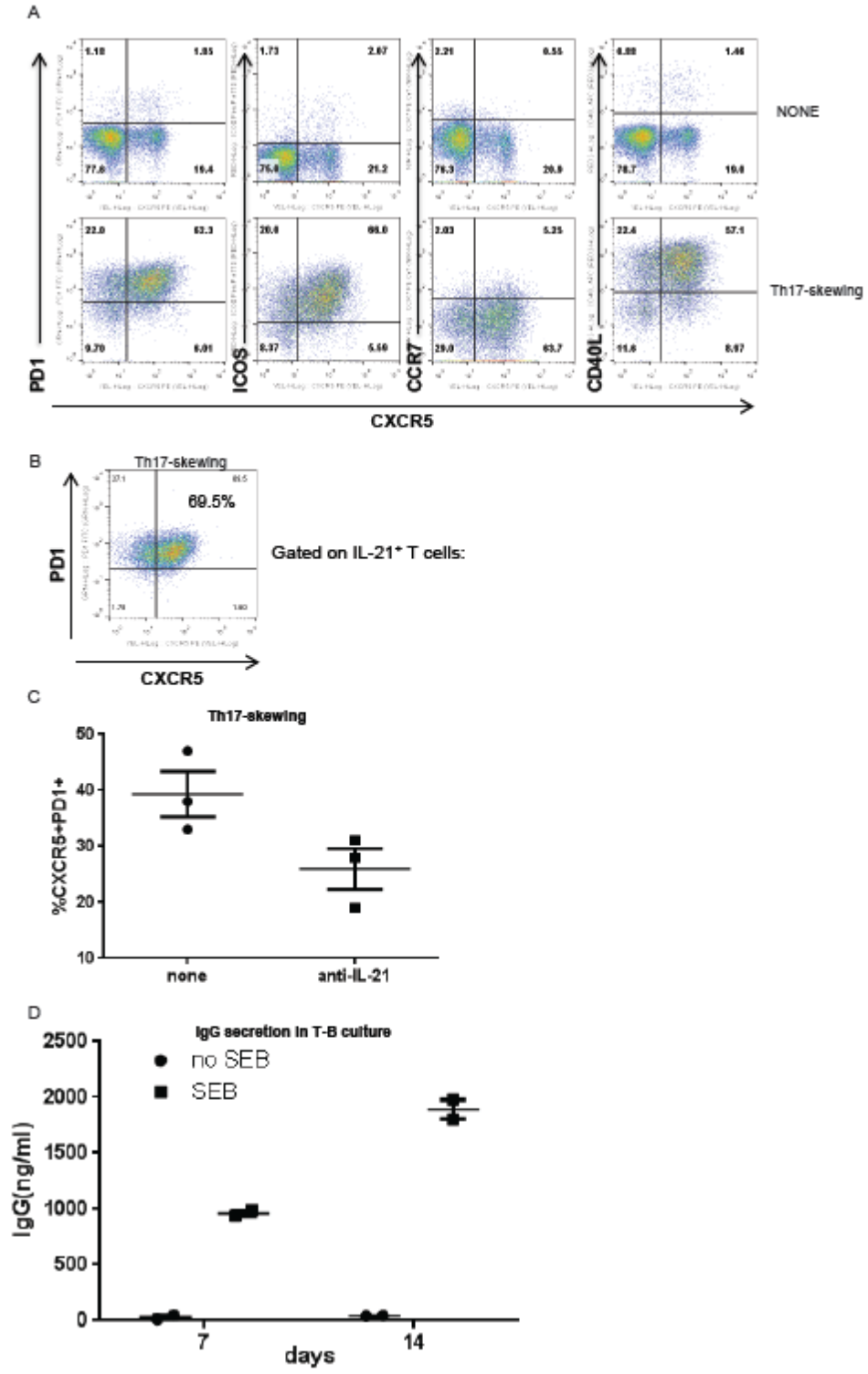

Fig. S1. The T_H17 cell–like skewing of human $CD4^+$ T cells induces a T_{FH} cell-like phenotype. (**A** to **D**) Human peripheral blood $CD4^+$ T cells were stimulated with anti-CD3 and anti-CD28 monoclonal antibodies alone (none) or in combination with IL-1β and TGF-β (T_H17-skewing) for 48 hours. (A and B)

