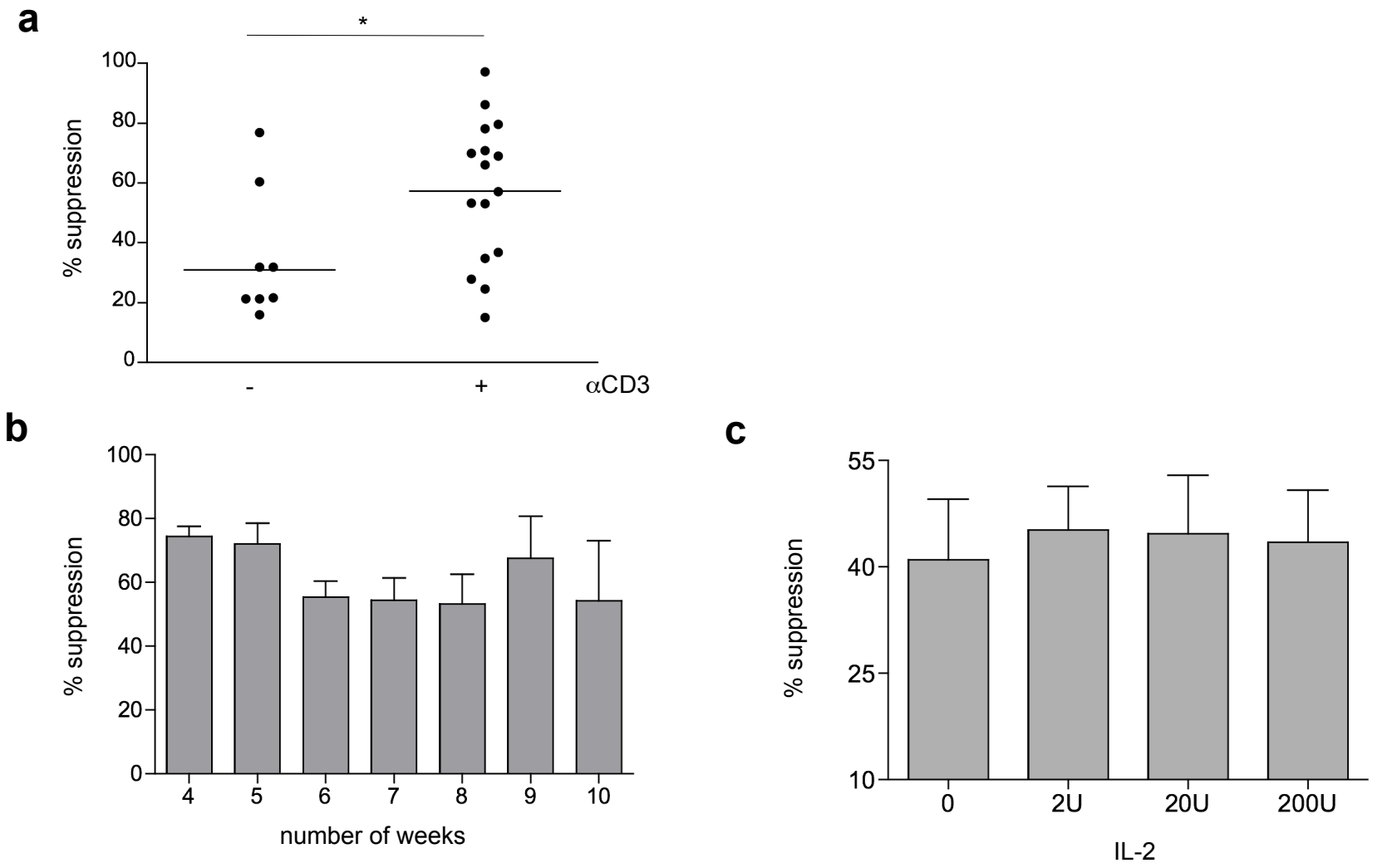
