World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:18, No:01, 2024

UCP1 Regulates Cardiolipin Metabolism and Mediates Mitochondrial Homeostasis Maintenance of ANXA1 in Diabetic Nephropathy

Authors : Zi-Han Li, Lu Fang, Liang Wu, Dong-Yuan Chang, Manyuan Dong, Liang Ji, Qi Zhang, Ming-Hui Zhao, Sydney C. W. Tang, Lemin Zheng, Min Chen

Abstract : Uncoupling of mitochondrial respiration by chemical uncouplers has proven effective in ameliorating obesity, insulin resistance, and hyperglycemia, which were risk factors for diabetic nephropathy (DN). Recently, we found that ANXA1 could improve mitochondrial function to mitigate DN progression. However, the underlying mechanism is not fully clear yet. Here, we identified uncoupling protein 1 (UCP1), an inner membrane protein of mitochondria, as a key to mitochondrial homeostasis improved by ANXA1. Specifically, ANXA1 attenuated mitochondrial dysfunction via appropriately upregulating UCP1 by stabilizing its transcription factor GATA binding protein 3 (GATA3) by combining it with thioredoxin. Moreover, specific overexpression of UCP1 in the renal cortex rescued renal injuries in diabetic Anxa1-KO mice. UCP1 deletion aggravated renal injuries in HFD/STZ-induced diabetic mice. Mechanistically, UCP1 reduced mitochondrial fission through the aristaless-related homeobox (ARX)/cardiolipin synthase 1 (CRLS1) pathway. Therapeutically, CL316243, a UCP1 agonist, could attenuate established DN in db/db mice. This work established an alternative principle to harness the power of uncouplers for the treatment of DN.

Keywords : diabetic nephropathy, uncoupling protein 1, mitochondrial homeostasis, cardiolipin metabolism
Conference Title : ICMHS 2024 : International Conference on Medicine and Health Sciences
Conference Location : Zurich, Switzerland
Conference Dates : January 11-12, 2024