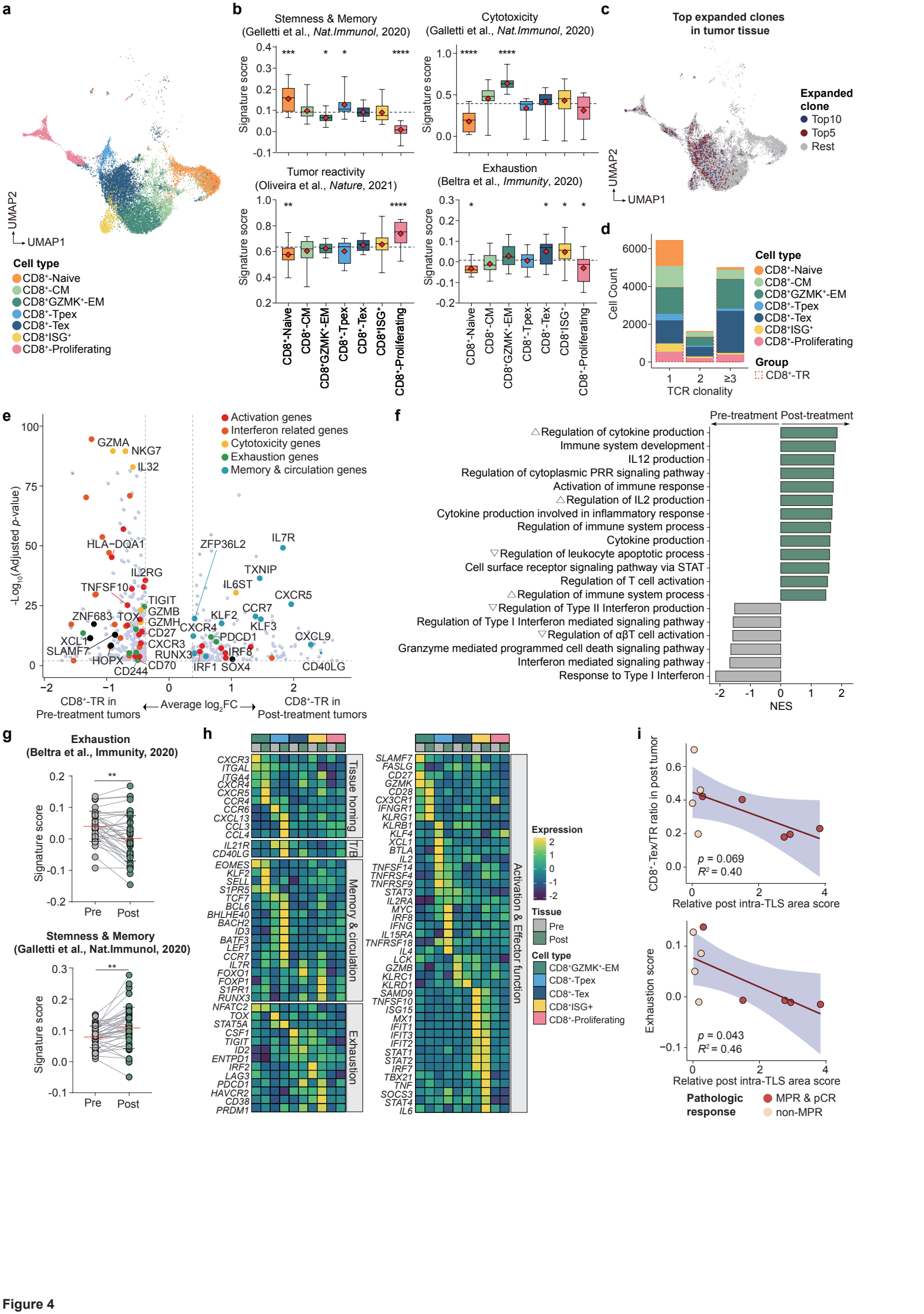

a
UMAP2
UMAP1
Cell type
CD8+-Naive
CD8+-CM
CD8+GZMK+-EM
CD8+-Tpex
CD8+-Tex
CD8+ISG+
CD8+-Proliferating
b
Stemness & Memory
(Gelletti et al., Nat.Immunol, 2020)
Cytotoxicity
(Galletti et al., Nat.Immunol, 2020)
Tumor reactivity
(Oliveira et al., Nature, 2021)
Exhaustion
(Beltra et al., Immunity, 2020)
Signature score
c
Top expanded clones
in tumor tissue
Expanded clone
Top10
Top5
Rest
d
Cell Count
TCR clonality
Cell type
Group
CD8+-TR
e
-Log10(Adjusted p-value)
Activation genes
Interferon related genes
Cytotoxicity genes
Exhaustion genes
Memory & circulation genes
GZMA
NKG7
IL32
HLA-DQA1
IL2RG
TNFSF10
TIGIT
GZMB
GZMH
CD27
CXCR3
RUNX3
HOPX
CD70
CD244
ZNF683
TOX
XCL1
SLAMF7
ZFP36L2
IL7R
TXNIP
IL6ST
CXCR5
CCR7
KLF2
CXCR4
KLF3
PDCD1
IRF8
IRF1
SOX4
CXCL9
CD40LG
CD8+-TR in
Pre-treatment tumors
Average log2FC
CD8+-TR in
Post-treatment tumors
f
Pre-treatment
Post-treatment
△Regulation of cytokine production
Immune system development
IL12 production
Regulation of cytoplasmic PRR signaling pathway
Activation of immune response
△Regulation of IL2 production
Cytokine production involved in inflammatory response
Regulation of immune system process
Cytokine production
▽Regulation of leukocyte apoptotic process
Cell surface receptor signaling pathway via STAT
