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The potential roles of NAD(P)H:quinone oxidoreductase 1 in the development of diabetic nephropathy and actin polymerization

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Objectives:

Diabetic nephropathy (DN) is a major complication of diabetes mellitus. NAD(P)H:quinoneoxidoreductase 1 (NQO1) is an antioxidant enzyme that has been involved in the progression of several kidneyinjuries. However, the roles of NQO1 in DN are still unclear. We investigated the effects of NQO1 deficiency instreptozotocin (STZ)-induced DN mice.

Methods:

Wild-type (WT) and NQO1 KO male mice on C57BL/6N genetic backgroundwere used. For the diabetic nephropathy model, STZ was dissolved in citrate buffer (0.1 M; pH 4.5) andprepared immediately before use. Age-matched 8-week-old WT and NKO male mice were administered STZ(50 mg/kg body weight, intraperitoneal injection) after 4 h fasting, for five consecutive days. ACR weremeasued. Renal histology and molecular evaluation were done.

Results:

NQO1 was upregulated in the glomerulus and podocytes under hyperglycemic conditions. NQO1knockout (NKO) mice showed more severe changes in blood glucose and body weight than WT mice after STZtreatment. Furthermore, STZ-mediated pathological parameters including glomerular injury, blood ureanitrogen levels, and foot process width were more severe in NKO mice than WT mice. Importantly, urinealbumin-to-creatinine ratio (ACR) was higher in healthy, non-treated NKO mice than WT mice. ACR responseto STZ or LPS was dramatically increased in the urine of NKO mice compared to vehicle controls, while itmaintained a normal range following treatment of WT mice. More importantly, we found that NQO1 canstimulate actin polymerization in an in vitro biochemical assay without directly the accumulation on F-actin.

Conclusions:

NQO1 has an important role against the development of DN pathogenesis and is a novelcontributor in actin reorganization via stimulating actin polymerization.