

Supplementary BOX I. The annotation of CD4⁺/CD8⁺T cell sub-populations based on scRNASeq-data analyses.

Abbreviations: Overall expression representation of; HI, high-level; MED, medium-level; LO, low-level; +, minimal-level; MIN, minimal-to-negligible level; and NULL, negligible-to-zero level.

SKCM-CD8⁺T cells

Cluster 0 Pre-T_{EM}-like (Pre effector-memory like) IFNG^{MED}, GZMA^{HI}, PRFI^{HI}, KLRG1⁺, EOMES⁺, TBX21⁺, CCR7^{NULL}, SELL^{MIN}, CD44^{MED}

Cluster 1 T_{EFF}-like (Effector-like) TBX21⁺, TNF^{NULL}, IFNG^{MED}, PRFI^{HI}, GZMA^{HI}, GZMB^{HI}, GZMK^{MED}, CCL5^{HI}, CCL3^{LO}, CCL4^{MED}, BTLA⁺, CTLA4^{MED}, PDCDI^{MED}, ICOS^{LO}, LAG3^{MED}

Cluster 2 T_{RM} (Resting-memory) IFNG⁺, GZMB^{MIN}, GZMA^{MIN}, PRFI^{HI}, KLRG1^{LO}, TOX^{MED}, EOMES^{LO}, TBX21^{MIN}, TNF^{NULL}, CCR7^{MIN}, SELL^{MIN}, CD44^{MED}

Cluster 3 Pre-T_{EM} (Pre effector-memory) IFNG^{MED}, GZMA^{HI}, PRFI^{HI}, KLRG1^{LO}, EOMES^{MED}, TBX21^{NULL}, TNF^{NULL}, CCR7^{NULL}, SELL^{MIN}, CD44^{MED}

Cluster 4 T_{CM} (Central-memory) CCR7^{MED}, SELL^{HI}, IL7R^{HI}, CD27^{HI}, TBX21^{NULL}, EOMES^{LO}, PRFI^{LO}, GZMA/B^{MIN}

Cluster 5 T_{EMRA} (Effector memory re-expressing CD45RA) CCR7^{NULL}, CD27^{LO}, GZMA/B^{HI}, GZMK^{MED}, PRFI^{MED}, IFNG⁺, TNF⁺, TOX^{LO}, PDCDI^{MIN}, CTLA4^{MIN}

Cluster 6 T_{EFF} (Effector) TBX21⁺, TNF⁺, IFNG^{HI}, PRFI^{HI}, GZMA^{HI}, GZMB^{HI}, GZMK^{HI}, CCL5^{HI}, CCL3^{HI}, CCL4^{HI}, BTLA⁺, CTLA4^{HI}, PDCDI^{HI}, ICOS^{MED}, LAG3^{MED}

Cluster 7 T_{SEFF} (Suppressed-effector) TBX21^{NULL}, TNF^{NULL}, IFNG⁺, STAT1^{LO}, PRFI^{HI}, GZMA^{HI}, GZMB^{MIN}, GZMK^{HI}, CCL5^{HI}, CCL3^{MED}, CCL4^{HI}, BTLA^{NULL}, CTLA4^{LO}, PDCDI^{HI}, ICOS^{LO}, LAG3^{MED}

Cluster 8 T_{DPE}-like (Double-positive effector-like) KLRG1^{MED}, IL7R^{LO}, STAT1^{HI}, TBX21^{NULL}, TIGIT^{MED}, PRFI^{MED}, PDCDI^{LO}, GZMA^{LO}, GZMB^{NULL}, GZMK^{HI}

Cluster 9 MAIT-like (Mucosal associated invariant T cells) CD8A^{MIN}, CD8B^{NULL}, CD44^{HI}, CCR7^{NULL}, SELL^{MIN}

Cluster 10 T_{EM} (Effector-memory) IFNG^{HI}, GZMB^{HI}, GZMA^{MED}, PRFI^{HI}, KLRG1^{LO}, EOMES⁺, TBX21⁺, TNF⁺, CCR7^{NULL}, SELL^{NULL}, CD44^{MED}

