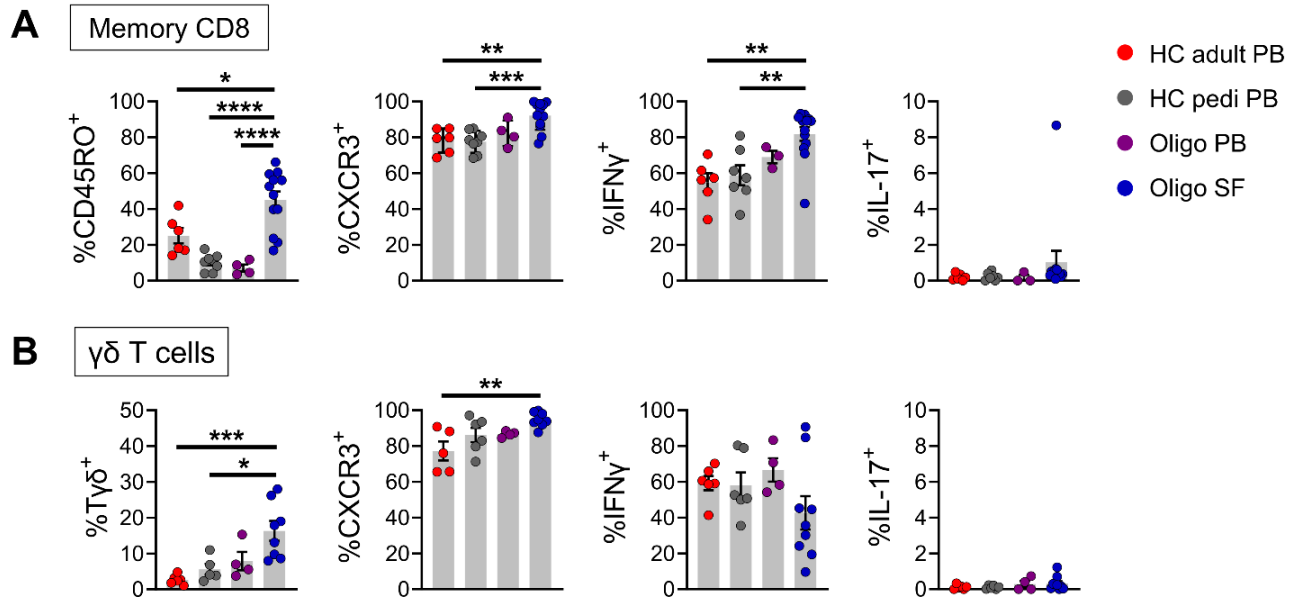


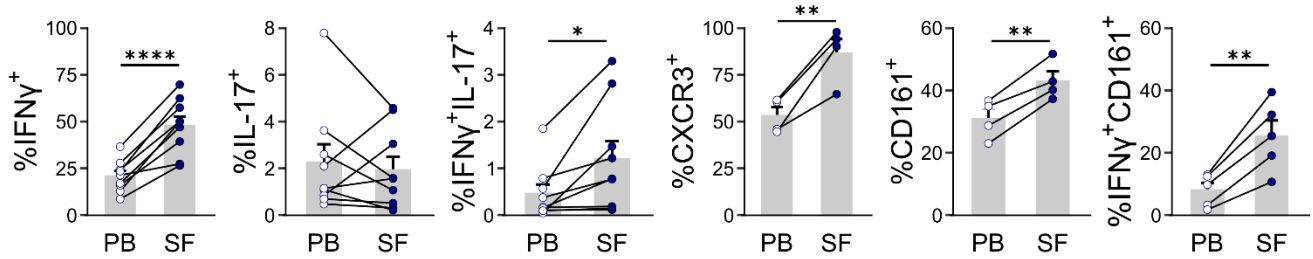
## SUPPLEMENTARY FIGURES



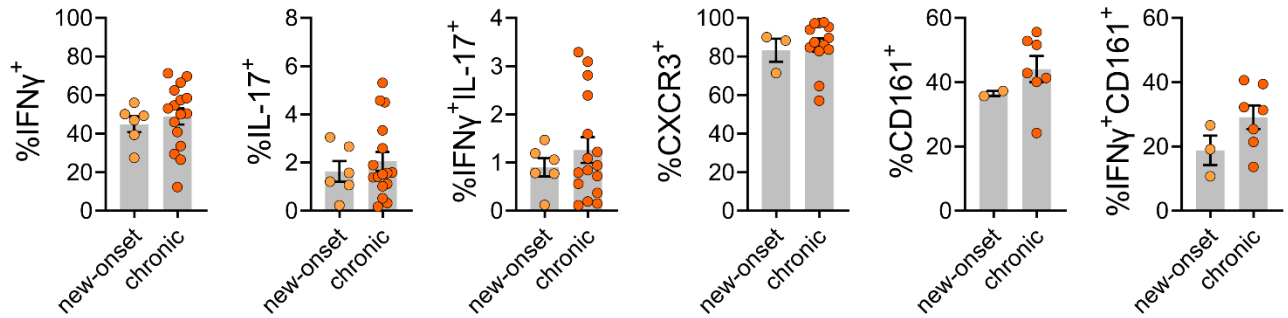
**Figure S1: CD8 memory T cells and  $\gamma\delta$  T cells are enriched in the SF of oligo JIA patients, and upregulate Th1 markers.**

A) Percent of total CD8<sup>+</sup> T memory (Tmem, CD3<sup>+</sup>CD8<sup>+</sup>CD45RO<sup>+</sup>) cells among total CD8<sup>+</sup> T cells and of CD8<sup>+</sup> Tmem expressing different cytokines and chemokines in the SF of oligo JIA patients (n=12-13) and in the PB of patients (n=3-4) and controls (adult: n=6, pediatric: n=7-8). B) Percent of total  $\gamma\delta$  T lymphocytes (CD3<sup>+</sup>T $\gamma\delta$ <sup>+</sup>) and of  $\gamma\delta$  T cells expressing different cytokines and chemokines in the SF of oligo JIA patients (n=8-9) and in the PB of patients (n=4) and controls (adult: n=5-6, pediatric: n=5-6). HC, healthy control; pedi, pediatric; oligo, oligoarticular juvenile idiopathic arthritis; PB, peripheral blood; SF, synovial fluid. Summary data on all bar graphs are mean  $\pm$  standard error. P-value <0.05 (\*); <0.01 (\*\*), <0.001 (\*\*\*), <0.0001 (\*\*\*\*). Statistical testing: one-way ANOVA followed by multiple t-tests with Turkey correction.

