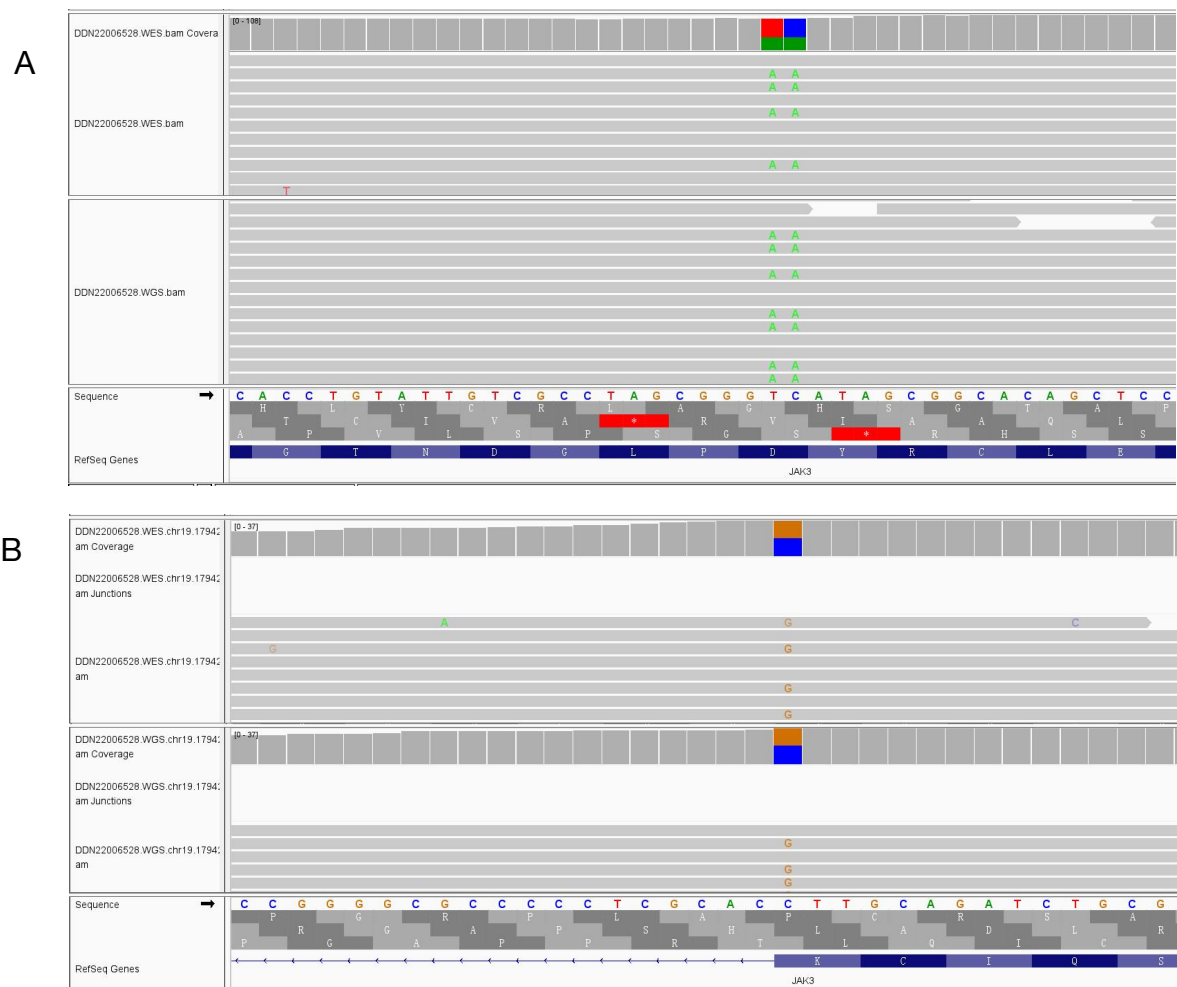




Supplementary Fig 1. Integrative Genomics Viewer Plot of JAK3 Gene Variant. (A)

Whole-genome and whole-exome sequencing reads mapping to JAK3 locus

c.2524_2525, with variant nucleotides displayed in green. The WES coverage depth is 95 reads, with the wild-type TC accounting for 58% and the variant TT accounting for 42%.