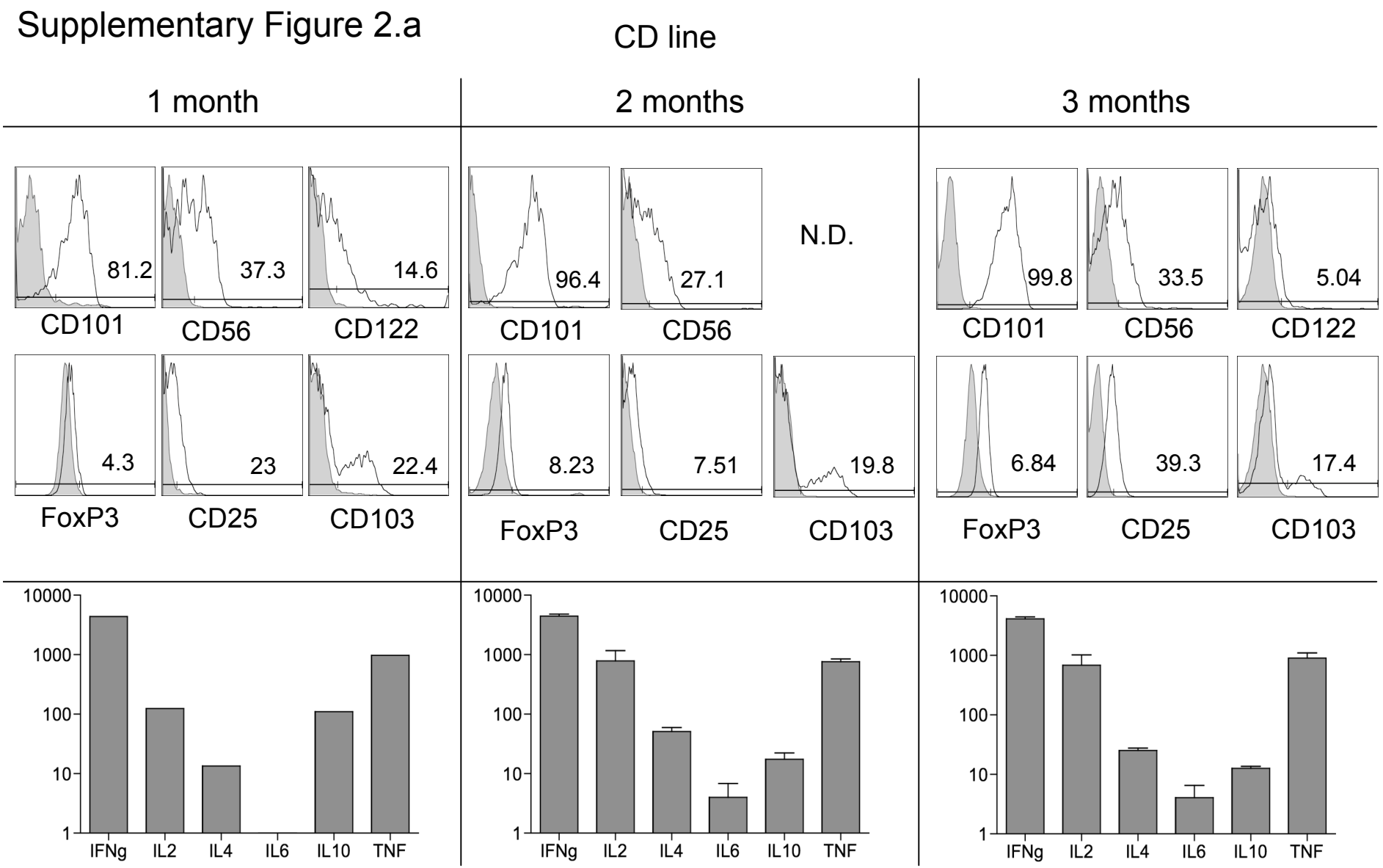
Supplementary Figure 1



