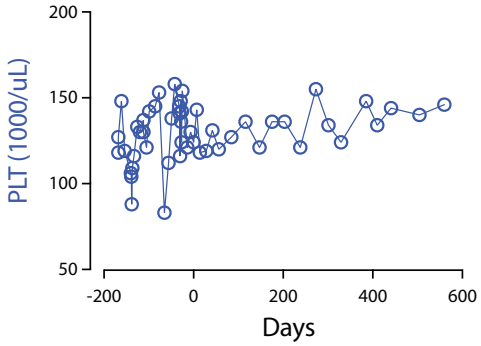
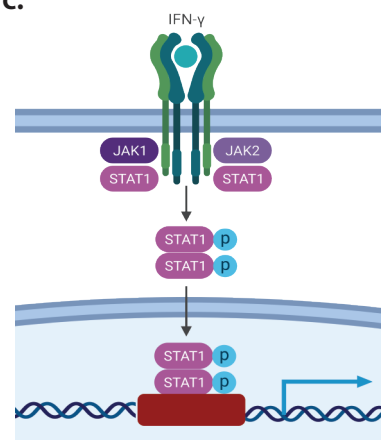
Rosenberg et al. Supplemental Figure 1

a.

b.



c.



d.

	Reference Range	Presentation Value	Nadir Value
Hematology			
Hemoglobin (g/dl)	12.0–16.0	3.9	3.9
Mean corpuscular volume (fL)	80-94	80	80
Hematocrit (%)	36.0–46.0	11.4	11.4
Reticulocytes (%)	0.5-2.5	Undetectable	Undetectable
White-cell count (per µl)	4500–11,000	0.9	0.6
Differential count (%)			
Neutrophils	40–70	39	
Lymphocytes	22–44	41	
Monocytes	4–11	19	
Eosinophils	0–8	0	
Platelet count (per µl)	150,000–400,000	118,000	83,000
Chemistries			
Sodium (mmol/liter)	135–145	141	
Potassium (mmol/liter)	3.4–5.0	3.6	
Chloride (mmol/liter)	98–108	103	
Carbon dioxide (mmol/liter)	23–32	29	
Urea nitrogen (mg/dl)	8–25	17	
Creatinine (mg/dl)	0.60–1.50	0.74	
Glucose (mg/dl)	70–110	107	
Iron Saturation (%)	14-50	96%	
Total iron binding capacity (ug/dL)	230-404	230	
Ferritin (ug/L)	20-300	651	
Folate (ng/mL)	>4.7	11.5	
Vitamin B12 (pg/mL)	>231	864	
Lactate dehydrogenase (IU/liter)	110–210	157	
Alanine aminotransferase (U/liter)	10–55	32	
Aspartate aminotransferase (U/liter)	10–40	20	
Bilirubin (mg/dl)			
Total	0.0–1.0	0.5	
Direct	0.0–0.4	<0.2	
Infectious Workup			
Human Immunodeficiency Virus		negative	
		IgM negative, IgG	
Parvovirus		positive, PCR negative	
Hepatitis B Virus		Immune	
Hepatitis C Virus antibody		negative	
Cytomegalovirus		IgM negative, IgG positive	
		IgM negative, IgG	
Epstein Barr Virus Viral Capsid Antigen		positive, PCR negative	
Serum Protein Electrophoresis		Normal	
Rheumatologic Workup			
Antinuclear Antibody		1:160	
anti-dsDNA antibody		negative	
anti-Smith antibody		negative	
anti-Ro antibody		negative	
anti-La antibody		negative	
anti-ribonucleoprotein antibody		negative	
anti-neutrophil cytoplasmic antibody		negative	
anti-cyclic citrullinated protein antibody		negative	
Rheumatoid factor		negative	
Celiac autoantibody panel		negative	