The abundances of CXCR5, PD1, ICOS, CCR7, CD40L, and IL-21 were determined by flow cytometric analysis. Data in (A) and (B) are from a single experiment and are representative of three experiments. (C) IL-21 was blocked in the culture through the addition of recombinant human IL-21R Fc chimeric protein, and its effects on the percentage of $CXCR5^{+}PD1^{+}$ T cells was assessed by flow cytometric analysis. (D) T_H17-skewed cells were co-cultured with autologous B cells for 7 or 14 days in the presence of SEB (0.05 ng/ml) and IgG secretion was determined by ELISA. Data in (C) and (D) are means ± SEM of three independent experiments. Statistical analysis was performed with the Wilcoxon test.

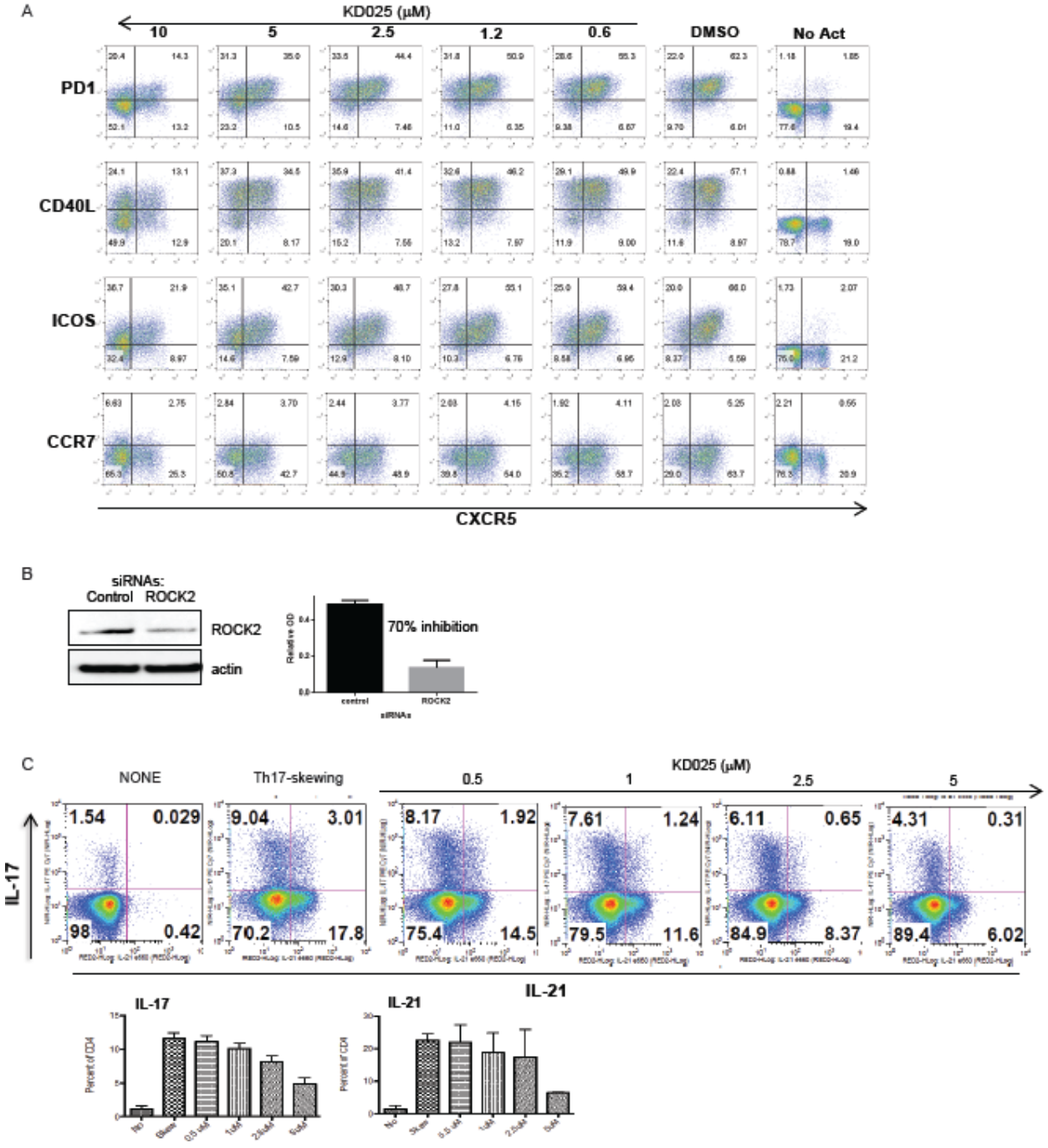

Fig. S2. ROCK2 is required for generation and function of **human T_{FH} cells.** (**A** to **C**) Human peripheral blood $CD4^+$ T cells were treated with the selective ROCK2 inhibitor KD025 (A and C) or were transfected with control or ROCK2-specific siRNAs (B) and then were stimulated with anti-CD3 and anti-CD28 monoclonal antibodies in combination with IL-1β and TGF-β (Th17-skewing) for 48 hours. (A and C) The relative abundances of CXCR5, PD1, ICOS, CCR7, CD40L, and intracellular IL-21 and IL-17 were determined by flow cytometric analysis. (B) Cell extracts were analyzed by Western blotting with antibodies against the indicated proteins. Data in (A) are from one experiment and are representative of

three experiments, whereas data in (B) and (C) are means ± SEM of three independent experiments. Statistical analysis was performed with the Wilcoxon test.

