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(57) Abstract: Provided herein are nucleic acids, expression cassettes, modified lymphocytes and compositions comprising the same which include a sequence encoding a fusion protein, TCR or CAR that includes a domain of LTBR. In certain embodiments, die cell is a T cell. Methods of treatment using the provided compositions are also described.

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METHODS AND COMPOSITIONS COMPRISING FUSION PROTEINS FOR IMPROVED IMMUNOTHERAPIES

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REFERENCE TO AN ELECTRONIC SEQUENCE LISTING

The contents of the electronic sequence listing (NYG-LIPP-158PCT.xml; Size: 304,622 bytes; and Date of Creation: March 15, 2023) is herein incorporated by reference in its entirety.

BACKGROUND

Cellular immunotherapies with engineered autologous patient T cells redirected against a chosen tumor antigen have yielded great efficacy against blood cancers, resulting in five approvals for chimeric antigen receptors (CARs) by the US Food and Drug Administration (FDA) so far[6]. By contrast, CAR therapy for solid tumors has shown a much lower efficacy overall, owing to the suppression of T cell effector function in the tumor microenvironment. Even for blood malignancies, with the exception of B acute lymphoblastic leukemia, most patients do not experience a durable response, with resistance being primarily due to T cell dysfunction rather than antigen loss[7]. Considerable efforts have been devoted to identifying genes and pathways that contribute to T cell dysfunction[8,9]. However, comprehensive, genome-wide screens for modulators of T cell function thus far have been limited to loss-of-function screens[2–4].

The advances in CRISPR genome engineering have made it possible to readily knock out every gene in the genome in a scalable and customizable manner. Although its large size makes it challenging (albeit not impossible[10]) to deliver Cas9 via lentivirus to primary T cells, alternative approaches have been developed, which rely on transient delivery of Cas9 protein[2] or mRNA[11], or on constitutive Cas9 expression in engineered isogenic mouse strains[3]. These approaches, however, are not amenable to gain-of-function screens in human cells, which require continuous expression of the transcriptional activator that drives target gene expression.

What is needed is improved compositions and methods for more effective immunotherapies.

SUMMARY OF THE INVENTION

Provided herein, in a first aspect, is a lymphocyte genetically modified to express a chimeric antigen receptor (CAR). The CAR includes an antigen binding domain; a transmembrane domain; and a signaling domain. In certain embodiments, at least one domain comprises an LTBR domain. In other embodiments, at least one domain comprises a domain from a gene of Table 3. In certain embodiments, the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof. In certain embodiments, the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or a fragment, deletion, or variant thereof. In certain embodiments, the LTBR intracellular domain has a deletion in at least amino acids 393 to 435.

In another embodiment, the CAR includes an antigen binding domain; a transmembrane domain; a co-stimulatory signaling domain; and a signaling domain. In certain embodiments, at least one domain comprises an LTBR domain. In other embodiments, at least one domain comprises a domain from a gene of Table 3. In certain embodiments, the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof. In certain embodiments, the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or a fragment, deletion, or variant thereof. In certain embodiments, the LTBR intracellular domain has a deletion in at least amino acids 393 to 435.

In another aspect, a nucleic acid molecule is provided. The molecule includes a sequence that encodes a chimeric antigen receptor (CAR). The CAR includes an antigen binding domain; a transmembrane domain; and a signaling domain. In certain embodiments, at least one domain comprises an LTBR domain. In other embodiments, at least one domain comprises a domain from a gene of Table 3. In certain embodiments, the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof. In certain embodiments, the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or a fragment, deletion, or variant thereof. In certain embodiments, the LTBR intracellular domain has a deletion in at least amino acids 393 to 435. In another embodiment, the CAR includes an antigen binding domain; a transmembrane domain; a co-stimulatory signaling domain; and a signaling domain. In certain embodiments, at least one domain comprises an LTBR domain. In other embodiments, at least one domain comprises a domain from a gene of Table 3. In certain embodiments, the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof. In certain embodiments, the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or a fragment, deletion, or variant thereof. In certain embodiments, the LTBR intracellular domain has a deletion in at least amino acids 393 to 435.

In another aspect, an expression cassette is provided that includes a nucleic acid molecule that includes a sequence that encodes a chimeric antigen receptor (CAR).

In another aspect, a method treating cancer in a subject in need thereof is provided. The method includes administering a composition comprising a modified lymphocyte as described herein.

In another aspect, a method of treating a viral disease in a subject in need thereof is provided. The method includes administering a composition comprising a modified lymphocyte

In another aspect, a method of treating an autoimmune in a subject in need thereof is provided. The method includes administering a composition comprising a modified lymphocyte

In another aspect, a fusion protein comprising an LTBR domain and at least one domain from a second protein, that is not LTBR is provided.

In another aspect, a host cell comprising a nucleic acid molecule or expression cassette as described herein, is provided.

Other aspects and advantages of the invention will be readily apparent from the following detailed description of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1A – FIG. 1D show a genome-scale overexpression screen to identify genes that boost the proliferation of primary human T cells. (FIG. 1A) Overview of the pooled ORF screen. $CD4^+$ and $CD8^+$ T cells were separately isolated from peripheral blood from three healthy donors. The barcoded genome-scale ORF library was then introduced into CD3/CD28-stimulated T cells, followed by selection of transduced cells. After 14 days of culture, T cells were labelled with carboxyfluorescein succinimidyl ester (CFSE) and restimulated to induce proliferation. By comparing counts of specific ORF barcodes before and after cell sorting, we identified ORFs enriched in the CFSElow population. (FIG. 1B) Normalized enrichment of individual barcodes for the indicated genes in the $CD4^+$ screen. (FIG. 1C) Robust rank aggregation of genes in both $CFSE^{low}CD4^+$ and $CFSE^{low}CD8^+$ T cells, based on consistent enrichment of individual barcodes for each gene. (FIG. 1D) Enrichment in individual donors and T cell populations of top-ranked genes (grouped by function and relevance to T cell proliferation) selected for further study. Neutral genes (MHC-I complex and cell-type specific differentiation markers) are included for comparison. Gene names are colored on the basis of the differential expression in CD3/CD28-stimulated and resting T cells (green, upregulated; red, downregulated; grey, no change; black, no expression)[41].

FIG. 2A – FIG. 2F show overexpression of top-ranked ORFs increases the proliferation, activation and cytokine secretion of $CD4^+$ and $CD8^+$ T cells. (FIG. 2A) CD4+ and $CD8^+$ T cells

from screen-independent donors were separately isolated and then transduced with lentiviruses encoding top-ranked ORFs together with a selection marker. After transduction and selection, T cells were restimulated before measurement of proliferation, expression of activation markers and cytokine secretion. (FIG. 2B) Proliferation of T cells transduced with top-ranked genes as the relative proliferation, which is defined as the ratio of stimulated cells to the corresponding unstimulated control, normalized to tNGFR. A minimum of two donors was tested per overexpressed gene, in biological triplicate. Boxes show 25th–75th percentiles with a line at the mean; whiskers extend to maximum and minimum values. *DUPD1* is also known as *DUSP29*. (FIG. 2C) Mean relative proliferation of ORF-transduced T cells in $CD4^+$ and $CD8^+$ T cells, normalized to tNGFR. Significant genes in both T cell subsets or either of them are marked (Student's two-sided *t* test $P < 0.05$ and false discovery rate < 0.1). (FIG. 2D) Representative expression of CD25 or CD154 after restimulation. The numbers on the histograms correspond to the percentage of gated cells ($CD8^+CD154^+$) or the mean fluorescence intensity (MFI). Dashed lines indicate the gate used to enumerate $CD154^+$ cells ($CD8^+$) or MFI for control (tNGFR) cells. (FIG. 2E) Secretion of IL-2 and IFNγ after restimulation, normalized to tNGFR. Only genes that significantly increase T cell proliferation in $CD4^+$, $CD8^+$ or both T cell subsets are shown. A minimum of two donors was tested in triplicate per gene. Boxes show 25th–75th percentiles with a line at the mean; whiskers extend to maximum and minimum values. (FIG. 2F) Intersection between different T cell activation phenotypes that are significantly ($P < 0.05$) improved by a given ORF in $CD8^+$ or $CD4^+$ T cells.

FIG. 3A – FIG. 3E show single-cell OverCITE-seq identifies shared and distinct transcriptional programs that are induced by gene overexpression in T cells. (FIG. 3A) OverCITE-seq captures overexpression (ORF) constructs, transcriptomes, TCR clonotypes, cell-surface proteins and treatment hashtags in single cells. (FIG. 3B) ORF assignment rate in resting and CD3/CD28-stimulated T cells. (FIG. 3C) Antibody-derived tag sequencing (ADTs; right) yields similar NGFR expression in tNGFR-transduced T cells to flow cytometry (left) with tNGFR-transduced T cells. Untransduced cells (left) or cells assigned a non-tNGFR ORF (right) are shown in grey. (FIG. 3D) Uniform manifold approximation and projection (UMAP) representation of single-cell transcriptomes after unsupervised clustering of OverCITE-seq-captured ORF singlets. The inset in the top left identifies stimulated and resting T cells as given by treatment hashtags. For each cluster, a subset of the top 20 differentially expressed genes is shown. *HIST1H1B* is also known as *H1-5* and *HIST1H3C* is also known as *H3C3*. (FIG. 3E) ORF prevalence in two representative clusters. Standardized residual values are from a chi-squared test. ORFs of interest are shown.

FIG. 4A – FIG. 4K show LTBR overexpression improves T cell function through activation of the canonical NF-κB pathway. (FIG. 4A) Differential expression of genes in resting LTBR and tNGFR (negative control) T cells. Genes highlighted in red are those with a twofold or greater change in expression and an adjusted $P < 0.05$. (FIG. 4B) Significantly enriched GO biological processes in LTBR-overexpressing T cells ($p < 0.05$). (FIG. 4C) Cell viability of $CD8^+$ T cells transduced with LTBR or tNGFR lentivirus, either restimulated with CD3/CD28 for four days or left unstimulated ($n = 2$ donors with 3 biological replicates each). (FIG. 4D) PD-1 expression on resting LTBR or tNGFR T cells stimulated with a 3:1 excess of CD3/CD28 beads every three days, for up to three rounds of consecutive stimulation. (FIG. 4E) ICAM-1 expression (resting) and IL-2 secretion (activated) by T cells transduced with Flag-tagged LTBR mutants, normalized to wild-type LTBR ($n = 6$ replicates across two experiments). (FIG. 4F) Enrichment of transcription factor motifs in differentially accessible chromatin (top 10 motifs from each comparison). (FIG. 4G) Quantification of phosphorylated RELA (phospho-RELA) in LTBR or tNGFR T cells stimulated with CD3/CD28 antibodies for the indicated periods of time. (FIG. 4H, FIG. 4I) Quantification of phosphorylated IκBα (FIG. 4H) or mature NF-κB2 (FIG. 4I) in resting or CD3/CD28-stimulated (15 min) LTBR or tNGFR cells. (FIG. 4J) IFNγ secretion by stimulated LTBR or tNGFR cells after CRISPR knockout of the indicated genes ($n = 18$, 3 sgRNAs in 2 donors in 3 biological replicates). IFNγ quantities are normalized to corresponding non-targeting (NT) controls (either LTBR or tNGFR) to allow comparisons of the relative effects of gene knockout on T cell activation. (FIG. 4K) Expression levels of core LTBR genes ($n = 274$ genes) in LTBR and tNGFR cells after CRISPR knockout of *RELA* or *RELB* (normalized to non-targeting control in LTBR cells). Boxes show 25th–75^{th} percentiles with a line at the median; whiskers extend to 1.5 times the interquartile range. Unpaired two-sided *t* test *P* values (FIG. 4C, FIG. 4G – FIG. 4K): not significant (NS) $P > 0.05$, $*P < 0.05$, $**P < 0.01$, $***P < 0.001$, $****P < 0.0001$. Error bars, s.e.m.; $n = 3$ biological replicates, unless stated otherwise.

FIG. 5A – FIG. 5I show top-ranked genes improve antigen-specific T cell responses and tumor killing. (FIG. 5A – FIG. 5G) Co-delivery of anti-CD19 CARs and ORFs to T cells from healthy donors. (FIG. 5A) Schematic of tricistronic vector and CAR T cell experiments. (FIG. 5B, FIG. 5C) Secretion of IFNγ (FIG. 5B) and IL-2 (FIG. 5C) after overnight co-incubation of $CD8^+$ T cells with Nalm6 cells at a 1:1 ratio ($n = 3$ biological replicates, representative of 2 donors). (FIG. 5D) Representative images of Nalm6 GFP^+ cells co-incubated for 48 h with CAR T cells or untransduced control T cells. Scale bar, 200 μm. (FIG. 5E) Nalm6 GFP^+ cell proliferation (normalized total GFP per well) after co-incubation with T cells co-expressing 19-28z CAR and LTBR or tNGFR (negative control) at the indicated effector-to-target ratios. (FIG. 5F) Quantification of Nalm6 GFP^+ clearance for T cells co-expressing 19-28z or 18-BBz CARs

and top-ranked genes (n = 3 biological replicates, representative of 2 donors), normalized to tNGFR at an effector-to-target ratio of 0.25 and after 48 h of co-incubation. (FIG. 5G) 19-BBz CAR T cells co-expressing LTBR or tNGFR were co-incubated at a 1:1 ratio with Nalm6 cells every 3 days for up to 3 rounds of stimulation (n = 3 biological replicates). Seven days after repeated antigen stimulation, CAR T cells were re-exposed to Nalm6 cells. IFNγ secretion was measured after overnight incubation. (FIG. 5H) Co-delivery of anti-CD19 CARs and ORFs to total PBMCs from a patient with diffuse large B cell lymphoma. Transduced T cells were incubated alone, or co-incubated with $CD19^+$ Nalm6 or $CD19^-$ Jurkat cell lines at a 1:1 ratio (n = 3 biological replicates, representative of 2 patients). Secretion of IFNγ and IL2 was measured after overnight incubation. For the Nalm6 condition, numbers above indicated column pairs are the fold increase in cytokine secretion by LTBR cells over tNGFR (negative control) cells. (FIG. 5I) Delivery of ORFs to Vγ9Vδ2 T cells. Secretion of IFNγ and IL-2 after overnight co-incubation with the pancreatic ductal adenocarcinoma (PDAC) line Capan-2, pre-treated with zoledronate to boost phosphoantigen accumulation (n = 3 biological replicates). Data are mean ± s.e.m. where appropriate.

