SUPPLEMENTARY MATERIAL

Supplementary Table 2. Comparison of Nanostring nCounter gene expression data with published DNA methylation data in TABs. Transcripts were considered up-regulated or down-regulated with fold changes in normalized expression between TMI and normal TABs > 2.0 or < -2.0 and Benjamini-Yekutieli adjusted p-values < 0.05. CpG sites were considered differentially methylated between TMI and normal TABs with $\Delta\beta > |0.20|$ and p-values < 0.05. Only genes exclusively associated with hypomethylated or hypermethylated CpG sites were included in the analysis.

Up-regulated genes with reported hypomethylated CpG sites	Up-regulated genes with reported hypomethylated CpG sites	Down-regulated genes with reported hypermethylated CpG sites	Up-regulated genes with reported hypermethylated CpG sites
AMICA1	IRF1	ABL1	ATG7
BATF	IRF5	CLU	CD37
BID	IRF8	CX3CL1	HLA-DPB1
BTLA	ITGA4	FEZ1	JAK3
C1QB	ITGAL	IGF1R	NLRP3
C3AR1	ITGB2	ITGA1	POU2F2
CASP8	ITK	JAM3	SBNO2
CCL18	LAG3	LRRN3	
CCL22	LAMP3	PDGFRB	
CCL5	LTA	RRAD	
CCR2	LTB	TGFB2	
CCR5	LY9		
CCR7	MS4A1/CD20		
CD163	MSR1		
CD28	NCF4		
CD3D	NLRC5		
CD3E	PIK3CG		
CD4	PRF1		
CD44	PSMB8		
CD5	PSMB9		
CD53	PTPRC/CD45		
CD74	RIPK2		
CD80	SELPLG		
CD84/SLAMF5	SH2D1A		
CD96	SLAMF1		
CTLA4	SLAMF6		
CXCR3	SLAMF7		
CXCR6	SPN		
DUSP4	STAT1		
FYN	STAT4		
GZMA	TAP1		
HAVCR2	TAP2		
HLA-A	TCF7		
HLA-DMA	TLR1		
HLA-DMB	TNF		
HLA-DPA1	TNFRSF1B		
HLA-DRA	TNFRSF4/OX40		
IL10RA	TNFRSF9/4-1BB		
IL12RB1	TNFSF14		
IL17RA	TNFSF8		
IL2RA	ZAP70		
IL2RG			
INPP5D			
IRAK2			

Supplementary Table 3. Comparison of Nanostring nCounter gene expression data with published RNA sequencing data in TABs. Transcripts were considered up-regulated or down-regulated with fold changes between TABs with TMI and normal TABs > 2.0 or < -2.0 and adjusted p-values < 0.05.

Up-regulated genes in TMI both by Nanostring nCounter and RNA sequencing	Up-regulated genes in TMI both by Nanostring nCounter and RNA sequencing	Up-regulated genes in TMI both by Nanostring nCounter and RNA sequencing	Down-regulated genes in TMI both by Nanostring nCounter and RNA sequencing
APOE	CTLA4	LCP1	CCL14
BLNK	CTSH	LILRB2	CFD
C1QA	CTSS	MARCO	CLU
C1QB	CXCL10	MS4A1/CD20	CX3CL1
C3AR1	CXCR4	NCF4	ITGB4
CASP1	CYBB	NLRC5	MCAM
CASP8	DUSP4	PDCD1LG2/PD-L2	
CCL18	FCER1G	PIK3CD	
CCL19	FCGR2B	PIK3CG	
CCL3	FCGR3A	PLAU	
CCL4	HCK	PLAUR	
CD14	HLA-A	POU2F2	
CD163	HLA-B	PSMB9	
CD2	HLA-C	PTPRC/CD45	
CD209	HLA-DMB	PYCARD	
CD247	HLA-DPB1	RUNX1	
CD33	HLA-DRA	SIGIRR	
CD37	IL12RB1	SLAMF7	
CD3D	IL15RA	SLC11A1	
CD3E	IL16	SPN	
CD44	IL17RA	SPP1	
CD53	IL1RN	STAT1	
CD6	IL21R	SYK	
CD68	IL32	TAP2	
CD7	IRAK1	TAPBP	
CD74	IRF1	TBX21	
CD83	IRF3	TCF7	
CD84/SLAMF5	IRF5	TIGIT	
CD8A	IRF7	TLR6	
CD96	ITGAL	TNFAIP3	
CFB	ITGAM	TNFRSF14	
CHIT1	ITGAX	TNFSF13	
CKLF	ITGB2	TNFSF13B	
CLEC4A	ITK	TNFSF8	
CLEC7A	JAK3	TREM1	
COL3A1	KLRB1	VCAM1	
CR1	KLRK1	ZAP70	
CSF1R	LCK		