Supplemental Figure 1: Additional clinical parameters, related to Figure 1

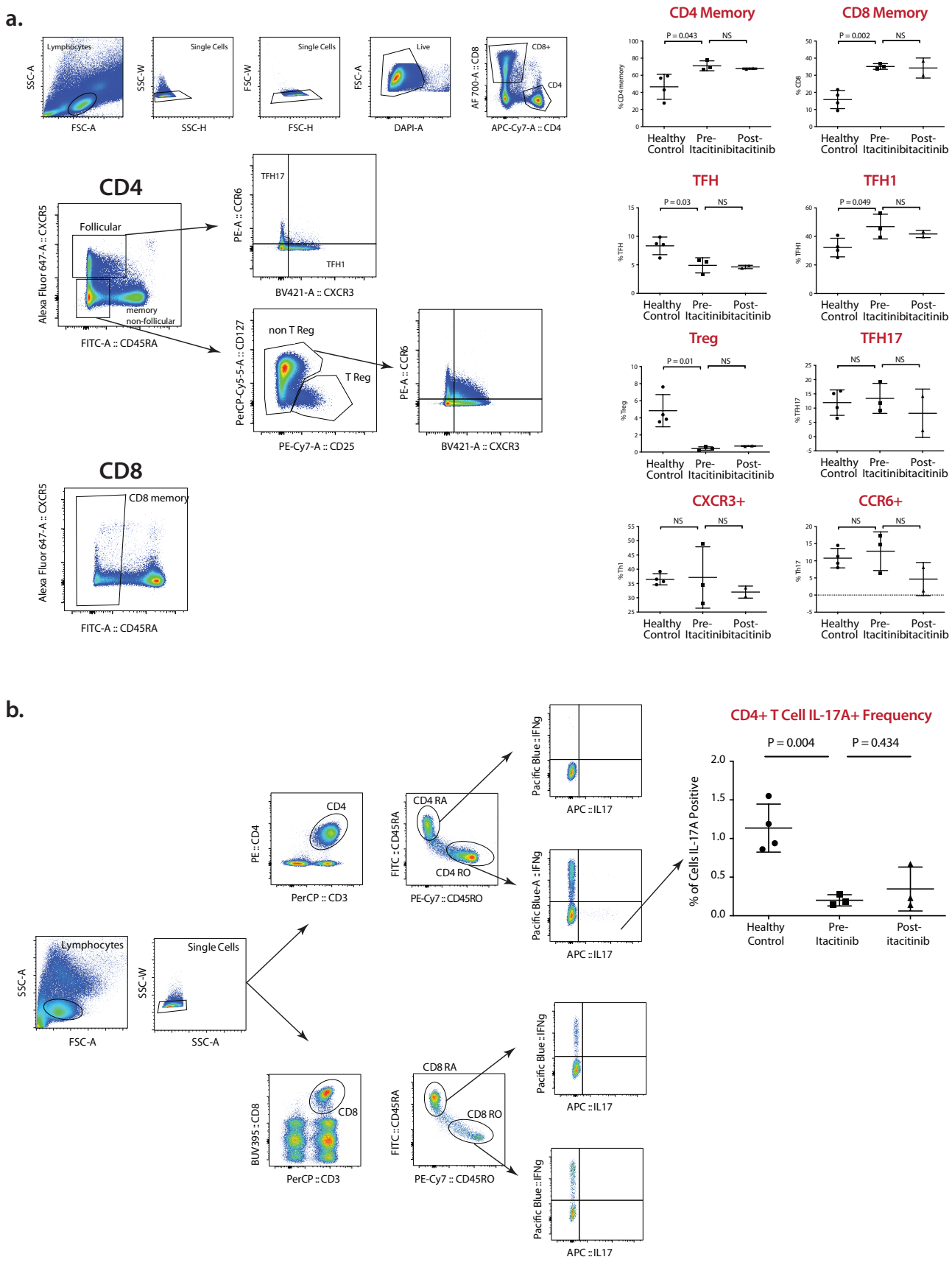
a. The patient's chronic mucocutaneous candidiasis.

b. The patient's platelet counts over time.

c. Schematic of JAK-STAT signaling showing interferon-γ binding its receptor, activating JAK1 and JAK2 to phosphorylate STAT1. STAT1 dimerizes, translocates to the nucleus, and activates target genes.

d. Laboratory values as part of an infectious and rheumatologic workup of pancytopenia.

