GW23-e1148 **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±7 vs 107±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±3.0 vs 75.6 ±1.9 mg/10 g body weight; 25.6±2.8 vs 5.7±0.4 μg/24 h; 1.63 ±0.22 vs 0.51±0.05 ng/24 h; 211±13 vs 336±17 ml/24 h, $p<0.05$). Periodic acid-Schiff staining showed that DOCA-salt treatment caused obvious glomerulosclrosis compared with the sham mice (0.41±0.05 vs 0.10±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 ±0.36 vs 0.43±0.20, $p<0.05$). Immunostaining studies showed that DOCA-salt treatment increased monocyte/macrophage infiltration in kidney compared with the sham mice (43±4 vs 13 ±2 cells/mm^2, $p<0.05$). 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.