Background Tubulo-interstitial damage during lupus nephritis (LN) is associated with poor renal prognosis in the long run. Here, we describe the progression of tubulo-interstitial fibrosis and immune cells infiltration with emphasis on CD8+ T cells, in parallel with renal outcomes in a mouse lupus model. Further, a strong correlation is identified between effector functions of CD8+ T cells and fibrotic processes, opening new avenues of research in the pathogenesis of LN.

Methods We collected blood, urine and kidneys from 39 B6/ Sle1.Sle2.Sle3 lupus-prone mice, before disease onset and at different stages of disease progression. RNA was extracted from kidneys and hybridized on Mouse Gene 2.0 ST exon arrays. Histopathological scores (NIH Activity and Chronicity Indexes) and digital quantification of fibrosis, IgGk deposits, CD8+ and CD3+ T cells were performed on total kidney. Renal CD8+ T cell phenotypes were determined by flow cytometry. Plasma urea and albuminuria were measured by immunoenzymatic assays.

Results IgGk deposits, CD8+ T cell infiltration and interstitial fibrosis increase with the progression of renal disease, evaluated by histopathological scores and plasma urea. Further, digital quantifications allowed us to identify a significant correlation (r=0.45, p=0.011) between local CD8+ T cell population and fibrosis, while total CD3+ cells population and IgGk deposits did not display such association. Moreover, characterization of CD8+T cell subpopulations showed that fibrosis is more specifically linked to effector functions of CD8+ T cells. Transcriptomic analyses supported this association, with a high correlation between mean expression of effector functions transcripts and the presence of a fibrotic signature (r=0.92, p<0.0001).

Conclusions Our results support the association between CD8+ T cell tubulo-interstitial infiltration and renal outcomes in a mouse lupus model. Further, a strong correlation is identified between effector functions of CD8+ T cells and fibrotic processes, opening new avenues of research in the pathogenesis of LN.

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