The WGS coverage depth is 37 reads, with the wild-type TC accounting for 48% and the

variant TT accounting for 62%. (B) Whole-genome and whole-exome sequencing reads

mapping to JAK3 locus c.2805, with variant nucleotides displayed in brown. The WES

coverage depth is 36 reads, with the wild-type G accounting for 50% and the variant C

accounting for 50%. The WGS coverage depth is 36 reads, with the wild-type G

accounting for 53% and the variant C accounting for 47%.

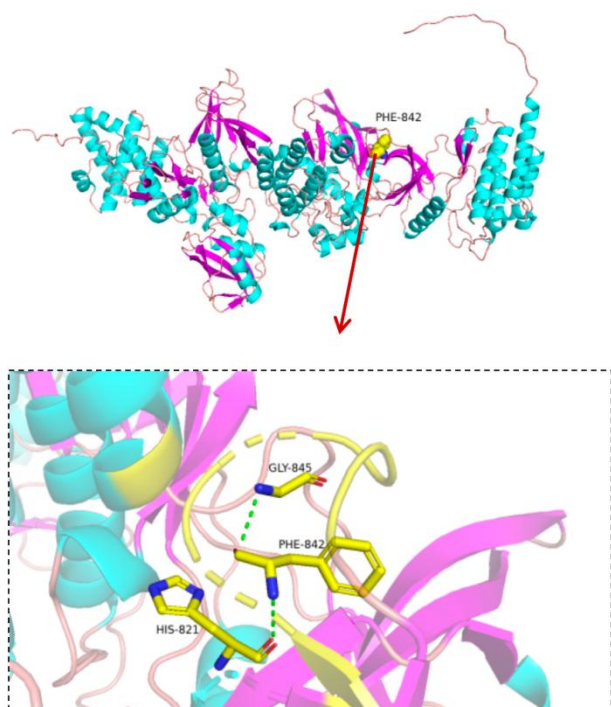
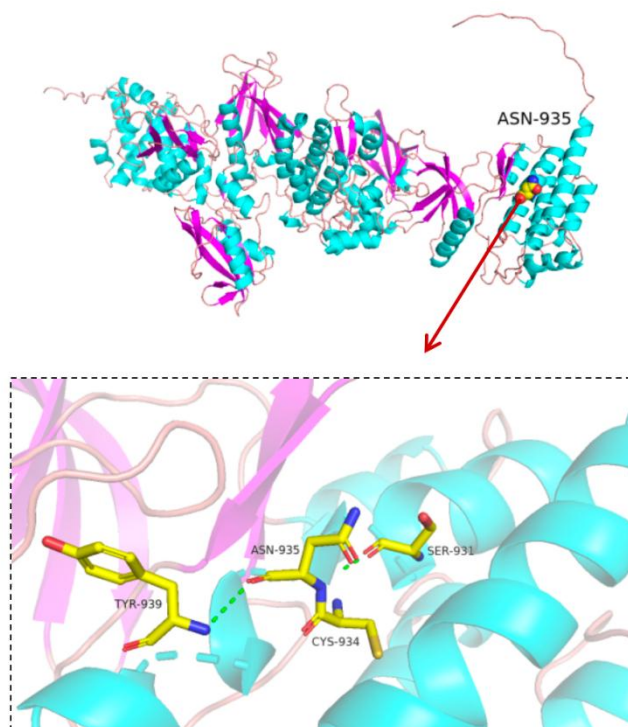
A JAK3 Gene c.2524_2525 delinsTT