Supplementary figure 1: (A) Initial stimulation of $CD8^+$ line with Visilizumab increases suppressor activity. *, $p \leq 0.05$, using an unpaired T test with Welch's correction. (B) Suppressor activity of CD8 lines was not affected by time in culture. (C) IL-2 was added to the suppressor assay in increasing amounts. IL-2 did not change the ability of $CD8^+$ Ts cells to mediate suppression. The effect of IL-2 was tested in 9 different NL lines.

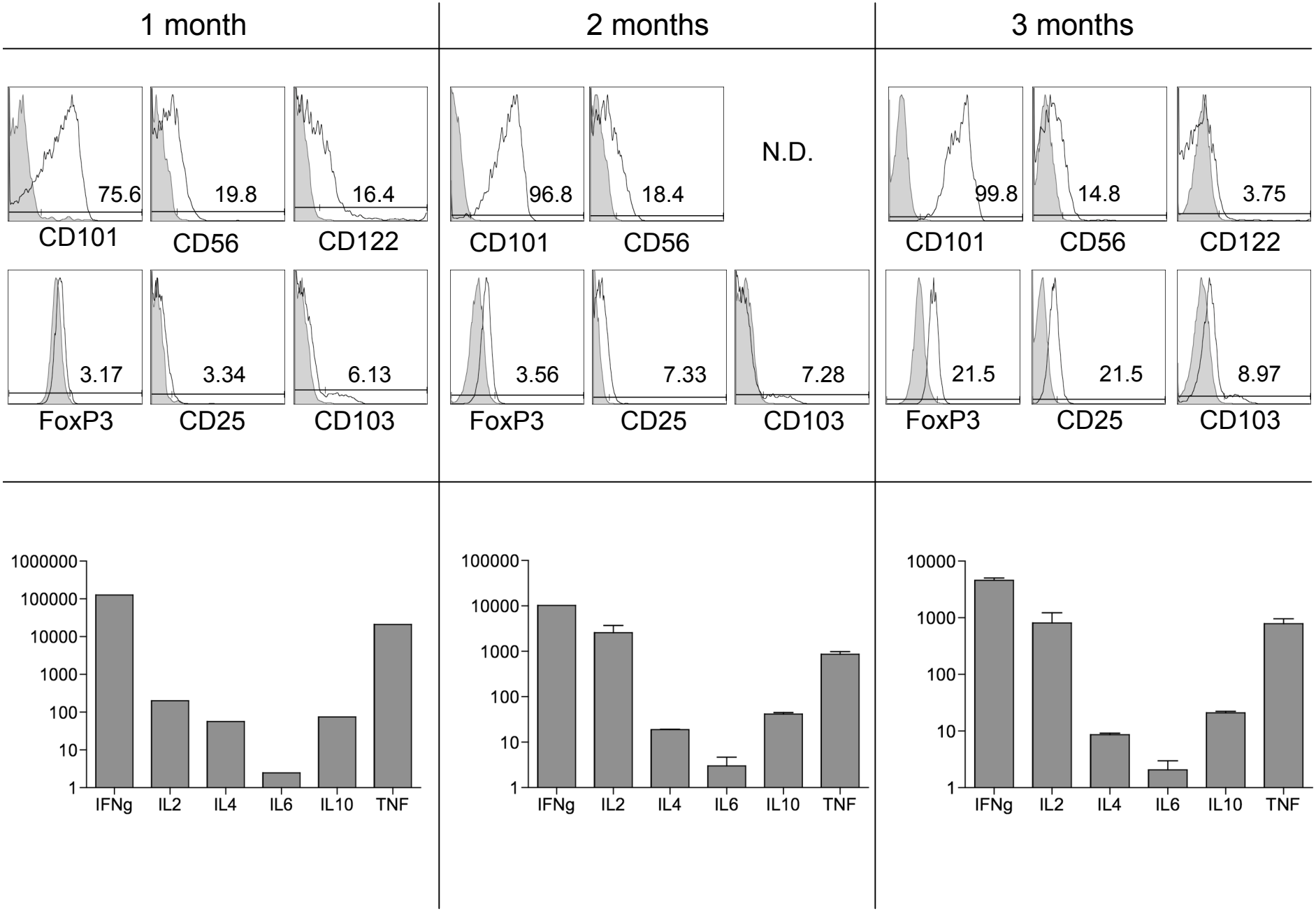
Supplementary Figure 2.a



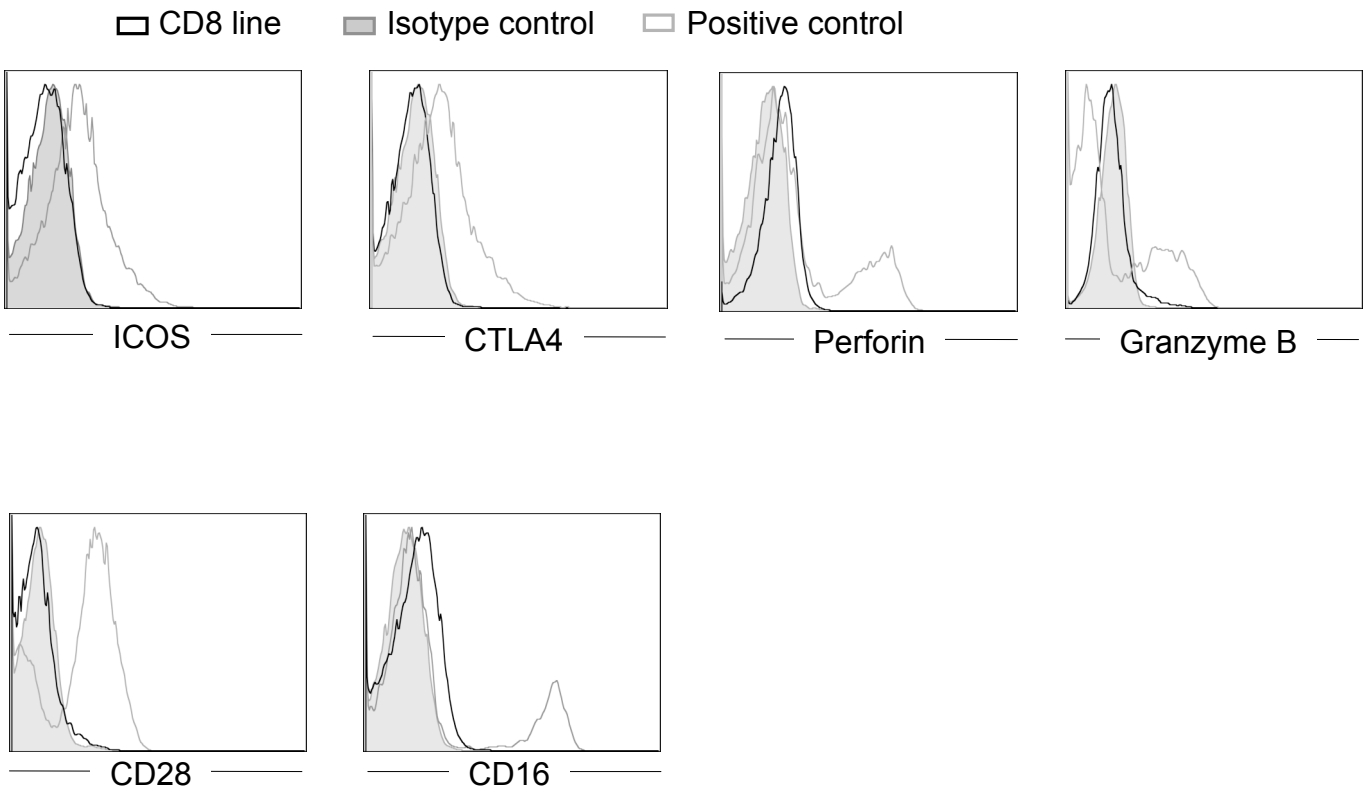
Supplementary figure 2: Characteristization of CD8$^+$ Ts lines over time. Surface staining, cytokines secretion profile and suppressor activity of CD8$^+$ Ts lines were measured at 1, 2 and 3 months in culture with IL7 and IL15. Surface expression of CD8$\alpha\beta$, CD3, $\alpha 4\beta 7$, CD101, CD56, CD122, FoxP3, CD25, CD103. open histograms, specific staining (antibodies to markers below the plots); filled histograms, isotype-matched control antibodies. Numbers adjacent to the outlined areas and above lines indicate the percentage of cells in the gate. Suppressor activity was unaffected over time (not shown). Cytokine levels in supernatants were measured 72h post aCD3/CD28 stimulation by Cytometric Bead Array. (A) CD CD8$^+$Ts lines. (B) NL CD8$^+$ Ts lines.

