2-O-06

Oral Sessions

Renin-angiotensin system-induced SPARC upregulation causes renal injury in hypertensive rats

Hiroe Toba¹, Takami Saito¹, Ryoki Kawashima¹, Shiho Sakaue¹, Yusuke Watanabe¹, Nessa Naseratun¹, Miyuki Kobara¹, Tetsuo Nakata¹

¹Dept. Clin. Pharmacol., Div. Pathol. Sci., Kyoto Pharmaceutical Univ.

Background: Secreted protein acidic and rich in cysteine (SPARC), one of the ECMs, promotes inflammation in aging hearts. Pro-inflammatory and -fibrotic properties of ADAMTS1 is reported, and SPARC promotes collagen production via ADAMTS1 upregulation. This study investigated the roles of SPARC in hypertensive renal injury.

Methods: Uninephrectomized rats were treated with DOCA and salt for 0, 1, 2, or 3 weeks (DOCA-salt) with/without losartan (30 mg/kg). Blood pressure, proteinuria, CCr, and renal NADPH oxidase activity was measured. Fibrillar collagens and macrophages were detected by Masson's trichrome staining and immunohistochemistry, respectively. The protein levels of MCP-1, TGF-beta, collagen I, SPARC, and ADAMTS1 were examined by immunoblotting.

Results: Blood pressure increased time-dependently from 2w. Proteinuria increased from 2w and CCr decreased at 3w. NADPH oxidase activity, macrophage numbers, and MCP-1 increased in DOCA-salt. TGF-beta, tubulointerstitial fibrosis, and glomerulosclerosis increased time-dependently from 2w. The collagen I protein, in particular collagen I with larger molecular weight, increased in 3w. SPARC increased and peaked at 2w and reversed to the control levels at 3 weeks, and ADAMTS1 gradually increased until 3w, both of which were suppressed by Losartan.

Conclusions: Renal renin-angiotensin system-induced SPARC upregulation and subsequent ADAMTS1 production may mediate renal injury.