Supplementary material

PATIENTS AND METHODS

Patients

The parents provided consent and the patients were enrolled into an IRB approved protocol at the National Institutes of Health Clinical Center in Bethesda, MD (protocol 94E0165, NCT02974595).

28-gene interferon (IFN) score

Total RNA was extracted from peripheral blood collected into PAXgene tubes (Qiagen). Gene expression of 28 selected IFN-stimulated genes (ISGs) was determined by Nanostring assay (NanoString Technologies, Seattle, WA) and an IFN-score was calculated, as per Kim et al., 2018. Standardized IFN score is the sum of 28 Nanostring counts that were standardized by subtracting the mean of healthy controls and dividing by standard deviation of the healthy controls.

STAT phosphorylation by flow cytometry

PBMC from the patients and controls were left unstimulated or were stimulated with IFNα (10ng/ml), IFNγ (10ng/ml), IL-6 (10ng/ml), IL-21(50ng/ml), and APC-conjugated anti-CD4 monoclonal antibody (mAb) at 37°C and 5% CO2 for 20 min. The intracellular phosphorylation of STAT1 was assessed by flow cytometry. After washing, cells were fixed with Cytofix (BD Biosciences, San Jose, CA) at 37°C for 10 min and then permeabilized with Perm Buffer III (BD Biosciences) for 30 min on ice. Next, cells were washed and stained with FITC conjugated anti pSTAT1 (BD Biosciences). The cells were washed, and pSTAT1 expression was analyzed by flow cytometry upon gating on live CD4+ cells or monocytes.