<i>Patient</i>	E L C R Y F P L G D N
<i>Human</i>	E L C R Y D P L G D N
<i>Rhesus</i>	E L C R Y D P L G D N
<i>Mouse</i>	E L C R Y D P L G D N
<i>Dog</i>	E L C R Y D P L G D N
<i>Pallas</i>	E L C R Y D P L G D N
<i>Chicken</i>	E L C R Y D P L G D S
<i>Zebrafish</i>	E L C R Y D P W G D N

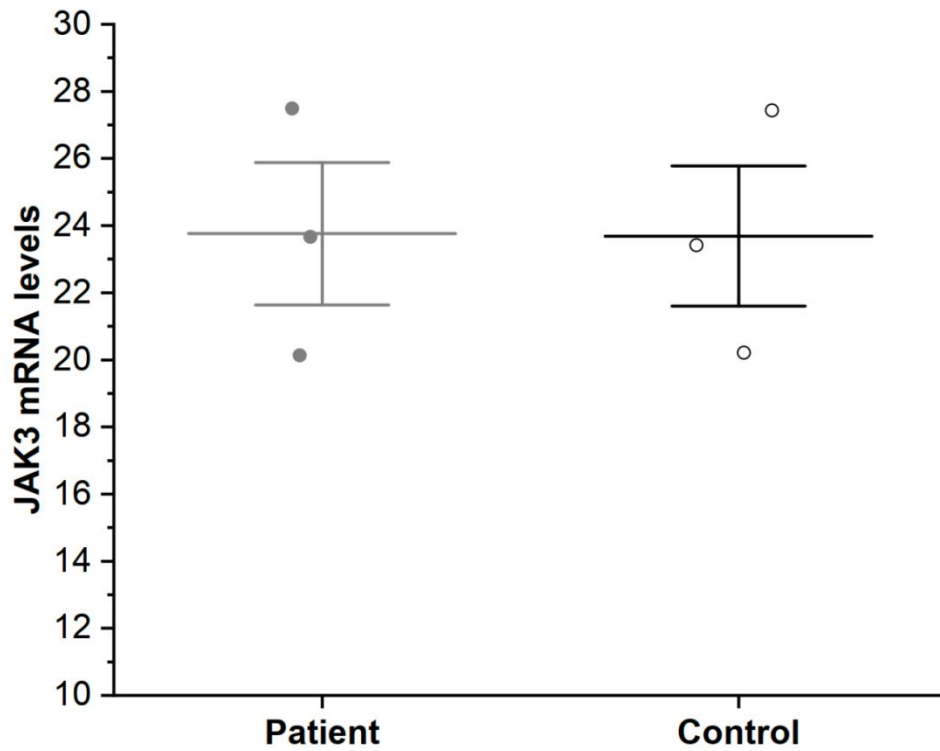
B JAK3 Gene c.2805G>C

<i>Patient</i>	Y S S Q I C N G M E Y L
<i>Human</i>	Y S S Q I C K G M E Y L
<i>Rhesus</i>	Y S S Q I C K G M E Y L
<i>Mouse</i>	F A W Q I C K G M E Y L
<i>Dog</i>	Y A S Q I C K G M E Y L
<i>Pallas</i>	F A W Q I C K G M E Y L
<i>Chicken</i>	Y A W Q I C K G M E Y L
<i>Zebrafish</i>	F A S Q I C K G M E Y L

Supplementary Fig 2. Conservation Analysis of JAK3 Protein. Homologous protein sequences were downloaded from the HomoloGene database on the NCBI website, and sequence alignment and visualization were performed using UniproUGENE software. Comparative analysis across multiple species shows that both the 842nd and 935th amino acids of the JAK3 gene are highly conserved. The patient's c.2524_2525delinsTT variant results in an aspartic acid to phenylalanine substitution at position 842 (A), while the c.2805G>C variant leads to a lysine to asparagine substitution at position 935 (B).

