Pro-inflammatory molecules; basic FGF, VEGF, PDGF-88, IL1, IL6, TNF, IL17a, IL8, MCP1, IP10, MIP1, MIP1, Eotaxin, RANTES, IL2, IL4, IL5, IL9,IL12, IL13, IL15, IFN, G-CSF, GM-CSF, IL7, IL10 were measured in plasma by Milliplex 26-plex. Total RNA was isolated from plasma and the profile of miRs was determined by Real-time quantitative RT-PCR analysis. We calculated an integrated index using endothelial function, cytokine levels, and miR data, to look at the relation between laboratory and clinical data following treatment.

Results: Leukocyte and platelet counts, CRP and serum albumin levels were similar before and after treatment. The groups did not differ in eGFR, Ca, P, and 25-OH-vitamin D3 levels after treatment, but there was a dose dependent response in PTH levels. Since the number of patients was small, we merged both treatment groups (1 and 2 μg) for the analysis. VEGF, PDGF, Basic-FGF, Eotaxin, IL8, IP10, MIP1 , IFN , IL9, IL12, IL7, IL17, G-CSF, and IL10 decreased significantly following the treatment, compared to placebo, as did miR 432-5p, miR 495-3p, and miR 576-5p. The integrated index showed a significant relation between macro- and microvascular endothelial function and microcirculation, with cytokines such as basic-FGF, PDGF and VEGF, together with miR 432. In terms of miR 495, the integrated value showed significance for microvascular endothelial function.

Conclusions: Paricalcitol treatment in moderate CKD reduces inflammation and levels of selected miRs, involved in the atherosclerosis process and platelet function. The decline in cytokines and miRs could be linked to our previous clinical findings, using the integrated index. This study suggests a role for VDRA in patients with moderate CKD but further studies are warranted to more deeply characterize the effects of vitamin D on immune and endothelial cells, expression of cytokines and regulation of miRs in the process of the disease

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INTESTINAL TH17 CELLS DRIVE RENAL TISSUE INJURY IN CRESCENTIC GLOMERULONEPHRITIS

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Introduction: The relationship between microbiota-induced TH17 cells in the small intestine and pathogenic TH17 responses in autoimmune diseases is still unclear.

Methods: Renal TH17 cells from patients with ANCA-associated glomerulonephritis and nephritic mice using the nephrotoxic nephritis model (NTN) were analyzed by flow cytometry including intracellular cytokine staining. Migration of T cells in nephritic mice was analyzed using photoconvertible Kaede-transgenic mice.

Results: Here, we report high frequencies of CD4+RORgt+TH17 cells in the kidneys of patients with ANCA-associated crescentic glomerulonephritis and in a mouse model of crescentic glomerulonephritis. By labeling intestinal cells in photoconvertible Kaede-transgenic mice, we were able to demonstrate that a significant proportion of the TH17 cells in the inflamed kidney originated from the small intestine and infiltrated the kidney via the CCR6/CCL20 axis. In line, experiments in germ free mice and in mice treated with a cocktail of four antibiotics revealed that the TH17 response in the kidney and the consecutive tissue injury in crescentic glomerulonephritis depended on microbiota-induced intestinal TH17 cells. Furthermore, in a therapeutic and well-tolerable approach, treatment of mice with a single antibiotic (vancomycin) significantly reduced intestinal TH17 cells and subsequently renal TH17 infiltration and tissue damage.

Conclusions: These findings identified a direct relationship between microbiota-induced TH17 cells and the destructive TH17 response in autoimmunity, suggesting that therapeutic manipulation of the intestinal microbiota might provide new opportunities for the treatment of TH17-driven autoimmune disorders.

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PAIRED IMMUNOGLOBULIN-LIKE TYPE 2 RECEPTOR ALPHA NEGATIVELY REGULATES ANTIBODY- MEDIATED GLOMERULONEPHRITIS

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Introduction: Systemic and local immune responses of leukocytes are important for host defense, but uncontrolled inflammation can lead to various organopathy. In addition, once cross reaction has formed between the external antigen and the autoantigen, various autoimmune diseases and allergic diseases can be induced. PILR expressed mainly on macrophages, dendritic cells and granulocytes, contains two immunoreceptor tyrosine-based inhibitory motifs (ITIMs) in its cytoplasmic domain. PILR has described for its negative regulatory functions for activation of leukocyte 2 integrin in acute inflammation including LPS-induced endotoxin shock model. Here, we investigated roles of PILR in antibody-mediated glomerular inflammation.

Methods: Antibody-mediated glomerulonephritis was induced by intravenous administration of nephrotoxic serum (NTS) after pre-immunization with rabbit IgG in C57BL/6 (WT) and PILR -/- mice. Functional analysis for renal injury was performed by urine albumin and serum creatinine (sCr) concentrations at day 7, 14 and 21. Diseased kidneys from both mouse strains were harvested for histology, renal leukocyte infiltrates by flow cytometry and renal cytokine profiles by ELISA after induction of glomerulonephritis. In vitro, m2 integrin-dependent neutrophil adhesion on immune-complex (IC) formed with BSA-anti BSA IgG was evaluated in both mouse strains.

Results: PILR was specifically expressed on glomerular Ly6B+cells (neutrophils and monocytes) in diseased WT mice. Similar amount of pathogenic rabbit IgG deposition on GBM was observed in WT and PILR -/- mice on day 14 kidney specimen, but BUN and sCr concentrations were significantly elevated in PILR -/- mice compare to WT mice at day 14 and 21, and those were highly associated with deteriorated proteinuria. In histological analysis, glomerular damages, corroborated with both glomerular PAS deposits and glomerular crescent formation, were significantly severe in PILR -/- mice at day 14 and 21 ($p<0.05$). Moreover, glomerular neutrophil accumulation was remarkably observed in PILR -/- mice compare to WT mice. In addition, total infiltration of Ly6Ghigh neutrophils, F4/80+ macrophages and CD3+CD4+ T cells in whole kidneys were increased in PILR -/- mice than WT mice at day 14 and 21. Renal proinflammatory cytokine profiles for IL-1 and IL-6 on day 21 also demonstrated severe renal inflammation in PILR -/-mice. In vitro,