Cluster 11 Pre-T_{EFF} (Pre-effector) TBX21^{NULL}, TNF^{NULL}, IFNG^{MED}, PRFI^{MED}, GZMA^{HI}, GZMB^{NULL}, GZMK^{HI}, CCL5^{HI}, CCL3^{MIN}, CCL4^{HI}, BTLA⁺, CTLA4^{MIN}, PDCDI^{LO}, ICOS^{LO}, LAG3^{LO}

Cluster 12 Early-T_{EFF} (Early-effector) TBX21^{NULL}, TNF^{NULL}, IFNG^{MED}, PRFI^{HI}, GZMA^{LO}, GZMB^{MIN}, GZMK^{MIN}, CCL5^{HI}, CCL3^{LO}, CCL4^{HI}, BTLA⁺, CTLA4^{LO}, PDCDI^{MED}, ICOS^{LO}, LAG3^{MED}

Cluster 13 T_N (Naive) CCR7^{MED}, IL7R^{HI}, SELL^{MED}, CTLA4^{NULL}, TOX^{NULL}, EOMES^{NULL}, GZMA/B/K^{NULL}, PRFI^{LO}, ICOS^{MIN}, IFNG^{NULL}, TNF^{NULL}

Cluster 14 T_{TIPM} (Tumour-infiltrating peripheral-memory) SELL^{LO}, PRFI^{LO}, GZMA^{MED}, GZMB^{NULL}, GZMK^{HI}, IFNG^{MIN}, TNF^{NULL}, CCR7^{MED}, CD27^{MED}, TBX21^{NULL}

Cluster 15 T_{RDM} (Resident-memory) ITGAE^{HI}, KLRG1^{MIN}, CCR7^{NULL}, SELL^{MIN}, KLF2^{NULL}, EOMES^{NULL}, TBX21^{NULL}

SKCM-CD4⁺T cells

Cluster 0 KLRBI^{HI}CD4⁺T

Cluster 1 T_{REG} (Regulatory) FOXP3^{HI}, TIGIT^{HI}, IKZF2^{MED}, CTLA4^{HI}, IL2RA^{MED}, TNFRSF18^{HI}, TNFRSF9^{MED}, ENTPD1^{MED}, IL10^{MED}

Cluster 2 T_{RN} (Resting-Naive) CXCR4^{HI}, CTLA4^{NULL}, CXCR3^{NULL}, CXCR5^{NULL}, CCR5^{NULL}, FOXP3^{NULL}, GATA3^{MIN}, ICOS^{NULL}, IKZF2^{NULL}, PDCDI^{NULL}, STAT1^{LO}

Cluster 3 T_{FH} (Follicular-helper) BATF^{HI}, BCL6^{MED}, MAF^{HI}, PDCDI^{HI}, STAT3^{MED}, ICOS^{HI}, CXCR5^{LO};

Cluster 4 T_{IFNS} (Interferon-stimulated) STAT1^{HI}, STAT3^{MED}, STAT4^{LO}, STAT6^{LO}, PDCDI^{NULL}, CTLA4^{MIN}, REL^{MED}

Cluster 5 T_{H2} (type-II polarised) GATA3^{MED}, FOXP3^{NULL}, CXCR3^{NULL}

Cluster 6 TIGIT^{HI}CD4⁺T

Cluster 7 T_{HI} (Type-I polarised) CXCR3^{HI}, CCR5^{LO}, CXCR6⁺, ICOS^{LO}, TNF⁺, CTLA4^{LO}, CD28^{MED}, TOX^{MIN}, STAT1^{MED}, PDCDI^{LO}

Cluster 8 T_N (Naive) CXCR4^{LO}, CD28^{LO}, CCR5^{NULL}, CXCR3^{NULL}, FOXP3^{NULL}, GATA3^{MIN}, ICOS^{MIN}, PDCDI^{NULL}, STAT1^{LO}, TIGIT^{MIN}, TNF^{NULL}

Cluster 9 ICOS^{HI}CD4⁺T

Cluster 10 T_{H22-like} (Type-22 polarised-like) CCR4^{HI}, AHR^{MED}, STAT1^{LO}, CTLA4^{MIN}, PDCDI^{NULL}, ICOS^{MED}

