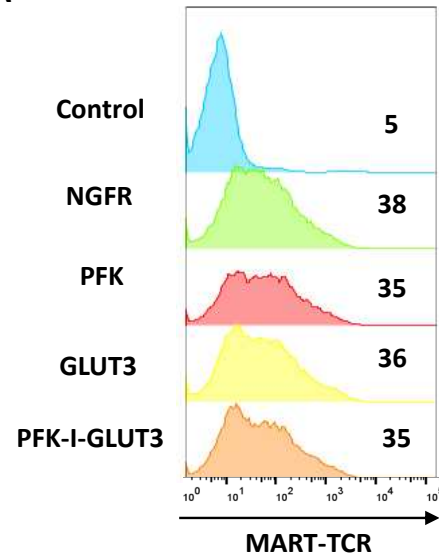
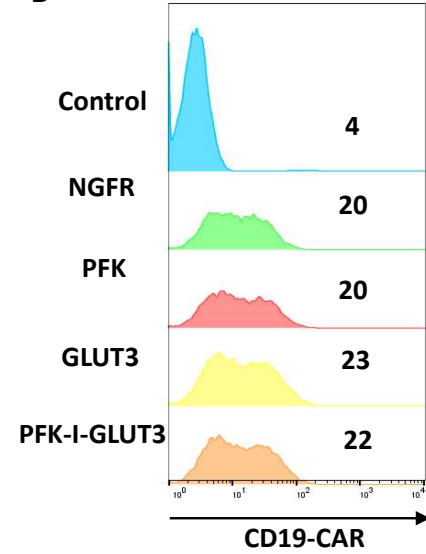


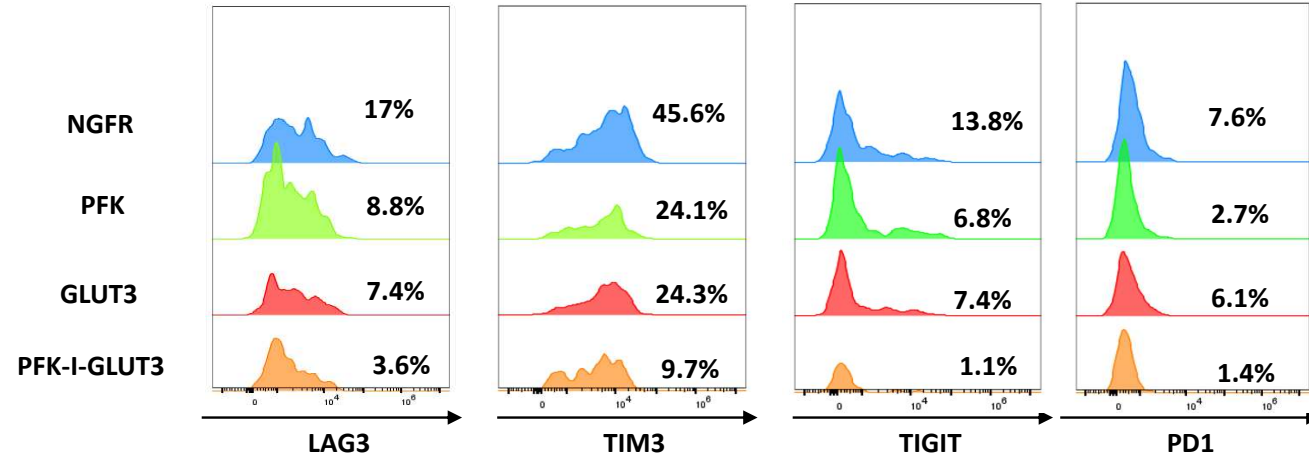
Supplementary Figure S1

A**B**

Supplementary Figure S1

Primary human PBLs were transduced with either TCR/CAR and different metabolic gens. TCR (A) and CAR (B) expression was evaluated by flow cytometry 30 days after transduction in NGFR, PFK, GLUT3 and PFK-I-GLUT3 co-transduced population. The MFI is indicated and no significant difference was noted between the different populations.

