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Elucidating Asprosin's Role as an Intracellular Metabolism Regulator in Diabetic Kidney Disease

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Objectives : Asprosin is an adipokine with a multifaceted function that encompasses inducing insulin resistance, promoting inflammation, and stimulating appetite. We seek to establish its pivotal role as a mediator in regulating cellular energy metabolism, particularly in the context of diabetic kidney disease.
Methods : Type 2 diabetic db/db mice were categorized into two groups: one received Asprosin neutralizing antibodies (250 μg/mouse/21 days), targeting the 28-amino acid peptide located proximal to Asprosin's C-terminus (KKKELNQLEDRYDKDYLSGELGDNLKMK), while the other received an AMP-activated protein kinase (AMPK) activator (Metformin) associated with the regulation of Asprosin receptors (OLFR734/G proteins-cAMP-PKA). Additionally, we cultured renal constituent cells (mesangial cells, glomerular endothelial cells) in high glucose and palmitic acid conditions and treated them with an AMPK inhibitor (Compound C) after silencing Asprosin expression using siRNA. We assessed the levels of Asprosin, AMPK, and their respective downstream signaling pathways.
Results : Asprosin was found to be overexpressed in the serum and kidney tissues of db/db mice, as well as in renal constituent cells cultured under high glucose and palmitic acid conditions. Interfering with Asprosin led to reduced body and liver weight in mice, improved glucose tolerance, and mitigated renal injury in vivo. Asprosin knockdown ameliorated lipid accumulation and inflammatory infiltration, both in vitro and in vivo. Moreover, Asprosin absence activated the AMPK/Sirts/mTOR signaling pathway, while the AMPK inhibitor Compound C reversed the effects of Asprosin on lipid accumulation and inflammatory response, confirming Asprosin's direct role in intracellular lipid metabolism.
Conclusions : The mechanism of intracellular energy metabolism regulation mediated by Asprosin presents promising potential for targeted organ therapy in the development and prevention of diabetic kidney disease. Inhibiting Asprosin suppressed lipid accumulation and inflammation in diabetic kidney disease through the activation of AMPK-associated signaling pathway.