Rosenberg et al. Supplemental Figure 2

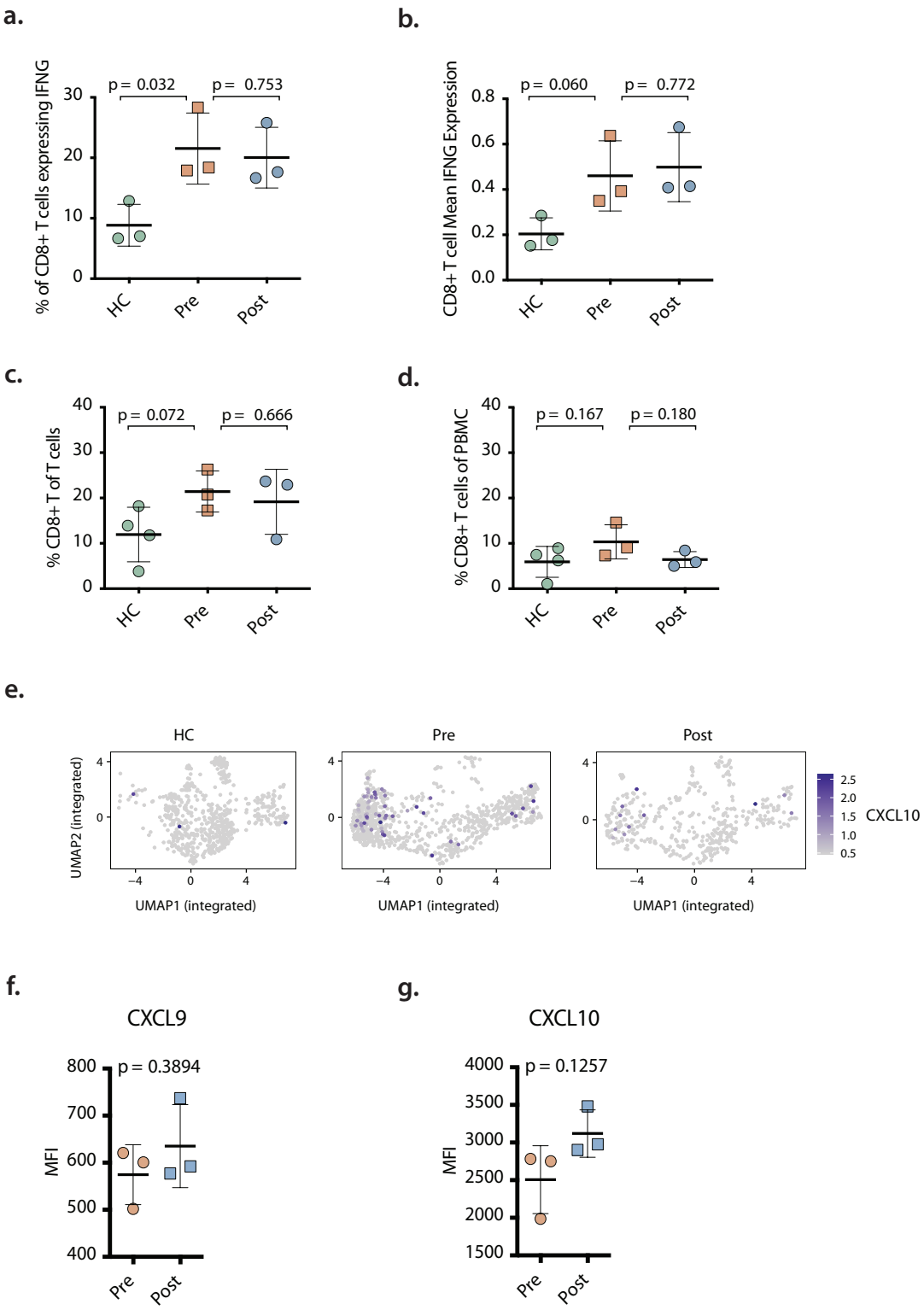


Supplemental Figure 2: Immunophenotyping, related to Figure 2

a. Flow cytometric immunophenotyping gating strategy is shown (left). Cell type frequencies for each cell type are plotted by condition (healthy controls, pre-itacitinib, or post-itacitinib) (right).

b. Flow cytometric intracellular cytokine staining gating strategy is shown (left). Memory CD4+ T cell IL-17A-secreting cell frequencies are plotted (right). CD4+ T cell interferon-γ-secreting frequencies are found in Figure 2 of the main manuscript, as are CD8+ T cell interferon-γ-secreting frequencies. All P values are calculated using unpaired t-test.

Rosenberg et al. Supplemental Figure 3



Supplemental Figure 3: Single-cell RNA-sequencing cell function and frequency, and additional plasma cytokine concentrations, related to Figure 3

a. For all samples with at least 15 CD8+ cells, the percent of CD8+ T cells expressing interferon-γ is plotted. For HC n = 3, pre-itacitinib n = 3, and post-itacitinib n = 3.

b. Mean interferon-γ transcript levels are plotted as in a.

c. Using single cell RNA-sequencing, for each time point as described in Figure 2, the number of cells in the CD8+ T cell cluster was divided by the total number of cells in that time point's T cell-containing cluster or

d. divided by the total number of PBMC sequenced. The percentage was then plotted, and p-values determined by unpaired t-test. For HC n = 4, pre-itacitinib n = 3, and post-itacitinib n = 3. All P values calculated using unpaired t test.

e. Expression of CXCL10 is plotted by condition. For HC n = 4, pre-itacitinib n = 3, and post-itacitinib n = 3.