FIG. 6A – FIG. 6Q show design of the human ORF library screen in primary T cells. (FIG. 6A) Barcoded vector design for ORF overexpression. (FIG. 6B) Distribution of the number of barcodes per ORF in the library. (FIG. 6C) Vector design for quantifying the effect of different promoters and ORF insert sizes on lentiviral transduction efficiency. EFS – elongation factor-1α short promoter, CMV – cytomegalovirus promoter, PGK – phosphoglycerate kinase-1 promoter. (FIG. 6D) Sequential gating strategy and representative histograms of cells transduced with marker gene rat CD2 under different promoters. (FIG. 6E) Percentage of positive cells and (FIG. 6F) mean fluorescence intensity (MFI) of rat CD2 (rCD2) expressed from the EFS and CMV promoters, following puromycin selection of transduced primary $CD4^+$ T cells. Each data point indicates individual transduction (n = 3 biological replicates). Error bars are SEM. (FIG. 6G) Distribution of ORF sizes in the genome-scale library. The size of TCR-rCD2 construct tested in panels FIG. 6E and FIG. 6F is marked. (FIG. 6H) Titration of CD3/CD28 antibodies. T cells were labelled with CFSE, stimulated and incubated for 4 days. Gate for proliferating T cells was set to include cells that proliferated at least twice (third CFSE peak). (FIG. 6I) Expansion of T cells from three healthy donors transduced with the ORF library. (FIG. 6J) Representative CFSE profile of restimulated $CD8^+$ and $CD4^+$ T cells before the sort. The $CFSE^{low}$ sort gate is marked. (FIG. 6K) Recovery of individual barcodes or corresponding ORFs in transduced T cells and plasmid used for lentivirus production. Respective samples from three donors were computationally pooled together at equal number of reads prior to counting how many barcodes or ORFs were present with a minimum of one read. (FIG. 6L) Distribution of reads corresponding

to ORFs of different sizes. ORFs were assigned to ten quantiles based on their size, with Q1 being smallest size and Q10 being the largest size (n = 1,161 ORFs per quantile). Box shows 25–75 percentile with a line at the median; whiskers extend to 1.5 × interquartile range. (FIG. 6M) Enrichment of genes in both $CFSE^{low}$ $CD4^+$ and $CD8^+$ T cells, calculated by collapsing individual barcodes into corresponding genes. Significantly enriched genes (log_2 fold change higher than 0.5 and adjusted p-value lower than 0.05) are marked in red. Immune response genes of interest are marked. (FIG. 6N) Overlap of significantly enriched genes from FIG. 6M in individual screen populations ($CD4^+$, $CD8^+$) analyzed separately. (FIG. 6O) Normalized enrichment of individual barcodes for indicated genes in the $CD8^-$ screen. (FIG. 6P) GO biological processes for significantly enriched genes in FIG. 6M. (FIG. 6Q) Overlap of significantly enriched genes with differentially expressed genes between CD3/CD28 stimulated and naive T cells[41].

FIG. 7A – FIG. 7J show overexpression of select ORFs in screen independent donors. (FIG. 7A) Histograms of selected ORF expression in T cells after puromycin selection. (FIG. 7B) Quantification of tNGFR expression in transduced $CD4^+$ and $CD8^+$ T cells. Puromycin selection was complete after 7 days post transduction. To maintain T cells in culture, they were restimulated with CD3/CD28 on days 21 and 42. (FIG. 7C) Correlation between ORF sizes and changes in proliferation relative to tNGFR. Mean log_2 fold-changes are shown. (FIG. 7D) Proliferation of restimulated $CD8^+$ or (FIG. 7E) $CD4^+$ T cells relative to tNGFR in individual donors (n = 3 biological replicates). Mean and SEM are shown. (FIG. 7F, FIG. 7G) Proliferation of T cells transduced with ORFs that significantly improved T cell proliferation (see FIG. 2C) measured by dilution of CellTrace Yellow. Representative CellTrace Yellow histograms and fitted distributions (FIG. 7F) as well as quantifications of the proliferation index (FIG. 7G) are shown (n = 3 biological replicates). P values: < 0.0001, 0.0008, <0.0001, 0.011, 0.0031, 0.0007, < 0.0001, 0.28, 0.004, < 0.0001, 0.58, 0.01, 0.0003, < 0.0001, 0.036, 0.0049 (left to right). (FIG. 7H) Viability of ORF-transduced T cells 4 days after CD3/CD28 restimulation. Representative data from one donor (out of 4 donors tested) are shown (n = 3 biological replicates). (FIG. 7I, FIG. 7J) Cell cycle analysis of T cells stimulated with CD3/CD28 for 24 h. Gating was performed based on isotype and fluorescence minus one controls. Representative gating (FIG. 7I) as well as (FIG. 7J) quantification of cells in the S-G2-M phases (for stimulated T cells) are shown (n = 6 biological replicates from two donors). P values: 1, 0.29, 0.0065, 0.17, 0.0051, 1, 0.13, 0.55, 0.0004, 0.98, 0.0088, 0.68, 0.91, 0.7, 1 (left to right). Statistical significance for panels FIG. 7G and FIG. 7I: one way ANOVA with Dunnett`s multiple comparisons test * p <0.05, ** p < 0.01, *** p < 0.001, **** p < 0.0001. Error bars indicate SEM.

FIG. 8A – FIG. 8E show functional response of ORF-overexpressing T cells. (FIG. 8A) Quantitative expression of CD25 or CD154 following restimulation. A minimum of two donors was tested in triplicate per gene. Only genes that significant increase T cell proliferation in $CD4^+$, $CD8^+$ or both T cell subsets are shown. Mean and SEM are shown. (FIG. 8B, FIG. 8C) Sensitivity to antigen dose. T cells were incubated with indicated anti-CD3 antibody concentrations for 24 h and the amount of secreted IFNγ was quantified. Representative dose-response curve fitting (FIG. 8B) and IC_{50} quantifications (FIG. 8C) are shown (n = 2 biological replicates). (FIG. 8D) Quantification of secreted IL-2 and IFNγ in T cells incubated alone or with CD3/CD28 antibodies for 24 h. Representative data from one out of four donors (n = 3 biological replicates) are shown. (FIG. 8E) Multiplexed quantification of selected secreted cytokines and chemokines by ORF-transduced T cells after 24 h of CD3/CD28 stimulation. Means of duplicate measurements (from independent samples) z-score normalized to tNGFR are shown.

FIG. 9A – FIG. 9J show OverCITE-seq identifies ORFs and their transcriptional effects. (FIG. 9A) Quality parameters of cells as identified by gel bead barcodes. Negative, singlets and doublets are assigned based on cell hashing. (FIG. 9B) Proportion of stimulated and resting T cells among cells assigned to each ORF. Chi-squared test p-values are shown for ORFs with significantly shifted (uneven) distributions of stimulated and rested cells. (FIG. 9C) Cell-cycle corrected scaled expression of the overexpressed gene in the cells transduced with the respective ORF and negative control (tNGFR). Two-sided Wilcoxon test p-values shown above the violin plots indicate the statistical significance of gene expression level between specific ORF and tNGFR-transduced T cells. Box shows 25--75 percentile with a line at the median; whiskers extend to maximum and minimum values. N = 71 (ADA), 147 (AHCY), 190 (AHNAK), 119 (AKR1C4), 124 (ATF6B), 179 (BATF), 137 (CALML3), 189 (CDK1), 129 (CDK2), 236 (CLIC1), 84 (CRLF2), 91 (CXCL12), 88 (CYP27A1), 129 (DBI), 26 (DCLRE1B), 261 (DUPD1), 25 (FOSB), 119 (GPD1), 124 (GPN3), 199 (IFNL2), 60 (IL12B), 70 (IL1RN), 156 (ITM2A), 74 (LTBR), 88 (MRPL18), 167 (MRPL51), 107 (MS4A3), 69 (NFYB), 355 (NGFR), 261 (RAN), 182 (SLC10A7), and 56 (ZNF830) single cells. (FIG. 9D) Expression of all ORF genes by cells assigned each ORF. Each row is z-score normalized. (FIG. 9E) Distribution of individual ORF frequencies in clusters. Numbers of ORF cells and the chi-squared test residuals are displayed. Chi-squared test p-values indicating whether ORF distribution in each cluster significantly differs from overall ORF distribution are shown on top of the plot. Proportions of stimulated and resting T cells in each cluster are shown underneath the cluster label. (FIG. 9F, FIG. 9G) Spearman correlations between transcriptional profiles of selected ORF cells in resting (FIG. 9F) and stimulated (FIG. 9G) populations. (FIG. 9H) Fold change of top differentially expressed genes between cells with the indicated ORFs in resting and stimulated T cells. For each

condition, the ORFs with the strongest transcriptional changes (compared to tNGFR cells) are shown. (FIG. 9I) Differential gene expression in stimulated ORF T cells compared to resting T cells. Genes with significant expression changes in at least one ORF are shown (DESeq2 adjusted $p < 0.05$). For all genes, we display $\log_2$ fold-change of each ORF(stimulated) to tNGFR (resting), normalized to $\log_2$ fold-change of tNGFR (stimulated) to tNGFR (resting). Genes of interest in each cluster are labelled. (FIG. 9J) Mean TCR clonotype diversity in ORF cells.

FIG. 10A – FIG. 10M show functional analysis of *LTBR* overexpression in T cells. (FIG. 10A) *LTBR* expression in the indicated human primary tissues from the Genotype-Tissue Expression (GTEx) project v8[75] ($n = 948$ donors). Box shows 25–75 percentile with a line at the median. (FIG. 10B) *LTBR* expression in peripheral blood mononuclear cells (PBMCs) from 31,021 cells from 2 donors[76]. Cell types indicated are derived from Harmony tSNE clustering of single-cell transcriptomes. (FIG. 10C) Overlap between significantly upregulated genes in LTBR cells compared to tNGFR cells identified in single-cell or bulk RNA-seq. (FIG. 10D, FIG. 10E) TCF1 expression in LTBR or tNGFR transduced T cells. (FIG. 10D) Representative histograms of TCF1 expression and the gate for TCF1+ cells (dashed line) are shown, as well as (FIG. 10E) quantification of $TCF1^+$ cells ($n = 3$ biological replicates). (FIG. 10F – FIG. 10H) ICAM-1, CD70, CD74, and MHC-II expression in LTBR and tNGFR T cells. Representative histograms (FIG. 10F), quantification (FIG. 10G) in $n = 3$ donors ($CD8^+$) or $n = 4$ donors ($CD4^+$) and time course (FIG. 10H) of expression in LTBR and tNGFR cells after CD3/CD28 stimulation ($n = 3$ biological replicates). (FIG. 10I) Differentiation phenotype of NGFR and LTBR transduced T cells ($n = 4$ donors, $CD4^+$ and $CD8^+$ separately). CM: Central memory. EM: Effector memory. Differentiation was defined based on CD45RO and CCR7 expression (naive: $CD45RO^{neg}$ $CCR7^+$, CM: $CD45RO^+$ $CCR7^+$, EM: $CD45RO^+$ $CCR7^{neg}$, effector $CD45RO^{neg}$ $CCR7^{neg}$). (FIG. 10J) Representative dot plots of T cell viability after CD3/CD28 stimulation. Viable cells are in the lower left quadrant. (FIG. 10K) Cell viability of $CD4^+$ T cells transduced with LTBR or tNGFR lentivirus, either restimulated with CD3/CD28 for four days or left unstimulated ($n = 2$ donors with 3 biological replicates each). (FIG. 10L, FIG. 10M) LTBR and tNGFR cells were stimulated with a 3:1 excess of CD3/CD28 beads every three days for up to three rounds of stimulation. Following repeated stimulation, expression of TIM-3 and LAG-3 (FIG. 10L) was measured in resting cells, and secretion of IFNγ and IL2 (FIG. 10M) was measured in restimulated cells ($n = 3$ biological replicates). Statistical significance for panels FIG. 10E, FIG. 10I, and FIG. 10K: two-sided unpaired *t*-test; for panel FIG. 10G: two-sided paired *t*-test. Error bars indicate SEM.

FIG. 11A – FIG. 11K show LTBR ligands and expression of LTBR via mRNA or with deletion and point mutants. (FIG. 11A) IL2 secretion after 24 h stimulation with CD3/CD28 antibodies. Where indicated, recombinant soluble LTA (1 ng/mL) or LIGHT (10 ng/mL) were

added together with CD3/CD28 antibodies. $CD4^+$ T cells from one donor were tested in triplicate. (FIG. 11B, FIG. 11C) $CD4^+$ and $CD8^+$ T cells from two donors were co-incubated for 24 h with CD3/CD28 antibodies or recombinant soluble LTA or LIGHT and then IL2 (FIG. 11B) and IFNγ (FIG. 11C) were measured. (n = 3 biological replicates). (FIG. 10D, FIG. 10E) Differentiation phenotype (FIG. 10D) or proliferation (FIG. 10E) after restimulation of tNGFR and LTBR transduced T cells (n = 3 biological replicates) incubated either with IL2 alone or with LTA (1 ng/mL) or LIGHT (10 ng/mL) for the duration of culture. CM: Central memory. EM: Effector memory. Unpaired two-sided t-test p values are shown. (FIG. 11F, FIG. 11I) Transient LTBR or tNGFR expression via mRNA nucleofection (FIG. 101F). T cells were either nucleofected with LTBR or tNGFR mRNA (n = 3 biological replicates), and the surface expression of LTBR (FIG. 11G), tNGFR (FIG. 11H) or four genes upregulated in LTBR cells (FIG. 11I) was monitored over 21 days. At each timepoint the expression of target genes was normalized to matched tNGFR control. (FIG. 11J) Schematic representation of FLAG-tagged LTBR mutants. (FIG. 11K) LTBR and FLAG expression in T cells transduced with LTBR mutants. Error bars indicate SEM.

