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Letter to Editor

Elabela: A Novel Biomarker and Therapeutic Target in Diabetic Kidney Disease

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Dear Editor,

Diabetic kidney disease (DKD), a significant microvascular complication associated with diabetes mellitus, represents the foremost cause of end-stage renal disease globally, resulting in a considerable burden on patients and healthcare systems (1). The intricate pathophysiology of DKD encompasses hyperglycemia-induced mechanisms, oxidative stress, inflammation, and fibrosis. In the context of ongoing research aimed at identifying novel biomarkers and therapeutic targets, Elabela has emerged as a promising candidate for the early prediction and management of DKD.

Elabela, also referred to as Toddler or Apela, is a peptide composed of 54 amino acids, which includes a secretory signal. Its mature form consists of 32 amino acids and was independently identified by two distinct research groups (2,3). Elabela functions as an endogenous ligand for the apelin receptor (APJ), a G protein-coupled receptor (GPCR) that plays a critical role in early embryonic development, particularly in endoderm differentiation and cardiovascular formation (2,3). Although its expression is predominantly limited to specific adult tissues, Elabela is primarily located in the kidneys, prostate, and pluripotent stem cells (2,4). The detection of Elabela mRNA in the adult human kidneys, as noted by Chng et al (2), has spurred further investigations into its physiological relevance in renal function.

The investigation of the tissue distribution of Elabela through reverse transcription polymerase chain reaction (RT-PCR) conducted by Wang et al (4) and Deng et al (5) has substantiated its predominant expression in mature renal tissues. As a circulating hormone peptide (3), Elabela has been demonstrated to enhance cardiac contractility, induce vasodilation, regulate fluid homeostasis, and exhibit anti-atherosclerotic and antioxidative properties via its interaction with the apelin receptor (6,7). Moreover, gene therapy utilizing Elabela has shown renoprotective effects by preserving glomerular structural integrity, mitigating renal fibrosis, and suppressing the expression of fibrotic molecules in hypertensive rodent models (8,9). These findings indicate that Elabela may play a significant role in renal physiology and the progression of renal diseases.

Clinical studies have consistently demonstrated a progressive decline in serum Elabela levels among patients with chronic kidney disease, with a significant correlation identified between Elabela levels and estimated glomerular filtration rate (eGFR) (10). Zhang et al (11) documented a systematic decrease in serum Elabela levels across various stages of DKD, ranging from normal albuminuria to advanced macroalbuminuria accompanied by elevated serum creatinine. Importantly, an inverse relationship was identified between serum Elabela levels and the albumin/creatinine ratio, serum creatinine, retinopathy, and blood pressure, while a positive correlation was established with eGFR. These findings were corroborated by Onalan et al (12), who reported significantly elevated Elabela levels in healthy individuals compared to diabetic patients, with further reductions observed in patients exhibiting worsening albuminuria and renal dysfunction. Similarly, Mohamed et al (13) reported a pronounced decline in serum Elabela levels in patients with progressive diabetic nephropathy, thereby reinforcing its potential role as a clinical prognostic marker.

Preclinical studies provide robust evidence for the therapeutic potential of Elabela in the context of DKD. The administration of Elabela in streptozotocin-induced diabetic murine models significantly decreased markers indicative of renal inflammation and fibrosis, resulting in enhanced renal function and protection against podocyte

injury (14). Zheng et al (15) demonstrated that Elabela effectively inhibits the progression of DKD by activating renal tubular autophagy, a process that is otherwise compromised by hyperglycemic conditions. Furthermore, Chen et al (16) elucidated that Elabela administration alleviates diabetic glomerular endothelial damage, with its protective effects being partially mediated through the modulation of the AMPK/NLRP3 signaling pathway.

In conclusion, the significant association between diminished serum Elabela levels and the progression of DKD, coupled with its observed renoprotective effects in preclinical models, underscores its potential utility as both a biomarker and a therapeutic target. Notwithstanding these encouraging findings, further research is necessary to clarify the specific mechanisms that underpin the protective role of Elabela in DKD. Future investigations concentrating on large-scale clinical trials and mechanistic pathways will be critical in assessing its translational application in the management of diabetic nephropathy.

Competing Interests
The author declares no conflict of interests.

Ethical Approval
Not applicable.

