, Chen P, Ali E, et al. Application of logistic regression, support vector machine and random forest on the effects of titanium dioxide nanoparticles using macroalgae in treatment of certain risk factors associated with kidney injuries. Environ Res. 2023;220:115167.
85. Nguyen MT, Devarajan P. Biomarkers for the early detection of acute kidney injury. Pediatr Nephrol. 2008;23(12):2151-7.
86. Iatrou A, Clark EM, Wang Y. Nuclear dynamics and stress responses in Alzheimer's disease. Mol Neurodegener. 2021;16(1):1-5.