FIG. 12A – FIG. 12I show chromatin accessibility in LTBR T cells. (FIG. 12A) Principal component (PC) analysis of global accessible chromatin regions of LTBR and tNGFR T cells, either resting or stimulated with CD3/CD28 for 24 h. (FIG. 12B) Differentially accessible chromatin regions between stimulated and resting tNGFR, stimulated and resting LTBR, resting LTBR and resting tNGFR, and stimulated LTBR and stimulated tNGFR. Numbers of peaks gained/lost are shown (using absolute $\log_2$ fold change of 1 and adjusted p value < 0.1 as cut-off). (FIG. 12C, FIG. 12D) Changes in chromatin accessibility (FIG. 12C) for differentially expressed (adjusted $p < 0.05$) genes or in gene expression (FIG. 12D) for differentially accessible (adjusted $p < 0.05$) regions. Two-sided t-test p values are shown. Box shows 25–75 percentile with a line at the median; whiskers extend to 1.5 × interquartile range. N = 614 genes (FIG. 12C) or genomic regions (FIG. 12D). (FIG. 12E, FIG. 12F) Chromatin accessibility profiles at loci more (FIG. 12E) or less open (FIG. 12F) in LTBR compared to tNGFR cells, resting or stimulated for 24 h. The y-axis represents normalized reads (scale: 0–860 for *BATF3*, 0–1950 for *IL13*, 0–1230 for *TRAF1*, 0–1000 for *TNFSF4*, 0–300 for *PDCD1*, 0–2350 for *LAG3*). (FIG. 12G) Chromatin accessibility in resting or stimulated LTBR and tNGFR cells. Each row represents a peak significantly enriched in LTBR over matched tNGFR control ($\log_2$ fold change > 1, DESeq2 adjusted p value < 0.05). Peaks were clustered using k-means clustering and selected genes at/near peaks from each cluster are indicated. (FIG. 12H) Correlations for each ATAC sample (biological replicate) based on the bias-corrected deviations. (FIG. 12I) Top transcription factor (TF) motifs enriched in the differentially accessible chromatin regions in resting LTBR cells compared to resting tNGFR cells.

FIG. 13A – FIG. 13P show proteomic and functional genomic assays of NF-κB activation. (FIG. 13A) Phospho-RELA staining by intracellular flow cytometry in LTBR and tNGFR cells. Gating for identification of phospho-RELA+ cells is shown. (FIG. 13B, FIG. 13C) Western blot quantification of key proteins in the NF-κB pathway in LTBR and tNGFR cells, resting or stimulated with CD3/CD28 for 15 min. Representative gels (FIG. 13B) or quantification of band intensity relative to GAPHD (FIG. 13C) are shown (n = 3 biological replicates). Unpaired two-sided t test p values are shown. (FIG. 13D) Representation of the LTBR signaling pathway. Each gene is colored based on the differential expression in LTBR over matched tNGFR cells ($CD4^+$ and $CD8^+$ T cells, resting or stimulated for 24 h). (FIG. 13E – FIG. 13G) Simultaneous gene knockout via CRISPR and ORF overexpression. T cells were transduced with a lentiviral vector co-expressing a single guide RNA (sgRNA) and the LTBR ORF. After transduction, Cas9 protein was delivered via nucleofection. (FIG. 13F) Representative expression of target genes in LTBR cells co-expressing an sgRNA targeting *B2M*, an essential component of the MHC-I complex, or *TRBC1/2*, an essential component of the αβ TCR. (FIG. 13G) Quantification of IFNγ after restimulation (n = 3 sgRNAs). (FIG. 13H – FIG. 13O) Representative protein-level based quantification of gene knockout efficiency. Representative histograms (FIG. 13H, FIG. 13J, FIG. 13L) and quantification of relative expression levels of LTA, LIGHT, and RELA (FIG. 13I, FIG. 13K, FIG. 13M) are shown (n = 3 sgRNAs). Dashed lines represent gates used to enumerate cells expressing a given protein. Representative gel (FIG. 13N) and quantification of RELB expression (FIG. 13O) are shown (n = 3 sgRNAs for RELB and 2 non-targeting control sgRNAs). (FIG. 13P) Identification of 274 genes identified as enriched in both $CD4^+$ and $CD8^+$ T cells transduced with LTBR over matched tNGFR controls ("core LTBR" genes). Error bars indicate SEM.

FIG. 14A – FIG. 14P show co-delivery of ORFs with CD19-targeting CARs. (FIG. 14A) Transduction efficiency of CAR+ORF lentiviral vectors or ORF alone (n = 4 biological replicates). (FIG. 14B, FIG. 14C) CAR expression level as determined by staining with anti-mouse Fab $F(ab')_2$. Representative histograms (FIG. 14B) and quantification of CAR expression relative to tNGFR (FIG. 14C) is shown for two healthy donors and two patients with diffuse large B cell lymphoma (DLBCL). (FIG. 14D) Expansion curves of CAR+ORF transduced T cells (n = 4 biological replicates). (FIG. 14E) LTBR expression in autologous $CD14^+$ monocytes and T cells transduced with LTBR alone or CAR+LTBR. (FIG. 14F – FIG. 14I) Expression of ICAM-1 (FIG. 14F), CD70 (FIG. 14G), CD74 (FIG. 14H) and MHC-II (FIG. 14I) by T cells transduced with LTBR ORF only, CAR + LTBR or CAR + tNGFR. All data are normalized to tNGFR only (no CAR). Unpaired two-sided t test p values are shown. (FIG. 14J – FIG. 14M) Expression of exhaustion markers PD-1 (FIG. 14J), TIM-3 (FIG. 14K), LAG-3 (FIG. 14L) and CD39 (FIG.

14M) in CAR+ORF T cells. (FIG. 14N) Differentiation phenotype of CAR+ORF T cells. CM: Central memory. EM: Effector memory. Differentiation was defined based on CD45RO and CCR7 expression (naive: $CD45RO^{neg}$ $CCR7^{+}$, CM: $CD45RO^{+}CCR7^{+}$, EM: $CD45RO^{+}$ $CCR7^{neg}$, effector $CD45RO^{neg}$ $CCR7^{neg}$). (FIG. 14O, FIG. 14P) Expression of activation markers CD25 (FIG. 14O) and CD69 (FIG. 14P) in CAR+ORF T cells incubated alone or with Nalm6 cells for 24 h. Error bars indicate SEM. $N = 3$ biological replicates, unless indicated otherwise.

FIG. 15A – FIG. 15P show top-ranked genes from the ORF screen boost antigen-specific T cell responses. (FIG. 15A, FIG. 15B) Co-delivery of anti-CD19 CARs and ORFs to T cells from healthy donors. (FIG. 15A) IFNγ and (FIG. 15B) IL2 secretion after overnight co-incubation of $CD4^{+}$ T cells with Nalm6 cells at 1:1 ratio ($n = 3$ biological replicates, representative of two donors). (FIG. 15C, FIG. 15D) IFNγ (FIG. 15C) or IL-2 (FIG. 15D) secretion by CAR+ORF or ORF only T cells co-incubated for 24 h either alone or with Nalm6 cells. (FIG. 15E) Cytotoxicity of 19-BBz CAR T cells expressing tNGFR or LTBR ORF after co-incubation with Nalm6 GFP cells. (FIG. 15F) Quantification of Nalm6 clearance (relative to Nalm6 co-incubated with untransduced T cells) for CAR+ORF or ORF alone T cells at different effector:target ratios. Unpaired two-sided *t*-test *p* values: 0.011, 1.3x10−4, 0.072, 0.02, 0.021, 0.52, 0.087, 1, 0.51 (left to right). (FIG. 15G) Representative images of T cells transduced with 19-28z CAR and NGFR or LTBR, co-incubated with $CD19^{+}$ Nalm6 GFP cells for 48 h at 1:1 ratio. Scale bar: 200 μm. (FIG. 15H – FIG. 15J) Repeated stimulation of CAR+ORF T cells with Nalm6 cells. IL-2 secretion (FIG. 15I), or Nalm6 survival (FIG. 15J), by 19-BBz CAR LTBR or tNGFR T cells re-challenged with Nalm6 after repeated stimulation with Nalm6 cells every three days, for up to three rounds of stimulation. (FIG. 15K) Secretion of cytokines IL2 and IFNγ by CAR/LTBR or CAR/tNGFR T cells from two patients with DLBCL after overnight incubation with Nalm6 target cells. Two-sided paired *t*-test *p* value is shown. (FIG. 15L) Representative staining of ORF-transduced T cells endogenously expressing Vγ9Vδ2 TCR. (FIG. 15M) Quantification of ORF-transduced T cells expressing Vγ9Vδ2 TCR. (FIG. 15N, FIG. 15O) IL2 (FIG. 15N) or IFNγ (FIG. 15O) secretion after 24 h co-incubation of ORF transduced Vγ9Vδ2 T cells with leukemia cell lines. (FIG. 15P) IL2 or IFNγ secretion after 24 h co-incubation of ORF transduced Vγ9Vδ2 T cells with BxPC3, a pancreatic ductal adenocarcinoma cell line. Cell lines in panels (FIG. 15N – FIG. 15P) were pre-treated with zoledronic acid prior to co-incubation. Error bars indicate SEM. $N = 3$ biological replicates are shown, unless indicated otherwise.

FIG. 16A – FIG 16F show Top-ranked genes improve antigen-specific CAR T cell responses in solid tumor. (FIG. 16A) Codelivery of anti-mesothelin CARs and ORFs to T cells from healthy donors. (FIG. 16B – FIG. 16D) Secretion of cytokines IFNγ and IL2 by CD4+ and CD8+ T cells co-transduced with anti-mesothelin CARs and ORF, after an overnight co-

incubation with a mesothelin-high cell line Capan-2 (FIG. 16B, FIG. 16C) or mesothelin-low cell line BxPC3 (FIG. 16D). No specific cytokine secretion was observed in T cells incubated alone. *N* = 3 biological replicates. Dashed line indicated the level of cytokine secretion in regular CAR T cells (i.e., co-expressing tNGFR). (FIG. 16E, FIG. 16F) Killing of GFP+ mesothelin-high Capan-2 or mesothelin-low BxPC3 after co-incubation with engineered CAR T cells at 1:2 T cell to cancer cell ratio for 48 h. Cancer cell killing was normalized by dividing the integrated GFP signal in wells containing regular CAR T cells (i.e. co-expressing tNGFR) by the integrated GFP signal in specified samples. Ratio above one indicates higher killing, i.e. lower GFP signal in specified samples (and thus lower number of cancer cells) than in matched CAR control (CAR + tNGFR). WT or no CAR = untransduced T cells.

FIG. 17A – FIG. 17D show Top-ranked genes improve antigen-specific TCR T cell responses in solid tumor. (FIG. 17A) Codelivery of anti-NY-ESO-1 TCR and ORFs to T cells from healthy donors. (FIG. 17B, FIG. 17C) Secretion of cytokines IFNγ and IL-2 by CD8+ T cells co-transduced with anti-NY-ESO-1 TCR and ORF, after an overnight coincubation with a melanoma cell line A375. No specific cytokine secretion was observed in T cells incubated alone. N = 3 biological replicates. Dashed line indicated the level of cytokine secretion in regular TCR T cells (i.e., co-expressing tNGFR). (FIG. 17E, FIG. 17F) Killing of GFP+ A375 cells co-incubation with engineered TCR T cells at 1:1 T cell to cancer cell ratio for 48 h. Cancer cell killing was normalized by dividing the integrated GFP signal in wells containing only A375 cells but no T cells by the integrated GFP signal in specified samples. No TCR = untransduced T cells.

FIG. 18A – FIG. 18G provide an overview of OverCITE-seq.

FIG. 19 is a listing of the clinical trials relating to chimeric antigen receptors available on clinicaltrials.gov.

FIG. 20 is a listing of the clinical trials relating to T cell receptors available on clinicaltrials.gov.

FIG. 21A – FIG. 21N show insertion of the intracellular domain of LTBR into the CAR signaling domains results in superior efficacy. (FIG. 21A) Schematic representation of anti-CD19 CARs utilizing the CD28 costimulatory domain. (FIG. 21B) Schematic representation of anti-CD19 CARs utilizing the 41-BB costimulatory domain. (FIG. 21C, FIG. 21D) Surface expression of the CAR in T cells transduced with the constructs shown in FIG. 21A and FIG. 21B, respectively. No CAR indicates untransduced T cells. (FIG. 21E, FIG. 21F) Expression of LTBR-induced genes CD54 (also known as ICAM-1) and CD74 in resting T cells transduced with constructs shown in FIG. 21A and FIG. 21B, respectively. Surface expression was normalized to the matched control (CAR T cells co-expressing tNGFR). *N* = 2 individually transduced samples (CD4+ and CD8+ T cells). (FIG. 21G, FIG. 21H) Differentiation of T cells transduced with

constructs shown in FIG. 21A and FIG. 21B, respectively (naïve: CD45RO- CCR7+, central memory [CM]: CD45RO+ CCR7+, effector memory [EM]: CD45RO+ CCR7-, effector: CD45RO- CCR7-). (FIG. 21I – FIG. 21L) Secretion of cytokines IFNγ and IL2 by CD4+ and CD8+ T cells transduced with constructs shown in FIG. 21A and FIG. 21B, respectively, after an overnight co-incubation with a CD19+ leukemia cell line Nalm6. No specific cytokine secretion was observed in T cells incubated alone. *N* = 3 biological replicates. Dashed line indicated the level of cytokine secretion in regular CAR T cells (i.e. co-expressing tNGFR). (FIG. 21M, FIG. 21N) Killing of GFP+ CD19+ leukemia cell line Nalm6 after co-incubation with engineered CAR T cells at high (1:2 T cell to cancer cell ratio) or low (1:8 T cell to cancer cell ratio) for 48 h or 96 h. Cancer cell killing was normalized by dividing the integrated GFP signal in wells containing regular CAR T cells (i.e. coexpressing tNGFR) by the integrated GFP signal in specified samples. Ratio above one indicates higher killing, i.e. lower GFP signal in specified samples (and thus lower number of Nalm6 cancer cells) than in matched CAR control (CAR + tNGFR). WT or no CAR = untransduced T cells.