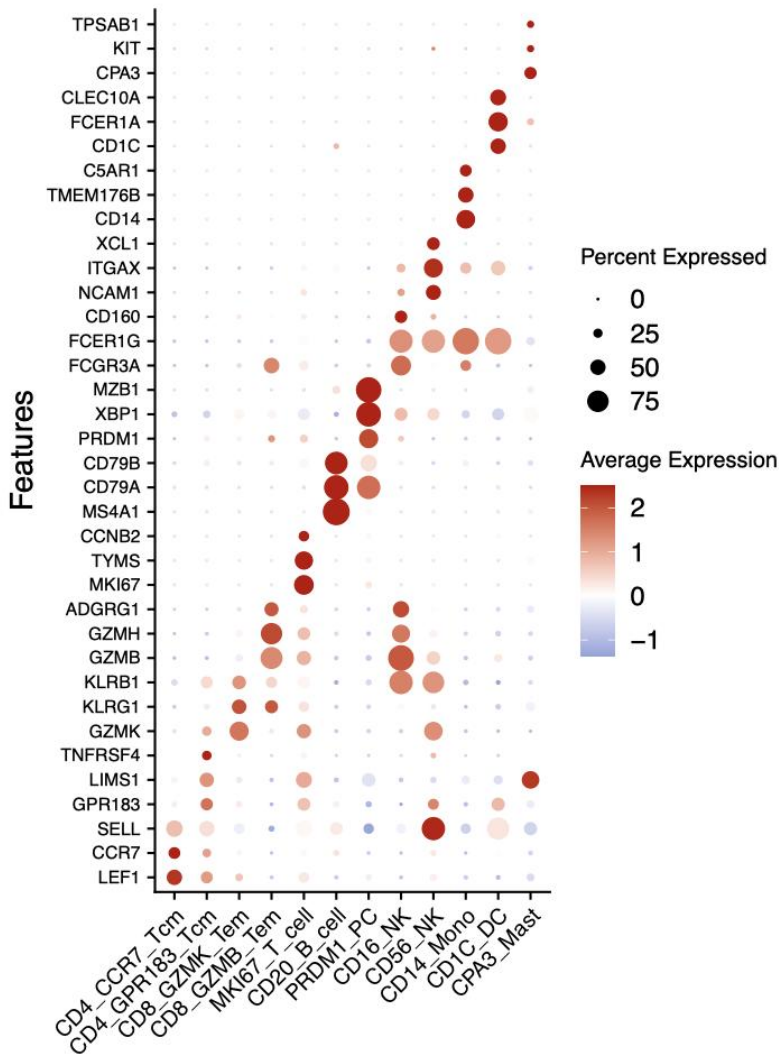
A JAK3 Gene c.2524_2525 delinsTT**B JAK3 Gene c.2805G>C****Supplementary Fig 3. Visual Analysis of Structural Impacts of Variants at Positions 842**

and 935 in the JAK3 Protein. The 3D protein structure analysis was conducted using protein sequences downloaded from the NCBI website (<https://www.ncbi.nlm.nih.gov/>). Homology modeling of the protein structure was performed using the online analysis tool Swiss-Model (<https://swissmodel.expasy.org/interactive>). The selected model's PDB file was downloaded and visualized using PyMOL viewer software, and images were saved. The c.2524_2525delinsTT variant results in an aspartic acid (D) to phenylalanine (F) substitution at position 842, altering the local hydrogen bonding network and potentially affecting protein conformation. Similarly, the c.2805G>C variant leads to a lysine (K) to asparagine (N) substitution at position 935, disrupting the hydrogen bond interactions with surrounding residues. Blue represents α -helices, purple represents β -sheets, and pink loops represent loop structures. The observed hydrogen bonds are displayed as stick models, with each color representing different atoms: yellow for carbon (C), gray for hydrogen (H), blue for nitrogen (N), red for oxygen (O), and orange for sulfur (S). Hydrogen bonds are shown in green.