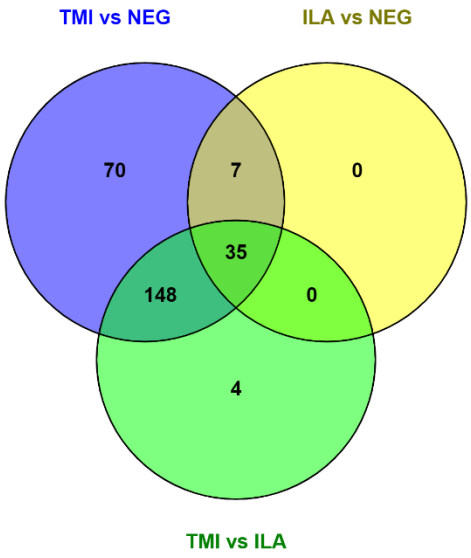
Supplementary Table 4. Characteristics of the validation cohorts of patients.

Demographic, clinical and laboratory characteristics	TMI	ILA	NEG
Number	7	7	7
Age at disease onset, median (IQR), years	78 (74 – 82)	74 (62 – 82)	78 (76 – 83)
Males / females, n	0 / 7	0 / 7	5 / 2
Any cranial symptoms[a], n (%)	7 (100)	4 (57)	1 (14)
Any visual symptoms[b], n (%)	1 (14)	3 (43)	4 (57)
Systemic signs/symtoms[c], n (%)	6 (86)	4 (57)	2 (29)
Polymyalgia rheumatica, n (%)	4 (57)	3 (43)	2 (29)
ESR, median (IQR), mm/h	82 (81 – 88)	61 (35 – 82)	53 (27 – 66)
CRP, median (IQR), mg/dl[d]	3.8 (2.8 – 11.0)	8.4 (1.3 – 10.9)	2.1 (0.8 – 3.5)
Prednisone at TABs, n (%)[e]	0 (0)	5 (71)	0 (0)

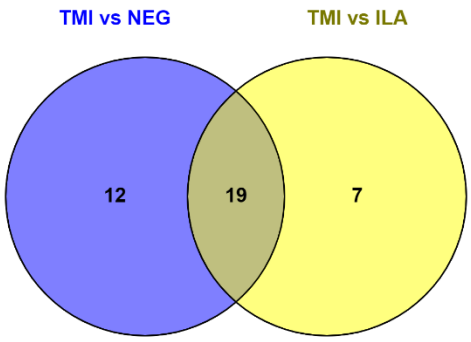
[a]At least one of the following: headache, scalp tenderness, jaw claudication.
[b]At least one of the following: sight loss, diplopia, amaurosis fugax.
[c]At least one of the following: fever, fatigue, anorexia, weight loss of at least 4 kg.
[d]Upper limit of the normal reference range = 0.5 mg/dl.
[e] 50 mg/day for 8 days; 50 mg/day for 14 days; 25 mg/day for 10 days; 25 mg/day for; 5 mg/day for 12 days.
IQR: interquartile range; TAB: temporal artery biopsy; TMI: transmural inflammation; ILA: inflammation limited to adventitia; NEG, normal temporal artery biopsies without inflammation from patients without GCA; n: number.

Supplementary Figure 1. Comparison of the deregulated genes in the histological patterns. The lists of deregulated genes between TMI and NEG (n = 291), TMI and ILA (n = 213), ILA and NEG (n = 42) were intersected by means of Venn diagrams. Transcripts were considered up-regulated or down-regulated with fold changes > 2.0 or < -2.0 and adjusted p-values < 0.05 (TMI *vs* NEG and TMI *vs* ILA) or p-values not corrected for multiple testing < 0.05 (ILA *vs* NEG). In addition genes detected in TABs with TMI or ILA but not detected in normal TABs with p < 0.05 by Fisher's exact test were included and considered up-regulated. (A) Up-regulated genes. (B) Down-regulated genes. TMI = transmural inflammation in temporal artery biopsies. ILA = inflammation limited to adventitia. NEG = normal, non-inflamed temporal artery biopsies.