FIG. 22A – FIG. 22C show LTBR potentiates the activity of a 1st generation CAR. (FIG. 22A) Schematic representation of anti-CD19 CARs (generation 0 – no signaling domains, 1st generation – only CD3z, 2nd generation – 4-1BB and CD3z) co-expressed together with tNGFR (negative control) or LTBR. (FIG. 22B, FIG. 22C) Secretion of cytokines IFNγ and IL2 by CD4+ and CD8+ T cells transduced constructs shown in FIG. 22A after an overnight co-incubation with a CD19+ leukemia cell line Nalm6. No specific cytokine secretion was observed in T cells incubated alone. *N* = 3 biological replicates. Dashed line indicated the level of cytokine secretion in regular 2nd generation CAR T cells (i.e., co-expressing tNGFR). WT – untransduced T cells.

FIG. 23A – FIG. 23B show extracellular LTBR potentiates T cell function when fused to the stalk, transmembrane and signaling domains of a 2nd generation CAR. (FIG. 23A) Schematic representation of constructs tested. (FIG. 23B) Secretion of cytokines IFNγ and IL2 by CD4+ and CD8+ T cells transduced constructs shown in FIG. 23A after an overnight co-incubation with CD3 and CD28 antibodies. No specific cytokine secretion was observed in T cells incubated alone. *N* = 2 biological replicates. Dashed line (where applicable) shows cytokine secretion in untransduced (WT – wild type) T cells.

FIG. 24A – FIG. 24E CARs with only the intracellular LTBR signaling domain boost T cell response to TCR stimulation and activate the NFκB pathway. (FIG. 24A) Schematic representation of CAR constructs composed of the antigen targeting moiety, a stalk (CD8 or CD28), a transmembrane domain derived either from the same protein as the stalk or from LTBR, and the intracellular domain of LTBR. (FIG. 24B) Schematic representation of 2nd generation CARs or CARs lacking any signaling domain, co-expressed with tNGFR (negative control) or

LTBR. (FIG. 24C) Secretion of cytokines IFNγ and IL2 by CD4+ and CD8+ T cells transduced constructs shown in FIG. 24A and FIG. 24B after an overnight co-incubation with CD3 and CD28 antibodies. No specific cytokine secretion was observed in T cells incubated alone. *N* = 3 biological replicates. Dashed line (where applicable) shows cytokine secretion in T cells expressing only the anti-CD19 targeting moiety but no signaling domains (19-CD8 + tNGFR). WT – untransduced (wild-type) cells. (FIG. 24D) Expression of CD74 either on resting T cells or T cells co-incubated with CD19+ target cells overnight. Dashed lines show CD74 expression in T cells expressing only the anti-CD19 targeting moiety but no signaling domains (19-CD8 + tNGFR) – incubated alone or with target cells. WT – untransduced (wild-type) cells.

FIG. 25A – FIG. 25C show schematic representations of incorporating LTBR into the TCR complex. (FIG. 25A) αβTCR designs; (FIG. 25A) γδTCR designs; (FIG. 25A) αβT cell co-receptor designs.

FIG. 26A – FIG. 26K show LTBR co-delivery improves antitumor activity of B7-H3 CAR T cells. FIG. 26A shows differentiation of transduced and untransduced T cells (naïve: CD45RO- CCR7+, central memory: CD45RO+ CCR7+, effector memory: CD45RO+ CCR7-, effector: CD45RO- CCR7-). Expression of surface markers CD54 (FIG. 26B) and CD74 (FIG. 26C). *n* = 3. Secretion of IFNγ (FIG. 26D) or IL2 (FIG. 26E) after overnight co-incubation of engineered T cells with B7-H3+ cell lines BT12, BT16 and A375, and a B7-H3^{negative} cell line Nalm6. *n* = 3. Killing of GFP+ B7-H3+ cell lines BT12, BT16 and A375 (FIG. 26F) or GFP+ B7-H3^{negative} cell line Nalm6 (FIG. 26G) after co-incubation with engineered CAR T cells at 2:1 T cell to cancer cell ratio. FIG. 26H – FIG. 26K show in vivo testing of B7-H3 CAR T cells in NSG mice implanted with A375 cells in the left flank. Due to the aggressive tumor growth in the majority of animals, the experiment was terminated on day 25. (FIG. 26H) Experimental design. On day 13 post tumor inoculation, tumor volume was measured using calipers. Based on the tumor burden, mice were staged into five groups (*n* = 4-5 mice per group) so that there was no difference in median burden between groups. After staging, mice were injected with 1:1 mix of human CD4 and CD8 T cells, either untransduced or transduced with B7-H3 CAR and control gene tNGFR or LTBR. High dose = 5 million T cells per mouse; low dose = 1 million T cells per mouse. (FIG. 26I) Body weight changes after tumor implantation. (FIG. 26J) Mean tumor size per group. Mice were removed from the study and euthanized once the tumor exceeded 200 mm^3 volume or at veterinarian's, blinded to the study design, discretion. (FIG. 26K) Tumor size in individual mice.

FIG. 27A – FIG. 27G show CAR fusions with truncated LTBR intracellular tail. (FIG. 27A) Literature-based annotation of the functional elements within the LTBR signaling tail. Numbers indicate amino acid numbering as per https://www.uniprot.org/uniprotkb/P36941. (FIG.

27B) Schematic depicting fusion of LTBR intracellular tail to the C-terminus of a 19-28-z CAR. For V1-V9 variants of the intracellular tail, dashed lines indicate which part of LTBR protein was included in the fusion with a CAR. All sequences (amino acid and protein) are listed in the sequence listing. (FIG. 27C) Surface expression of 19-28-z CAR in transduced T cells. (FIG. 27D) Differentiation of transduced and untransduced T cells (naïve: CD45RO- CCR7+, central memory: CD45RO+ CCR7+, effector memory: CD45RO+ CCR7-, effector: CD45RO- CCR7-). (FIG. 27E) Intracellular/nuclear expression of TCF1. The relative levels of TCF1 were normalized to the signal in 19-28-z + tNGFR CAR T cells. (FIG. 27F) Surface expression of CD54 and CD74, normalized to the signal in 19-28-z + tNGFR CAR T cells. (FIG. 27G) Secretion of IL2 and IFNγ cytokines upon overnight co-incubation of anti-CD19 CAR T cells with CD19+ leukemia cells Nalm6. Absolute quantities of secreted cytokines were normalized to the quantity secreted by 19-28-z + tNGFR CAR T cells.

FIG. 28A – FIG. 28N show LTBR signaling tail fusion to a mesothelin targeting CAR. (FIG. 28A) Construct designs. (FIG. 28B) CAR surface expression on transduced T cells. (FIG. 28C) CAR T cell proliferation in response to antigenic stimulation. T cells were isolated, transduced with lentivirus and selected. 14 days after isolation CAR T cells were co-incubated with mesothelin+ PDAC cell line Capan-2 at 1:1 ratio (n = 3). T cells were periodically counted and split to adjust to a 0.5 x 10^6 cell/mL density. (FIG. 28D) Killing of GFP+ mesothelin+ Capan-2 cell line after co-incubation with engineered CAR T cells at 1:4 T cell to cancer cell ratio. (FIG. 28E) Cytokine secretion after 24 h co-incubation of engineered CAR T cells with mesothelin+ Capan-2 cell line. (FIG. 28F) Surface expression of CD54 and CD74 on engineered CD4 and CD8 T cells. Median fluorescence intensity of staining for each sample was z-score normalized by subtraction to the median fluorescence intensity of the corresponding control (either Meso-BB-z or Meso-28-z) and divided by the standard deviation of the sample group. (FIG. 28G) Intracellular expression of TCF1 in engineered T cells. Median fluorescence intensity of staining for each sample was z-score normalized by subtraction to the median fluorescence intensity of the corresponding control (either Meso-BB-z or Meso-28-z) and divided by the standard deviation of the sample group. (FIG. 28H) Cytokine secretion after 24 h co-incubation of engineered CAR T cells pan-T cell stimulation using CD3/CD28. (FIG. 28I) Schematic depicting sequential co-transduction of T cells with two lentiviral particles, one encoding a mesothelin targeting CAR and the other a natural full length LTBR or a fusion of LTBR intracellular domain with a CAR. (FIG. 28J) CAR surface expression on sequentially transduced T cells. (FIG. 28K) LTBR surface expression on sequentially transduced T cells. (FIG. 28L) Surface expression of CD54 and CD74 on sequentially transduced CD4 and CD8 T cells, normalized to corresponding untransduced T cells. (FIG. 28M, FIG. 28N) IFNγ (FIG. 28M) or

IL2 (FIG. 28N) secretion after 24 h co-incubation of sequentially transduced CAR T cells with mesothelin+ Capan-2 cell line.

FIG. 29A – FIG. 29I show LTBR signaling tail fusion to the members of the TCR-CD3 complex. (FIG. 29A) Construct designs for TCR fusions. (FIG. 29B) TCR surface expression on transduced T cells. (FIG. 29C) Surface expression of CD54 and CD74 on transduced T cells. (FIG. 29D) Cytokine secretion upon 24 h co-incubation of engineered T cells with NY-ESO-1+ melanoma line A375. (FIG. 29E) Construct designs for CD3 fusions. (FIG. 29F) Schematic depiction of sequential transduction of T cells with lentiviral particles encoding an NY-ESO-1 TCR and CD3 genes, natural or fused on the C-terminus with the LTBR signaling tail. (FIG. 29G) TCR surface expression on sequentially transduced T cells. (FIG. 29H) Surface expression of CD54 and CD74 on sequentially transduced T cells. (FIG. 29I) Cytokine secretion upon 24 h co-incubation of sequentially transduced T cells with NY-ESO-1+ melanoma line A375.

FIG. 30A – FIG. 30G show LTBR signaling tail fusion to the members of the CD8 complex. (FIG. 30A) Construct designs for CD8 fusions. (FIG. 30B) Schematic depiction of sequential transduction of T cells with an NY-ESO-1 TCR and CD8 genes, natural or fused with the LTBR intracellular tail. (FIG. 30C, FIG. 30D) Surface expression of CD54 (FIG. 30C) and CD74 (FIG. 30D) on transduced T cells. (FIG. 30E) Intracellular expression of TCF1 in transduced T cells. (FIG. 30F) Cytokine secretion upon 24 h co-incubation of engineered T cells with HLA-A2+ cell line HEK293T pulsed with indicated concentration of the NY-ESO-1 derived peptide epitope. (FIG. 30G) Antigen sensitivity of engineered T cells calculated based on the sigmoidal fitting of the levels of the indicated cytokine secretion as a function of peptide concentration. MFI – median fluorescence intensity.

FIG. 31 shows ORF library vector engineering. Lentivirus encoding puromycin resistance and a barcoded ORF library (as indicated) was produced in HEK293T cells, concentrated and used to transduce activated T cells. Two days after transduction, engineered T cells from each condition were split and one set was selected with puromycin while the other was treated with vehicle. After a two-day selection, T cells were counted and transduction efficiency was determined by dividing the live cell number in the condition treated with puromycin to the matched, untreated control. Dashed line indicates survival of untransduced T cells treated with puromycin.

DETAILED DESCRIPTION OF THE INVENTION

The engineering of autologous patient T cells for adoptive cell therapies has revolutionized the treatment of several types of cancer[1]. However, further improvements are needed to increase response and cure rates. Provided herein are modified T cells that include

nucleic acids encoding fusion proteins that include LTBR, or domains thereof. When overexpressed in T cells, LTBR induced profound transcriptional and epigenomic remodeling, leading to increased T cell effector functions and resistance to exhaustion in chronic stimulation settings through constitutive activation of the canonical NF-κB pathway. *LTBR* and other highly ranked genes improved the antigen-specific responses of chimeric antigen receptor T cells and γδ T cells, highlighting their potential for future cancer-agnostic therapies[5]. We provide improved CAR, TCR and related T cell therapies for treatment of cancer and other diseases.

Unless defined otherwise in this specification, technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs and by reference to published texts, which provide one skilled in the art with a general guide to many of the terms used in the present application.

As used throughout this specification and the claims, the terms "comprising", "containing", "including", and its variants are inclusive of other components, elements, integers, steps and the like. Conversely, the term "consisting" and its variants are exclusive of other components, elements, integers, steps and the like.

It is to be noted that the term "a" or "an", refers to one or more, for example, "T cell", is understood to represent one or more T cell(s). As such, the terms "a" (or "an"), "one or more," and "at least one" is used interchangeably herein.

As used herein, the term "about" means a variability of plus or minus 10% from the reference given, unless otherwise specified.

Furthermore, "and/or" where used herein is to be taken as specific disclosure of each of the two specified features or components with or without the other. Thus, the term "and/or" as used in a phrase such as "A and/or B" herein is intended to include "A and B," "A or B," "A" (alone), and "B" (alone). Likewise, the term "and/or" as used in a phrase such as "A, B, and/or C" is intended to encompass each of the following aspects: A, B, and C; A, B, or C; A or C; A or B; B or C; A and C; A and B; B and C; A (alone); B (alone); and C (alone).

The term "nucleic acid" or "polynucleotide" refers to deoxyribonucleic acids (DNA) or ribonucleic acids (RNA) and polymers thereof in either single- or double-stranded form. Unless specifically limited, the term encompasses nucleic acids containing known analogues of natural nucleotides that have similar binding properties as the reference nucleic acid and are metabolized in a manner similar to naturally occurring nucleotides. Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (e.g., degenerate codon substitutions), alleles, orthologs, SNPs, and complementary sequences as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions may be achieved by generating sequences in which the third position of one or more selected (or all) codons is

substituted with mixed-base and/or deoxyinosine residues (Batzer et al., Nucleic Acid Res. 19:5081 (1991); Ohtsuka et al, J. Biol. Chem. 260:2605-2608 (1985); and Rossolini et al., Mol. Cell. Probes 8:91-98 (1994)).

The terms "nucleic acid sequence," "nucleotide sequence," or "polynucleotide sequence" are used interchangeably and refer to a contiguous nucleic acid sequence. The sequence can be either single stranded or double stranded DNA or RNA, e.g., an mRNA.