Supplementary Figure 2.b

NL line



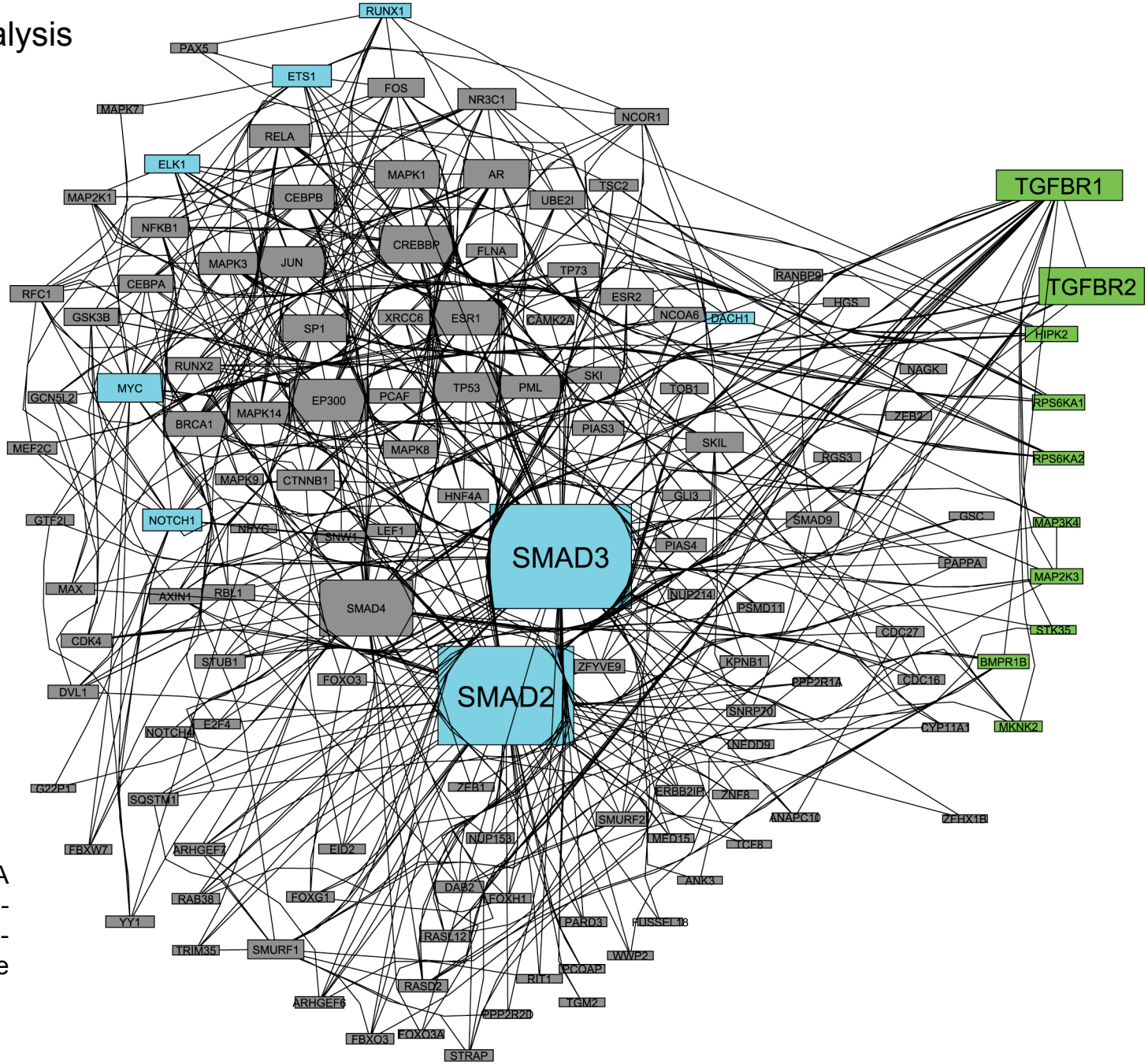
Supplementary Figure 3



Supplementary figure 3: Surface staining of $CD8^+$ Ts lines from NL, UC and CD subgroups is equivalent. There is no surface or intracytoplasmic expression of ICOS, CTLA4, perforin, granzyme B, CD28 and CD16. *open black histograms*, specific staining (antibodies to markers below the plots); *filled histograms*, isotype-matched control antibodies; *open grey histograms,* positive staining control.

