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Immature Renal Dendritic Cells Recruit Regulatory CXCR6+ Invariant Natural Killer T Cells to Attenuate Crescentic GN

Jan-Hendrik Riedel*, Hans-Joachim Paust*, Jan-Eric Turner, André P. Tittel, Christian Krebs, Erik Disteldorf, Claudia Wegscheid, Gisa Tiegs, Joachim Velden, Hans-Willi Mittrücker, Natalio Garbi, Rolf A.K. Stahl, Oliver M. Steinmetz, Christian Kurts and Ulf Panzer (*contributed equally)

ABSTRACT: Immature renal dendritic cells (DCs) are protective early in murine crescentic GN, but the mechanisms underlying this protection are unknown. Here, depletion of DCs reduced the recruitment of invariant natural killer T (iNKT) cells, which attenuate GN, into the kidney in the early stage of experimental crescentic GN. More than 90% of renal iNKT cells expressed the chemokine receptor CXCR6, and renal DCs produced high amounts of the cognate ligand CXCL16 early after induction of nephritis, suggesting that renal DC-derived CXCL16 might attract protective CXCR6+ iNKT cells. Consistent with this finding, CXCR6-deficient mice exhibited less iNKT cell recruitment and developed nephritis that was more severe, similar to the aggravated nephritis observed in mice depleted of immature DCs. Finally, adoptive transfer of CXCR6-competent NKT cells ameliorated nephritis. Taken together, these results suggest an immunoprotective mechanism involving immature DCs, CXCL16, CXCR6, and regulatory iNKT cells, which might stimulate the development of new therapeutic strategies for GN.

STATEMENT: *This paper identifies for the first time a chemokine/chemokine-receptor mediated crosstalk between dendritic cells and NKT cells as the missing link between the migration of regulatory invariant NKT cells to the inflamed kidney and the disease-attenuating effect of immature DCs seen during the early phase of crescentic glomerulonephritis. This study was only rendered possible by the extensive interdisciplinary network of scientists and their specific expertise from several different institutes of the UKE.*

BACKGROUND: This study was performed at the III. Medizinische Klinik – Experimental Nephrology in the group of Prof. Panzer who holds a professorship at the UKE since 2010. This group is part of the Klinische Forschergruppe KFO228 “Immunopathogenesis and Therapy of Glomerulonephritis” which was just recently awarded funding for the second 3-year period by the DFG. This study is part of the dissertation of Mr. Riedel, he and Dr. Paust contributed equally to this work. They were interested in the functional role of dendritic cells and their interactions with NKT cells via chemokine/chemokine-receptor crosstalk in a model of renal autoimmune disease.