RENAL VASOCONSTRICTION AND NATRIURESIS INDUCED BY TUMOR NECROSIS FACTOR (TNF)-α ARE MEDIATED BY TNF RECEPTOR TYPE 1

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Infusion of TNF-α exerts renal vasoconstriction as well as natriuresis in mice. To define the receptor subtypes involved in these renal vascular and tubular actions of TNF-α, experiments were conducted to assess the responses to human recombinant TNF-α (0.33ng/min/g BW; i.v. infusion for 75 min) in gene knockout mice for either TNF receptor type 1 (TNFR1KO; n=6) or type 2 (TNFR2KO; n=6) and compared these results with those obtained in corresponding wild type (WT; C57BL6; n=6) mice. Renal blood flow (RBF) and glomerular filtration rate (GFR) were determined by PAH and inulin clearances respectively. As reported previously, TNF-α infusion in WT mice resulted in decreases of 20±5% (P<0.03) in RBF, 40±2% (P<0.003) in GFR as well as increases in 83±27% (0.05>P>0.01) in urine flow (V) and 363±104% (P<0.05) in sodium excretion (U NaV). These responses are completely absent in TNFR1KO mice. TNF-α infusion in TNFR1KO mice resulted in non-significant changes in renal parameters (RBF; 8±22%; GFR, -18±14%; V, 15±16%; U NaV, -47±12%). However, TNF-α infusion in TNFR2KO mice showed similar changes in renal parameters as observed those in the WT mice. The responses in TNFR2KO mice are as follows: RBF; -22±10% (0.05>P>0.01); GFR, -36±7% (P<0.002); V, 91±19% (P<0.007); U NaV, 327±70% (P<0.01). These data demonstrate that TNF receptor type 1, not the type 2, is involved in mediating acute renal vascular and tubular actions of TNF-α.