Nucleic acids described herein can be cloned using routine molecular biology techniques, or generated de novo by DNA synthesis, which can be performed using routine procedures by service companies having business in the field of DNA synthesis and/or molecular cloning (e.g. GeneArt, GenScript, Life Technologies, Eurofins). The nucleic acid sequences encoding aspects of a CRISPR-Cas editing system described herein are assembled and placed into any suitable genetic element, e.g., naked DNA, phage, transposon, cosmid, episome, etc., which transfers the sequences carried thereon to a host cell, e.g., for generating non-viral delivery systems (e.g., RNA-based systems, naked DNA, or the like), or for generating viral vectors in a packaging host cell, and/or for delivery to a host cells in a subject. In one embodiment, the genetic element is a vector. In one embodiment, the genetic element is a plasmid. The methods used to make such engineered constructs are known to those with skill in nucleic acid manipulation and include genetic engineering, recombinant engineering, and synthetic techniques. See, e.g., Green and Sambrook, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring Harbor, NY (2012).

"Variants" of proteins or peptides as defined in the context of the present invention may be generated, having an amino acid sequence which differs from the original sequence in one or more mutation(s), such as one or more substituted, inserted and/or deleted amino acid(s). Preferably, these fragments and/or variants have the same biological function or specific activity compared to the full-length native protein, e.g., its specific inhibitory property. "Variants" of proteins or peptides as defined in the context of the present invention may comprise conservative amino acid substitution(s) compared to their native, i.e., non-mutated physiological, sequence. Substitutions in which amino acids, which originate from the same class, are exchanged for one another are called conservative substitutions. In particular, these are amino acids having aliphatic side chains, positively or negatively charged side chains, aromatic groups in the side chains or amino acids, the side chains of which can enter into hydrogen bonds, e.g., side chains which have a hydroxyl function. This means that e.g., an amino acid having a polar side chain is replaced by another amino acid having a likewise polar side chain, or, for example, an amino acid characterized by a hydrophobic side chain is substituted by another amino acid having a likewise hydrophobic side chain (e.g., serine (threonine) by threonine (serine) or leucine (isoleucine) by

isoleucine (leucine)). Insertions and substitutions are possible, in particular, at those sequence positions which cause no modification to the three-dimensional structure or do not affect the binding region. Modifications to a three-dimensional structure by insertion(s) or deletion(s) can easily be determined e.g., using CD spectra (circular dichroism spectra) (Urry, 1985, Absorption, Circular Dichroism and ORD of Polypeptides, in: Modern Physical Methods in Biochemistry, Neuberger et al. (ed.), Elsevier, Amsterdam). A variant may also include a non-natural amino acid.

A "variant" of a protein or peptide may have at least 70%, 75%, 80%, 85%, 90%, 95%, 98% or 99% amino acid identity over a stretch of 10, 20, 30, 50, 75, 100 or more amino acids of such protein or peptide, or over the full length of the protein or peptide.

The term "gene" can refer to a segment of DNA involved in producing or encoding a polypeptide chain. It may include regions preceding and following the coding region (leader and trailer) as well as intervening sequences (introns) between individual coding segments (exons).

As used herein, the terms "coding region" and "region encoding" and grammatical variants thereof, refer to an open reading frame (ORF) in a polynucleotide that upon expression yields a polypeptide or protein.

"Polypeptide," "peptide," and "protein" are used interchangeably herein to refer to a polymer of amino acid residues. As used herein, the terms encompass amino acid chains of any length, including full-length proteins, wherein the amino acid residues are linked by covalent peptide bonds.

The term "domain" refers to a region of the protein's polypeptide chain that is self-stabilizing and that folds independently from the rest of the protein. The protein domain need not be identical to the native protein from which it is derived, but may be a variant thereof, including a variant that has a deletion, truncation, etc.

The term "encoding" refers to the inherent property of specific sequences of nucleotides in a polynucleotide, such as a gene, a cDNA, or an mRNA, to serve as templates for synthesis of other polymers and macromolecules in biological processes having either a defined sequence of nucleotides (i.e., rRNA, tRNA, and mRNA) or a defined sequence of amino acids and the biological properties resulting therefrom. Thus, a gene, cDNA, or RNA, encodes a protein if transcription and translation of mRNA corresponding to that gene produces the protein in a cell or other biological system. Both the coding strand, the nucleotide sequence of which is identical to the mRNA sequence and is usually provided in sequence listings, and the non-coding strand, used as the template for transcription of a gene or cDNA, can be referred to as encoding the protein or other product of that gene or cDNA.

Unless otherwise specified, a "nucleic acid sequence encoding an amino acid sequence" includes all nucleic acid sequences that are degenerate versions of each other and that encode the same amino acid sequence. A nucleic acid sequence that encodes a protein or an RNA may also include introns to the extent that the nucleotide sequence encoding the protein may in some version contain an intron(s).

The term "expression" is used herein in its broadest meaning and comprises the production of RNA, of protein, or of both RNA and protein. Expression may be transient or may be stable.

The terms "expressing" and "overexpression" refer to increasing the expression of a gene or protein. The terms refer to an increase in expression, for example, in increase in the amount of mRNA or protein expressed in a T cell, other lymphocyte or host cell, of at least 10%, as compared to a reference control level, or an increase of least about 20%, or at least about 30%, or at least about 40%, or at least about 50%, or at least about 60%, or at least about 70%, or at least about 80%, or at least about 90%, or at least about 100%, or at least about 200%, or at least about 300% or at least about 400%. Various methods for expression and/or overexpression are known to those of skill in the art, and include, but are not limited to, stably or transiently introducing a exogenous polynucleotide encoding a fusion protein, TCR, or CAR to be expressed and/or overexpressed in the cell or inducing expression or overexpression of an endogenous gene encoding the protein in the cell.

The term "autologous" refers to any material derived from the same subject to whom it is later to be re-introduced.

The term "exogenous" refers to any material introduced from or produced outside an organism, cell, tissue or system.

The term "expression vector" refers to a vector comprising a recombinant polynucleotide comprising expression control sequences operatively linked to a nucleotide sequence to be expressed. An expression vector comprises sufficient cis-acting elements for expression; other elements for expression can be supplied by the host cell or in an in vitro expression system. Expression vectors include all those known in the art, such as cosmids, plasmids (e.g., naked or contained in liposomes) and viruses (e.g., lentiviruses, retroviruses, adenoviruses, and adeno-associated viruses) that incorporate the recombinant polynucleotide.

As used herein, an "expression cassette" refers to a nucleic acid molecule which encodes one or more ORFs or genes, e.g., an effector-enhancing gene, or a CAR or TCR or component thereof. An expression cassette also contains a promoter and may contain additional regulatory elements that control expression of one or more elements of a gene editing system in a host cell. In one embodiment, the expression cassette may be packaged into the capsid of a viral vector

(e.g., a viral particle). In one embodiment, such an expression cassette for generating a viral vector as described herein is flanked by packaging signals of the viral genome and other expression control sequences such as those described herein.

The term "regulatory element" or "regulatory sequence" refers to expression control sequences which are contiguous with the nucleic acid sequence of interest and expression control sequences that act in trans or at a distance to control the nucleic acid sequence of interest. As described herein, regulatory elements comprise but are not limited to: promoter; enhancer; transcription factor; transcription terminator; efficient RNA processing signals such as splicing and polyadenylation signals (polyA); sequences that stabilize cytoplasmic mRNA, for example Woodchuck Hepatitis Virus (WHP) Posttranscriptional Regulatory Element (WPRE); sequences that enhance translation efficiency (i.e., Kozak consensus sequence); sequences that enhance protein stability; and when desired, sequences that enhance secretion of the encoded product. Also, see Goeddel; Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, CA (1990). Regulatory sequences include those which direct constitutive expression of a nucleic acid sequence in many types of target cell and those which direct expression of the nucleic acid sequence only in certain target cells (e.g., tissue-specific regulatory sequences).

A "promoter" is defined as one or more a nucleic acid control sequences that direct transcription of a nucleic acid. As used herein, a promoter includes necessary nucleic acid sequences near the start site of transcription, such as, in the case of a polymerase II type promoter, a TATA element. A promoter also optionally includes distal enhancer or repressor elements, which can be located as much as several thousand base pairs from the start site of transcription. The term "constitutive" when referring to a promoter specifies a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a cell under most or all physiological conditions of the cell. The term "inducible" or "regulatable" when referring to a promoter specifies a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a cell substantially only when an inducer which corresponds to the promoter is present in the cell. In certain embodiments, the inducible promoter is activated in response to T cell stimulation. In certain embodiments, the promoter is an NFAT, AP1, NFκB, or IRF4 promoter. The term "tissue-specific" when referring to a promoter specifies a nucleotide sequence which, when operably linked with a polynucleotide encodes or specified by a gene, causes the gene product to be produced in a cell substantially only if the cell is a cell of the tissue type corresponding to the promoter. Additional promoter elements, e.g., enhancers, regulate the frequency of transcriptional initiation. Typically, these are located in the region 30-110 bp upstream of the start site, although

a number of promoters have been shown to contain functional elements downstream of the start site as well. The spacing between promoter elements frequently is flexible, so that promoter function is preserved when elements are inverted or moved relative to one another. In the thymidine kinase (tk) promoter, the spacing between promoter elements can be increased to 50 bp apart before activity begins to decline. Depending on the promoter, it appears that individual elements can function either cooperatively or independently to activate transcription. Exemplary promoters include the CMV IE gene, EF-1α., ubiquitin C, or phosphoglycerokinase (PGK) promoters.

The term "operably linked" refers to functional linkage between one or more regulatory sequences and a heterologous nucleic acid sequence resulting in expression of the latter. For example, a first nucleic acid sequence is operably linked with a second nucleic acid sequence when the first nucleic acid sequence is placed in a functional relationship with the second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Operably linked DNA sequences can be contiguous with each other and, where necessary to join two protein coding regions, are in the same reading frame.

The term "lentivirus" refers to a genus of the Retroviridae family. Lentiviruses are unique among the retroviruses in being able to infect non-dividing cells; they can deliver a significant amount of genetic information into the DNA of the host cell, so they are one of the most efficient methods of a gene delivery vector. HIV, SIV, and FIV are all examples of lentiviruses.

In certain embodiments, one or more genes are encoded by a nucleic acid sequence that is delivered to a host cell by a vector or a viral vector, of which many are known and available in the art. In one embodiment, provided is a vector comprising an expression cassette as described herein. In one embodiment, a vector is a non-viral vector. In another embodiment, a vector is a viral vector. A "viral vector" refers to a synthetic or artificial viral particle in which an expression cassette containing a nucleic acid sequence of interest is packaged in a viral capsid or envelope. Examples of viral vectors include but are not limited to lentivirus, adenoviruses, retroviruses (γ-retroviruses and lentiviruses), poxviruses, adeno-associated viruses (AAVs), baculoviruses, herpes simplex viruses. In one embodiment, the viral vector is replication defective. A "replication-defective virus" refers to a viral vector, wherein any viral genomic sequences also packaged within the viral capsid or envelope are replication-deficient, *i.e.*, they cannot generate progeny virions but retain the ability to infect cells.

The term "lentiviral vector" refers to a vector derived from at least a portion of a lentivirus genome, including especially a self-inactivating lentiviral vector as provided in Milone et al., Mol. Ther. 17(8): 1453-1464 (2009). Other examples of lentivirus vectors that may be used

in the clinic, include but are not limited to, e.g., the LENTIVECTOR® gene delivery technology from Oxford BioMedica, the LENTIMAX™ vector system from Lentigen and the like. Nonclinical types of lentiviral vectors are also available and would be known to one skilled in the art.

Provided herein, in one aspect, is an engineered lentiviral vector comprising the sequence of SEQ ID NO: 132, or a sequence sharing at least 90% identity with SEQ ID NO: 132. In certain embodiments, the sequence shares at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity with SEQ ID NO: 132. The engineered vector is useful for, inter alia, the ORF screens described herein. In certain embodiments, an open reading frame (ORF) for a gene of interest is inserted within the vector sequence. In certain embodiments, a barcode is inserted within the vector sequence. SEQ ID NO: 133 provides an exemplary embodiment in which various primer binding sites, meganuclease recognition sites for restriction digests, and cloning recombination sites have been inserted in the sequence at the site that the ORF and/or barcode can be inserted. Primer binding sites, restriction sites, cloning sites and the like can be included in addition to the ORF and/or barcode. In certain embodiments, the ORF and/or barcode is/are inserted after nucleotide 3291 of SEQ ID NO: 132.

In certain embodiments, the vector is a non-viral plasmid that comprises an expression cassette described herein, e.g., naked DNA, naked plasmid DNA, RNA, and mRNA; coupled with various compositions and nano particles, including, e.g., micelles, liposomes, cationic lipid - nucleic acid compositions, poly-glycan compositions and other polymers, lipid and/or cholesterol-based - nucleic acid conjugates, and other constructs such as are described herein. See, e.g., X. Su et al, Mol. Pharmaceutics, 2011, 8 (3), pp 774–787; web publication: March 21, 2011; WO2013/182683, WO 2010/053572 and WO 2012/170930, all of which are incorporated herein by reference.

Plasmids, other cloning and expression vectors, properties thereof, and constructing/manipulating methods thereof that can be used in accordance with the present invention are readily apparent to those of skill in the art. In one embodiment, an expression cassette as described herein is engineered into a suitable genetic element (a vector) useful for generating viral vectors and/or for introduction to a host cell, e.g., naked DNA, phage, transposon, cosmid, episome, etc., which transfers the sequences carried thereon. The selected vector may be delivered by any suitable method, including transfection, electroporation, liposome delivery, membrane fusion techniques, high velocity DNA-coated pellets, viral infection and protoplast fusion. The methods used to make such constructs are known to those with skill in nucleic acid manipulation and include genetic engineering, recombinant engineering, and

synthetic techniques. See, e.g., Sambrook et al, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring Harbor, NY.

The term "transfected" refers to a process by which exogenous nucleic acid is transferred or introduced into the host cell. A "transfected" cell is one which has been transfected with exogenous nucleic acid. The cell includes the primary subject cell and its progeny.

