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Autoimmune Renal Disease is Exacerbated by S1P-Receptor-1-Dependent Intestinal Th17 Cell Migration to the Kidney

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ABSTRACT:
Th17 cells are most abundant in the gut, where their presence depends on the intestinal microbiota. Here, we examined whether intestinal Th17 cells contribute to extra-intestinal Th17 responses in autoimmune kidney disease. We found high frequencies of Th17 cells in the kidneys of patients with antineutrophil cytoplasmatic antibody (ANCA)-associated glomerulonephritis. We utilized photoconversion of intestinal cells in *Kaede* mice to track intestinal T cell mobilization upon glomerulonephritis induction, and we found that Th17 cells egress from the gut in a S1P-receptor-1-dependent fashion and subsequently migrate to the kidney via the CCL20/CCR6 axis. Depletion of intestinal Th17 cells in germ-free and antibiotic-treated mice ameliorated renal disease, whereas expansion of these cells upon *Citrobacter rodentium* infection exacerbated pathology. Thus, in some autoimmune settings, intestinal Th17 cells migrate into target organs, where they contribute to pathology. Targeting the intestinal Th17 cell "reservoir" may present a therapeutic strategy for these autoimmune disorders.

STATEMENT:
"By photolabelling intestinal cells, we provide direct evidence that microbiota-induced Th17 cells egress from the gut S1PR1-dependently and infiltrate the kidney via CCL20/CCR6 in immune-mediated diseases. This finding might build the basis for therapies targeting the intestinal Th17 cell "reservoir" to treat extraintestinal T_h17 autoimmunity."

BACKGROUND:
This work was planned and performed by Christian Krebs and Ulf Panzer at the III. Medizinische Klinik (Nephrology). These authors have a strong interest in the pathogenesis of autoimmune diseases with a special focus on the contribution of Th17 cells in human and in experimental glomerulonephritis.

The work consists of fruitful cooperation's within the UKE including gastroenterology, microbiology and others that allowed a comprehensive analysis of the developmental origin of Th17 cells in immune-mediated renal disease.

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