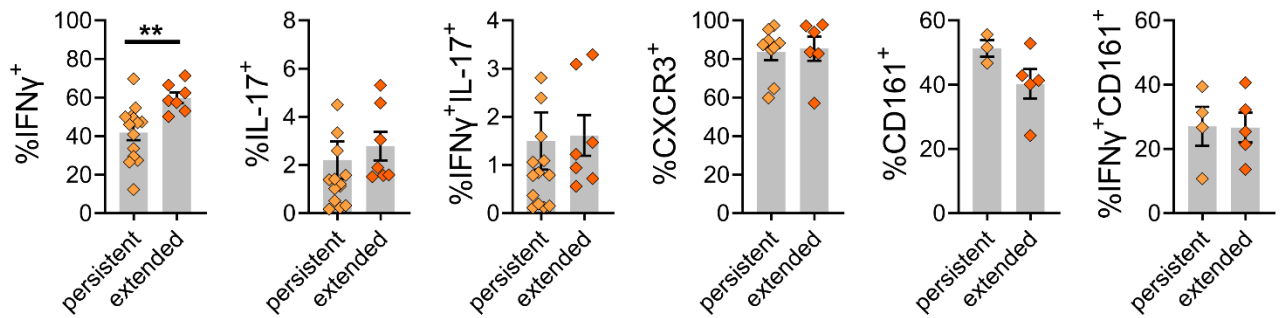
### A Paired oligo PB and SF samples



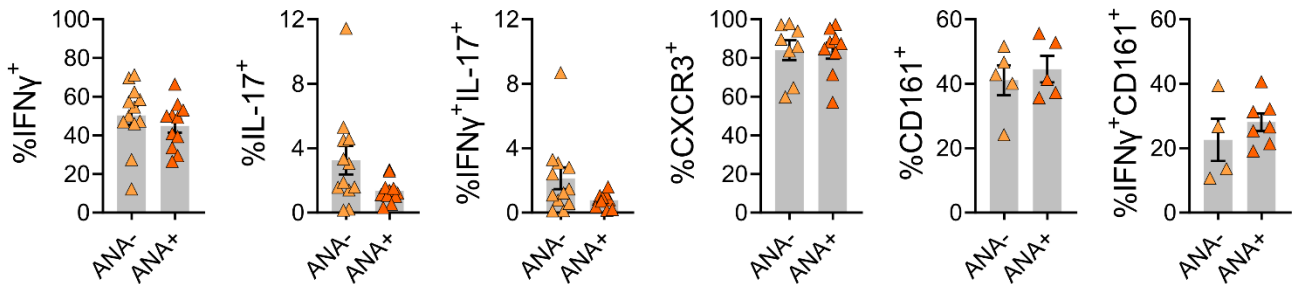
### B New-onset oligo SF vs. Chronic oligo SF



