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Renoprotective Effect of Dipeptidyl Peptidase-4 Inhibitor in Aging Mice

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Objectives : Dipeptidyl peptidase 4 (DPP-4) inhibitors are well known hypoglycemic agents. Recently, there have been increasing evidence of diverse protective effects besides lowering glucose levels, including renoprotective effect. However, the pathogenesis of the protective effects have not been clarified yet. We investigated the renoprotective effects of DPP-IV inhibitors via the renin-angiotensin system in the aging mice model.

Methods : Eighteen month-old C57BL/6 mice were divided into two groups according to DPP-IV inhibitor administration : LIN (N=8) and CONT (N=8). The LIN group (N=8) was administered with linagliptin 5mg/kg per oral daily. Both groups were followed for 24 weeks. Renal function, albuminuria, activities and expressions of DPP-4 and glucagon like peptide-1 (GLP-1) in renal tissue, neuropeptide Y and substance P in serum and renal tissue, histologic changes and expressions of angiotensin-converting enzyme (ACE), angiotensin-converting enzyme 2 (ACE2), angiotensin II (Ang II), angiotensin II type 1 receptor (AT1R), angiotensin II type 2 receptor (AT2R), prorenin receptor (PRR), Mas receptor (MasR), endothelial nitric oxide synthase (eNOS), NADPH oxidase 2 and oxidase 4 (Nox2 and Nox4), transforming growth factor-

Results : Renal function and albuminuria were not different between the two groups. In the LIN group, DPP-4 activities in renal tissue were decreased and serum substance P concentrations were increased. In renal tissue, expressions of ACE, PRR and AT1R were significantly decreased in the LIN group compared to the CON group ($p < 0.05$ for both), but ACE2, AT2R and MasR were not different (figure 1). Nox2 and Nox4, TGF-

Conclusions : DPP-4 inhibitors may provide renoprotective effects especially against the aging process of the kidney via a reduced PRR-ACE-AT1R axis.

Keywords : Dipeptidyl peptidase-IV, renin-angiotensin system, aging