As used herein, "transient" refers to expression of a non-integrated transgene for a period of hours, days or weeks, wherein the period of time of expression is less than the period of time for expression of the gene if integrated into the genome or contained within a stable plasmid replicon in the host cell.

RNA or DNA can be introduced into target cells using any of a number of different methods, for instance, commercially available methods which include, but are not limited to, electroporation (Amaxa Nucleofector-II (Amaxa Biosystems, Cologne, Germany)), (ECM 830 (BTX) (Harvard Instruments, Boston, Mass.) or the Gene Pulser II (BioRad, Denver, Colo.), Multiporator (Eppendorf, Hamburg Germany), cationic liposome mediated transfection using lipofection, polymer encapsulation, peptide mediated transfection, or biolistic particle delivery systems such as "gene guns" (see, for example, Nishikawa, et al. Hum Gene Ther., 12(8):861-70 (2001).

As used herein, the term "subject" means a mammalian animal, including a human, a veterinary or farm animal, a domestic animal or pet, and animals normally used for clinical research. In one embodiment, the subject of these methods and compositions is a human. Still other suitable subjects include, without limitation, murine, rat, canine, feline, porcine, bovine, ovine, non-human primate and others. As used herein, the term "subject" is used interchangeably with "patient".

Compositions

Provided herein are compositions which include nucleic acids, expression cassettes, and/or lymphocytes which include coding sequences for certain genes (or fragments thereof), which have been shown to enhance T cell survival, proliferation and/or effector function (collectively referred to herein as an "effector-enhancing gene"). In certain embodiments, the effector-enhancing gene comprises any of the genes identified in Table 1, 2, or 3.

TABLE 1

gene_symbol							
RPLP1	EMC10	SFTPC	PSMB1	SEC61G	PRAP1	KLK11	TSPAN1
HDHD2	CCR4	PAFAH1B3	THRA	SNAPIN	CBX8	TMEM43	CELA1
DBI	RIMS3	RPL29	SLC37A4	IGHV7-81	FGL1	PRSS8	HEMK1
UBE2A	IFNL2	CZIB	HNRNPK	OXA1L	KIAA0930	SLC39A1	METTL7B
WDR70	GLYCTK	C11orf16	ASB6	F2RL1	AHNAK	KRTAP19-5	TPI1
AHSA1	POLG2	PRTN3	RRAGB	PFKFB4	PDLIM3	GPN3	PRSS48
ARMC7	OR1D5	UBE2D1	MAPK3	LRRC29	CD59	GJB7	MEIS3
PKLR	SZRD1	GTPBP8	HLA-DOA	SPPL2C	LTBR	VSTM1	EXOSC5
TIMMDC1	DYRK4	CRADD	SPIC	DHX40	SLC10A7	TIMP4	H5FX3
TRH	CUTA	CDK17	HADH	RAN	ACTL8	LIG3	OSM
NFYB	RNF186	RAB24	RPL14	KDSR	MEI1	C1orf210	GSTK1
SPATS1	ACSM5	TAZ	IFT81	IL27	GTF3C6	CEP43	RUVBL2
PRND	TAFA2	PDK4	TMEM44	NRBP2	RTBDN	FKBP1A	EDDM3A
TRMT12	TFF1	FNDC8	TLE1	UHMK1	RAD51C	ETFBKMT	TARBP2
LENG1	CLN6	CCDC137	GNPDA1	QTRT1	ZCCHC12	FBXO6	PGAP2
SMOC1	FBXO30	CST8	BAX	S100A8	VWC2L	RHEX	MAGEA12
BOLL	CLEC19A	NLRP5	LGALS12	PDXK	PRR19	TRAF2	PEX11A
VASH1	TMEM263	LRP5L	DAND5	SLC52A1	COMMD8	NOL6	CA12
CTPS2	CALML3	FHIT	LTA4H	UBL4B	OR10G3	SNURF	GPR37L1
TSHB	F2RL2	SNAPC5	TXN	MID2	ADAT2	RAB8A	EID3
BATF	DCT	DTNA	ELN	CNOT2	CALCB	MAB21L2	GRIK2
ACP2	PLPPR2	BDKRB2	IFITM3	IDH3B	SYS1	IFNA21	ADPRS
SULT1C4	ASMTL	TANK	RPL13A	IL10	PSG1	TMIGD1	SLC23A3
CDC42	FBXL2	SEMA4G	ARSJ	WAS	DPH1	H2AC6	ADH4
ZNF830	RNF11	PIEZO1	APTX	ALKBH3	LRRC71	IGSF10	H3C10

MMP2	ZMYM3	CD1B	RIT2	GOSR2	CDK2	HMHB1	TRPV2
YPEL4	CAMKMT	SLC39A4	CPSF4	RNF114	DCLRE1B	PLA2G1B	HOXA6
EXOSC1	GPHB5	VRK2	ADAM2	HLF	UBE2D4	KCNJ12	NCR3
SPRR2B	NMS	ENHO	APEX2	SRP9	RORA	KLK2	KLK15
HOGA1	HAAO	SWSAP1	TMEM205	OR10W1	STK25	PPP1R8	WDFY1
LARS2	WDTC1	RALB	CAPNS2	AKAP7	SLC4A4	CSRP1	ZCRB1
EDA	RASGEF1C	POU2F2	NELFE	TMEM107	TRIM36	TIMM8B	EMP3
CCNE1	NFIC	NNAT	S100A9	TMEM134	CENPW	POU4F3	S1PR3
SPAG11A	CHMP2A	ECT2	IFRD2	PWP1	MS4A3	FANCC	TOR1AIP2
MRFAP1L1	HCFC2	C1D	CSF3	CLIC1	CDA	PCP2	MRPS12
SKAP1	GPATCH11	MORN4	GPNMB	C5orf24	PGS1	TRIM74	SSX3
ANXA9	DUPD1	DCUN1D3	XAGE3	RBIS	SH3RF3	PPP1R2B	HEPACAM2
CYP27A1	FCF1	TESC	RPP30	EVA1C	GLT1D1	KCNA4	CTRB1
MRPL50	HSD17B7	IL1RN	APBB1IP	USP24	LHFPL5	HSD11B2	SLC7A11
TRIM51	OR1N2	GPD1	CRHBP	SYNGR2	SERPINB4	RSKR	PEX12
SLC1A7	HHLA3	DOK6	AFTPH	DDIT4	STAU2	TBCCD1	TMED9
RPL30	MC3R	FAM216A	ZNF232	GGCX	EIF1AY	SYT10	C16orf70
PLSCR1	RASGEF1A	GALNT3	H2AC14	ITM2A	GPR3	ATP5MPL	SLC25A48
LIN37	PDP2	XIAP	SELENOH	SUN5	YIF1A	TBRG4	TGIF1
MASP2	MIF4GD	PATE1	S100A11	EDC3	OR6B2	ALDH1A3	MRPL17
ENPP1	GTF2B	ANGPT4	CDCP2	P2RY6	KLRD1	POFUT1	PCMTD1
MAPRE3	CTRB2	HAVCR2	BCL7A	SLC25A39	PRDX5	TEX35	SOSTDC1
REEP4	ANAPC16	MYL4	CERS4	RAP1A	ZNF689	DECR2	TNFAIP8
COPS8	DHRSX	H2BC21	OR3A2	DRAP1	RASSF1	S100A7	CABLES1

gene_symbol							
TP53	CCL13	TUBB	IL31	GLYAT	TAAR5	LRRC25	GSK3B
ITIH1	CTSE	ASCL3	CSH1	IL23A	VGLL3	LAMTOR1	PODXL2
PPIC	LSM1	PTPN7	STPG2	ASB1	BRWD1	TPPP3	ACSM3
EXOSC4	PAGE5	MRPL18	HSPBAP1	TSPAN31	FUT10	DKC1	CGB2
TM2D2	AHCY	FAM71F2	RHBDD2	RRAGA	DPEP2	BANF2	FMO4
LYPD4	MGAT4D	NMU	CCBE1	SRGN	SDC4	CD244	TBC1D20
LDHC	HPCAL1	SNCB	BNIPL	OR52W1	MRPL51	DMAP1	RPL18
CISH	TRIM5	LRTM1	LAMP2	TMEM37	FAM180A	RSPO1	TWIST2
CGGBP1	PHF23	DEFB134	CHST4	DCK	MRPS21	THNSL1	RTL8C
GABRB1	IFNE	CD14	ESM1	TIRAP	ING3	PELI1	GDAP1
PACC1	CXCL12	SUMO3	PRG3	DAB1	SEC31A	CEP112	SAMSN1
PKIB	IQCD	PHPT1	LRRC8D	OR4K17	PSMB6	ENPP3	SNRK
NBR1	ETFA	UHRF2	OLFM1	RAB27B	TNFSF14	HEATR9	RNF5
MKNK1	SMAP1	BIN3	TAC1	SELENOW	NACA	PTCHD1	STX8
CPXM2	PTRH2	AGAP1	CA2	MATN1	PRR15L	WDR1	PELI2
IFTAP	PSMD4	CRIP1	C3AR1	DEFB132	VAMP2	GFAP	CRYBA1
HAUS1	SERAC1	SLC17A4	GUCA2A	ORM2	NAGK	SRSF12	OCEL1
WDR4	B3GAT3	TRAPPC6A	MRPL53	KRT14	OTX1	NEIL2	AK3
TMPRSS6	LAPTM5	GRPEL1	HMCES	GRID1	PRSS37	INSL5	EME1
SPINK9	WDR20	FOSB	GAK	NPY	SLC25A4	F11R	ABHD14B
AKR1C4	CKMT1A	SLC31A2	PPP2R5E	DEFB135	PAX9	CLEC3A	MOB3C
MLLT11	SLC14A1	WFDC3	DOK1	RNASEH2B	ROGDI	ATF6B	WDR62
TCEAL7	CRLF2	PLA2G12A	CDK1	GHITM	ARL11	POLR2C	KIF26B
UBQLN3	ZNF706	TMEM143	CTSW	CDC25C	C2orf73	FSCB	THEM4
PSMA2	LAD1	SPANXN5	FAM78A	TNIP1	MAPRE2	MMP16	HUWE1
IL12B	SIRT5	GALP	SMIM14	MTG1	NELFCD	LRAT	LCN10
COX7A2L	TTC9C	BOD1L1	KRTAP3-3	TMEM126A	WDR77	RPL21	ELF2

PYGB	HCST	NIT1	RALGPS2	HAPLN3	AMIGO3	DYNAP	HPRT1
OR10X1	YARS2	REEP3	ZDHHC5	DDIT3	TMEM189	UBE2M	PPP2R2B
ACBD4	BEX3	SLC35C2	MPDU1	TRIM47	CLDN14	UTP4	MRPL49
MIER2	PSMD3	PIFO	SLC39A11	OR13G1	INSIG2	OR2H1	BMPER
HP1BP3	QPRT	SGCA	CASTOR1	AGPAT4	ZDHHC6	C8orf37	C6orf141
CD3E	CA5B	TRMT44	PRB3	AK2	LMBRD1	EIF4E3	ADAP2
CNR2	PLD3	RNF182	STMN2	PCSK4	IRX6	ADA	SMCP
UPP2	LMAN2L	PDCD1	RACK1	PGLYRP1	GNB1L	DDX49	TMEM68
TRIP6	CA11	DBF4B	PFN4	BBS1	H2BC15	H6PD	R3HDM4
SNRPA	TRIM22	SUPT4H1	DIMT1	TEX38	CCDC127	SSMEM1	IRF4
OR2M4	MYL6	SHFL	SCG5	CORO2B	PPIG	RNF185	CEP20
SPINT4	MLX	BRD2	DERL1	TEX12	SLFN5	TNFSF18	PHKG1
PYCR2	CALML5	MDFI	CHGB	SPIB	C2CD4B	ARHGAP28	APCDD1
MRPL15	WNT7B	JAGN1	GPR17	LETM1	SLC26A5	REXO2	IL18RAP
EOLA2	DUS1L	TMEM182	SMU1	FXYD1	CCL17	STX1A	UBXN1
POLD3	TRPV5	KRT20	FAM32A	HOMER1			

Provided herein are expression cassettes that include nucleic acid sequences that encode fusion proteins that include at least a fragment of one or more effector-enhancing genes. In certain embodiments, the gene comprises any of the genes identified in Table 1, above, or a fragment or variant thereof. In another embodiments, the gene comprises any of the genes identified in Table 2, below, or a fragment or variant thereof. In another embodiments, the gene comprises any of the genes identified in Table 3, below, or a fragment or variant thereof. Desirable fragments include protein domains, such as an intracellular signaling domain, a transmembrane domain, or extracellular domain. In certain embodiment, the expression cassette includes more than one effector-enhancing gene fragment.

As used herein, where reference to a specific gene of Table 1, Table 2, or Table 3 is mentioned, it is intended that the use of the coding sequence for the full-length protein, a fragment having a deletion or truncation, a domain, or a variant having one or more substitutions in the amino acid, is intended. For example, in certain embodiments, the nucleic acid encodes a protein sequence having a deletion in the N terminus. In certain embodiments, the nucleic acid

encodes a protein sequence having a deletion in the C terminus. In one embodiment, the nucleic acid encodes a protein having of at least 5, at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50, at least 55, at least 60, at least 65, at least 70, at least 75, at least 80, at least 85, at least 90, at least 95, at least 100, at least 105, at least 110, at least 115, at least 120, or at least 125 amino acids.

In one embodiment, the effector-enhancing gene is LTBR. LTBR, a receptor endogenously expressed by professional antigen presenting cells but not lymphocytes, was identified as a strong synthetic driver of both T-cell proliferation and secretion of key cytokines: IL-2 and IFNγ. Using a multimodal single-cell sequencing approach, it was shown that LTBR induces profound transcriptional changes when overexpressed in T-cells, activating cellular programs involved in antigen presentation and prevention of apoptosis. As described herein, a platform was developed for testing combinatorial perturbations in T-cells, by co-expressing a gene of interest (e.g. LTBR) together with CRISPR sgRNAs targeting other genes, to map signaling networks in T-cells. Also demonstrated herein is that mRNA delivery of LTBR as an alternative to constitutive lentiviral expression, highlighting the translational potential of our screening approach.

