



Oral Communication Abstract

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Targeting Nox with Pan-Nox Inhibitor in aging diabetic kidney

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Objectives: Aging process is a risk factor for altered glucose metabolism and insulin resistance. Moreover, diabetes with serious complications has been steadily increasing in older patients. Chronic inflammation and increased oxidative stress are commonly shared features of aging and diabetes mellitus. Therefore, we investigated the effect of pan-nox inhibitor on aging diabetic mice.

Methods: Diabetes was induced by intraperitoneal injection of streptozotocin at a 50mg/kg/day for 5 days in 52-week-old week C57BL/6J mice. An orally active pan-Nox inhibitor was administered by oral gavage at a dose of 60mg/kg/day for 12 weeks in aging mice and diabetes induced aging mice.

Results: Nox inhibition significantly improved insulin resistance in both aging and diabetic aging mice. Additionally, fasting glucose and HbA1c level were significantly improved with Nox inhibition in diabetic aging group. Interestingly, oxidative stress measured by 8-isoprostane was significantly increased in both aging and diabetic mice. Pannox inhibitor significantly reduced plasma 8-isoprostane level in aging group, and urinary 8-isoprostane level in diabetic group. In diabetic aging condition, there was trend to decrease in urinary albumin and nephrin excretion with Nox inhibition. Simply aging did not significantly altered PAI-1 and collagen IV expressions in the kidney compared to diabetic condition. However, nox 1 and 4 expressions was as well as increased in aging mice and diabetic mice. Pannox inhibitor significantly reduced renal PAI-1, collagen IV expressions in diabetic aging mice. Klotho level was significantly reduced in both aging and diabetic mice and Nox inhibition restored klotho level in aging mice, but not in diabetic mice.

Conclusions: Our results provide evidence that pan-Nox inhibition may improve systemic insulin resistance and oxidative stress in aging diabetic status, and therefore may have potential protective effects on aging diabetic kidney.