Cluster 11 T_{DFF} (Dysfunctional-precursor) PDCDI^{MED}, CCR6^{MED}, STAT1^{NULL}, IL21R^{LO}, TNF^{NULL}, ICOS^{NULL},

Cluster 12 T_{IN} (Inflamed-naive) CXCR4^{MED}, CD28^{LO}, CCR5^{LO}, CXCR3^{MIN}, FOXP3^{NULL}, GATA3^{LO}, ICOS^{MED}, PDCDI^{MIN}, STAT1^{MED}, TIGIT^{MED}, TOX^{MED}, TNF^{NULL}

GBM-CD8⁺T cells

Cluster 0 T_{DFF} (Dysfunctional-precursor) CD8A^{MED}, CD8B^{LO}, IL7R^{MED}, KLRG1^{LO}, IFNG^{NEG}, GZMB^{NULL}, GZMA^{NULL}, PRFI^{LO}, TNF^{LO}, CD44^{MED}

Cluster 1 CD27^{HI}CD8⁺T_{DF} (Dysfunctional) IL7R^{LO}, CD27^{HI}, TOX⁺, TIGIT⁺, PDCDI^{LO}, GZMA^{HI}, GZMB^{NEG}, GZMK^{HI}, PRFI^{LO}, ICOS^{LO}, IFNG^{NULL}, TNF^{LO}

Cluster 2 Pre-T_{EFF} (Pre-effector) TNF^{NEG}, CD27^{NULL}, ICOS^{NEG}, IFNG^{LO}, STAT1^{LO}, PRFI^{MED}, GZMA^{MED}, GZMB^{HI}, CCL4^{MED}, TOX^{NULL}, PDCDI^{LO}

Cluster 3 TOX^{HI}CD8⁺T_{INV} (Invariant) CD8A^{LO}, CD8B^{LO}, TOX^{HI}, CCL4^{HI}, CD27^{LO}, CD44^{HI}, IFNG⁺, GZMB^{NEG}, GZMA^{HI}, PRFI^{MED}, KLRG1^{MED}, IL7R^{NULL}

Cluster 4 T_{RDF} (Resident-dysfunctional) IL7R^{HI}, ITGAE^{MED}, KLRG1^{NULL}, CD27^{MED}, GZMA^{MED}, PRFI^{MED}, ICOS^{LO}, IFNG^{NEG}, STAT1^{NULL}, TNF^{NULL}, TOX^{NEG}, PDCDI^{LO}, TIGIT^{LO}

GBM-CD4⁺T cells

Cluster 0 T_N (Naive) IL7R^{HI}, SELL^{HI}, CD28^{LO}, CTLA4^{NEG}, GZMA^{NULL}, PRFI^{LO}, ICOS^{LO}, PDCDI^{LO}, TIGIT^{LO}, TNF^{NULL}

Cluster 1 T_{IF} (Inflammatory) CCL4^{HI}, TNF^{HI}, CD28^{LO}, CTLA4^{NEG}, GZMA^{LO}, PRFI^{HI}, ICOS^{NULL}, PDCDI^{LO}, TIGIT^{LO}, TOX^{MED}

Cluster 2 ICOS^{MED}CD4⁺T_{DF} (Dysfunctional) ICOS^{MED}, CTLA4^{NEG}, TOX^{LO}, CD28^{LO}, PDCDI^{LO}, GZMA^{HI}, PRFI^{NEG}

Cluster 3 T_{DF} (Dysfunctional) CTLA4^{NEG}, TOX^{NEG}, CD28^{LO}, ICOS^{NULL}, PDCDI^{LO}, GZMA^{NULL}, PRFI^{NULL}

Cluster 4 ICOS^{HI}T_{REG}-like (Regulatory-like) ICOS^{HI}, CTLA4^{HI}, IL2RB^{HI}, TIGIT^{LO}, SELL^{MED}, TNF^{NEG}, PRFI^{LO}, GZMA^{NULL}, PDCDI^{NEG}

Cluster 5 T_{PC} (Precursor) IL7R^{HI}, IL2RB^{MED}, CTLA4^{NULL}, TOX^{LO}, CD28^{MED}, ICOS^{NEG}, PDCDI^{LO}, GZMA^{HI}, PRFI^{NULL}