In a certain embodiment, the expression cassette comprises a nucleic acid encoding LTBR, or a fragment thereof. *LTBR* (lymphotoxin-beta receptor), which encodes for tumor necrosis factor receptor superfamily member 3, is essential for the development and organization of secondary lymphoid tissues and chemokine release. A representative nucleic acid sequence of LTBR can be found at Accession ID NM_002342.3.

SEQ ID NO: 1

ATGCTCCTGCCTTGGGCCACCTCTGCCCCCGGCCTGGCCTGGGGGCCTCTGGTGCTGG
GCCTCTTCGGGCTCCTGGCAGCATCGCAGCCCCAGGCGGTGCCTCCATATGCGTCGG
AGAACCAGACCTGCAGGGACCAGGAAAAGGAATACTATGAGCCCCAGCACCGCATC
TGCTGCTCCCGCTGCCCGCCAGGCACCTATGTCTCAGCTAAATGTAGCCGCATCCGG
GACACAGTTTGTGCCACATGTGCCGAGAATTCCTACAACGAGCACTGGAACTACCTG
ACCATCTGCCAGCTGTGCCGCCCCTGTGACCCAGTGATGGGCCTCGAGGAGATTGCC
CCCTGCACAAGCAAACGGAAGACCCAGTGCCGCTGCCAGCCGGGAATGTTCTGTGCT
GCCTGGGCCCTCGAGTGTACACACTGCGAGCTACTTTCTGACTGCCCGCCTGGCACT
GAAGCCGAGCTCAAAGATGAAGTTGGGAAGGGTAACAACCACTGCGTCCCCTGCAA
GGCCGGGCACTTCCAGAATACCTCCTCCCCCAGCGCCCGCTGCCAGCCCCACACCAG
GTGTGAGAACCAAGGTCTGGTGGAGGCAGCTCCAGGCACTGCCCAGTCCGACACAA
CCTGCAAAAATCCATTAGAGCCACTGCCCCCAGAGATGTCAGGAACCATGCTGATGC
TGGCCGTTCTGCTGCCACTGGCCTTCTTTCTGCTCCTTGCCACCGTCTTCTCCTGCATC

TGGAAGAGCCACCCTTCTCTCTGCAGGAAACTGGGATCGCTGCTCAAGAGGCGTCCG
CAGGGAGAGGGACCCAATCCTGTAGCTGGAAGCTGGGAGCCTCCGAAGGCCCATCC
ATACTTCCCTGACTTGGTACAGCCACTGCTACCCATTTCTGGAGATGTTTCCCCAGTA
TCCACTGGGCTCCCCGCAGCCCCAGTTTTGGAGGCAGGGGTGCCGCAACAGCAGAGT
CCTCTGGACCTGACCAGGGAGCCGCAGTTGGAACCCGGGGAGCAGAGCCAGGTGGC
CCACGGTACCAATGGCATTCATGTCACCGGCGGGTCTATGACTATCACTGGCAACAT
CTACATCTACAATGGACCAGTACTGGGGGGACCACCGGGTCCTGGAGACCTCCCAGC
TACCCCCGAACCTCCATACCCCATTCCCGAAGAGGGGGACCCTGGCCCTCCCGGGCT
CTCTACACCCCACCAGGAAGATGGCAAGGCTTGGCACCTAGCGGAGACAGAGCACT
GTGGTGCCACACCCTCTAACAGGGGCCCAAGGAACCAATTTATCACCCATGAC

The full-length amino acid sequence of LTBR is SEQ ID NO: 2 (Uniprot P36941):

MLLPWATSAPGLAWGPLVLGLFGLLAASQPQAVPPYASENQTCRDQEKEYYEPQHRICC
SRCPPGTYVSAKCSRIRDTVCATCAENSYNEHWNYLTICQLCRPCDPVMGLEEIAPCTSK
RKTQCRCQPGMFCAAWALECTHCELLSDCPPGTEAELKDEVGKGNNHCVPCKAGHFQN
TSSPSARCQPHTRCENQGLVEAAPGTAQSDTTCKNPLEPLPPEMSGTMLMLAVLLPLAFF
LLLATVFSCIWKSHPSLCRKLGSLLKRRPQGEGPNPVAGSWEPPKAHPYFPDLVQPLLPIS
GDVSPVSTGLPAAPVLEAGVPQQQSPLDLTREPQLEPGEQSQVAHGTNGIHVTGGSMTIT
GNIYIYNGPVLGGPPGPGDLPATPEPPYPIPEEGDPGPPGLSTPHQEDGKAWHLAETEHCG
ATPSNRGPRNQFITHD

The LTBR protein can be divided into three regions, or domains: the extracellular domain (amino acids 31-227 of SEQ ID NO: 2); the transmembrane (or helical) domain (amino acids 228-248 of SEQ ID NO: 2); and the cytoplasmic (or intracellular) domain (amino acids 249-435 of SEQ ID NO: 2). The signal peptide of the immature protein is at amino acids 1-30 of SEQ ID NO: 2. When a domain is referred to herein, it is intended that variants, including N-terminal or C-terminal truncated variants, are included.

In certain embodiments, the expression cassette comprises a nucleic acid encoding a fragment of LTBR. In certain embodiments, the nucleic acid encodes a protein sequence having a deletion of amino acids 2-31, 32-41, 32-151, 32-180, 393-435, 377-435, 324-377, 297-435, or 262-435 as compared to the native protein (SEQ ID NO: 2). In certain embodiments, the nucleic acid encodes a protein sequence having a deletion in the N terminus. In certain embodiments, the nucleic acid encodes a protein sequence having a deletion in the C terminus. In one embodiment, the LTBR is has a deletion of residues 393-435. In certain embodiments, the LTBR has a deletion of at least 5, at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50, at least 55, at least 60, at least 65, at least 70, at least 75, at least 80, at least

85, at least 90, at least 95, at least 100, at least 105, at least 110, at least 115, at least 120, or at least 125 amino acids.

In certain embodiments, the expression cassette comprises a nucleic acid encoding a fragment that is a domain of LTBR. In certain embodiments, the nucleic acid encodes the extracellular domain of LTBR (amino acids 31-227 of SEQ ID NO: 2). In certain embodiments, the nucleic acid encodes the transmembrane domain of LTBR (amino acids 228-248 of SEQ ID NO: 2). In certain embodiments, the nucleic acid encodes the cytoplasmic (or intracellular) domain of LTBR (amino acids 249-435 of SEQ ID NO: 2). In other embodiments, the domain is a variant of one of the LTBR domains, including a variant that has a deletion. Desirable variants of the cytoplasmic domain include those with amino acids 249-378, 249-379, 249-380, 249-381, 249-382, 249-383, 249-384, 249-385, 249-386, 249-387, 249-388, 249-389, 249-390, 249-391, or 249-392 all of SEQ ID NO: 2. Further desirable variants include those with amino acids 249-378, 249-379, 249-380, 249-381, 249-382, 249-383, 249-384, 249-385, 249-386, 249-387, 249-388, 249-389, 249-390, 249-391, or 249-392 all of SEQ ID NO: 2 having 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid substitutions as compared to SEQ ID NO: 2. In certain embodiments, the LTBR fragment comprises amino acids 249-396 of SEQ ID NO: 2. In certain embodiments, the LTBR fragment comprises amino acids 249-393 of SEQ ID NO: 2. In certain embodiments, the LTBR fragment comprises amino acids 249-387 of SEQ ID NO: 2. In certain embodiments, the LTBR fragment comprises amino acids 249-377 of SEQ ID NO: 2. In certain embodiments, the LTBR fragment comprises amino acids 262-435 of SEQ ID NO: 2. In certain embodiments, the LTBR fragment comprises amino acids 297-435 of SEQ ID NO: 2. In certain embodiments, the LTBR fragment comprises amino acids 324-435 of SEQ ID NO: 2. In certain embodiments, the LTBR fragment comprises amino acids 345-435 of SEQ ID NO: 2. In certain embodiments, the LTBR fragment comprises amino acids 358-435 of SEQ ID NO: 2.

In other embodiments, the expression cassette comprises a nucleic acid encoding two or more domains of LTBR. In one embodiment the nucleic acid encodes the cytoplasmic domain (or variant thereof) and the transmembrane domain of LTBR. In another embodiment, the nucleic acid encodes the cytoplasmic domain (or variant thereof), transmembrane domain, and extracellular domain of LTBR.

The fusion proteins described herein also include at least a fragment, including a domain, of second protein, different from the first. In certain embodiments, the second protein is a protein that is a component of a T cell receptor. In other embodiments, the second protein is a protein that interacts with T cell receptor. Such proteins include CD4, CD8A, CD8B, CD3E, CD3D, CD3G, and CD3Z.

In one embodiment a fusion protein includes an LTBR domain, or variant thereof, and CD4. In another embodiment a fusion protein includes an LTBR domain, or variant thereof, and CD8A and/or CD8B. In another embodiment a fusion protein includes an LTBR domain, or variant thereof, and CD3E. In another embodiment a fusion protein includes an LTBR domain, or variant thereof, and CD3D. In another embodiment a fusion protein includes an LTBR domain, or variant thereof, and CD3G. In another embodiment a fusion protein includes an LTBR domain, or variant thereof, and CD3Z. In certain embodiments, the LTBR domain is an intracellular domain. In certain embodiments, the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or variant thereof. In certain embodiments, the LTBR intracellular domain has a deletion in at least amino acids 393 to 435.

Various isoforms of the genes identified in Table 1 are known in the art. Some are described in Table 2 below. In another embodiment, an expression cassette is provided which includes the coding sequence for any of the alternative isoforms. Alternative coding sequences accounting to the degeneracy of the genetic code, including codon optimized coding sequences, for these genes can be identified by the person of skill in the art, and utilized as an alternative embodiment of the compositions and methods described herein.

Table 2

Gene ID	Symbol	Transcript	Length (nt)	Protein	Length (aa)	Isoform	Gene name
100	ADA	NR_136160.2	1431				adenosine deaminase
100	ADA	NM_001322050.2	1380	NP_001308979.1	228	2	adenosine deaminase
100	ADA	NM_001322051.2	1424	NP_001308980.1	339	3	adenosine deaminase
100	ADA	NM_000022.4	1496	NP_000013.2	363	1	adenosine deaminase
10538	BATF	NM_006399.5	913	NP_006390.1	125		basic leucine zipper ATF-like transcription factor
1109	AKR1C4	NM_001818.5	1192	NP_001809.4	323		aldo-keto reductase family 1 member C4
1388	ATF6B	NM_001136153.2	2617	NP_001129625.1	700	b	activating transcription factor 6 beta
1388	ATF6B	NM_004381.5	2626	NP_004372.3	703	a	activating transcription factor 6 beta
1622	DBI	NM_001282635.3	804	NP_001269564.1	104	1	diazepam binding inhibitor, acyl-CoA binding protein
1622	DBI	NM_001282636.3	718	NP_001269565.1	63	7	diazepam binding inhibitor, acyl-CoA binding protein
1622	DBI	NM_001282633.3	680	NP_001269562.1	104	1	diazepam binding inhibitor, acyl-CoA binding protein

1622	DBI	NM_020548.9	675	NP_065438.1	104	1	diazepam binding inhibitor, acyl-CoA binding protein
1622	DBI	NM_001178043.4	594	NP_001171514.1	97	6	diazepam binding inhibitor, acyl-CoA binding protein
1622	DBI	NM_001178041.4	690	NP_001171512.1	129	5	diazepam binding inhibitor, acyl-CoA binding protein
1622	DBI	NM_001282634.3	650	NP_001269563.1	104	1	diazepam binding inhibitor, acyl-CoA binding protein
1622	DBI	NM_001178042.4	645	NP_001171513.1	104	1	diazepam binding inhibitor, acyl-CoA binding protein
1622	DBI	NM_001079862.4	564	NP_001073331.1	87	3	diazepam binding inhibitor, acyl-CoA binding protein
1622	DBI	NM_001352432.3	896	NP_001339361.1	63	7	diazepam binding inhibitor, acyl-CoA binding protein
1622	DBI	NM_001178017.3	756	NP_001171488.1	148	4	diazepam binding inhibitor, acyl-CoA binding protein
1622	DBI	NM_001079863.3	698	NP_001073332.1	88	2	diazepam binding inhibitor, acyl-CoA binding protein
191	AHCY	XM_011528657.2	1436	XP_011526959.2	434	X1	adenosylhomocysteinase
191	AHCY	XM_017027709.2	1801	XP_016883198.1	432	X2	adenosylhomocysteinase
191	AHCY	XM_011528658.3	1798	XP_011526960.2	434	X1	adenosylhomocysteinase
191	AHCY	XM_011528656.3	1803	XP_011526958.2	434	X1	adenosylhomocysteinase
191	AHCY	XM_011528659.1	2196	XP_011526961.1	404	X3	adenosylhomocysteinase
191	AHCY	NM_001161766.2	2368	NP_001155238.1	404	2	adenosylhomocysteinase
191	AHCY	NM_001362750.2	1774	NP_001349679.1	432	1	adenosylhomocysteinase
191	AHCY	NM_000687.4	2150	NP_000678.1	432	1	adenosylhomocysteinase
191	AHCY	XM_017027710.2	2136	XP_016883199.1	306	X4	adenosylhomocysteinase
191	AHCY	XM_005260317.2	2601	XP_005260374.1	404	X3	adenosylhomocysteinase
191	AHCY	NM_001322085.2	3092	NP_001309014.1	404	2	adenosylhomocysteinase
191	AHCY	NM_001322084.2	3270	NP_001309013.1	404	2	adenosylhomocysteinase
191	AHCY	NM_001322086.2	3281	NP_001309015.1	434	3	adenosylhomocysteinase
2819	GPD1	NM_005276.4	2887	NP_005267.2	349	1	glycerol-3-phosphate dehydrogenase 1
2819	GPD1	NM_001257199.2	2818	NP_001244128.1	326	2	glycerol-3-phosphate dehydrogenase 1
282616	IFNL2	NM_172138.2	951	NP_742150.1	200		interferon lambda 2
338599	DUSP29	XM_011539747.2	4872	XP_011538049.1	220	X1	dual specificity phosphatase 29