Supplementary Figure 4a

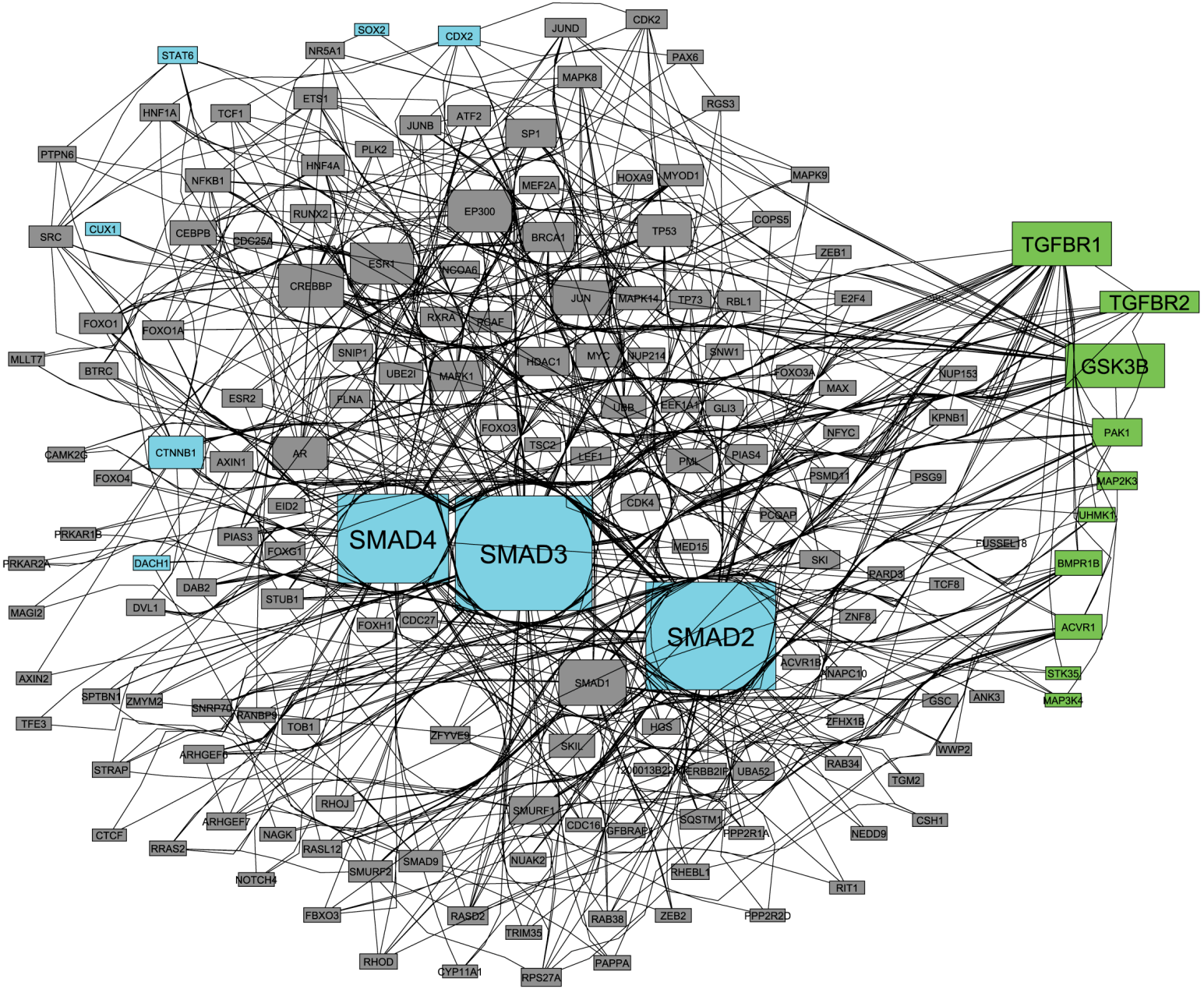
Positive correlation analysis



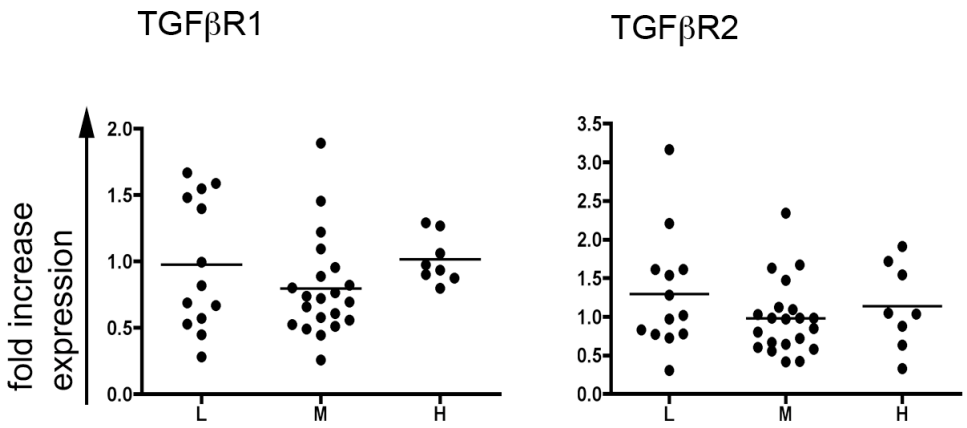
Supplementary figure 4: (A and B) Detailed protein-protein interaction sub-networks presented in figure 4.