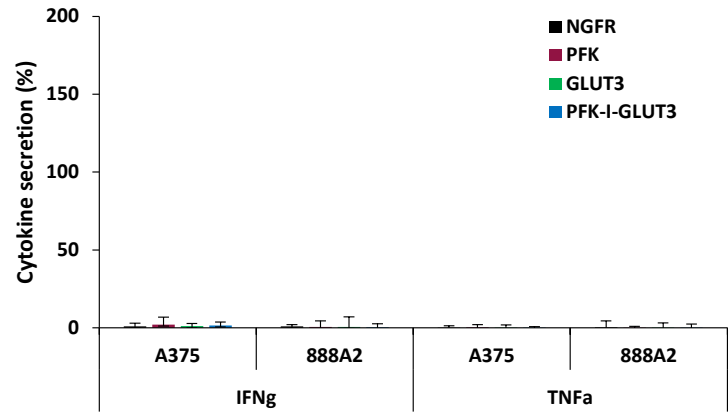
Supplementary Figure 2



Supplementary Figure S2

Representative results from flow cytometric analysis of PFK, GLUT3, PFK-I-GLUT3 and NGFR engineered T-cells stained for LAG3, TIM3, TIGIT and PD1 expression. The percent of positive cells is indicated.

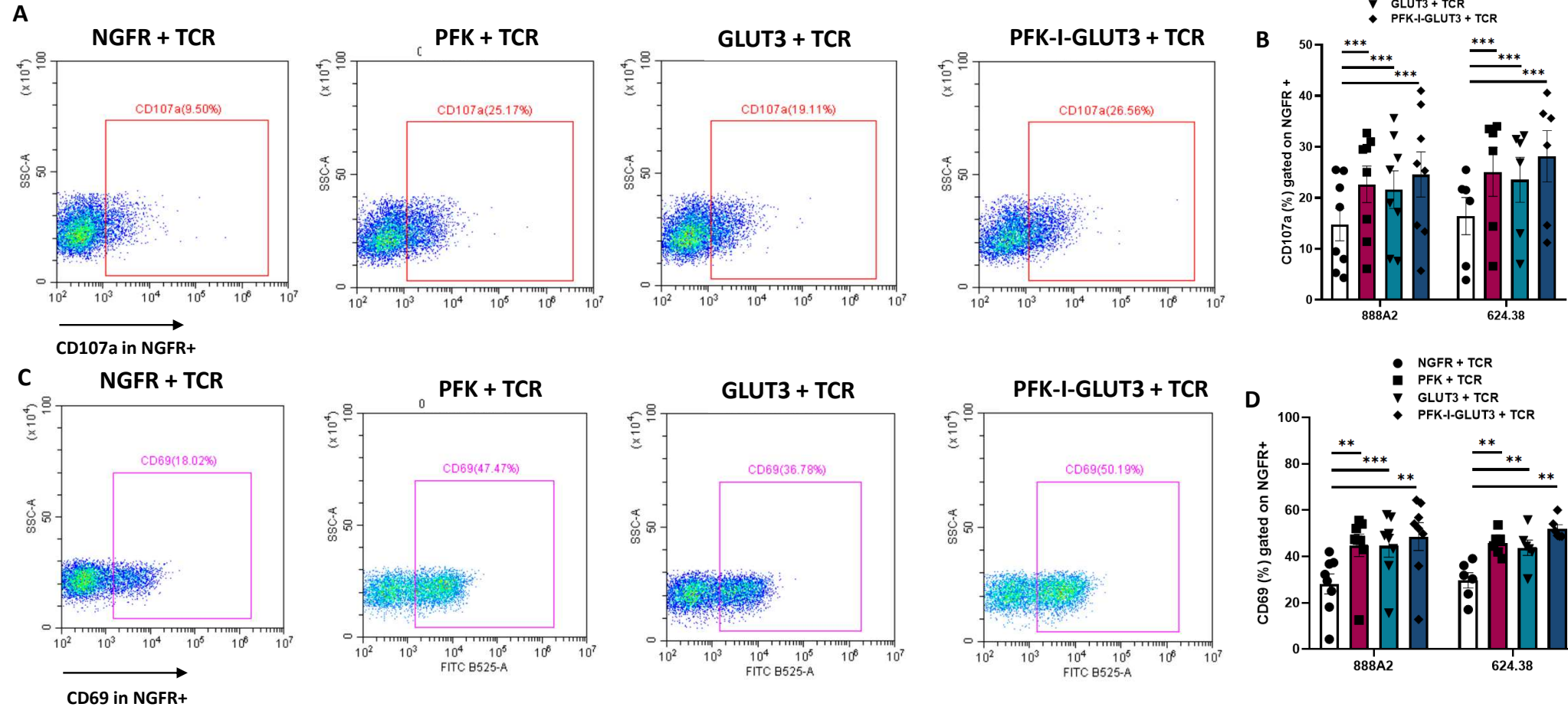
Supplementary Figure 3



Supplementary Figure S3

NGFR, PFK, GLUT3 and PFK-I-GLUT3 (without TCR) were co-cultured overnight with tumor cells. IFN γ and TNF α secretion were measured by ELISA. As expected, no significant cytokine secretion was detected in the absence of TCR signal (Signal 1).

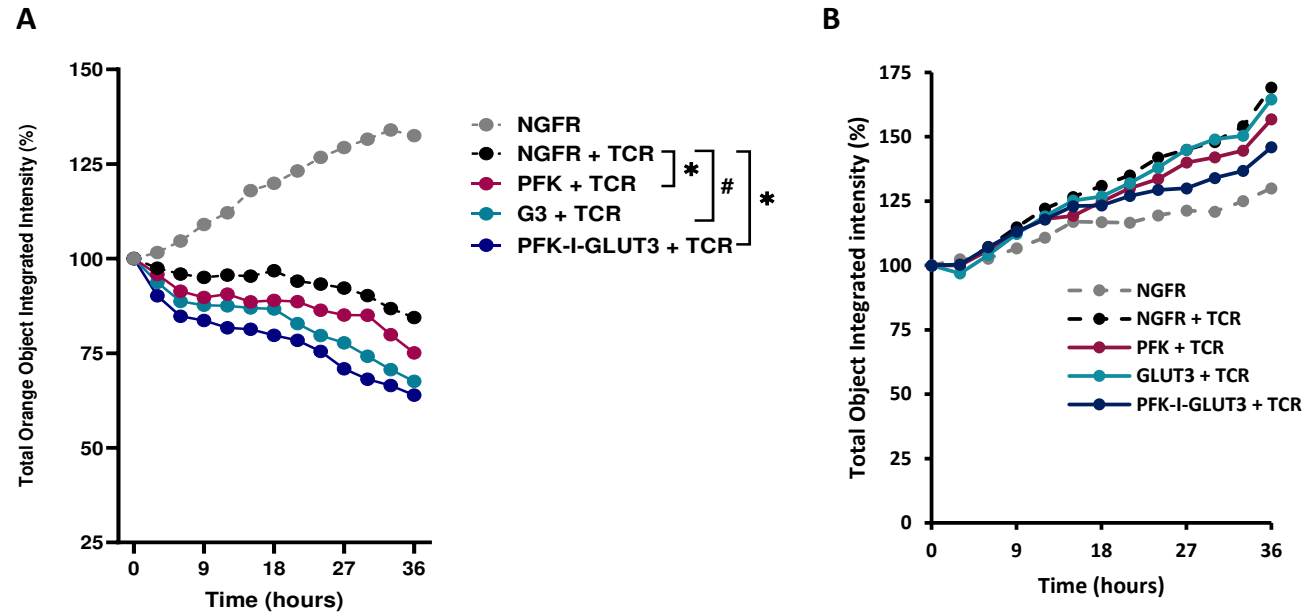
Supplementary Figure 4



Supplementary Figure S4

Primary human PBLs were transduced with a MART-1 specific TCR as well as with PFK/NGFR, Glut3/NGFR, PFK-IRES-Glut3/NGFR or NGFR only (control) CD107a (A-B) and CD69 (C-D) expression were measured by flow cytometry, gated on the NGFR⁺ population. Results are presented from 6 independent experiments (with at least 3 different donors). A representative result (A, C) and the mean+SEM (B, D) are presented. Statistical significance between the groups and control was determined using a *Student's* paired t-test.

Supplementary Figure 5



Supplementary Figure S5

Engineered-T cells (as indicated) were co-cultured with 888A2 (C) and negative control A375 (D) at a ratio of 2:1 (E:T) for 36 hours. The mCherry⁺ live population was measured using an Incucyte apparatus. This result is representative of 3 different cytotoxicity assay performed with 3 different donors.