Regulation of T cell activation
△Regulation of immune system process
▽Regulation of Type II Interferon production
Regulation of Type I Interferon mediated signaling pathway
▽Regulation of αβT cell activation
Granzyme mediated programmed cell death signaling pathway
Interferon mediated signaling pathway
Response to Type I Interferon
NES
g
Exhaustion
(Beltra et al., Immunity, 2020)
Stemness & Memory
(Galletti et al., Nat.Immunol, 2020)
Signature score
Pre
Post
h
Tissue homing
T/B
Memory & circulation
Exhaustion
Activation & Effector function
CXCR3
ITGAL
ITGA4
CXCR4
CXCR5
CCR4
CCR6
CXCL13
CCL3
CCL4
IL21R
CD40LG
EOMES
KLF2
SELL
S1PR5
TCF7
BCL6
BHLHE40
BACH2
ID3
BATF3
LEF1
CCR7
IL7R
FOXO1
FOXP1
S1PR1
RUNX3
NFATC2
TOX
STAT5A
CSF1
TIGIT
ID2
ENTPD1
IRF2
LAG3
PDCD1
HAVCR2
CD38
PRDM1
SLAMF7
FASLG
CD27
GZMK
CD28
CX3CR1
IFNGR1
KLRG1
KLRB1
KLF4
XCL1
BTLA
IL2
TNFSF14
TNFRSF4
TNFRSF9
STAT3
IL2RA
MYC
IRF8
IFNG
IL15RA
TNFRSF18
IL4
LCK
GZMB
KLRC1
KLRD1
SAMD9
TNFSF10
ISG15
MX1
IFIT1
IFIT3
IFIT2
STAT1
STAT2
IRF7
TBX21
TNF
SOCS3
STAT4
IL6
Expression
Tissue
Pre
Post
Cell type
CD8+GZMK+-EM
CD8+-Tpex
CD8+-Tex
CD8+ISG+
CD8+-Proliferating
i
CD8+-Tex/TR ratio in post tumor
p = 0.069
R2 = 0.40
Relative post intra-TLS area score
Exhaustion score
p = 0.043
R2 = 0.46
Pathologic response
MPR & pCR
non-MPR

Figure 4