Summary

Systemic lupus erythematosus (SLE) is one example of an autoimmune disease, characterized by a breakdown of self-tolerance to autoantigens leading to inflammation and tissue destruction in multiple organ systems, including the kidney. Lupus nephritis (LN) is a major contributor to the morbidity and mortality in SLE and is associated with the infiltration of T cells into the kidney. However, the relation between kidney-infiltrating T cells and intrarenal inflammation is not completely understood. An acquired deficiency of the cytokine Interleukin-2 and consecutive disturbances in regulatory T cell (Treg) biology are essentially involved in the pathogenesis of SLE. The aim of this thesis was to investigate whether intrarenal T cells contribute to kidney inflammation and whether an intrarenal IL-2 deficiency exists in the inflamed kidney contributing to an impaired Treg homeostasis and Tcon hyperactivity. Furthermore, it was evaluated whether an IL-2 based immunotherapy can re-establish the Treg/ Tcon homeostasis and has an effect on the progression of LN. In NZB/W mice, flow cytometric analyses of renal lymphocytes revealed a progressive infiltration of Treg and Tcon in the kidney with advancing disease. Intrarenal Treg show typical signs of an IL-2 deficiency together with a progressive hyperactivity of intrarenal Tcon. These Treg defects were associated with a diminished *in vitro* production of IL-2 by kidney-infiltrating Tcon. Furthermore, IL-2 therapy was able to increase the intrarenal Treg pool and reduced the intrarenal Tcon hyperactivity; ultimately leading to a longer survival of IL-2 treated mice. Together, this provides additional scientific rationales for an IL-2 based immunotherapy in human SLE and in particular in lupus nephritis, as a major contributor to the morbidity in this disease.