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**ROLE OF CHEMOKINE RECEPTOR 2 IN RENAL INJURY DURING DOCA-SALT HYPERTENSION**

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**Objectives** This study was designed to determine the role of chemokine receptor 2 (CCR2), a receptor of MCP-1, in the development of salt-sensitive hypertension-induced renal damage.

**Methods** We induced hypertension by uninephrectomy and deoxycorticosterone (DOCA)-salt in C57BL/6 mice with or without a selective CCR2 antagonist, RS504393. Sham mice underwent uninephrectomy without receiving DOCA and saline.

**Results** After 4 week treatment, systolic blood pressure (SBP) measured by tail-cuff method increased in the DOCA-salt-treated mice compared with the sham mice ( $142 \pm 7$  vs  $107 \pm 6$  mm Hg,  $p < 0.01$ ). DOCA-salt treatment also induced renal hypertrophy, increased urinary albumin and 8-isoprostane excretion and decreased creatinine clearance compared with the sham mice ( $110.9 \pm 3.0$  vs  $75.6 \pm 1.9$  mg/10 g body weight;  $25.6 \pm 2.8$  vs  $5.7 \pm 0.4$   $\mu$ g/24 h;  $1.63 \pm 0.22$  vs  $0.51 \pm 0.05$  ng/24 h;  $211 \pm 13$  vs  $336 \pm 17$  ml/24 h,  $p < 0.05$ ). Periodic acid-Schiff staining showed that DOCA-salt treatment caused obvious glomerulosclerosis compared with the sham mice ( $0.41 \pm 0.05$  vs  $0.10 \pm 0.03$ ,  $p < 0.05$ ). Masson trichrome staining revealed that tubulointerstitial injury in kidney also increased in the DOCA-salt-treated mice compared with the sham mice ( $2.29 \pm 0.36$  vs  $0.43 \pm 0.20$ ,  $p < 0.05$ ). Immunostaining studies showed that DOCA-salt treatment increased monocyte/macrophage infiltration in kidney compared with the sham mice ( $43 \pm 4$  vs  $13 \pm 2$  cells/mm<sup>2</sup>,  $p < 0.05$ ). Blockade of the CCR2 with RS504393 (4 mg/kg/day, sc) had no effect on SBP. However, they prevented renal morphological damage and inhibited the increase in urinary albumin and 8-isoprostane excretion and the decrease in creatinine clearance ( $p < 0.05$ ).

**Conclusions** Our data showed that blockade of CCR2 with RS504393 prevented renal damage induced by DOCA-salt hypertension independently of their effects on blood pressure. The results suggest that CCR2-mediated monocyte/macrophage infiltration may contribute to renal damage induced by salt-sensitive hypertension.