Supplementary Figure 4b

Negative correlation analysis

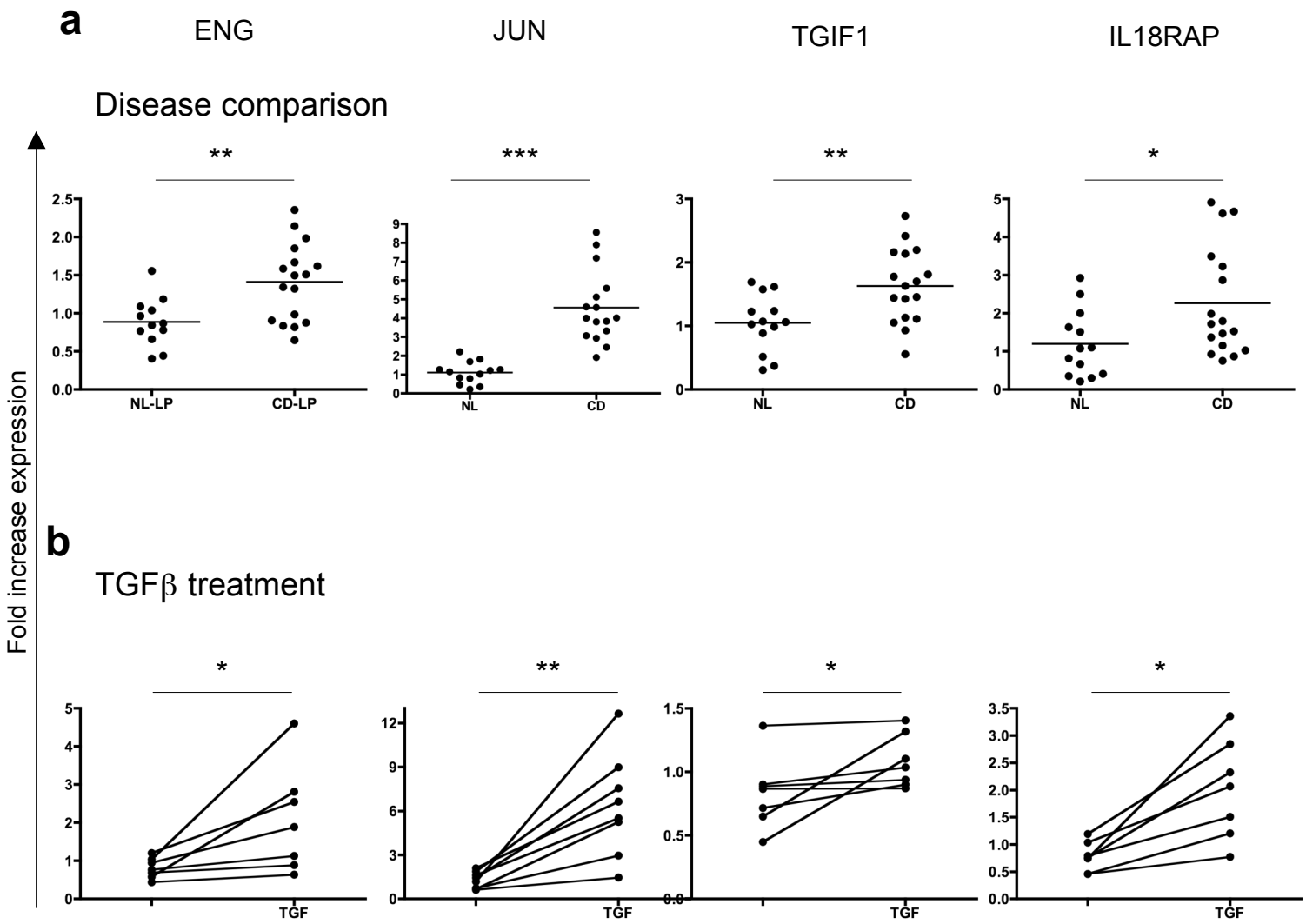


Supplementary Figure 5



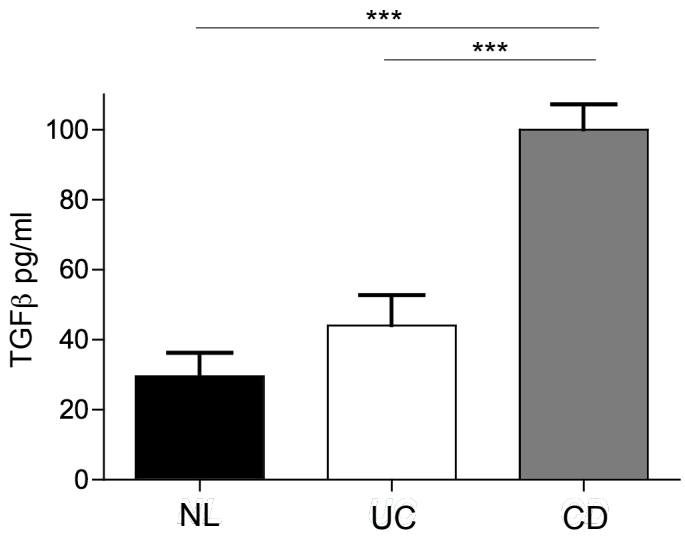
Supplementary figure 5: TGFBR mRNA levels. One million cells of low, medium and high $CD8^+$ Ts lines were stimulated with αCD3/CD28 beads for 72h. mRNA was extracted and used as a template for cDNA. qPCR was performed to evaluate the expression levels of TGFBR1 and TGFBR2.

Supplementary Figure 6



Supplementary figure 6: Validation of the microarray results. (A) One million cells of both NL and CD derived $CD8^+$ Ts lines were stimulated in the presence or absence of αCD3/CD28 beads for 72h. mRNA was extracted and used as a template for cDNA. qPCR was performed to evaluate the expression levels of ENG, Jun, TGIF1 and IL18RAP, using an unpaired T test with Mann Whitney correction (B) One million cells of both NL and UC $CD8^+$ Ts lines were either stimulated in the presence or absence of TGFβ (2ng/ml) for 72h. mRNA was extracted and used as a template for cDNA. qPCR was performed to evaluate the expression levels of ENG, Jun, TGIF1 and IL18RAP, using non parametric Wilcoxon matched pairs T test. *, $p<0.05$. **, $p<0.01$. ***, $p<0.001$.

Supplementary Figure 7



Supplementary figure 7: Bioactive levels of TGFβ in tissue explants derived from NL, UC and CD patients. Error bars represent standard deviation. ***, $p<0.001$, using a nonparametric test, one way analysis of variance, Bonferroni's post test correction.

Supplementary Table 1a

Stimulation				% of CD8+ T cells after 15 days in culture
