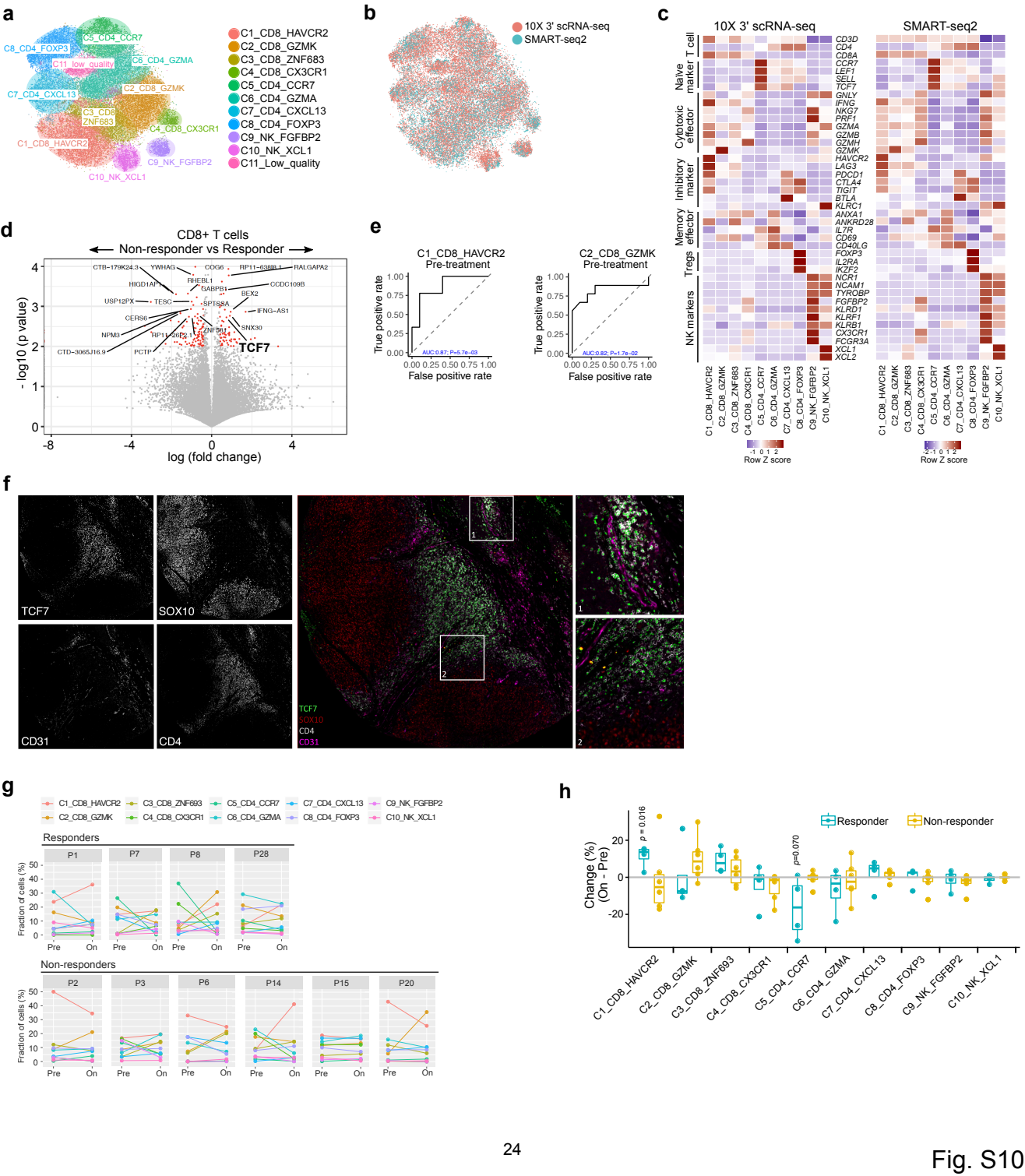
a
C5_CD4_CCR7
C8_CD4_FOXP3
C11_low_quality
C6_CD4_GZMA
C7_CD4_CXCL13
C2_CD8_GZMK
C3_CD8_ZNF683
C4_CD8_CX3CR1
C1_CD8_HAVCR2
C9_NK_FGFBP2
C10_NK_XCL1
C1_CD8_HAVCR2
C2_CD8_GZMK
C3_CD8_ZNF683
C4_CD8_CX3CR1
C5_CD4_CCR7
C6_CD4_GZMA
C7_CD4_CXCL13
C8_CD4_FOXP3
C9_NK_FGFBP2
C10_NK_XCL1
C11_Low_quality
b
10X 3' scRNA-seq
SMART-seq2
c
10X 3' scRNA-seq
SMART-seq2
Naive marker T cell
Cytotoxic effector
Inhibitory marker
Memory effector
Tregs
NK markers
CD3D
CD4
CD8A
CCR7
LEF1
SELL
TCF7
GNLY
IFNG
NKG7
PRF1
GZMA
GZMB
GZMH
GZMK
HAVCR2
LAG3
PDCD1
CTLA4
TIGIT
BTLA
KLRC1
ANXA1
ANKRD28
IL7R
CD69
CD40LG
FOXP3
IL2RA
IKZF2
NCR1
NCAM1
TYROBP
FGFBP2
KLRD1
KLRF1
KLRB1
CX3CR1
FCGR3A
XCL1
XCL2
C1_CD8_HAVCR2
C2_CD8_GZMK
C3_CD8_ZNF683
C4_CD8_CX3CR1
C5_CD4_CCR7
C6_CD4_GZMA
C7_CD4_CXCL13
C8_CD4_FOXP3
C9_NK_FGFBP2
C10_NK_XCL1
Row Z score
d
CD8+ T cells
Non-responder vs Responder
- log10 (p value)
log (fold change)
CTB-179K24.3
YWHAG
CDC6
RP11-638I8.1
RALGAPA2
RHEBL1
HIGD1AP1
CABP81
CCDC109B
BEX2
USP12PX
TESC
SPTSSA
IFNG-AS1
CERS6
SNX30
NPM3
TP11-36P2.1
ZNF561
TCF7
CTD-3065J16.9
PCTP
e
C1_CD8_HAVCR2
Pre-treatment
C2_CD8_GZMK
Pre-treatment
True positive rate
False positive rate
AUC:0.87; P=5.7e-03
AUC:0.82; P=1.7e-02
f
TCF7
SOX10
CD31
CD4
TCF7
SOX10
CD4
CD31
g
C1_CD8_HAVCR2
C2_CD8_GZMK
C3_CD8_ZNF683
C4_CD8_CX3CR1
C5_CD4_CCR7
C6_CD4_GZMA
C7_CD4_CXCL13
C8_CD4_FOXP3
C9_NK_FGFBP2
C10_NK_XCL1
Responders
P1
P7
P8
P28
Non-responders
P2
P3
P6
P14
P15
P20
Fraction of cells (%)
Pre
On
h
Responder
Non-responder
p = 0.016
p=0.070
Change (%) (On - Pre)
C1_CD8_HAVCR2
C2_CD8_GZMK
C3_CD8_ZNF693
C4_CD8_CX3CR1
C5_CD4_CCR7
C6_CD4_GZMA
C7_CD4_CXCL13
C8_CD4_FOXP3
C9_NK_FGFBP2
C10_NK_XCL1