A

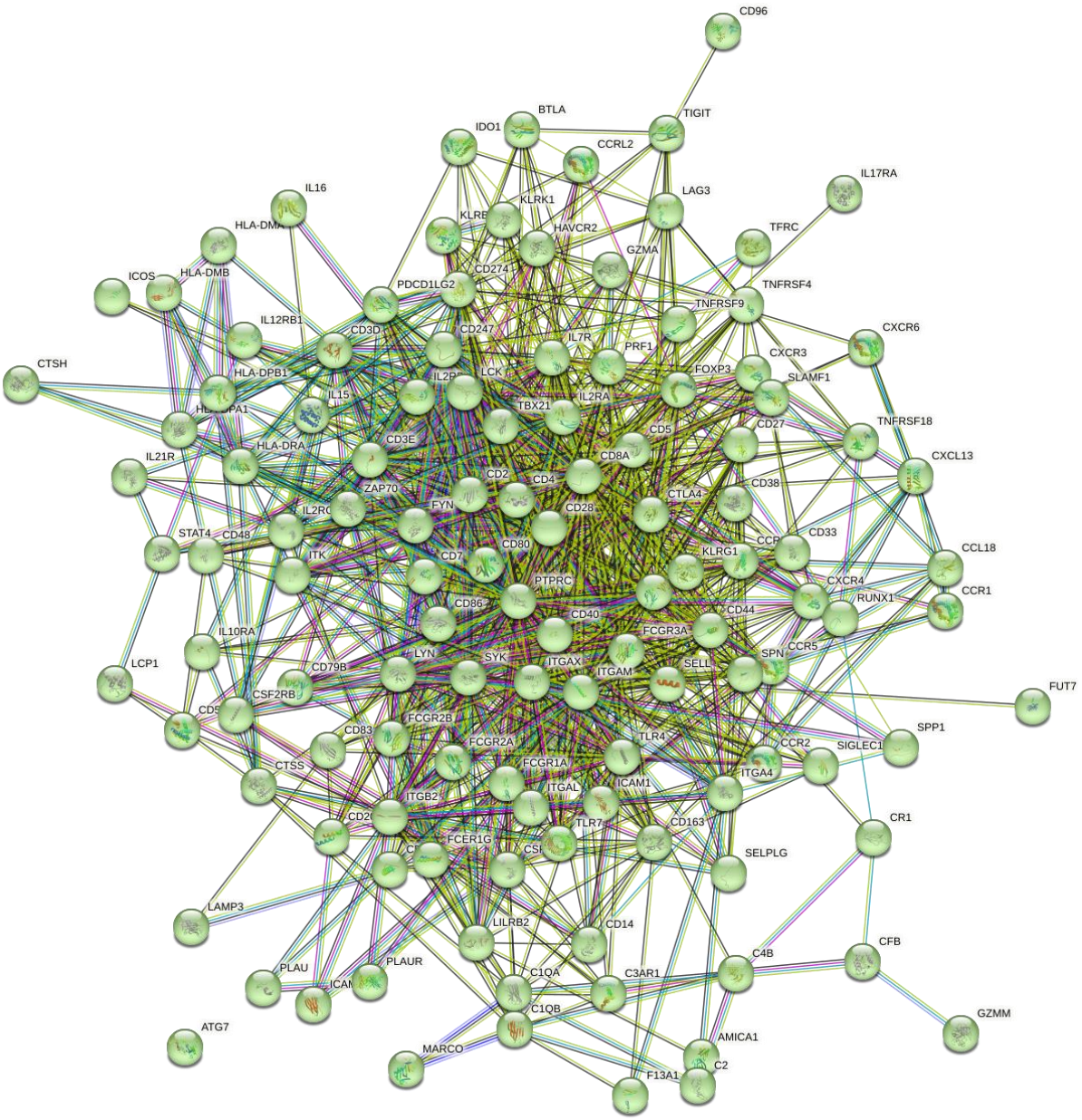


B



Supplementary Figure 2. Interactions among proteins encoded by the DEGs between TABs with TMI and normal TABs by STRING software analysis. The list of genes up-regulated plus detected/undetected (n = 260) or down-regulated (n = 31) in TMI versus normal TABs were uploaded in the STRING software. Network analysis was performed applying high confidence interaction score (=0.700) followed by k-means clustering (feasible only for the up-regulated genes). The network nodes are proteins. The edges show the predicted functional associations with up to 7 differently colored lines: red line = gene fusion evidence; green line = neighborhood evidence; blue line = co-occurrence evidence; purple line = experimental evidence; yellow line = textmining evidence; light blue line = database evidence; black line = co-expression evidence. A, B, C images show interactions among the up-regulated DEGs clustered by k-means algorithm. D shows interactions among the down-regulated DEGs.