Primary stimulation 5 days w/ Visilizumab	Secondary stimulation			
	Irradiated PBMCs	IL-15	IL-7	
-	-	-	-	11.76
-	+	-	-	6.19
-	+	+	-	15.62
-	+	+	+	16.94
+	+	-	-	30.43
+	+	+	-	56.27
+	+	+	+	48.6

Supplementary Table 1b

	NL		CD	
	% naïve cells	Patients number	% naïve cells	Patients number
CD45Rhi $CD62L^+$	6.44% ±8.3%	5	7.22% ± 6.62%	6

Supplementary table 1: Assessment of $CD8^+$ T cells derived from different LP culture conditions (A) % of $CD8^+$ T cells at day 15 from different culture conditions. (B) % of naive $CD8^+$ cells in freshly isolated LPLs derived from NL and CD patients. Naive cells were defined as $CD3^+$ $CD8^+$ cells expressing high levels of CD45RA and CD62L.

Supplementary Table 2

	NL		UC		CD	
	% in positive gate	Number of $CD8^+$ Ts lines	% in positive gate	Number of $CD8^+$ Ts lines	% in positive gate	Number of $CD8^+$ Ts lines
CD8β	92.8% ± 6.25%	3	98.05% ± 1.77%	2	92.87% ± 0.85%	3
Integrin α4β7	99.5% ± 0.26%	3	99.07% ± 0.31%	3	99.43% ± 0.12%	3
CD101	96.57% ± 2.72%	3	98.5% ± 1.41%	2	94.23% ± 8.78%	3
CD56	39.31% ± 26.06%	4	19.8% ± 10.04%	2	33.47% ± 5.88%	3
CD122	16.33% ± 9.5%	4	10.75% ± 0.07%	2	17.43% ± 4.86%	3
FoxP3	45.05% ± 14.11%	6	32% ±8.23%	3	25.8% ± 1.27%	2
CD103	11.9% ± 10.92%	3	4.16% ± 0.45%	2	9.18% ±8%	3
CD25	30.37% ± 6.82%	3	34.97% ± 26.48%	3	24.8% ± 12.98%	3

Supplementary table 2: detailed summary table for figure 3B, indicating the number of cell lines stained for a specific cell marker, as well as % of cells in the positive gate based on the type of cell lines stained NL, UC or CD.