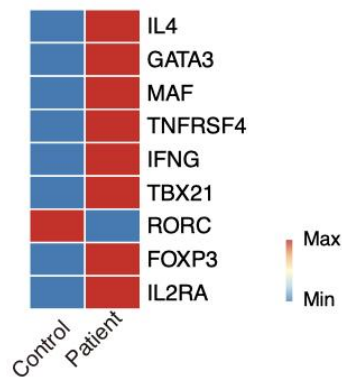


Supplementary Fig 4. Comparison of JAK3 mRNA Levels in Peripheral Blood Between Patient and Healthy Control. The JAK3 mRNA levels in the patient with JAK3 mutation are comparable to those in control group.

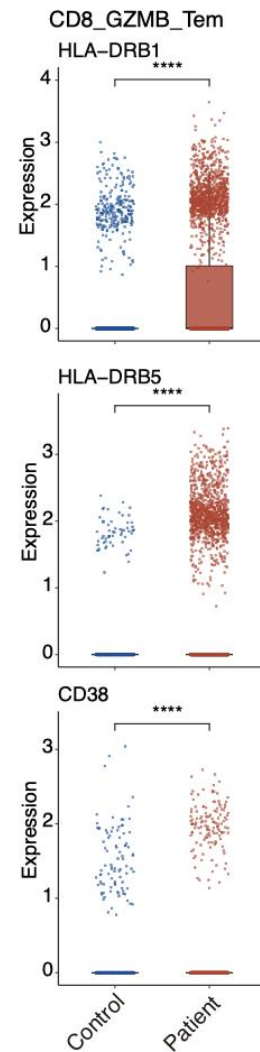
A



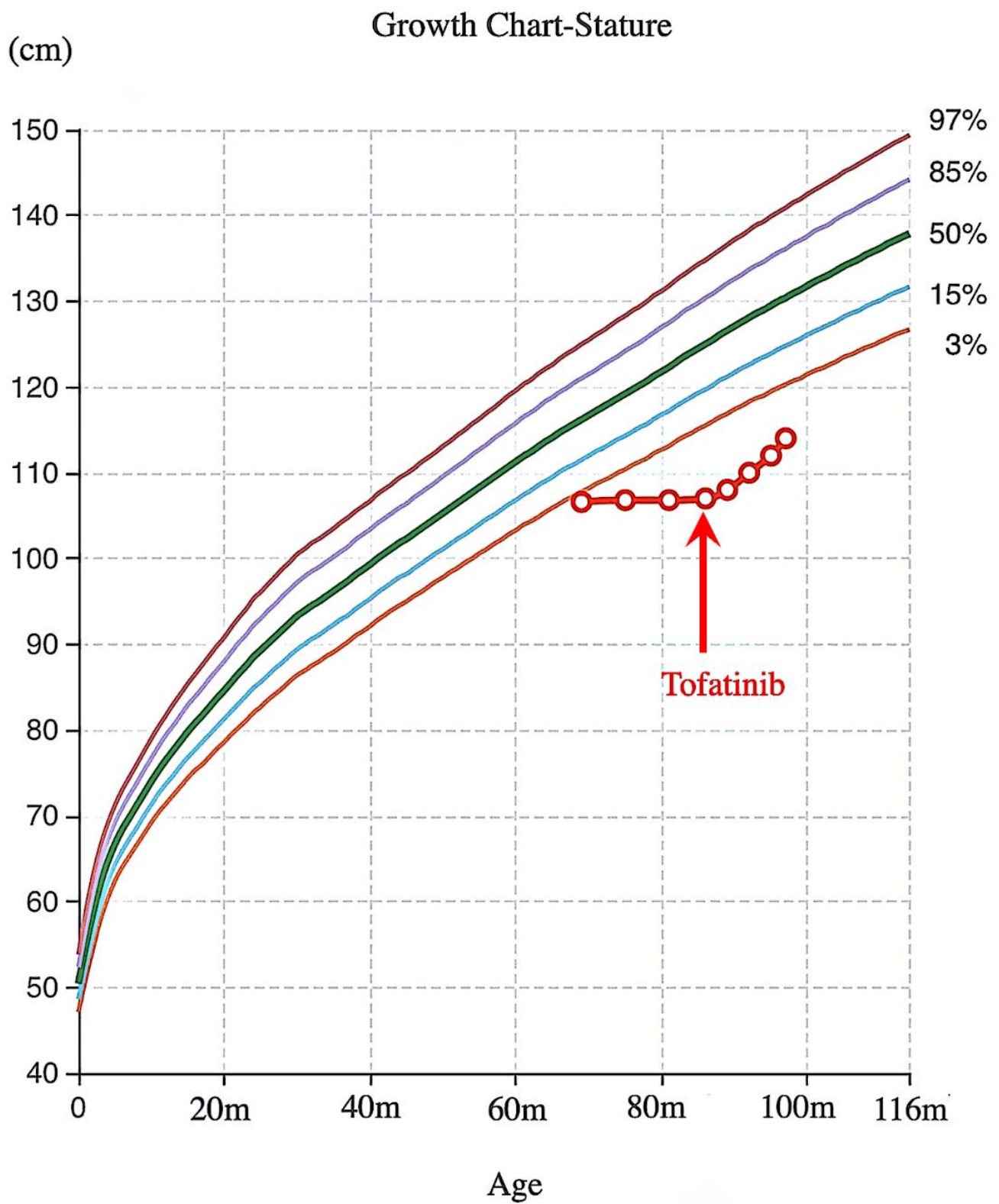
B



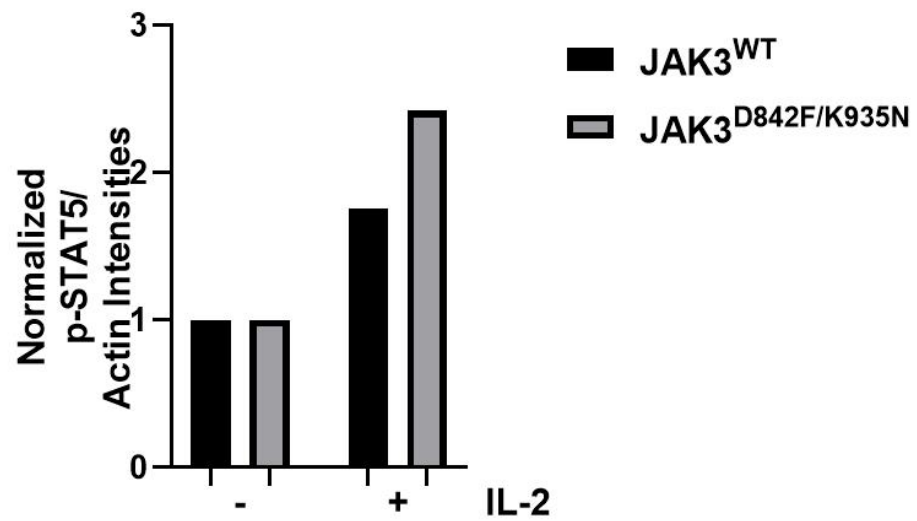
C



Supplementray Fig 5. (A) Dot plots showing the expression of selected canonical genes in each sub-cluster. (B) Heatmap illustrating the expression of genes associated with Th1, Th2, Th17, and Treg differentiation within the CD4⁺CCR7⁺ central memory T cell (Tcm) population, comparing control and patient samples. (C) Boxplots comparing the expression levels of HLA-DR genes and CD38 in CD8⁺GZMB⁺ effector memory T cells (Tem) between control and patient samples.



Supplementary Fig 6. Growth curve of the patient.



Supplementary Fig 7. Quantification of p-STAT5 protein expression by western blot analysis normalized on β -actin.