### C Persistent oligo SF vs. Extended oligo SF

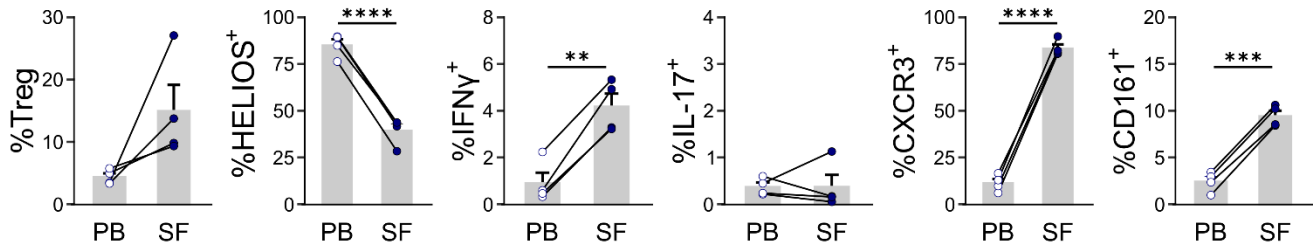


### D ANA- oligo SF vs. ANA+ oligo SF

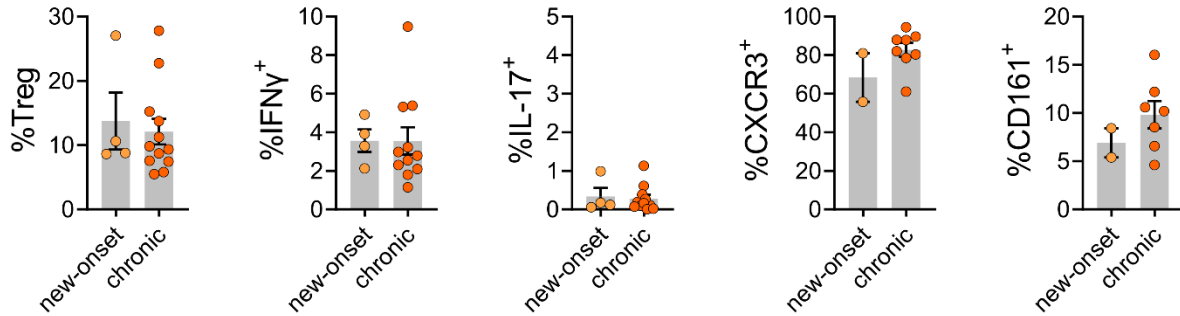


**Figure S2: Th1 polarization of CD4<sup>+</sup> Tmem cells in the SF of new-onset and chronic oligo JIA patients.** A) Percent of CD4<sup>+</sup> Tmem (CD3<sup>+</sup>CD4<sup>+</sup>CD45RO<sup>+</sup>) cells expressing different cytokines and chemokines in paired PB and SF samples from oligo JIA patients (n=4-9). B) Percent of CD4<sup>+</sup> Tmem cells expressing different cytokines and chemokines in oligo JIA SF samples obtained at disease onset (n=2-5) or in chronic disease phase (n=7-16). C) Percent of CD4<sup>+</sup> Tmem cells expressing different cytokines and chemokines in the SF of patients progressing to persistent (n=3-13) or extended (n=5-7) forms of oligo JIA. D) Percent of CD4<sup>+</sup> Tmem cells expressing different cytokines and chemokines in the SF of oligo JIA patients with (n=5-11) or without (n=4-12) antinuclear autoantibody (ANA). All analyses were gated on CD3<sup>+</sup>CD4<sup>+</sup>CD45RO<sup>+</sup> cells (CD4<sup>+</sup> Tmem). PB, peripheral blood; SF, synovial fluid; oligo, oligoarticular juvenile idiopathic arthritis; ANA, antinuclear autoantibody. Summary data on all bar graphs are mean ± standard error. P-value <0.05 (\*); <0.01 (\*\*), <0.001 (\*\*\*), <0.0001 (\*\*\*\*). Statistical testing: Paired (a) and unpaired (b and c) t-tests.

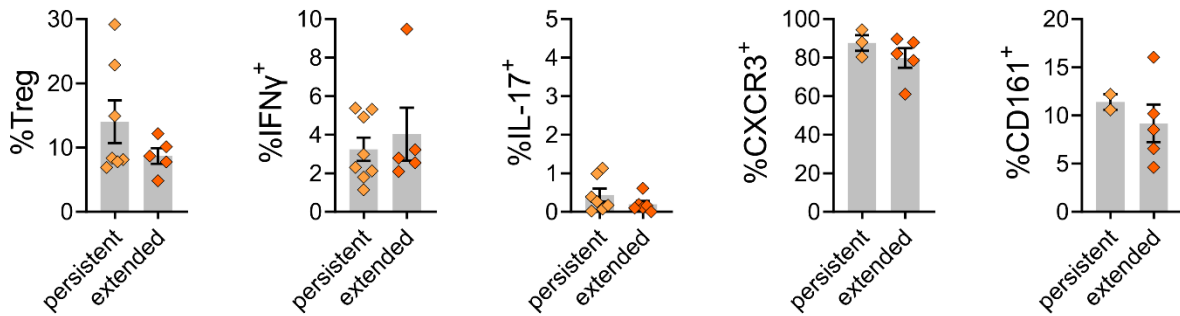
### A Paired oligo PB and SF samples



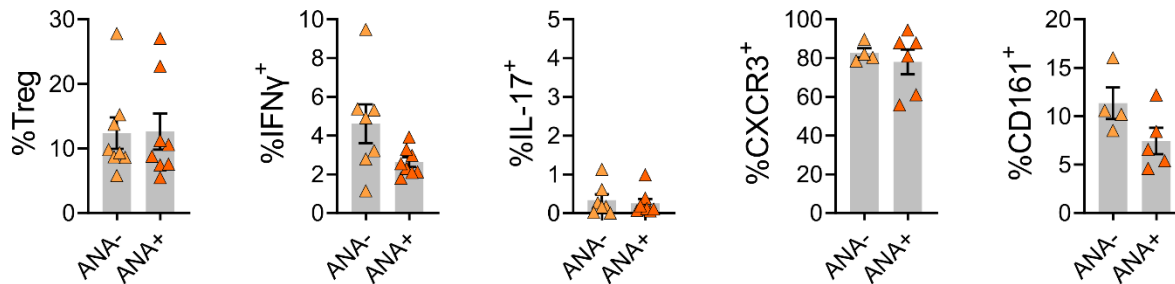
### B New-onset oligo SF vs. Chronic oligo SF



