the index date. Fully adjusted models included chronic kidney disease, Charlson comorbidity index, glucocorticoids, and cardiovascular medication use assessed at the time of SLE diagnosis.

**Results** We identified 290 SLE cases who died and 502 matched controls among 792 individuals with SLE. The mean age at index date was 65.6 years for cases and 64.7 years for controls. The majority were female (87.9% of cases and 91.4% of controls). The mean SLE disease duration was 5.3 years for both groups. Adjusted odd ratios (ORs) for all-cause mortality relative to the remote users were 0.35 (95% CI: 0.20, 0.59) for current users and 3.78 (95% CI: 2.07, 6.91) for subjects who recently discontinued HCQ (table 1). HCQ non-users had the same risk of death as remote users (OR 0.93 [95% CI: 0.59, 1.44]). Similar trends were seen for the risk of mortality due to CVD.

**Conclusions** In this study, we found a nearly four-fold increased risk of death associated with recent HCQ discontinuation and a substantially increased risk of CVD death. This could be partially explained by a direct protective effect of HCQ that is rapidly lost following discontinuation. We also demonstrated a 65% reduced risk of death among current HCQ users compared with remote users. By leveraging remote users as the comparison group, we reduced the potential for confounding by indication.

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**Abstract 300 INSIGHTS FROM SINGLE-CELL RNA SEQUENCING OF SKIN AND KIDNEY IN LUPUS NEPHRITIS**

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**Background** Classification and treatment decisions in lupus nephritis (LN) are largely based on renal histology. Single-cell
RNA sequencing (scRNAseq) analysis may accurately differentiate types of renal involvement at the transcriptomic level, and better inform treatment decisions and prognosis.

Methods scRNAseq was performed on kidney and non-lesional skin tissue collected from 20 SLE patients undergoing a clinically indicated renal biopsy. Cell types were determined using principal component analysis and t-distributed stochastic neighbor embedding (tSNE) plotting, resulting in the definitive identification of keratinocytes, tubular cells, mesangial cells, fibroblasts, endothelial cells, and leukocytes.

Results LN patients expressed upregulated IFN response genes in both their tubular cells and keratinocytes. This IFN response signature in tubular cells predicted poor response to therapy 6 months post-biopsy. Tubular cells of non-responder patients also expressed upregulated extracellular matrix proteins and fibrotic markers (figure 1A and 1B). Using logistic regression analysis, a 4-gene tubular fibrosis score was created and able to predict response to treatment with an area under curve of 0.9 (figure 1C). Keratinocytes of non-responders also upregulated certain extracellular matrix genes and this response was not observed in peripheral blood mononuclear cells. Differential expression analysis between histology classes indicated an upregulation of IFN and TNF signaling in the tubular cells of patients with proliferative LN compared with membranous.

Conclusions scRNAseq from 2–10 mm of renal biopsy tissue in SLE can differentiate between the different classes of LN, and provide important insights into potential pathogenic mechanisms. Further, changes in the skin of LN patients can provide a useful source of biomarkers and may reflect important information concerning concurrent kidney pathological events.

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Results Multilayer integrative analysis of microRNA and mRNA regulation showed that 10 miRNAs were down-regulated and 19 miRNAs were up-regulated in SLE patient PBMCs compared with HCs. Bioinformatics analysis of regulatory networks between miRNAs and mRNAs showed that 19 miRNAs were related to metabolic processes. Two candidate miRNAs, NovelmiRNA-25 and miR-1273h-5p, which were signiﬁcantly increased in the PBMCs of SLE patients (p<0.05), represented diagnostic biomarkers with sensitivities of 94.74% and 89.47%, respectively (area under the curve=0.574 and 0.788, respectively). NovelmiRNA-25 expression in PBMCs was associated with disease activity in SLE patients, in both active and stable groups (p<0.05). NovelmiRNA-25 overexpression downregulated AMPD2 expression in HEK293T cells through direct targeting of the AMPD2 3'UTR (p<0.01), while inhibition of NovelmiRNA-25 activity led to increased AMPD2 expression (p<0.01). NovelmiRNA-25 overexpression also downregulated AMPD2 protein expression in HEK293T cells; AMPD2 protein expression in SLE patient PBMCs was decreased. Our results show that differentially expressed miRNAs play an important role in SLE.

Conclusions Our data demonstrate a novel mechanism in SLE development that involves the targeting of AMPD2 expression by NovelmiRNA-25. miRNAs may serve as novel biomarkers for the diagnosis and evaluation of disease activity of SLE and represent potential therapeutic targets for this disease.

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