University of Fribourg/Faculty of Science and Medicine / Department of Endocrinology, Metabolism, and Cardiovascular System

Hypoxia upregulates arginase-II expression: impact on renal and vascular damage

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Arginase-II (Arg-II). Arg-II is located in the mitochondria and is prominently expressed in the kidney, exclusively in the proximal tubular S3 segment cells under physiological conditions but is also inducible under stress or pathological conditions. The roles of this enzyme in kidney functions, endothelial activation, and macrophage polarization under hypoxic condition are still controversial.

Firstly, we investigated the function of Arg-II in the hypoxia-induced injury of renal proximal tubular epithelial cells under hypoxic conditions and its implication in age-associated renal fibrosis. We also tested the hypothesis that hypoxia-HIF-induced Arg-II in endothelial cells and macrophages promotes endothelial activation through enhanced mitochondrial oxidative stress and macrophage polarization.

Our data indicate that hypoxia enhances renal HIFs-Arg-II-TGF-β1 cascade, contributing to the pathogenesis of age-associated renal fibrosis. Secondly, we demonstrate hypoxia enhances endothelial ICAM-1 protein level and monocyte-endothelium interaction through HIF1α-Arg-II-mitochondrial ROS and suggests targeting this cascade could be a promising therapeutic strategy to prevent hypoxia-induced vascular damage/dysfunction. Lastly, our results show that HIF1α and/or HIF2α might mediate the hypoxia-induced increase in Arg-II expression, inducing mixed M1 and M2 macrophage polarization.

Jury:

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