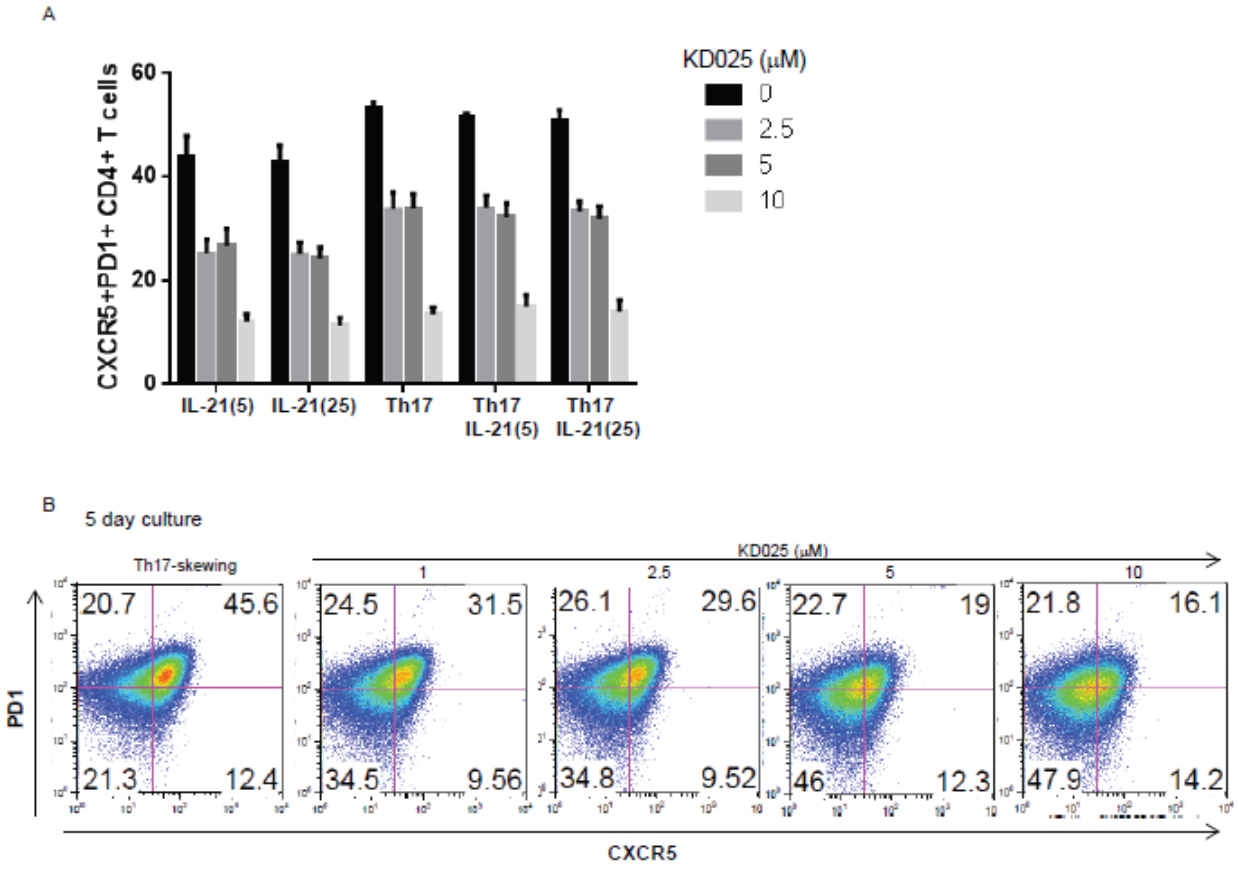

Fig. S3. KD025 decreases the percentage of CXCR5^{+}PD1^{+} T cells in the presence of IL-21 in vitro. (**A** and **B**) Human peripheral blood CD4^{+} T cells were left untreated or were treated with the indicated concentrations of KD025 before being stimulated with anti-CD3 and anti-CD28 monoclonal antibodies in combination with IL-1β and TGF-β (Th17) or with IL-21 (at 5 or 25 ng/ml) for 48 (A) or 120 (B) hours. The cells were then analyzed for surface PD1 and CXCR5 expression by flow cytometry. Data in (A) are means ± SEM of three independent experiments. Data in (B) are from a single experiment and are representative of three independent experiments. Statistical analysis was performed with the Wilcoxon test.

