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Expression of Ciliary Neurotrophic Factor and Its Receptor Following Experimental Obstructive Nephropathy

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Introduction: Ciliary neurotrophic factor (CNTF) is well known to be a growth/survival factor in neuronal tissue. However, little is known about its role in the kidney. Our previous study demonstrated that CNTF is induced mainly in the regenerating cells in the S3 segment of proximal tubule (S3), which are the most vulnerable with ischemia-reperfusion injury. We intended to investigate the expression of CNTF and it's specific receptor subunit, CNTF receptor alpha (CNTFR α), in a model of unilateral ureteral obstruction (UUO) which results in tubular injuries throughout the whole kidney.

Methods: Complete UUO was produced in Sprague-Dawley rats by left ureteral ligation. The animals were sacrificed on day 1, 3, 5, 7, 10, 14, 21 and 28 after UUO. Sham-operated, and both obstructed and contralateral unobstructed kidneys were fixed, and processed for both immunohistochemistry using a monoclonal antibody for rat CNTF and in situ hybridization using CNTFR α-specific digoxigenin labeled riboprobe.

Results: The immunoreactivity for CNTF in sham-operated and contralateral unobstructed kidneys were observed only in the descending thin limb (DTL) of loop of Henle. In obstructed kidney, CNTF-positivity were induced in some cells of S3 on day 1, and progressively expanded into the entire S3 and even into a part of S2 segment of the proximal tubule on day 7. After then, up-regulated CNTF expression in the proximal tubules in the OSOM was maintained until day 28. There is no detectable immunoreactivity of CNTF except both DTL and proximal tubules in the kidneys among the whole experimental groups. The hybridization signal of CNTFR α in sham-operated and contralateral unobstructed kidneys was detectable weakly in DTL, distal tubule (DT), thick ascending limb (TAL) and in some cells of S3. After obstruction injury, CNTFR α mRNA expression increased progressively in both the renal cortex and the medulla up to day 7, and maintained till day 28. In obstructed kidney, DT, TAL and S3 shows strong hybridization signal. In contrast, collecting duct and convoluted proximal tubule stained moderate to weakly.

Conclusion: These results, taken together with our previous study, suggest that the S3 proximal tubular cells may be the unique induction site of CNTF in response to renal injury, and that CNTF may play a role via its specific recpetor in the whole renal tubule in UUO.