### C Persistent oligo SF vs. Extended oligo SF

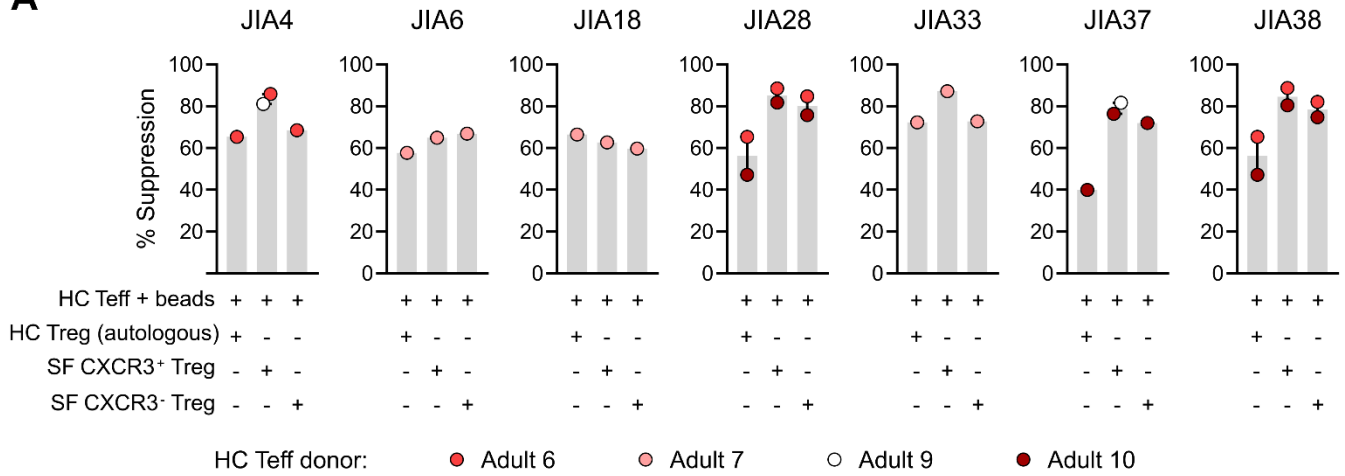


### D ANA- oligo SF vs. ANA+ oligo SF

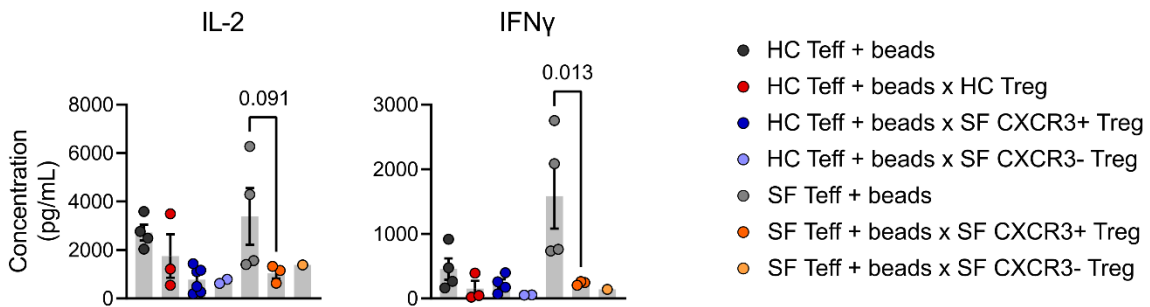


**Figure S3: Th1 polarization of regulatory T (Treg) cells in the SF of new-onset and chronic oligo JIA patients.** A) Percent of total Treg (CD25<sup>+</sup>CD127<sup>lo</sup>FOPX3<sup>+</sup>) among CD4<sup>+</sup> T cells, and of Treg cells expressing different cytokines and chemokines in paired PB and SF samples from oligo JIA patients (n=4). B) Percent of total Treg (CD25<sup>+</sup>CD127<sup>lo</sup>FOPX3<sup>+</sup>) among CD4<sup>+</sup> T cells, and of Treg cells expressing different cytokines and chemokines in oligo JIA SF samples obtained at disease onset (n=2-4) or in chronic disease phase (n=7-12). C) Percent of total Treg (CD25<sup>+</sup>CD127<sup>lo</sup>FOPX3<sup>+</sup>) among CD4<sup>+</sup> T cells and of Treg cells expressing different cytokines and chemokines in the SF of patients progressing to persistent (n=2-8) or extended (n=5) forms of oligo JIA. D) Percent of total Treg (CD25<sup>+</sup>CD127<sup>lo</sup>FOPX3<sup>+</sup>) among CD4<sup>+</sup> T cells and of Treg cells expressing different cytokines and chemokines in the SF of oligo JIA patients with (n=5-8) or without (n=4-8) antinuclear autoantibody (ANA). PB, peripheral blood; SF, synovial fluid; oligo, oligoarticular juvenile idiopathic arthritis; ANA, antinuclear autoantibody. Summary data on all bar graphs are mean  $\pm$  standard error. P-value <0.05 (\*); <0.01 (\*\*), <0.001 (\*\*\*), <0.0001 (\*\*\*\*). Statistical testing: Paired (a) and unpaired (b and c) t-tests.

**A**



**B**



**Figure S4: Th1-like Tregs maintain the ability to suppress Teff proliferation and cytokine production.** A) Per patient percent suppression (mean  $\pm$  standard error) in the proliferation of Teff cells ( $CD4^+CD25^+$ ) from a third-party control after co-culture at a ratio of 1:1 with autologous PB Tregs ( $CD4^+CD25^+CD127^{lo}$ ), oligo JIA CXCR3<sup>+</sup> SF Tregs or oligo JIA CXCR3<sup>-</sup> SF Tregs. Given the small number of subjects in each experiment, statistical testing was not preformed. B) Cytokine concentration (pg/mL, mean  $\pm$  standard error) detected in the supernatant of suppression assay co-cultures. Teffs from healthy controls were stimulated with anti-CD2/CD3/CD28 beads alone or co-cultured at a ratio of 1:1 with autologous Tregs, oligo JIA CXCR3<sup>+</sup> SF Tregs, or oligo JIA CXCR3<sup>-</sup> SF Tregs. Similarly, oligo JIA SF Teffs were stimulated with beads and co-cultured at a ratio of 1:1 with autologous oligo JIA CXCR3<sup>+</sup> SF Tregs or oligo JIA CXCR3<sup>-</sup> SF Tregs. The depicted data represents 4 independent experiments conducted with 4 healthy controls and 5 oligo JIA patients. HC, healthy control; oligo, oligoarticular; JIA, juvenile idiopathic arthritis; PB, peripheral blood; SF, synovial fluid. Statistical testing: one-way ANOVA followed by selected t-tests with Turkey correction.