Fig. S10

Fig. S10. Mapping the melanoma SMART-seq2 dataset

a,b t-SNE plots showing T-/NK-cells clustered by CCA-alignment of SMART-seq2 dataset (melanoma) and 10X 3' scRNA-seq dataset (LC, CRC, OvC), and colour-coded for cluster names (**a**) or technologies (**b**). **c** Heatmaps comparing marker gene expression signatures of CCA-aligned clusters of T-/NK-cells originated from different technologies (left: 10x scRNA-seq, right: SMART-seq2). **d** Volcano plot showing differentially expressed genes in CD8+ T cells from immunotherapy responders and non-responders. **e** Receiver operating characteristic (ROC) analysis was performed to evaluate the predictive effect of C1_CD8_HAVCR2 and C2_CD8_GMZK on response to checkpoint immunotherapy. The area under the ROC curve (AUC) was used to quantify response prediction in pre-treatment biopsies. **f** Images of a representative core, showing 4 single markers (left, greyscale) and a composite RGB-coloured image on the right, with two magnified areas: 1) $TCF7^{+}$ $CD4^{+}$ T-cells (green, white) outside a blood vessel (CD31, purple) at the periphery of the tumour (SOX10, red), and 2) $TCF7^{+}$ $CD4^{+}$ T-cells in the peritumoural area, entering the tumour (SOX10, red) at its interface. **g** Percentage changes of T-/NK-cell clusters in melanoma patient biopsies from pre-treatment (Pre) and on-treatment (On) lesions per patient. The plots were grouped by responder (n=4) and non-responder (n=6). One responder (P4) was excluded due to lack of initial response. **h** Percentage changes of T-/NK-cells in on-treatment (On) and pre-treatment (Pre) lesions per patient. The change (%) = On (%) – Pre (%).