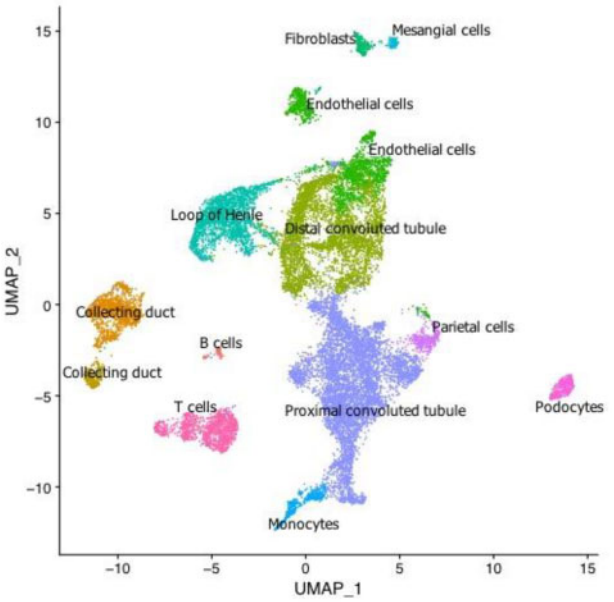
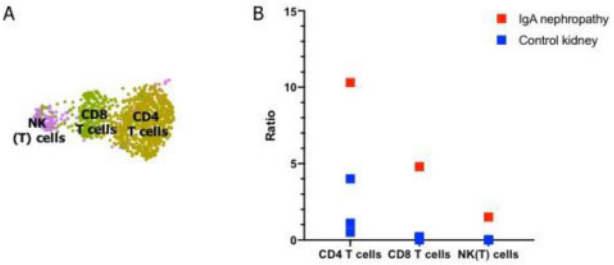
towards CD8 lymphocytes and NK(T) cells (Figure 2). NK cells were solely present in IgA nephropathy compared to healthy kidney (1.5% versus 0% in all healthy kidneys).





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SINGLE-CELL TRANSCRIPTOME OF COVID19 ASSOCIATED IGA NEPHROPATHY*

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BACKGROUND AND AIMS: Acute kidney injury is common in patients infected with the novel coronavirus SARS-CoV-2. Predominant findings in case series of kidney biopsies include acute tubular injury and collapsing podocytopathy. We performed single-cell RNA sequencing on kidney biopsy of a patient with COVID19-associated Henoch-Schönlein vasculitis, to investigate the underlying molecular changes.
METHOD: A 46-year-old woman presented with cutaneous vasculitis, arthritis, fever and microscopic hematuria. SARS-CoV-2 PCR on nasopharyngeal swab turned positive. Despite quick spontaneous resolution of symptoms, hematuria persisted and proteinuria increased in the next weeks. Subsequent kidney biopsy showed IgA nephropathy. Kidney biopsy was dissociated into a single-cell suspension and RNA was sequenced. 6126 kidney cells passed quality filters. Publicly available single cell sequencing data of 3 healthy kidney samples were integrated to allow comparison. The skin biopsy, performed at the initial presentation, was stained for the SARS-CoV-2 spike protein and the ACE2 protein using immunohistochemistry.
RESULTS: Unsupervised clustering analysis of kidney identified 12 distinct cell types (Figure 1). T-lymphocytes were significantly enriched in COVID19 associated IgA nephropathy (16.7% versus 0.5%, 1.2% and 4.1% in healthy kidney, IgA nephropathy/healthy kidney ratio of relative % of T-/NK-cell clusters of 8.5), with a deviation

Several genes involved in immune activation, oxidative stress and injury were upregulated in podocytes and mesangial cells. For example, one of the genes upregulated in podocytes was macrophage migration inhibitory factor (MIF) which is known to be involved in podocyte injury and mesangial sclerosis. In endothelial cells pathways involved in NK cell immunity, antigen presentation, interferon gamma signaling, and viral entry were upregulated. In T lymphocytes pathways of antigen presentation and T cell cytotoxicity were enriched.
In the skin biopsy, immunohistochemistry was positive for SARS-CoV-2 spike protein inside inflammatory cells, while the ACE2 receptor was positive in the same inflammatory cells, as well as inside endothelial cells.
CONCLUSION: Although both innate and adaptive immunity are considered to be involved in IgA nephropathy, our single cell sequencing data demonstrates that mainly T-lymphocytes, especially CD8 cells and NK cells, are enriched in COVID19 associated IgA nephropathy. Further elucidation of the involved pathways and the T cell receptor is planned. Interestingly, the SARS-CoV-2 virus could be identified inside the inflammatory cells in the skin in the context of cutaneous vasculitis, suggesting a direct pathologic effect.