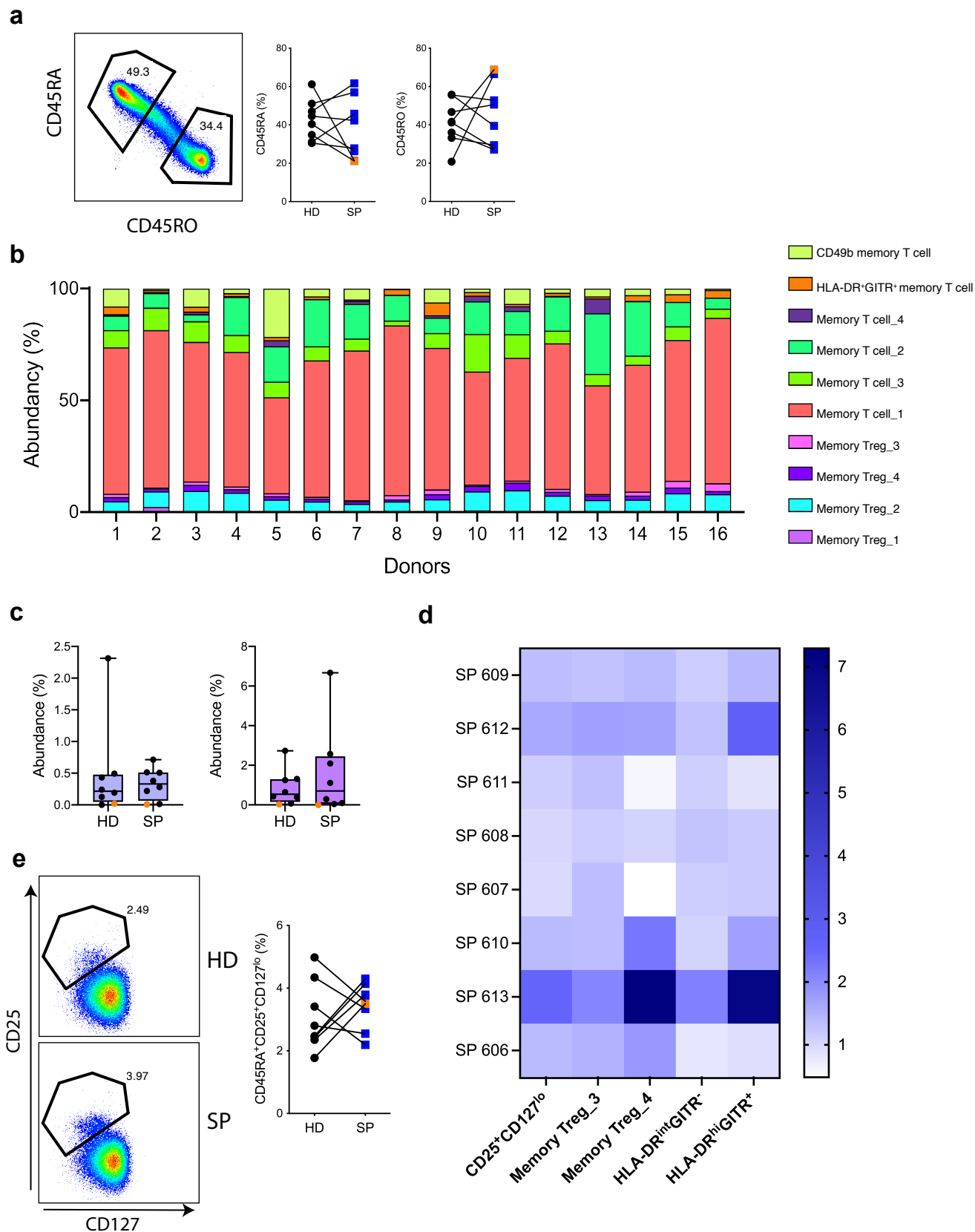


ID	Sex	Age at current sample (years)	Time since mAb+ve (years)	Current GADA DK Units/ml	Current IA-2A DK units/ml	Current IAA units	Current ZnT8A units	Antibodies present at first mAb+ve sample	Stage of Diabetes Progression
SP 606	Male	72.6	32	53.929	0.000	0.000	34.525	GADA, IA-2A, ZnT8A	Stage 3
SP 607	Male	49.1	30.8	34.323	0.000	0.000	0.851	GADA, ZnT8A	Stage 1
SP 608	Female	47.1	30.4	176.307	23.100	0.000	3.862	GADA, IA-2A, ZnT8A	Stage 2
SP 609	Male	33.5	26.2	114.170	0.275	0.000	1.481	GADA, IAA	Stage 1
SP 610	Female	40.6	25.6	4.524	35.430	0.000	0.361	GADA, IA-2A, ZnT8A	Stage 1
SP 611	Male	56.3	18.6	1026.042	4.791	1.640	0.435	GADA, IAA	Stage 1
SP 612	Male	31.2	18.2	319.394	0.000	0.000	0.312	GADA, IAA	Stage 1
SP 613	Male	31.7	18.6	143.477	6.748	0.000	4.670	GADA, IA-2A, ZnT8A	Stage 1

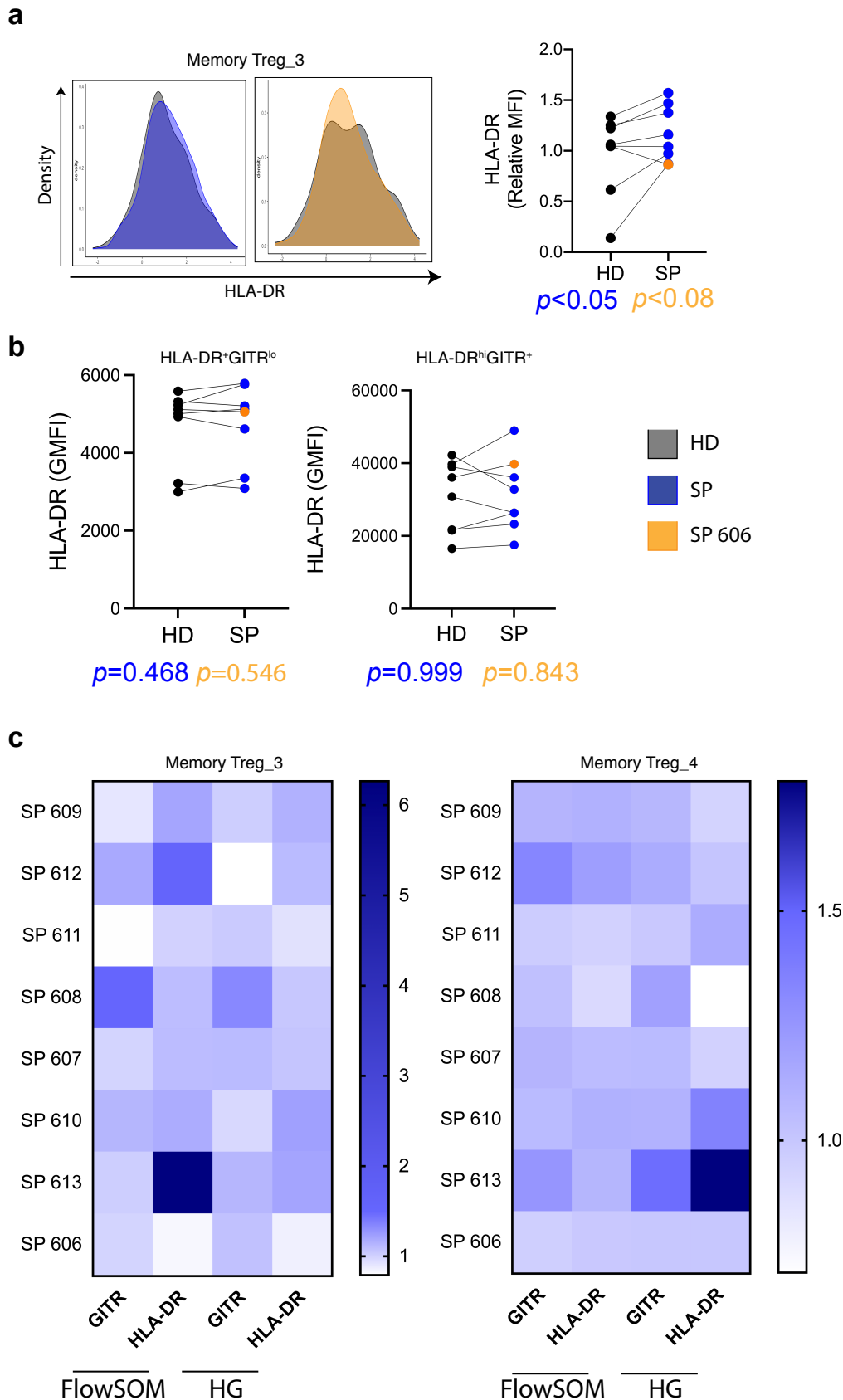
