

Supplementary Fig. S1. AMPK hyperactivity in TAK T cells upon stimulation.

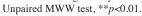
(A)CD4 T cells from healthy and TAK patients were activated with anti-CD3/CD28 beads for 3 days and analysed for phosphor-AMPK using Phosflow cytometry. Representative from 6 healthy-TAK pairs.

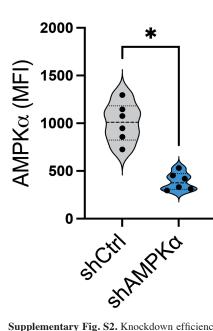
(B)CD4 T cells from healthy and SLE patients (n=5) were activated with anti-CD3/CD28 beads for 3 days and analysed for intracellular phosphor-AMPK.

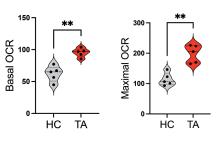
(C)CD8 T cells from healthy and TAK patients (n=5) were activated with anti-CD3/CD28 beads for 3 days and analysed for intracellular phosphor-AMPK.

(D)CD4 T cells from healthy and TAK patients were activated with anti-CD3/CD28 beads for 6 days and analysed for survival by detecting Annexin-V<sup>+</sup>7-AAD<sup>+</sup> fractions. Representative from 6 healthy-TAK pairs.

(E) Unstimulated CD4 T cells from healthy and TAK patients (n=5) were analysed for p-AMPK and survival using flow cytometry.

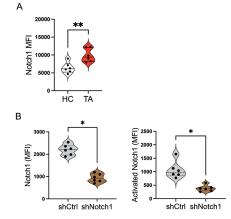






**Supplementary Fig. S3.** Higher mitochondrial metabolism in TAK T cells.

CD4 T cells from healthy and TAK patients (n=5) were activated with anti-CD3/CD28 beads for 3 days and analysed for mitochondrial OCR. \*\*p<0.01 with unpaired MWW test.

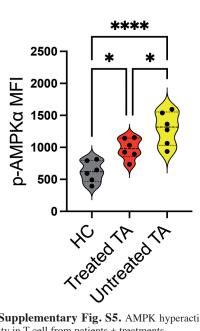


**Supplementary Fig. S4.** Genetic knockdown of Notch1 in TAK T cells.

(A) CD4 T cells from healthy and TAK patients (n=6) were stimulated with anti-CD3/CD28 beads for 3 days and analysed for Notch1 expression using flow cytometry.

(B) CD4 T cells from TAK patients (n=6) were transfected with Notch1 shRNA or the control, and activated with anti-CD3/CD28 beads for 24 hrs.

Unpaired (A) and paired (B) MWW test. \**p* < 0.05, \*\**p*<0.01.



**Supplementary Fig. S5.** AMPK hyperactivity in T cell from patients  $\pm$  treatments. CD4 T cells from healthy individuals and TAK patients  $\pm$  treatments were activated with anti-CD3/CD28 beads for 3 days and analysed for intracellular phosphor-AMPK. ANOVA with Turkey method from 6 individuals in each group, \**p*<0.05, \*\*\*\**p*<0.0001.

Supplementary Fig. S2. Knockdown efficiency of AMPK $\alpha$  in T cells.

CD4 T cells from TAK patients (n=6) were transfected with AMPK $\alpha$  shRNA or the control, and activated with anti-CD3/CD28 beads for 24 hrs. \*p<0.05 with paired MWW test.