A



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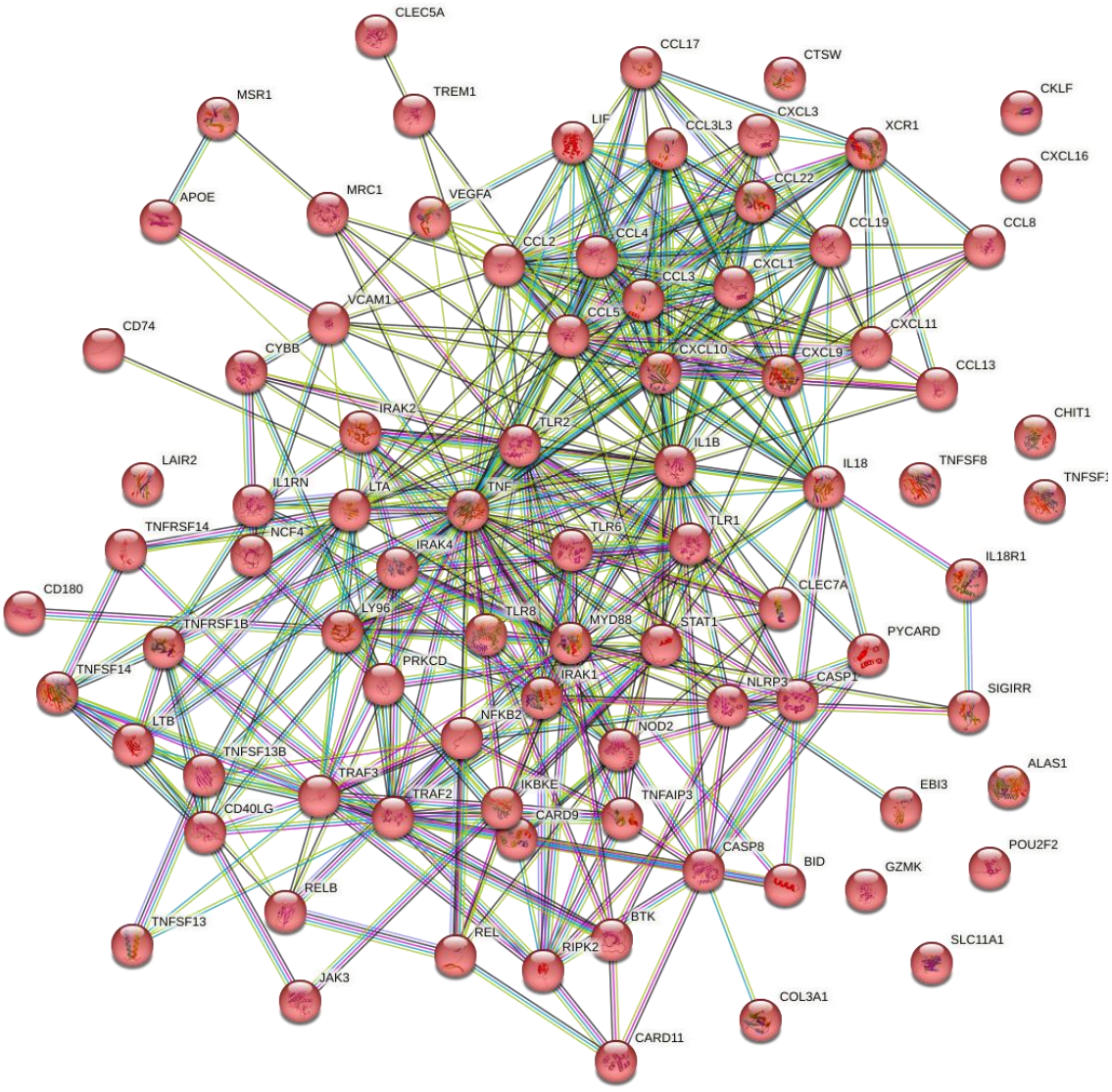
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MSR1
TREM1
CKLF
LIF
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XCR1
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APOE
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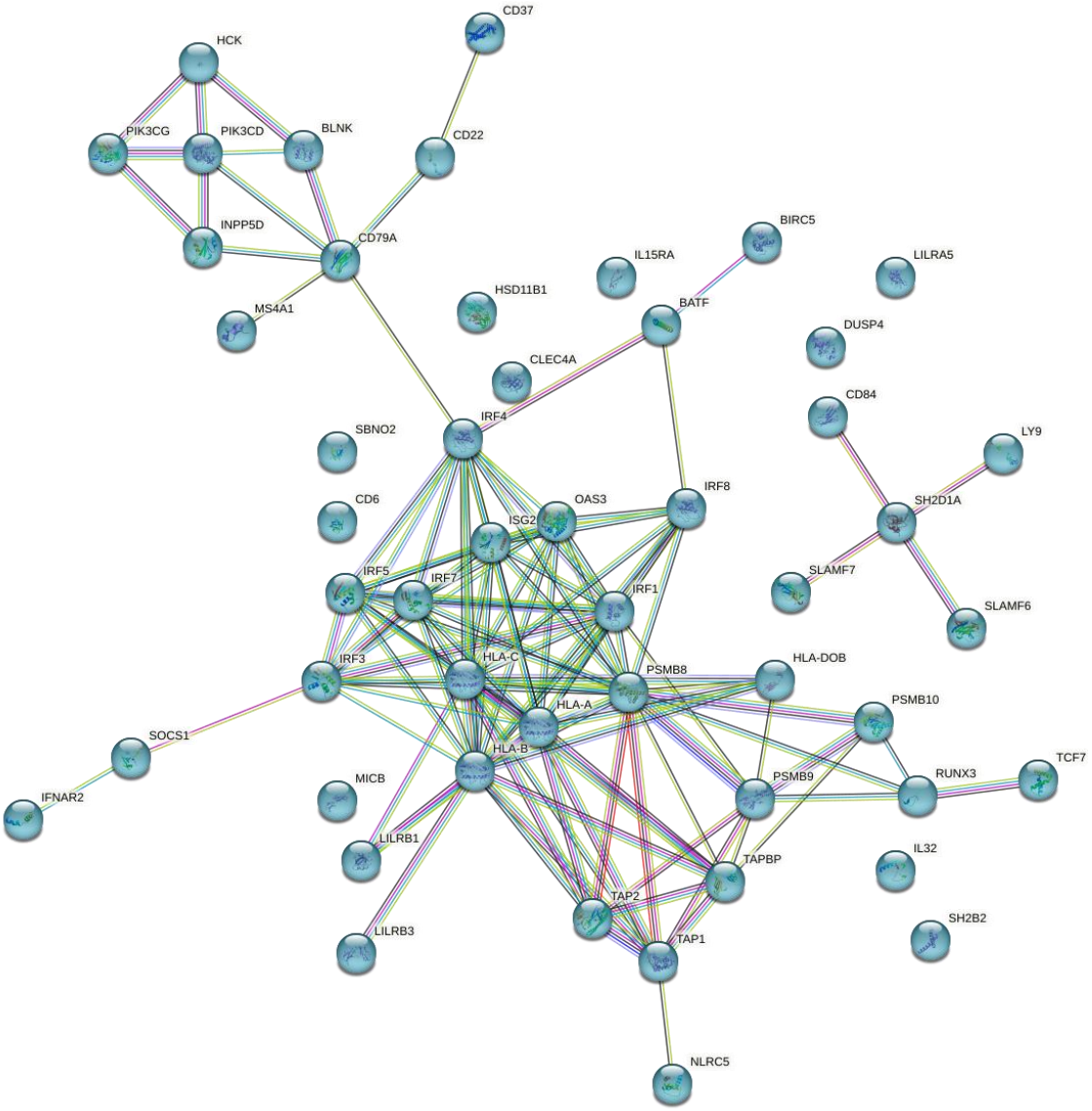
VEGFA
CCL22
CCL19
CCL8
CCL2
CCL4
CXCL1
CCL3
VCAM1
CCL5
CXCL11
CD74
CYBB
CXCL10
CXCL9
CCL13
IRAK2
TLR2
CHIT1
IL1B
LAIR2
IL18
TNFSF8
IL1RN
LTA
TNF
TNFRSF14
NCF4
TLR6
TLR1
IRAK4
IL18R1
CD180
CLEC7A
LY96
TLR8
MYD88
STAT1
PYCARD
TNFRSF1B
TNFSF14
PRKCD
IRAK1
NLRP3
CASP1
SIGIRR
LTB
NFKB2
NOD2
TNFSF13B
TRAF3
ALAS1
TRAF2
IKBKE
TNFAIP3
EBI3
CD40LG
CARD9
CASP8
BID
GZMK
POU2F2
RELB
TNFSF13
REL
BTK
RIPK2
SLC11A1
JAK3
COL3A1
CARD11