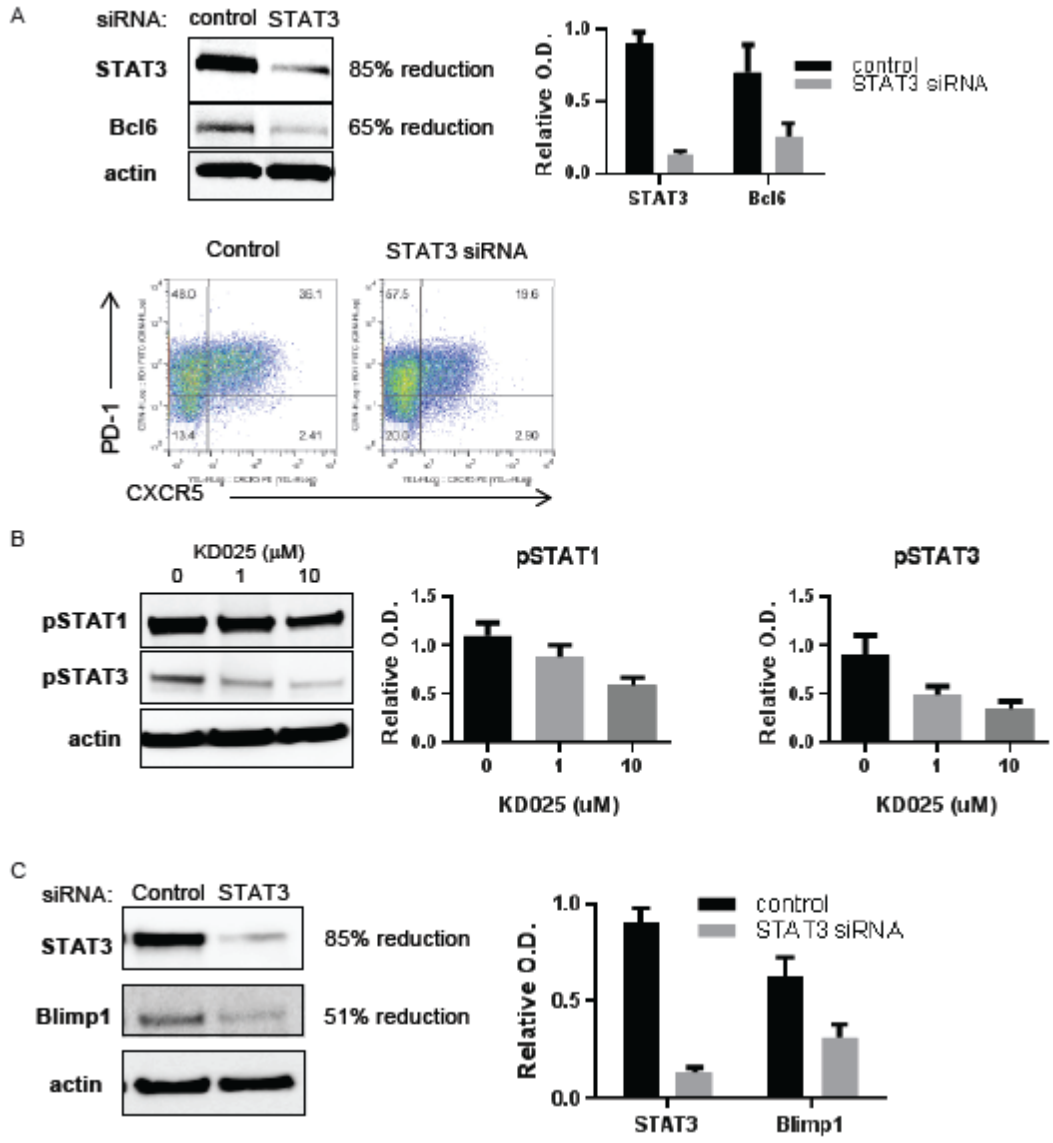

Fig. S4. STAT3 is required for Bcl6 and Blimp1 in human T_{FH} cells. (**A** to **D**) Human peripheral blood $CD4^+$ T cells were transfected with control or STAT3-specific siRNAs (A and C) or were treated with 10 μM KD025 (B and D) and then were stimulated under T_H17 cell–skewing conditions for 48 hours. (A to C) Cell extracts were analyzed by Western blotting with antibodies against the indicated proteins, which was followed by densitometric analysis of the bands of interest (bar graphs). (A) Bottom: The percentages of $CXCR5^+$ $PD1^+$ T cells were determined by flow cytometric analysis. Data are from a single experiment and are representative of three experiments. Data in (A) are means are means ± SEM of three independent experiments. Statistical analysis was performed with the Wilcoxon test.

