Bactericidal activity of renal tubular cells: the putative role of human beta-defensins

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Renal tubular epithelial cells (RTC) form a barrier between the host and ascending microbes in upper urinary tract infection. Previous studies have shown the ability of the kidney to produce defensins—antimicrobial peptides that play a pivotal role in unspecific host defense. To further clarify the role of renal epithelium for direct antibacterial activity we investigated the expression, regulation and production of antimicrobial peptides by cultured human RTC. Cell culture supernatants of RTC exert strong bactericidal activity against Escherichia coli and Klebsiella pneumoniae, two of the most important pathogens in urinary tract infections. The antimicrobial effect depends on salt concentration, a typical feature of human defensins. RT-PCR of RNA from cultured proximal and distal RTC showed constitutive expression of human beta-defensin 1 (hbd-1) and human beta-defensin 2 (hbd-2) whereas only hbd-1 expression could be detected in RNA preparation from renal biopsy material. Hbd-2 expression of RTC was induced by inflammatory processes as shown by semiquantitative competitive RT-PCR. Coincubation of the cultured cells with IL-1alpha or E. coli promote the strongest hbd-2 induction whereas TNF-alpha and LPS lead to a weaker or no (IL-6) hbd-2 induction. This is the first evidence that human RTC are able to produce antibacterial substances in a biologically relevant amount and that beta-defensins are candidate proteins responsible for this effect.

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