C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HCK
PIK3CG
PIK3CD
BLNK
CD22
INPP5D
CD79A
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BIRC5
IL15RA
LILRA5
HSD11B1
BATF
DUSP4
CLEC4A
CD84
IRF4
SBNO2
LY9
CD6
OAS3
IRF8
SH2D1A
ISG2
IRF5
IRF7
IRF1
SLAMF7
SLAMF6
IRF3
HLA-C
PSMB8
HLA-DOB
HLA-A
PSMB10
SOCS1
HLA-B
TCF7
MICB
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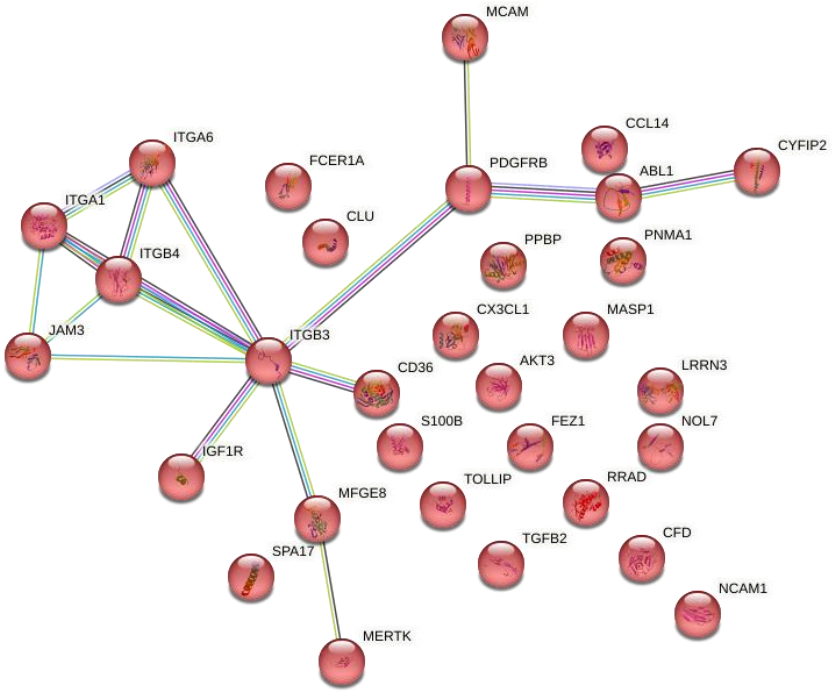
TAP2
SH2B2
LILRB3
TAP1
NLRC5

D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CCL14
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ABL1
ITGA1
CLU
PPBP
PNMA1
ITGB4
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MASP1
JAM3
ITGB3
AKT3
LRRN3
CD36
S100B
FEZ1
NOL7
IGF1R
TOLLIP
RRAD
MFGE8
TGFB2
CFD
SPA17
NCAM1
MERTK

Supplementary Figure 3. Validation of the increased expression in TABs with TMI of some DEGs that emerged from Nanostring nCounter profiling. The expression of CD45, CCL18, TNFRSF4/OX40, TNFRSF7/CD27, TNFRSF9/4-1BB was investigated by real-time PCR in a validation cohort. Normalized gene expression (= $2^{-\Delta Ct}$) is shown. POL2RA was used as housekeeping gene. CD45 was used to evaluate the degree of infiltrating leukocytes. Normalized expression was arbitrary set = 0.001 for genes that did not show amplification. Data were analyzed by the Kruskal-Wallis test with Dunns correction (* = $p < 0.05$; *** = $p < 0.001$) or Fisher's exact test (# = $p < 0.05$; ### = $p < 0.001$).