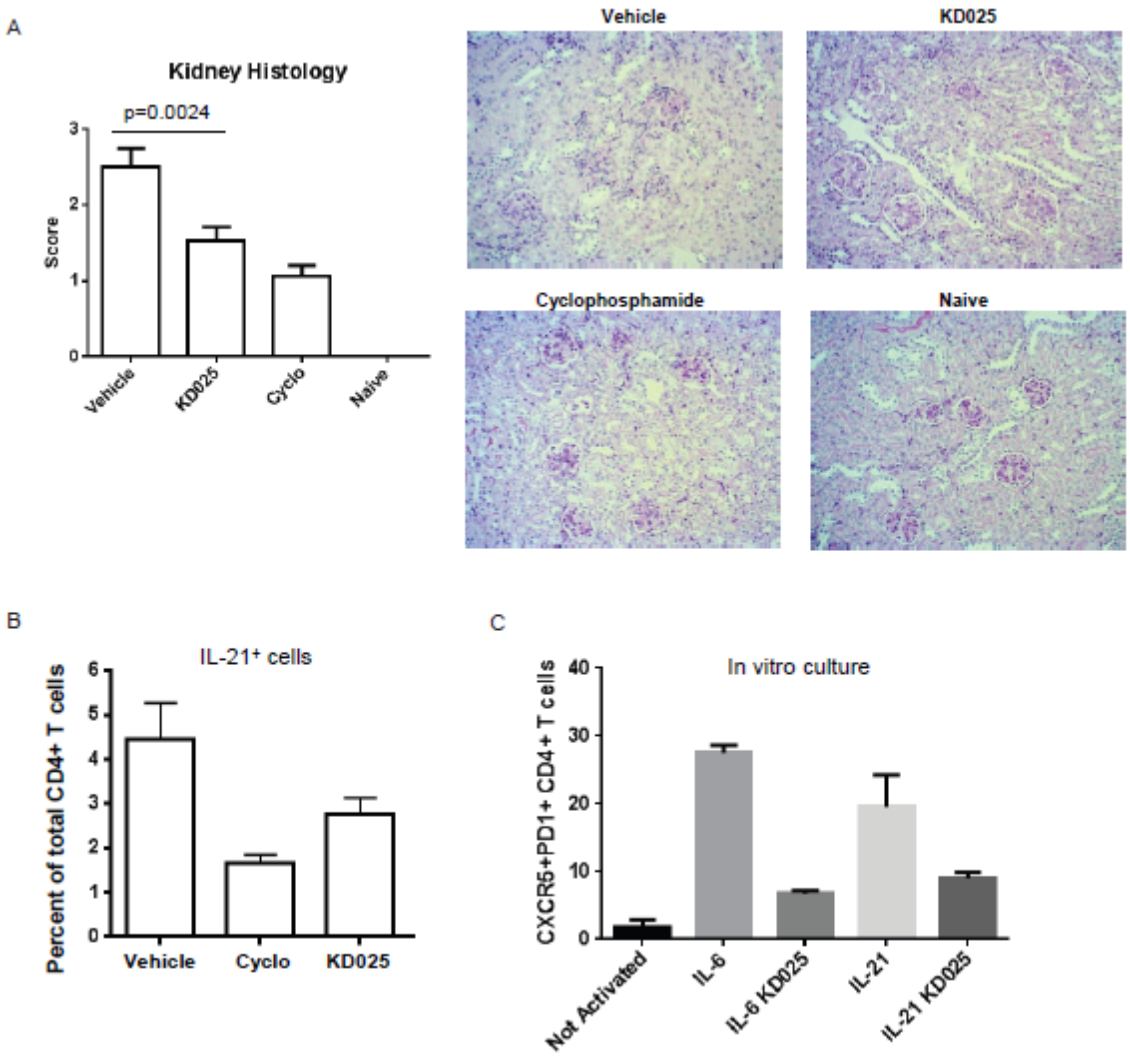

Fig. S5. KD025 stops the progression of kidney damage in MRL/lpr mice. (**A** and **B**) For a period of 6 weeks starting at 11 weeks of age, MRL/lpr mice (15 per group) were orally treated with vehicle or KD025 once a day or were injected intraperitoneally with cyclophosphamide once a week. (A) Right: Mice were sacrificed at the end of the treatment and kidney sections were subjected to histological analysis. Left: Kidney histological scores were determined. The data are means ± SEM. (B) The percentages of IL-21–producing cells in the spleens of the indicated mice were determined by intracellular flow cytometric analysis. (**C**) Naïve $CD4^+$ mouse T cells were stimulated with anti-CD3 and anti-CD28 monoclonal antibodies (8 μg/ml) in combination with anti-mouse IFN-γ antibody (10 μg/ml) and anti-mouse IL-4 antibody (10 μg/ml) and either IL-6 (10 ng/ml) or IL-21 (10 ng/ml) for 72 hours in the absence or presence of 10 μM KD025. The percentage of $CXCR5^+$ $PD1^+$ T cells was determined by flow cytometric analysis. Data are the average of three different experiments. (Statistical analysis was performed with the Mann-Whitney test.