## SUPPLEMENTARY TABLES

**Table S1: Clinical Characteristics of the Study Participants and Samples Contributed to the Studies.**

Subject	Sample	Group	JIA subtype		Sex	Age (yrs)		Joint involvement		ANA	Uveitis	Treatment at sampling	Flow	RNA-seq	Other
			at sampling	end of study		at onset	at sampling	at onset	at sampling						
Adult 1	PB	Control	NA	NA	F	NA	24-25	NA	NA	NA	NA	NA	Yes	No	No
Adult 2	PB	Control	NA	NA	F	NA	24-25	NA	NA	NA	NA	NA	Yes	No	No
Adult 3	PB	Control	NA	NA	M	NA	35-36	NA	NA	NA	NA	NA	Yes	Bulk	Suppr assay
Adult 4	PB	Control	NA	NA	M	NA	28	NA	NA	NA	NA	NA	Yes	No	No
Adult 5	PB	Control	NA	NA	M	NA	35	NA	NA	NA	NA	NA	No	Bulk	No
Adult 6	PB	Control	NA	NA	F	NA	26-28	NA	NA	NA	NA	NA	Yes	No	Suppr assay, Methylation
Adult 7	PB	Control	NA	NA	F	NA	35-36	NA	NA	NA	NA	NA	Yes	Bulk	Suppr assay, Methylation
Adult 8	PB	Control	NA	NA	F	NA	28-29	NA	NA	NA	NA	NA	Yes	Bulk	No
Adult 9	PB	Control	NA	NA	M	NA	36	NA	NA	NA	NA	NA	Yes	No	Suppr assay, Methylation
Adult 10	PB	Control	NA	NA	F	NA	22	NA	NA	NA	NA	NA	No	No	Suppr assay
Pedi 1	PB	Control	NA	NA	F	NA	16	NA	NA	NA	NA	NA	Yes	Bulk	No
Pedi 2	PB	Control	NA	NA	F	NA	11.5	NA	NA	NA	NA	NA	Yes	Bulk	No
Pedi 3	PB	Control	NA	NA	F	NA	7	NA	NA	NA	NA	NA	Yes	Bulk	No
Pedi 4	PB	Control	NA	NA	M	NA	11	NA	NA	NA	NA	NA	Yes	Bulk	No
Pedi 5	PB	Control	NA	NA	F	NA	6	NA	NA	NA	NA	NA	Yes	Bulk	No
Pedi 6	PB	Control	NA	NA	M	NA	6.5	NA	NA	NA	NA	NA	Yes	No	No
Pedi 7	PB	Control	NA	NA	M	NA	7	NA	NA	NA	NA	NA	Yes	No	No
Pedi 8	PB	Control	NA	NA	M	NA	14	NA	NA	NA	NA	NA	Yes	No	No
JIA 01	PB, SF	Oligo	Persistent	Persistent	F	4.5	9	2	1	-	No	ADA	Yes	Single-cell (SF)	No
JIA 02	PB, SF	Oligo	New-onset	Persistent	F	2	2	1	1	+	No	None	No	Bulk	No
JIA 02 (repeat)	SF	Oligo	Persistent	Persistent	F	2	4	1	1	+	No	ETA	Yes	Single-cell (SF)	No
JIA 03	SF	Oligo	Persistent	Persistent	F	3.5	9	1	1	-	No	None	Yes	No	No
JIA 03 (repeat)	PB, SF	Oligo	Persistent	Persistent	F	3.5	9.5	1	Unknown	-	No	None	No	Bulk	No
JIA 04	PB, SF	Oligo	New-onset	Persistent	F	10	10	1	1	+	No	None	No	Bulk	No
JIA 04 (repeat)	SF	Oligo	Persistent	Persistent	F	10	13	1	1	+	No	MTX	Yes	No	No
JIA 04 (repeat)	SF	Oligo	Persistent	Persistent	F	10	16	1	1	+	No	MTX	No	No	Suppr assay