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References
1. Zhang L, Long J, Jiang W, Shi Y, He X, Zhou Z, et al. Trends in chronic kidney disease in China. N Engl J Med. 2016;375(9):905-6. doi: 10.1056/NEJMc1602469.
2. Chng SC, Ho L, Tian J, Reversade B. ELABELA: a hormone essential for heart development signals via the Apelin receptor. Dev Cell. 2013;27(6):672-80. doi: 10.1016/j.devcel.2013.11.002.
3. Pauli A, Norris ML, Valen E, Chew GL, Gagnon JA, Zimmerman S, et al. Toddler: an embryonic signal that promotes cell movement via Apelin receptors. Science. 2014;343(6172):1248636. doi: 10.1126/science.1248636.
4. Wang Z, Yu D, Wang M, Wang Q, Kouznetsova J, Yang R, et al. Elabela-Apelin receptor signaling pathway is functional in mammalian systems. Sci Rep. 2015;5:8170. doi: 10.1038/srep08170.
5. Deng C, Chen H, Yang N, Feng Y, Hsueh AJ. Apela regulates fluid homeostasis by binding to the APJ receptor to activate Gi signaling. J Biol Chem. 2015;290(30):18261-8. doi: 10.1074/jbc.M115.648238.
6. Xu C, Wang F, Chen Y, Xie S, Sng D, Reversade B, et al. ELABELA antagonizes intrarenal renin-angiotensin system to lower blood pressure and protects against renal injury. Am J Physiol Renal Physiol. 2020;318(5):F1122-35. doi: 10.1152/ajprenal.00606.2019.
7. Xu J, Chen L, Jiang Z, Li L. Biological functions of Elabela, a novel endogenous ligand of APJ receptor. J Cell Physiol. 2018;233(9):6472-82. doi: 10.1002/jcp.26492.
8. Schreiber CA, Holditch SJ, Generous A, Ikeda Y. Sustained ELABELA gene therapy in high-salt diet-induced hypertensive rats. Curr Gene Ther. 2017;16(5):349-60. doi: 10.2174/1566523217666161121111906.
9. Chen Z, Wu C, Liu Y, Li H, Zhu Y, Huang C, et al. ELABELA attenuates deoxycorticosterone acetate/salt-induced hypertension and renal injury by inhibition of NADPH oxidase/ROS/NLRP3 inflammasome pathway. Cell Death Dis. 2020;11(8):698. doi: 10.1038/s41419-020-02912-0.
10. Lu X, Liu S, Luan R, Cui W, Chen Y, Zhang Y, et al. Serum Elabela and Apelin levels during different stages of chronic kidney disease. Ren Fail. 2020;42(1):667-72. doi: 10.1080/0886022x.2020.1792926.
11. Zhang H, Gong D, Ni L, Shi L, Xu W, Shi M, et al. Serum Elabela/Toddler levels are associated with albuminuria in patients with type 2 diabetes. Cell Physiol Biochem. 2018;48(3):1347-54. doi: 10.1159/000492093.
12. Onalan E, Doğan Y, Onalan E, Gozel N, Buran I, Donder E. Elabela levels in patients with type 2 diabetes: can it be a marker for diabetic nephropathy? Afr Health Sci. 2020;20(2):833-40. doi: 10.4314/ahs.v20i2.37.
13. Mohamed SM, Ramadan KS, Saedii AA, Ibrahim EA. Diagnostic significance of Elabela, FABP1, and FABP2 as biomarkers of diabetic nephropathy in type 2 diabetic patients. Indian J Clin Biochem. 2024. doi: 10.1007/s12291-024-01231-x.
14. Zhang Y, Wang Y, Luo M, Xu F, Lu Y, Zhou X, et al. Elabela protects against podocyte injury in mice with streptozocin-induced diabetes by associating with the PI3K/Akt/mTOR pathway. Peptides. 2019;114:29-37. doi: 10.1016/j.peptides.2019.04.005.
15. Zheng X, Yin L, Song J, Chen J, Gu W, Shi M, et al. ELABELA protects against diabetic kidney disease by activating high glucose-inhibited renal tubular autophagy. J Biomed Res. 2023;37(6):460-9. doi: 10.7555/jbr.37.20220214.
16. Chen Z, Wang Z, Hu Y, Lin H, Yin L, Kong J, et al. ELABELA/APJ axis prevents diabetic glomerular endothelial injury by regulating AMPK/NLRP3 pathway. Inflammation. 2023;46(6):2343-58. doi: 10.1007/s10753-023-01882-7.