A

Patient ID	Diagnosis	Gender	Age	Ethnicity	Severity w/o Medication	Current Medication	Severity with Medicaiton
AI-9076	SLE	Female	48	African American	Moderate-Severe	Aleve, Aspirin	Moderate
AI-9087	SLE	Female	30	African American	Moderate-Severe	Meloxicam 15mg/qd, Hydroxychloroquine 200mg/bid	Mild
AI-4157	SLE	Female	56	Hispanic/Latino	Severe	Paroxetine 40 mg, Hydroxychloroquine, Hydrocodone	Moderate
AI-9001	SLE	Female	53	Caucasian	Moderate-Severe	Plaquenil 200 mg/BID	Moderate-Severe
AI-9013	SLE	Female	31	African American	Severe	Mycophenolate Mofetil 250 mg/day, Plaquenil 250 mg/day, Prednisone 250 mg/day	Mild-Moderate
AI-2769	SLE	Male	33	Asian Pacific Islander	Moderate-Severe	prednisone/ 20mg/1xday CellCept/ 1500mg/2xday plaquenil/ 200mg/ 1xday	Moderate
10602	SLE	Female	38	Other	Severe	Plaquenil 200mg / 2 tablets, 2x per day	Mild-Moderate
AI-5324	SLE	Female	36	Hispanic / Latino	Severe	Plaquenil- 200mg/2x day Soma/350mg/2xday Norco/ 325mg/every 6 hours as needed	Moderate
AI-9026	SLE	Female	69	African American	Severe	hydroxychloroquina/200mg/bid, prednisone/5mg/bid, methotrexate/20mg/qw	Moderate
10806	SLE	Female	35	African American	Severe	Prednisone 5mg/1x day	Mild

