changed the recommended dosing from 6.5 mg/kg to 5 mg/kg. However, it is not clear that the lower dose of hydroxychloroquine will have the same efficacy for SLE activity or the same protective role against cardiovascular risk factors and thrombosis. We asked whether hydroxychloroquine blood levels could help identify those at greater future risk of retinopathy.

Methods We analyzed data on 537 SLE patients from a clinical cohort who had repeated assessments of HCQ blood concentrations, and were evaluated one or more times for retinopathy (300 single retinopathy exam, 149 two and 88 three or more assessments). The patients were 92% female and 42% Caucasian. Hydroxychloroquine blood levels were performed as previously described. In our analysis, HCQ toxicity was defined dichotomously by a retina expert: all those with a value of No or Possible were categorized as not having HCQ toxicity, and those who had a Yes were categorized as having it. Mean and maximum HCQ blood concentration over all cohort visits prior to the final retinopathy assessment were calculated. Risk of HCQ toxicity was then assessed in tertiles defined by these variables.

Results Significant risk factors for retinal toxicity are shown in table 1.

Conclusions Our data show that the risk of HCQ retinopathy is higher in men and Caucasians. As expected, it is higher in older patients and with greater duration. We also found that BMI and hypertension were predictive of HCQ retinopathy. For the first time, our data show the utility of HCQ blood levels in predicting retinopathy. This would allow clinicians to either decrease dose or increase monitoring in those with high blood levels.

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TYPE I INTERFERON MODULATES ADAM17 ACTIVITY IN PHOTSENSITIVE LUPUS MOUSE MODELS

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Background Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by systemic disease flares, renal complications, photosensitivity, and other clinical manifestations. A research area of particular interest to our lab is photosensitivity, an immune system reaction precipitated by ultraviolet radiation (UVR) exposure that results in

epidermal keratinocyte apoptosis and contributes to overall skin inflammation. Importantly, many SLE patients attribute a decrease in quality of life due to photosensitivity. Our lab has recently identified a mechanism in which a disintegrin and metalloprotease 17 (ADAM17) located on Langerhans cells (LCs) limits UVR-induced keratinocyte apoptosis and skin injury via keratinocyte epidermal growth factor receptor (EGFR) stimulation in mice and humans. While we have delineated the downstream effects of UVR-induced ADAM17 activity and expression in healthy and SLE skin, factors that regulate ADAM17 remain poorly understood. Previous studies have shown that elevated levels of type I interferon (IFN) are characteristic of SLE patients. Here, we hypothesize that type I interferon may regulate ADAM17 in LCs in lupus models.

Methods To quantify ADAM17 activity, we developed an assay that uses flow cytometry and co-culture systems. We use this assay in *in vitro* models and *in vivo* mouse models. To quantify the relative ratio of IFN-inducible genes, we use quantitative polymerase chain reaction (qPCR). To apply IFN- α to mice, we solubilize the protein and paint it on murine back skin.

Results *In vitro* methods showed that type I IFN was sufficient to reduce LC ADAM17 activity, and *in vivo* models showed that type I IFN receptor blockade corrected the LC ADAM17 defect in photosensitive lupus mouse models. We are analyzing qPCR data.

Conclusions We show that type I interferon (IFN) can reduce ADAM17 activity on epidermal cells. We also show that type I interferon receptor blockade in lupus mouse models rescues ADAM17 activity. Our data together suggest that type I IFN in lupus may contribute to Langerhans cell dysfunction and propensity to photosensitivity in SLE.

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AN UNCOMMON OVERLAP OF TWO COMMON RHEUMATOLOGICAL DISORDERS

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Background Juvenile systemic lupus erythematosus (SLE) is a heterogeneous multisystem autoimmune disease. Kawasaki disease (KD) is a common vasculitic disorder in children that manifests with fever and mucocutaneous involvement. While overlap of childhood SLE with other rheumatologic disorders has been described, it is extremely unusual in the

Abstract 17 Figure 1 Interferon is a sufficient and necessary condition to downregulate ADAM17 activity