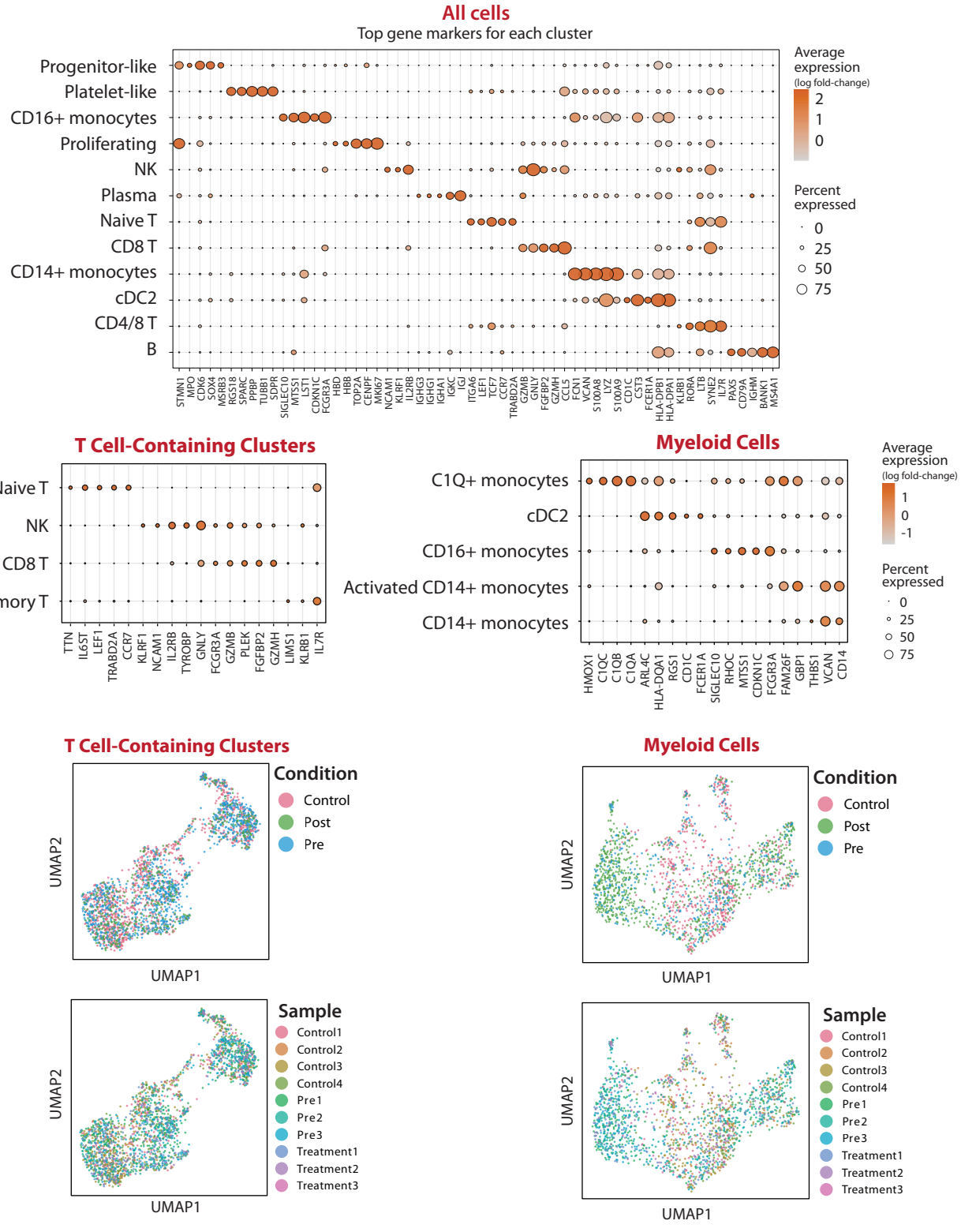
f.-g.Plasma cytokine levels measured in units of mean fluorescent intensity (MFI) from the patient at six time points pre- and post-itacitinib.

Rosenberg et al. Supplemental Methods Figure 1

a.

Sample	UMI (median)	Genes Detected (median)	# of Cells		Sample	UMI (median)	Genes Detected (median)	# of Cells
Healthy Control 1	1072	685	595		Pre-itacitinib 1	2142.5	1195.5	754
Healthy Control 2	1014	668	179		Pre-itacitinib 2	1630	952	639
Healthy Control 3	1117.5	699	814		Pre-itacitinib 3	1648	995	721
Healthy Control 4	794	538	607		Post-itacitinib 1	1144	748	577
					Post-itacitinib 2	786	573	259
					Post-itacitinib 3	1274	796	165

b.



c.

Supplemental Methods Figure 1: Single-cell RNA-sequencing cluster features, related to Figure 3

