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Autophagy: A Key to Kidney Health and Disease

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Introduction

Autophagy, a fundamental cellular recycling process, plays a critical role in maintaining renal health by clearing damaged organelles and misfolded proteins. Dysregulation of autophagy contributes significantly to the pathogenesis of various kidney diseases, including chronic kidney disease CKD, diabetic nephropathy, and acute kidney injury AKI. Enhancing or restoring autophagic flux shows promise as a therapeutic strategy to mitigate kidney damage and preserve renal function [1].

In diabetic nephropathy, impaired autophagy contributes to podocyte injury and glomerulosclerosis. Autophagy activators have demonstrated beneficial effects in preclinical models by improving podocyte function and reducing albuminuria. This suggests that modulating autophagy could be a valuable approach to slow the progression of diabetic kidney disease [2].

Acute kidney injury AKI is characterized by rapid loss of renal function, and autophagy plays a dual role, potentially protective in early stages but detrimental in chronic or severe injury. Understanding the temporal and context-dependent role of autophagy is crucial for developing targeted therapies for AKI [3].

Chronic kidney disease CKD involves progressive fibrosis and loss of nephron function, processes where autophagy defects are implicated. Autophagy impairment leads to the accumulation of damaged components, promoting inflammation and fibrosis. Modulating autophagy pathways could help reverse or halt fibrotic changes in CKD [4].

The role of autophagy in polycystic kidney disease PKD is complex. While initial studies suggested a protective role, more recent evidence points to autophagy as a potential therapeutic target for reducing cyst formation and renal damage, particularly when its flux is restored [5].

Metformin, a common drug for type 2 diabetes, has been shown to activate autophagy in renal cells. This mechanism may contribute to its renoprotective effects, particularly in the context of diabetic nephropathy, by improving cellular stress responses and reducing inflammation [6].

Imbalances in the gut microbiome are increasingly linked to kidney disease, and autophagy in intestinal epithelial cells plays a role in maintaining gut barrier integrity. Dysfunctional autophagy can exacerbate kidney injury by promoting inflammation and uremic toxin accumulation [7].

Mitochondrial dysfunction is a key feature in many kidney diseases, and autophagy, specifically mitophagy, is essential for clearing damaged mitochondria. Defective mitophagy leads to increased oxidative stress and further kidney damage, highlighting its therapeutic potential [8].

Autophagy is tightly regulated by various signaling pathways, including mTOR, AMPK, and FOXO. Understanding these regulatory mechanisms is crucial for developing strategies to pharmacologically modulate autophagy for therapeutic benefit in kidney diseases [9].

The role of selective autophagy receptors, such as p62 and NBR1, is paramount in targeting specific cellular components for degradation. These receptors are implicated in the pathogenesis of kidney diseases, and their modulation could offer novel therapeutic avenues [10].

Description

Autophagy, a fundamental cellular recycling process, plays a critical role in maintaining renal health by clearing damaged organelles and misfolded proteins. Dysregulation of autophagy contributes significantly to the pathogenesis of various kidney diseases, including chronic kidney disease CKD, diabetic nephropathy, and acute kidney injury AKI. Enhancing or restoring autophagic flux shows promise as a therapeutic strategy to mitigate kidney damage and preserve renal function [1].

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Conclusion

Autophagy is a vital cellular process for maintaining kidney health by removing damaged components. Its dysregulation is implicated in various kidney diseases, including CKD, diabetic nephropathy, and AKI. Therapeutic strategies targeting autophagy show promise for mitigating kidney damage and preserving function. In diabetic nephropathy, impaired autophagy contributes to podocyte injury, and activators have shown beneficial effects. AKI's complex role for autophagy requires understanding its temporal and context-dependent functions. CKD pathogenesis involves autophagy defects leading to fibrosis and inflammation, suggesting modulation as a therapeutic approach. Polycystic kidney disease also presents a complex role for autophagy, with restoration of flux being a therapeutic target. Metformin activates autophagy, potentially contributing to its renoprotective effects in diabetic nephropathy. Gut microbiome imbalances linked to kidney disease involve autophagy in intestinal cells maintaining gut barrier integrity. Mitophagy, a specific type of autophagy, is crucial for clearing damaged mitochondria, and its defects exacerbate kidney injury. Autophagy regulation by pathways like mTOR and AMPK is key for therapeutic development. Selective autophagy receptors also play a role in kidney pathophysiology, offering potential therapeutic targets.

Acknowledgement

None.

Conflict of Interest

None.

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