JIA 05	PB, SF	Oligo	Persistent	Extended	F	2.5	10	1	1	-	No	None	No	Bulk	No
JIA 05 (repeat)	PB, SF	Oligo	Persistent	Extended	F	2.5	14.5	1	1	-	No	ETA	Yes	No	No
JIA 06	PB, SF	Oligo	New-onset	Persistent	F	13	13	1	1	-	No	None	Yes	Bulk	Suppr assay
JIA 07	PB, SF	Oligo	New-onset	Persistent	F	3.5	3.5	2	2	-	No	None	No	Bulk	No
JIA 08	PB, SF	Oligo	New-onset	Persistent	F	5	5	2	2	-	Unknown	None	Yes	No	No
JIA 09	PB	Oligo	New-onset	Persistent	F	1.8	1.8	1	1	-	No	None	Yes	No	No
JIA 10	PB	Oligo	New-onset	Persistent	F	5	5	1	1	-	No	None	Yes	No	No
JIA 11	PB	Oligo	New-onset	Persistent	M	4	4	5	5	+	No	MTX*	Yes	No	No
JIA 12	PB	Oligo	New-onset	Persistent	M	4	4	1	1	+	No	None	Yes	No	No
JIA 13	SF	Oligo	New-onset	Persistent	F	2.5	2.5	2	4	+	Unknown	None	Yes	No	No
JIA 14	PB	Oligo	New-onset	Persistent	F	2	2.5	1	1	+	Yes	MTX	Yes	No	No
JIA 15	PB, SF	Oligo	Persistent	Persistent	F	2	12	2	1	-	No	MTX	No	Bulk	Methylation
JIA 16	PB, SF	Oligo	Persistent	Persistent	F	3	9	2	2	+	No	MTX	Yes	Bulk	Methylation
JIA 17	PB, SF	Oligo	Persistent	Persistent	F	3.5	10	1	1	-	Yes	MTX	Yes	Bulk	Methylation
JIA 18	SF	Oligo	Persistent	Persistent	F	5.5	6	1	1	+	No	None	Yes	No	Suppr assay
JIA 19	SF	Oligo	Persistent	Persistent	F	1	7	Unknown	2	+	No	None	Yes	No	No
JIA 20	SF	Oligo	Persistent	Persistent	F	4	10	1	1	-	Yes	None	Yes	No	No
JIA 21	SF	Oligo	Persistent	Persistent	F	2	4.5	2	2	-	Yes	None	Yes	No	Methylation
JIA 22	SF	Oligo	Persistent	Persistent	M	5	6	1	1	-	Unknown	None	Yes	No	No
JIA 23	SF	Oligo	Persistent	Persistent	F	13	15.5	1	1	+	No	None	Yes	No	No
JIA 24	SF	Oligo	Persistent	Persistent	F	6	11.5	1	2	-	No	None	Yes	No	No
JIA 25	PB, SF	Oligo	New-onset	Extended	M	15.5	16	2	2	+	No	None	No	Bulk	No
JIA 26	PB, SF	Oligo	New-onset	Extended	F	17	17	1	2	-	No	None	Yes	Bulk	No
JIA 27	PB, SF	Oligo	Persistent	Extended	F	6	8.5	1	1	-	No	None	Yes	No	No
JIA 28	SF	Oligo	Extended	Extended	F	6	14.5	1	1	-	No	None	Yes	No	Suppr assay
JIA 29	SF	Oligo	Extended	Extended	F	4	15	4	1	+	Yes	None	Yes	No	No
JIA 30	SF	Oligo	Extended	Extended	M	4	7	2	1	-	No	LEF, MTX	Yes	No	No
JIA 31	SF	Oligo	Extended	Extended	F	8.5	12	4	Unknown	+	No	MTX	Yes	No	No
JIA 32	PB, SF	Oligo	New-onset	Unknown	F	6	6.5	1	1	-	No	None	No	Bulk	No
JIA 33	SF	Oligo	New-onset	Unknown	M	2	2.5	3	3	+	No	None	Yes	No	Suppr assay Methylation
JIA 34	SF	Oligo	New-onset	Unknown	F	13	13.5	1	1	+	Unknown	None	Yes	No	No
JIA 35	PB, SF	Psoriatic	Persistent	Psoriatic	M	2	4.5	1	1	+	No	None	Yes	Bulk	No
JIA 36	PB, SF	ERA	Persistent	ERA	F	13	13.5	1	1	-	No	MTX	No	Bulk	No
JIA 37	SF	Oligo	Persistent	Persistent	F	2.5	8	1	2	-	Yes	MTX	No	No	Suppr assay
JIA 38	SF	Oligo	Persistent	Persistent	F	3	7.5	1	2	?	No	None	No	No	Suppr assay

NA, not applicable; PB, peripheral blood; SF, synovial fluid; Oligo, oligoarticular; ERA, enthesitis-related arthritis; JIA, juvenile idiopathic arthritis; F, female; M, male; yrs, years; ADA, adalimumab; ETA, etanercept; LEF, leflunomide; MTX, methotrexate; ANA, antinuclear antibodies; Suppr, suppression. \*jointly with systemic steroids.

**Table S2: Antibodies and dyes used in flow cytometry staining.**

Antibody or dye	Clone	Manufacturer	Catalog #	Staining
anti-CD4-FITC	RPA-T4	BD Biosciences	555346	Surface
anti-CD25-PE	BC96	eBioscience	12-0259-42	Surface
anti-CD127-PE/Cy7	A019D5	BioLegend	351320	Surface
anti-CD45RO-FITC	UCHL1	BioLegend	304204	Surface
anti-CD3-APC	UCHT1	eBioscience	17-0038-42	Surface
anti-CD3-PE/Cy7	OKT3	BioLegend	317334	Surface
anti-CD4-PE	OKT4	BioLegend	317410	Surface
anti-CD8-APC/Cy7	RPA-T8	BioLegend	301015	Surface
anti-Tgd-FITC	B1.1	BioLegend	11-9959-42	Surface
anti-CXCR3-Pacific Blue	G025H7	BioLegend	353724	Surface
anti-CXCR3-BV605	G025H7	BioLegend	353728	Surface
anti-CD161-BV605	HP-3G10	BioLegend	339916	Surface
anti-CTLA4-APC	L3D10	BioLegend	349908	Intracellular
anti-Helios-PerCp/Cy5.5	22F6	BioLegend	137230	Intracellular
anti-Helios-APC/eFluor780	22F6	eBioscience	47-9883-42	Intracellular
anti-FOXP3-pacific blue	PCH101	Invitrogen	48-4776-42	Intracellular
anti-IFN $\gamma$ -APC	4S.B3	BioLegend	502512	Intracellular
anti-IL-17A-PerCp/Cy5.5	BL168	BioLegend	512314	Intracellular
LIVE/DEAD™ Fixable Yellow Dead Cell Stain	NA	Invitrogen	L34959	Dead cells

**Table S3: Location of CpG sites analyzed in methylations studies.**

Locus	Region	Position*	CpG count
<i>FOXP3</i>	Treg-specific demethylation region (CNS2 region)	-2330 to -2263	9
<i>CTLA4</i>	Exon 2	2651 to 2757	5
<i>IKZF2</i>	Intron 4	27732 to 27748	3
<i>IKZF4</i>	Intron 5	1969 to 2083	2
<i>IL2RA</i>	Intron 1	24448 to 24517	4

\* Positions are specified counting from the ATG translation start codon.