ESM Table 1. Current islet autoantibody results for 8 slow progressors. The positive thresholds for GADA are ≥ 33 DK units/ml, IA-2A are ≥ 1.4 DK units/ml, IAA are ≥ 0.2 units and ZnT8 are ≥ 1.8 units.

ID	DRB1 (allele 1)	DRB1 (allele 2)	DQB1 (allele 1)	DQB1 (allele 2)	Genotype	Level of genetic risk
SP 606	04	12	0301	0302	DR4-DQ8/X	Moderate
SP 607	15	04	0302	0601	DR4-DQ8/X	Moderate
SP 608	04	11	0301	0302	DR4-DQ8/X	Moderate
SP 609	03	04	0201	0302	DR3-DQ2/DR4-DQ8	High
SP 610	04	04	0301	0302	DR4-DQ8/DR4-DQ7	Moderate
SP 611	04	07	02	0302	DR4-DQ8/X	Moderate
SP 612	01	03	02	0501	DR3-DQ2/X	Moderate
SP 613	03	04	0201	0302	DR3-DQ2/DR4-DQ8	High

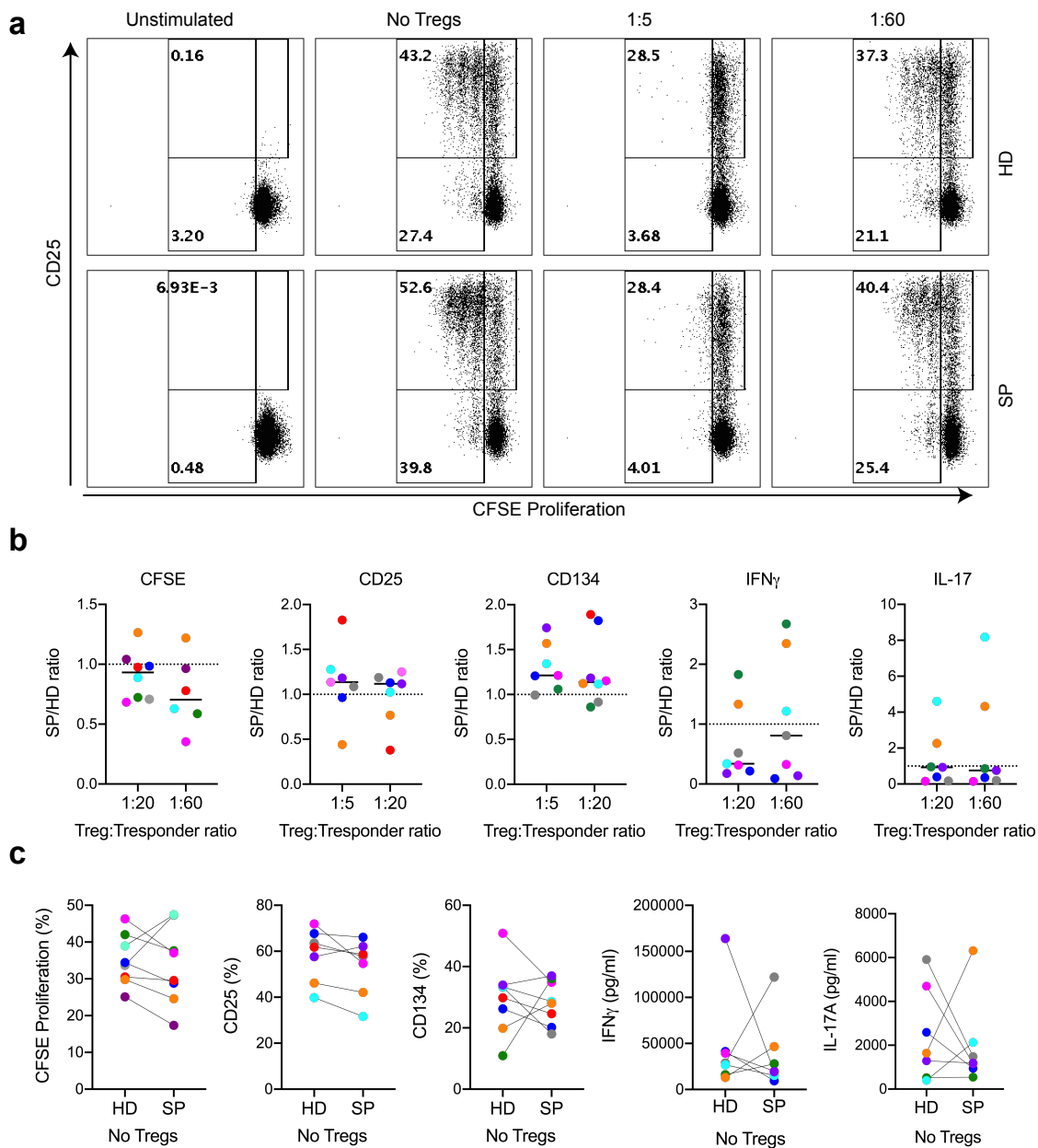
ESM Table 2. Table of genetic information for 8 slow progressors.



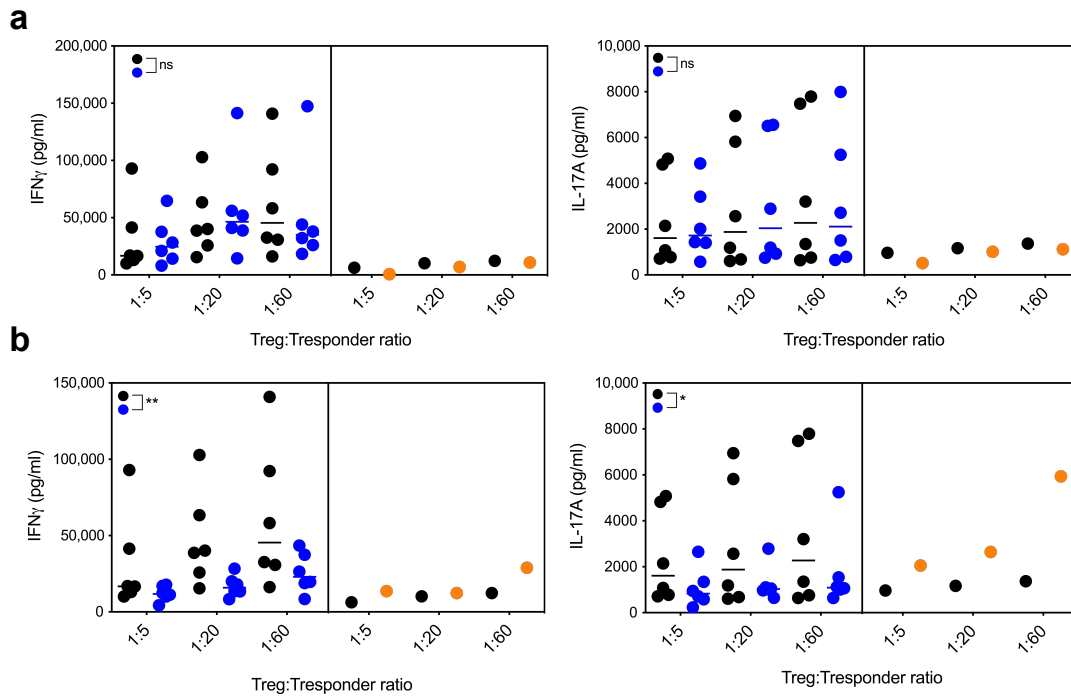