B

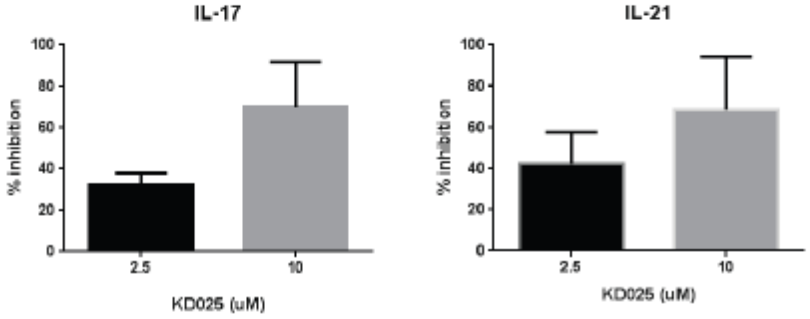

Fig. S6. KD025 inhibits IL-17 and IL-21 secretion by stimulated PBMCs from active SLE patients. (**A**) The clinical and demographic details of the active SLE patients studied. (**B**) PBMCs from six active SLE patients were treated with indicated concentrations of KD025 for 1 hour and then were stimulated under T_H17 cell–skewing conditions. Forty-eight hours later, IL-17 and IL-21 secretion was analyzed by ELISA. Data are means ± SEM of four independent experiments. Statistical analysis was performed with the Wilcoxon test.

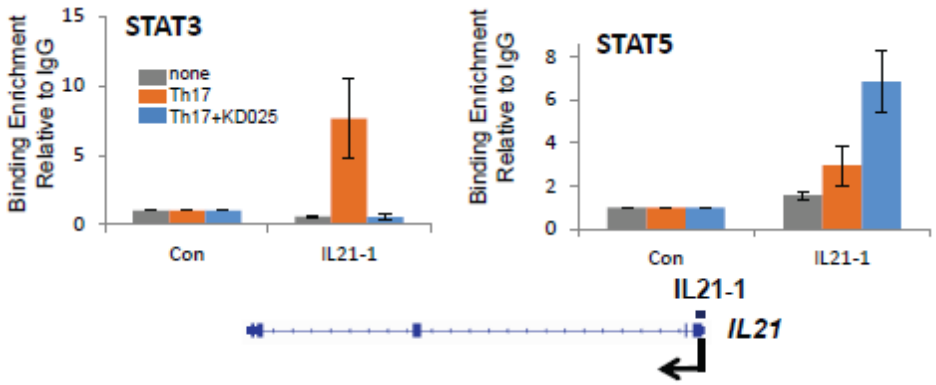

Fig. S7. KD025 oppositely regulates STAT3 and STAT5 binding to IL-21 promoter ChIP assays were performed with normal rabbit IgG and with antibodies specific for RNA pII, STAT3, or STAT5. Data) are means ± SEM of three different experiments. Statistical analysis was performed with the Wilcoxon test.

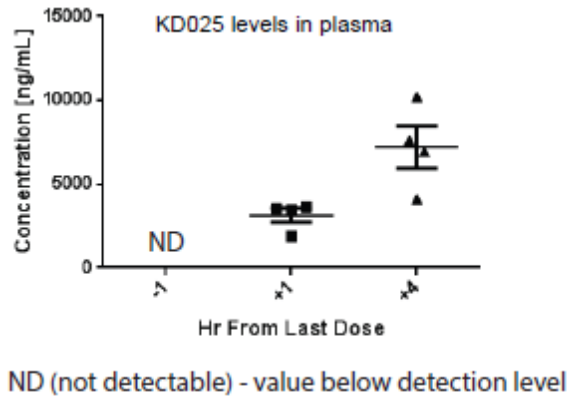

Fig. S8. Pharmacokinetic analysis of MRL/lpr mice treated with KD025 The concentration of KD025 was evaluated at the end of the treatment: -1, 1 hour before; +1, 1 hour after; and +4, 4 hours after the last dosing. ND (not detectable) - values are below detection level. Each point represents an individual mouse.