**Table S4: Significant hits in independent Gene Set Enrichment Analyses (GSEA) of SF Tregs versus PB Tregs and SF Teffs versus PB Teffs.** Tregs (CD4<sup>+</sup>CD25<sup>+</sup>CD127<sup>lo</sup>) and Teffs (CD4<sup>+</sup>CD25<sup>-</sup>) were sorted from paired SF and PB samples of JIA patients (n=14) and from the PB of pediatric (n=5) and adult (n=4) controls for bulk RNA-sequencing. The normalized enrichment score (NES), adjusted p-value and q-values as estimated by clusterProfiler are reported for significantly enriched pathways or gene sets, ranked from highest to lowest NES in the SF Treg compartment. DESeq2-estimated and rank-corrected log2 fold changes (LFC) in gene expression values served as input for a cutoff-free GSEA, run in R with clusterProfiler version 3.14.3. GSEA compared sequencing data to the Reactome database (immune system and metabolism subsets), the human Treg gene set described in Ferraro (2014) and the mouse peripheral/induced Treg gene set described in Hill (2007). n.s., not significant.

Pathway ID	Pathway or Gene set description	NES (Teff)	NES (Treg)	P-value (Teff)	P-value (Treg)	Q-values (Teff)	Q-values (Treg)
Treg_UP	Treg signature (Ferraro, 2014) - upregulated genes	2.734	2.538	0.00329	0.00297	0.00265	0.00207
R-HSA-6783783	Interleukin-10 signaling	2.325	2.532	0.00329	0.00297	0.00265	0.00207
R-HSA-2132295	MHC class II antigen presentation	2.092	2.505	0.00329	0.00297	0.00265	0.00207
R-HSA-877300	Interferon gamma signaling	2.162	2.503	0.00329	0.00297	0.00265	0.00207
R-HSA-909733	Interferon alpha/beta signaling	2.002	2.402	0.00329	0.00297	0.00265	0.00207
R-HSA-913531	Interferon Signaling	2.115	2.357	0.00329	0.00297	0.00265	0.00207
R-HSA-1236978	Cross-presentation of soluble exogenous antigens (endosomes)	n.s.	2.277	n.s.	0.00297	n.s.	0.00207
R-HSA-350562	Regulation of ornithine decarboxylase (ODC)	n.s.	2.269	n.s.	0.00297	n.s.	0.00207
R-HSA-389948	PD-1 signaling	2.264	2.234	0.00329	0.00297	0.00265	0.00207
R-HSA-6798695	Neutrophil degranulation	1.932	2.227	0.00329	0.00297	0.00265	0.00207
R-HSA-202427	Phosphorylation of CD3 and TCR zeta chains	2.209	2.192	0.00329	0.00297	0.00265	0.00207
R-HSA-449147	Signaling by Interleukins	1.987	2.164	0.00329	0.00297	0.00265	0.00207
R-HSA-202430	Translocation of ZAP-70 to Immunological synapse	2.175	2.134	0.00329	0.00297	0.00265	0.00207
R-HSA-202424	Downstream TCR signaling	1.585	2.106	0.02621	0.00297	0.02113	0.00207
R-HSA-202403	TCR signaling	1.508	2.081	0.04549	0.00297	0.03667	0.00207
R-HSA-202433	Generation of second messenger molecules	1.750	2.065	0.03377	0.00297	0.02722	0.00207
R-HSA-5668541	TNFR2 non-canonical NF-kB pathway	n.s.	2.046	n.s.	0.00297	n.s.	0.00207
R-HSA-388841	Costimulation by the CD28 family	1.967	2.029	0.00329	0.00297	0.00265	0.00207
R-HSA-351202	Metabolism of polyamines	n.s.	2.001	n.s.	0.00297	n.s.	0.00207
R-HSA-5669034	TNFs bind their physiological receptors	n.s.	1.995	n.s.	0.00297	n.s.	0.00207
R-HSA-1236974	ER-Phagosome pathway	n.s.	1.925	n.s.	0.00297	n.s.	0.00207
R-HSA-6785807	Interleukin-4 and Interleukin-13 signaling	1.543	1.916	0.04465	0.00297	0.03599	0.00207
R-HSA-1236975	Antigen processing-Cross presentation	n.s.	1.877	n.s.	0.00443	n.s.	0.00308
R-HSA-446652	Interleukin-1 family signaling	1.514	1.821	0.03886	0.00297	0.03133	0.00207
R-HSA-1169091	Activation of NF-kappaB in B cells	n.s.	1.821	n.s.	0.00894	n.s.	0.00622
R-HSA-2160916	Hyaluronan uptake and degradation	n.s.	1.800	n.s.	0.02123	n.s.	0.01477