a. Single-cell RNA-sequencing was performed on PBMCs from four different healthy controls and the patient at six different time points pre- and post-itacitinib treatment. For each sample, median unique molecular identifiers (UMIs) per cell, median genes detected per cell, and number of cells for each sample are shown.

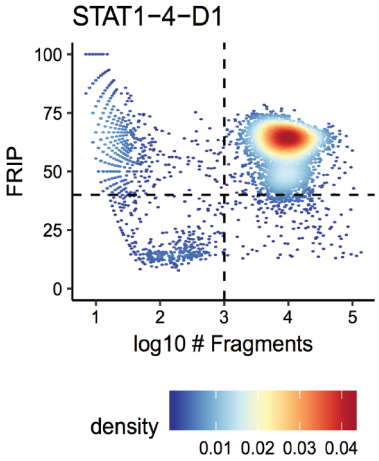
b. Cluster-defining genes for each cell type (top); cluster defining genes across T cell containing subclusters (bottom left); and cluster defining genes across myeloid subclusters (bottom right) are shown.

c. T cell-containing subclusters are shown by condition (Healthy control, pre-itacitinib, or post-itacitinib) (top left) and by sample (one of four healthy controls or one of six time points from the patient) (bottom left). The same is plotted for myeloid subclusters (top right) and (bottom right).

