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Methods: 18 lupus kidney (LN) and 34 transplanted kidney (KTx) samples were included in the study. Residual frozen kidney biopsies were collected after clinical diagnosis. The tissue from one donor was split into two. One portion was used for total RNA-Seq (tRNA-Seq) by SMARTer Stranded Total RNA-Seq Kit v2 - Pico Input Mamalian (Takara/Clontech). The rest was used for single nucleus RNA-Seq (snRNA-Seq) using Chromium Single Cell 3' Reagent Kits v3 (10x Genomics) (7 LN and 17 KTx). For the tRNA-Seq, the sequence reads were aligned to Ensembl genome annotation (Ens93) by STAR and the aligned reads were counted by htseq. snRNA-Seq score of tRNA-Seq was calculated using the reported method [1] per each module (M1.2, M3.4 and M5.12). For the snRNA-Seq, the sequenced reads were processed on the standard pipeline of CellRanger (10x Genomics) and the data was visualized using Seurat. snRNA-Seq of snRNA-Seq was computed by the method reported by Arazi A, et al [2].

Clinical outcomes of LN were examined on the medical records retrospectively and the clinical remission in 56 weeks for LN was defined as a urinary protein/creatinine ratio less than 0.5/gCr.

Results: 11 LN had clinical remission and 7 LN showed non remitted disease within 56 weeks after the biopsy. There were no statistical significance co-variants such as age, gender and WHO class in pathology, IFN score of M12, M3.4 and M5.12 were significantly increased in LN with remission within 56 weeks [median 0.773 vs 0.659, 0.595 vs 0.243 and 0.415 vs 0.100: p-value 0.03, 0.01 and 0.02 [Wilcoxon rank-test]] in tRNA-Seq. In the snRNA-Seq, the lupus kidney with low IFN score showed restricted IFN signature in the endothelial cells mainly, which can be detected even in the controls, but those with high IFN score indicated broadly spread IFN signature among all of the cell types.

Conclusion: LN with high IFN score in kidney tissue is correlated with remission within 56 weeks. LN with low IFN score showed IFN signature restricted to endothelial cells but those with a higher IFN score revealed broadly affected cell types with IFN signature. These results suggest that the IFN signature of LN may start from endothelial cells and then spread to whole kidney.


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