R-HSA-193368	Synthesis of bile acids and bile salts via 7alpha-hydroxycholesterol	n.s.	1.795	n.s.	0.02333	n.s.	0.01623
R-HSA-198933	Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell	1.686	1.789	0.00329	0.00443	0.00265	0.00308
R-HSA-622312	Inflammasomes	n.s.	1.788	n.s.	0.02368	n.s.	0.01647
R-HSA-1168372	Downstream signaling events of B Cell Receptor (BCR)	n.s.	1.785	n.s.	0.00894	n.s.	0.00622
R-HSA-447115	Interleukin-12 family signaling	1.678	1.761	0.03245	0.01554	0.02616	0.01081
R-HSA-9020591	Interleukin-12 signaling	1.831	1.747	0.00828	0.02367	0.00667	0.01646
R-HSA-9020702	Interleukin-1 signaling	n.s.	1.745	n.s.	0.00621	n.s.	0.00432
R-HSA-5676590	NIK-->noncanonical NF-kB signaling	n.s.	1.742	n.s.	0.01554	n.s.	0.01081
R-HSA-449836	Other interleukin signaling	n.s.	1.729	n.s.	0.03297	n.s.	0.02293
R-HSA-918233	TRAF3-dependent IRF activation pathway	n.s.	1.726	n.s.	0.04085	n.s.	0.02842
R-HSA-197264	Nicotinamide salvaging	n.s.	1.724	n.s.	0.03665	n.s.	0.02549
R-HSA-193775	Synthesis of bile acids and bile salts via 24-hydroxycholesterol	n.s.	1.721	n.s.	0.04123	n.s.	0.02868
R-HSA-189445	Metabolism of porphyrins	n.s.	1.721	n.s.	0.03665	n.s.	0.02549
R-HSA-192105	Synthesis of bile acids and bile salts	n.s.	1.718	n.s.	0.03725	n.s.	0.02591
R-HSA-1630316	Glycosaminoglycan metabolism	n.s.	1.712	n.s.	0.00780	n.s.	0.00542
R-HSA-390918	Peroxisomal lipid metabolism	n.s.	1.706	n.s.	0.03725	n.s.	0.02591
R-HSA-77289	Mitochondrial Fatty Acid Beta-Oxidation	n.s.	1.703	n.s.	0.03297	n.s.	0.02293
R-HSA-6803157	Antimicrobial peptides	2.002	1.701	0.00329	0.04070	0.00265	0.02831
R-HSA-193807	Synthesis of bile acids and bile salts via 27-hydroxycholesterol	n.s.	1.701	n.s.	0.04800	n.s.	0.03339
R-HSA-933541	TRAF6 mediated IRF7 activation	n.s.	1.689	n.s.	0.04315	n.s.	0.03002
R-HSA-8956321	Nucleotide salvage	n.s.	1.689	n.s.	0.04315	n.s.	0.03002
R-HSA-211976	Endogenous sterols	n.s.	1.687	n.s.	0.04315	n.s.	0.03002
R-HSA-5607764	CLEC7A (Dectin-1) signaling	n.s.	1.680	n.s.	0.00780	n.s.	0.00542
pTreg_DN	induced/peripheral Treg (Hill, 2007) - downregulated genes	n.s.	1.662	n.s.	0.00297	n.s.	0.00207
R-HSA-8956319	Nucleobase catabolism	n.s.	1.655	n.s.	0.04845	n.s.	0.03370
R-HSA-2162123	Synthesis of Prostaglandins (PG) and Thromboxanes (TX)	n.s.	1.654	n.s.	0.06257	n.s.	0.04352
R-HSA-2871837	FCERI mediated NF-kB activation	n.s.	1.651	n.s.	0.01554	n.s.	0.01081
R-HSA-70263	Gluconeogenesis	n.s.	1.645	n.s.	0.05211	n.s.	0.03625
R-HSA-2142845	Hyaluronan metabolism	n.s.	1.642	n.s.	0.06086	n.s.	0.04234
R-HSA-2029482	Regulation of actin dynamics for phagocytic cup formation	n.s.	1.641	n.s.	0.02333	n.s.	0.01623
R-HSA-8978868	Fatty acid metabolism	n.s.	1.641	n.s.	0.00453	n.s.	0.00315
R-HSA-844456	The NLRP3 inflammasome	n.s.	1.636	n.s.	0.06257	n.s.	0.04352
R-HSA-15869	Metabolism of nucleotides	n.s.	1.620	n.s.	0.01554	n.s.	0.01081
R-HSA-428157	Sphingolipid metabolism	n.s.	1.611	n.s.	0.02207	n.s.	0.01535
R-HSA-5607761	Dectin-1 mediated noncanonical NF-kB signaling	n.s.	1.604	n.s.	0.03281	n.s.	0.02282

R-HSA-71387	Metabolism of carbohydrates	n.s.	1.586	n.s.	0.00297	n.s.	0.00207
R-HSA-983705	Signaling by the B Cell Receptor (BCR)	n.s.	1.584	n.s.	0.01408	n.s.	0.00980
R-HSA-5621481	C-type lectin receptors (CLRs)	n.s.	1.583	n.s.	0.01408	n.s.	0.00980
R-HSA-936440	Negative regulators of DDX58/IFIH1 signaling	n.s.	1.580	n.s.	0.06879	n.s.	0.04785
R-HSA-451927	Interleukin-2 family signaling	1.878	1.575	0.00582	0.05351	0.00469	0.03723
R-HSA-983169	Class I MHC mediated antigen processing & presentation	n.s.	1.530	n.s.	0.00297	n.s.	0.00207
R-HSA-211945	Phase I - Functionalization of compounds	n.s.	1.530	n.s.	0.05351	n.s.	0.03723
R-HSA-2029480	Fcgamma receptor (FCGR) dependent phagocytosis	n.s.	1.500	n.s.	0.04315	n.s.	0.03002
R-HSA-1169410	Antiviral mechanism by IFN-stimulated genes	n.s.	1.476	n.s.	0.05466	n.s.	0.03802
R-HSA-1428517	The citric acid (TCA) cycle and respiratory electron transport	n.s.	1.469	n.s.	0.02207	n.s.	0.01535
R-HSA-983168	Antigen processing: Ubiquitination & Proteasome degradation	n.s.	1.460	n.s.	0.00890	n.s.	0.00619
R-HSA-8957322	Metabolism of steroids	n.s.	1.459	n.s.	0.03794	n.s.	0.02639
R-HSA-1483257	Phospholipid metabolism	n.s.	1.390	n.s.	0.04315	n.s.	0.03002
R-HSA-71291	Metabolism of amino acids and derivatives	-2.205	-2.135	0.00329	0.00297	0.00265	0.00207
Treg_DN	Treg signature (Ferraro, 2014) - downregulated genes	-1.850	-2.277	0.00582	0.00297	0.00469	0.00207
R-HSA-2408522	Selenoamino acid metabolism	-2.974	-3.124	0.00329	0.00297	0.00265	0.00207
R-HSA-2408557	Selenocysteine synthesis	-3.089	-3.218	0.00329	0.00297	0.00265	0.00207
R-HSA-9008059	Interleukin-37 signaling	1.757	n.s.	0.04062	n.s.	0.03274	n.s.
R-HSA-196757	Metabolism of folate and pterines	-1.901	n.s.	0.00329	n.s.	0.00265	n.s.