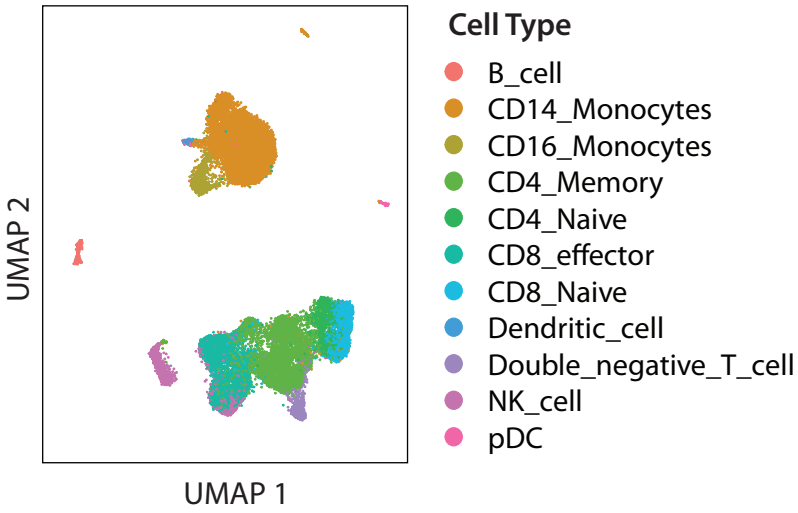
Rosenberg et al. Supplemental Methods Figure 2

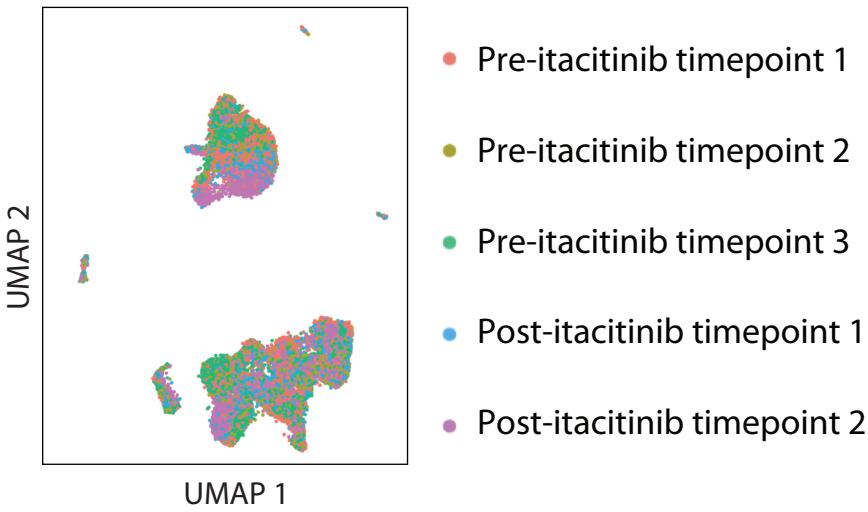
a.

Condition	# of cells
Pre-itacitinib 1	5325
Pre-itacitinib 2	3495
Pre-itacitinib 3	5706
Post-itacitinib 1	3713
Post-itacitinib 2	5530



b.





Supplemental Methods Figure 2: Single-cell assay for transposase-accessible chromatin with sequencing, related to Figure 3

a. Shown are the number of cells sequenced per time point sample (left) and a representative plot from one sample where each point is a cell plotted by log 10 number of fragments on the x-axis and by the fraction of reads in called peak regions (FRIP) on the y-axis.

b. Clustering of cell types using scATAC-seq, plotted in UMAP space, and labeled by cell type (top) and by time-point (bottom). N = 3 pre-itacitinib time points and n = 2 post-itacitinib time points.