Supplementary Table 1. JAK3 Gene Mutation Analysis and ACMG Evaluation

Gene	Exon Number	Nucleotide alteration	Amino acid change	Zygosity	From	SIFT Score	Mutation Taster Prediction	dbSNP	1000 Genomes Project	gnomAD	ACMG Evaluation
JAK3	exon 19	c.2524_2525delinsTT	p.Asp842Phe	Het	Father	<0.05	D	NC	NC	NC	PM1+PM2+ PM3+PP3
	exon20	c.2805G>C	p.Lys935Asn	Het	Mother	<0.05	D	NC	NC	NC	PM1+PM2+ PM3+PP3

Het: heterozygous; D: disease causing; NC: Not collected; ACMG: American College of Medical Genetics and Genomics.

Supplementary Table 2. List of Autoantibodies Tested in This Patient

Tested Autoantibodies
Antinuclear antibodies (ANA)
Anti-mitochondrial antibody (AMA)
Anti-mitochondrial M2 antibody (AMA-M2)
Anti-smooth muscle antibody (SMA)
Anti-liver/kidney microsomal antibody (LKM)
Anti-soluble liver antigen/hepatopancreatic antigen (SLA/LP)
Anticardiolipin antibody IgA
Anticardiolipin antibody IgG
Anticardiolipin antibody IgM
Anti-beta-2 glycoprotein I antibody IgA
Anti-beta-2 glycoprotein I antibody IgG
Anti-beta-2 glycoprotein I antibody IgM
Anti-double-stranded DNA antibody (anti-dsDNA)
Anti-histone antibody
Anti-nucleosome antibody
Anti-C1q antibody
Anti-SS-A (Ro) antibody
Anti-SS-B (La) antibody
Anti-Smith (Sm) antibody
Anti-U1 RNP antibody
Anti-Jo-1 antibody
Anti-topoisomerase I antibody (anti-Scl-70)
Anti-centromere antibody
Perinuclear anti-neutrophil cytoplasmic antibody (p-ANCA)
Cytoplasmic anti-neutrophil cytoplasmic antibody (c-ANCA)
Anti-myeloperoxidase antibody (anti-MPO)
Anti-proteinase 3 antibody (anti-PR3)
Thyrotropin receptor antibody (TRAb)
Thyroglobulin antibody (TgAb)
Thyroid peroxidase antibody (TPOAb)
Anti-PL-7 antibody
Anti-PL-12 antibody
Anti-EJ antibody
Anti-OJ antibody
Anti-Zo antibody
Anti-KS antibody
Anti-Ha antibody
Anti-Mi-2 α antibody
Anti-Mi-2 β antibody
Anti-TIF1 γ antibody
Anti-NXP2 antibody
Anti-MDA5 antibody
Anti-SAE1 antibody
Anti-SAE2 antibody

Anti-HMGCR antibody
Anti-SRP antibody
Anti-cN1A antibody
Anti-CENP-B antibody
Anti-RNP antibody
Anti-Th/To antibody
Anti-NOR-90 antibody
Anti-fibrillarin antibody
Anti-Ku antibody
Anti-PM-Scl100 antibody
Anti-PM-Scl75 antibody
Anti-Ro-52 antibody

Supplementary Table 3. Baseline serum cytokines and inflammatory markers.

Marker	Value	Normal
IL-2 (pg/mL)	1.96	(0.00–5.71)
IL-4 (pg/mL)	3.02	(0.00–2.80)
IL-6 (pg/mL)	2.56	(0.00–5.30)
IL-10 (pg/mL)	3.91	(0.00–4.91)
IL-17 (pg/mL)	8.84	(0.00–20.60)
IFN- γ (pg/mL)	2.05	(0.00–7.42)
TNF (pg/mL)	2.23	(0.00–4.60)
ESR (mm/h)	9	≤ 20
CRP (mg/L)	0.33	(0.00–10.00)
Fer (ug/L)	66.25	(16.40–323.00)