ESM Figure 1. Treg metaclusters in slow progressors. (a) Gating (left) and summary graphs for CD45RA (middle) and CD45RO (right) CD4⁺ T cells in slow progressors, matched to healthy donors. (b) CD45RA⁺Treg metaclusters (Memory T cell_1; Memory T cell_2; Memory T cell_3; Memory T cell_4; CD49b memory T cell; HLA-DR^{hi}GITR⁺ memory T cell; Memory Treg_1; Memory Treg_2; Memory Treg_3; Memory Treg_4) defined in each donor (n=16). (c) Memory Treg_1 (left) and Memory T cell_4 (right) box-plots (mean <math><0.05\%</math>). (d) Heatmap showing expression ratio (SP/HD) of defined Treg metaclusters Memory Treg_3 and Memory Treg_4 along with hierarchical gating emulating both Treg metaclusters for each individual slow progressor donor. (e) Gating to show CD25⁺CD127^{lo} Treg cells in the CD45RA CD4⁺ T cell compartment and summary graph showing no difference in naive Tregs.



ESM Figure 2. HLA-DR expression in Memory Treg_3 and Memory Treg_4 metaclusters. Memory Treg_3 metacluster from FLOW SOM, was examined for a change in HLA-DR expression marker. (a) FlowSOM HLA-DR expression concatenated from all HD (grey), all SP (blue) and SP 606 (orange) showing histograms (left) and summary graph (right). (b) Summary graphs of HLA-DR expression, from hierarchical gating in both HLA-DR⁺GITR^{lo} and HLA-DR^{hi}GITR⁺ Tregs (a, b) Wilcoxon matched-pairs signed rank test, p -value in orange is all donors included, p -value in blue is without donor SP 606 and matched HD not included in test. (c) Heatmap showing expression GITR and HLA-DR ratios (SP/HD), for each individual slow progressor donor, in defined Treg metaclusters or subsets defined by hierarchical gating: Memory Treg_3 (HLA-DR⁺GITR^{lo}) and Memory Treg_4 (HLA-DR^{hi}GITR⁺).



ESM Figure 3. Treg suppression in slow progressors (a) Representative flow plots for Treg suppression assay showing CFSE and CD25 gating on both slow progressor donor (SP) and matched healthy donor (HD). Unstimulated control, no Tregs (positive control) Treg:responder ratios 1:5 and 1:60 are shown (b) SP/HD ratios for CFSE, CD25, CD134, IFN γ and IL-17 when autologous Tregs and responders are cultured. (c) Response of CD4 effector T cells to polyclonal stimuli anti-CD3/28 for each individual slow progressor donor matched to healthy controls.



ESM Figure 4. Proinflammatory cytokine responses in Treg suppression assay. (a) HD responders were co-cultured with Tregs from matched healthy donors and slow progressors or SP 606. (b) autologous Treg: T responder assays (HD Tregs:HD responders; SP Tregs:SP responders). IFN γ (left) and IL-17 (right) production measured by Meso Scale Discovery. Healthy donor (HD, black dots), HD 606 plotted separately and slow progressors (SP, blue dots) or SP 606 donor (orange dots). ns, not-significant, **<0.01, *<0.05, repeated measures-two-way ANOVA.