338599	DUSP29	NM_001003892.3	1135	NP_001003892.1	220		dual specificity phosphatase 29
338599	DUSP29	NM_001384909.1	1267	NP_001371838.1	220		dual specificity phosphatase 29
338599	DUSP29	XM_017016176.1	1284	XP_016871665.1	112	X2	dual specificity phosphatase 29
3593	IL12B	NM_002187.3	2364	NP_002178.2	328		interleukin 12B
4055	LTBR	NM_001270987.2	2276	NP_001257916.1	416	2	lymphotoxin beta receptor
4055	LTBR	XM_005253688.2	2094	XP_005253745.1	399	X1	lymphotoxin beta receptor
4055	LTBR	XM_006718983.3	1127	XP_006719046.1	255	X2	lymphotoxin beta receptor
4055	LTBR	NM_002342.3	2134	NP_002333.1	435	1 precursor	lymphotoxin beta receptor
51184	GPN3	NM_001164372.2	1605	NP_001157844.1	323	2	GPN-loop GTPase 3
51184	GPN3	NM_016301.4	1457	NP_057385.3	284	1	GPN-loop GTPase 3
51184	GPN3	NM_001164373.2	1487	NP_001157845.1	294	3	GPN-loop GTPase 3
51184	GPN3	XM_017019394.1	1357	XP_016874883.1	262	X1	GPN-loop GTPase 3
51258	MRPL51	NM_016497.4	898	NP_057581.2	128		mitochondrial ribosomal protein L51
79026	AHNAK	NM_024060.4	1036	NP_076965.2	149	2	AHNAK nucleoprotein
79026	AHNAK	NM_001620.3	18761	NP_001611.1	5890	1	AHNAK nucleoprotein
79026	AHNAK	XM_017018270.1	18556	XP_016873759.1	5823	X1	AHNAK nucleoprotein
79026	AHNAK	NM_001346445.2	18697	NP_001333374.1	5890	1	AHNAK nucleoprotein
79026	AHNAK	NM_001346446.2	18713	NP_001333375.1	5890	1	AHNAK nucleoprotein
810	CALML3	NM_005185.4	1811	NP_005176.1	149		calmodulin like 3
9452	ITM2A	NM_001171581.2	1484	NP_001165052.1	219	2	integral membrane protein 2A
9452	ITM2A	NM_004867.5	1616	NP_004858.1	263	1	integral membrane protein 2A

Engineered T cell Receptors Containing LTBR Domains

The present disclosure provides nucleic acid sequences encoding engineered T cell receptors, e.g., T cell receptors (TCRs), that incorporate an LTBR domain. Also provided are chimeric antigen receptors (CAR) that incorporate an LTBR domain or variant thereof. Components of the TCR and CARs are further described herein. Also provided are the engineered TCRs and CARs, and modified T cells incorporating the same.

Also provided herein are nucleic acid sequences encoding engineered T cell receptors, e.g., T cell receptors (TCRs), that incorporate a domain or variant thereof from one of the genes of Table 3. Also provided are chimeric antigen receptors (CAR) that incorporate domain from one of the genes of Table 3. In certain embodiments, the domain is an intracellular domain from a gene selected from those of Table 3. Also provided are the engineered TCRs and CARs, and

modified T cells incorporating the same. As described below, embodiments incorporating LTBR domains are set forth. However, for each embodiment described for LTBR, an embodiment is intended for each of the genes of Table 3.

Table 3

ABCC5	CSF1R	GPR3	LYPD6B	OR6B2	SLC26A5	TSPAN31
ACE	CXCR1	GPR37L1	MAS1	OR8H2	SLC37A4	TSPAN9
ACP2	DCT	GRID1	MC3R	OXGR1	SLC39A4	VIPR1
ADAM2	DPEP2	GRIK2	MMP16	P2RX7	SLC41A2	VSTM1
AMIGO3	DYNAP	GRPR	MOG	P2RY6	SLC46A3	VTCN1
APCDD1	EDA	GSG1	MUC1	PDCD1	SLC4A4	ZDHHC5
ART4	EMP3	GYPC	NCR3	PIEZO1	SLC52A1	
BDKRB2	ENPP1	HAVCR2	OR10G3	PODXL2	SLC6A3	
C3AR1	EREG	HEPACAM2	OR10G6	PRND	SPPL2C	
CA12	ERMAP	HLA-DOA	OR10G9	PRPH2	STIM1	
CCR4	EVA1C	HLA-DPB1	OR10W1	PRSS8	SYNPR	
CD14	EVI2A	HTR1D	OR10X1	PTCHD1	TAAR5	
CD1B	F11R	IGF1R	OR13G1	PTCHD4	TAS2R3	
CD2	F2RL1	IL18RAP	OR1D5	RGR	TCIRG1	
CD244	F2RL2	KCNJ12	OR1N2	RHCG	TMEM132C	
CD300A	FAP	KCNMB1	OR1Q1	S1PR3	TMEM182	
CD4	FCGR2B	LAMP2	OR2G2	SCTR	TMEM255A	
CD48	FNDC4	LHFPL5	OR2H1	SDC1	TMEM37	
CD52	FOLR2	LMAN2L	OR2M4	SEMA4G	TMIGD1	
CD59	FZD10	LMBRD1	OR3A2	SGCA	TMPRSS11E	
CD79B	GABRA5	LRRC25	OR4D11	SLC10A6	TMPRSS6	
CLDN4	GABRB1	LRRTM3	OR4K17	SLC11A2	TNFSF18	
CNR2	GJB7	LRTM1	OR4X1	SLC14A1	TRPV2	
CRLF2	GPNMB	LTBR	OR51G1	SLC1A7	TRPV5	
CRTAM	GPR17	LYPD4	OR52W1	SLC26A1	TSPAN1	

Provided herein are nucleic acid molecules that comprise a coding sequence for any of the TCRs described herein modified to include a domain of LTBR or a gene of Table 3. Certain exemplary TCRs are provided in the sequence listing in SEQ ID Nos: 3-54. However, it is intended that nucleic acids encoding all the described TCRs, as well as the TCR proteins, are encompassed herewith.

The TCR is a disulfide-linked membrane-anchored heterodimer present on T cell lymphocytes, and the majority of T cells are αβ T cells having a TCR consisting of an alpha (α) chain and a beta (β) chain. Each chain comprises a variable (V) and a constant (C) domain, wherein the variable domain recognizes an antigen, or an MHC-presented peptide. TCRα and

TCRβ chains with a known specificity or affinity for specific antigens, e.g., tumor antigens described herein, can be introduced to a T cell using the methods described herein. TCRα and TCRβ chains having a desired, e.g., increased, specificity or affinity for a particular antigen can be isolated using standard molecular cloning techniques known in the art. Other modifications that increase specificity, avidity, or function of the TCRs or the engineered T cells expressing the TCRs can be readily envisioned by the ordinarily skilled artisan, e.g., promoter selection for regulated expression, mutations in the antigen binding regions of the TCRα and TCRβ chains. Any isolated or modified TCRα and TCRβ chain can be operably linked to or can associate with one or more intracellular signaling domains described herein. Signaling can be mediated through interaction between the antigen-bound αβ heterodimer to CD3 chain molecules, e.g., CD3zeta (ζ).

A smaller subset of T cells expresses a TCR having a (γ) gamma chain and a delta (δ) chain. Gamma-delta (γδ) T cells make up 3-10% of circulating lymphocytes in humans, and the Vδ2+ subset can account for up to 95% of γδ T cells in blood. Vδ2+ cells recognize non-peptide epitopes and do not require antigen presentation by major histocompatibility complexes ("MHC") or human leukocyte antigen ("HLA"). The majority of Vδ2+ T cells also express a Vγ9 chain and are stimulated by exposure to 5-carbon pyrophosphate compounds that are intermediates in mevalonate and non-mevalonate sterol/isoprenoid synthesis pathways. The response to isopentenyl pyrophosphate (5-carbon) is universal among healthy human beings. Another subset of γδ T cells, Vδ1+, make up a much smaller percentage of the T cells circulating in the blood, but are commonly found in the epithelial mucosa and the skin. γδ T cells have several functions, including killing tumor cells and pathogen-infected cells. Stimulation through the γδ TCR improves the capacity for cellular cytotoxicity, cytokine secretion and other effector functions. The TCRs of γδ T cells have unique specificities and the cells themselves occur in high clonal frequencies, thus allowing rapid innate-like responses to tumors and pathogens. See, e.g., Park and Lee, Exp Mol Med. 2021 Mar;53(3):318-327., which is incorporated herein by reference.

In certain embodiments, a T cell comprises a nucleic acid sequence encoding a TCR, e.g., a TCR that targets a tumor antigen, that includes an LTBR domain. In certain embodiments, the TCR includes the LTBR intracellular domain, or variant thereof as described herein. In one embodiment, the variant has a deletion in at least amino acids 393 to 435 of SEQ ID NO: 2. In one embodiment, the variant of the intracellular domain includes amino acids 249-392 of SEQ ID NO: 2. However, additional residues may be deleted. Thus, desirable variants of the intracellular domain include those with a sequence of amino acids 249-378, 249-379, 249-380, 249-381, 249-382, 249-383, 249-384, 249-385, 249-386, 249-387, 249-388, 249-389, 249-390, 249-391, or 249-392 all of SEQ ID NO: 2. Further desirable variants include those with a sequence of amino acids 249-378, 249-379, 249-380, 249-381, 249-382, 249-383, 249-384, 249-385, 249-386, 249-

387, 249-388, 249-389, 249-390, 249-391, or 249-392 all of SEQ ID NO: 2 having 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid substitutions as compared to SEQ ID NO: 2.

In certain embodiments, a T cell comprises a nucleic acid sequence encoding a TCR, e.g., a modified TCR that targets a tumor antigen described herein, that includes a domain from the genes of Table 3. In certain embodiments, the TCR includes an intracellular domain from the genes of Table 3, or variant thereof as described herein.

In one embodiment, the TCR comprises an LTBR intracellular domain fused to C-terminus of the TCR alpha chain. In another embodiment, the TCR comprises an LTBR intracellular domain fused to the C-terminus of the TCR beta chain. FIG. 25A, FIG. 29A. In one embodiment, the TCR comprises an LTBR intracellular domain fused to the C-terminus of the TCR delta chain. In another embodiment, the TCR comprises an LTBR intracellular domain fused to the C-terminus of the TCR gamma chain. In another embodiment, the TCR comprises an LTBR intracellular domain fused to the C-terminus of the CD3γ. In another embodiment, the TCR comprises an LTBR intracellular domain fused to the C-terminus of the CD3δ. In another embodiment, the TCR comprises an LTBR intracellular domain fused to the C-terminus of one or both CD3ε. In another embodiment, the TCR comprises an LTBR intracellular domain fused to the C-terminus of one or both CD3ζ. See FIG 25A and 25B.

In one embodiment, the TCR comprises an intracellular domain of a gene of Table 3 fused to C-terminus of the TCR alpha chain. In another embodiment, the TCR comprises an intracellular domain of a gene of Table 3 fused to the C-terminus of the TCR beta chain. FIG. 25A. In one embodiment, the TCR comprises an intracellular domain of a gene of Table 3 fused to the C-terminus of the TCR delta chain. In another embodiment, the TCR comprises an intracellular domain of a gene of Table 3 fused the C-terminus of the TCR gamma chain. In another embodiment, the TCR comprises an intracellular domain of a gene of Table 3 fused to the C-terminus of the CD3γ. In another embodiment, the TCR comprises an intracellular domain of a gene of Table 3 fused to the C-terminus of the CD3δ. In another embodiment, the TCR comprises an intracellular domain of a gene of Table 3 fused to the C-terminus of one or both CD3ε. In another embodiment, the TCR comprises an intracellular domain of a gene of Table 3 fused to the C-terminus of one or both CD3ζ.

In another embodiment, the LTBR intracellular domain is fused to the C-terminal intracellular tail of CD4. In another embodiment, the LTBR intracellular domain is fused to the C-terminal intracellular tails of CD8α and/or CD8β. See FIG. 25C.

In another embodiment, an intracellular domain of a gene of Table 3 is fused to the C-terminal intracellular tail of CD4. In another embodiment, an intracellular domain of a gene of Table 3 is fused to the C-terminal intracellular tails of CD8α and CD8β.

In other embodiments, at least one domain of LTBR is delivered to a lymphocyte via direct modification of the endogenous genome. Various techniques for modification of the endogenous genome are known in the art, including CRISPR, zinc finger nucleases, TALENs, etc. See, e.g., Azangou-Khyavy et al, CRISPR/Cas: From Tumor Gene Editing to T Cell-Based Immunotherapy of Cancer, Front. Immunol., 29 September 2020 | https://doi.org/10.3389/fimmu.2020.02062, which is incorporated herein by reference. In on embodiment, the LTBR intracellular domain, or fragment thereof, is inserted into the genome of a lymphocyte. In other embodiments, at least one domain of a gene of Table 3 is delivered to a lymphocyte via direct modification of the endogenous genome.

In certain embodiments, the TCR is a known TCR, such as those identified in FIG. 20, as modified as described herein to contain a domain of LTBR or a gene of Table 3 (or variant thereof). In certain embodiments, the TCR targets MART-1. Chodon T, et al, Adoptive transfer of MART-1 T-cell receptor transgenic lymphocytes and dendritic cell vaccination in patients with metastatic melanoma. Clin Cancer Res. 2014 May 1;20(9):2457-65. doi: 10.1158/1078-0432.CCR-13-3017. Epub 2014 Mar 14. PMID: 24634374; PMCID: PMC4070853. In other embodiments, the TCR targets MAGE A4. Hong et al, Phase 1 dose escalation and expansion trial to assess the safety and efficacy of ADP-A2M4 SPEAR T cells in advanced solid tumors. ASCO Meeting Library, 2020 ASCO Virtual Scientific Program, J Clin Oncol 38: 2020 (suppl; abstr 102). In other embodiments, the TCR targets WT1. Chapuis AG, et al. T cell receptor gene therapy targeting WT1 prevents acute myeloid leukemia relapse post-transplant. Nat Med. 2019 Jul;25(7):1064-1072. doi: 10.1038/s41591-019-0472-9. Epub 2019 Jun 24. PMID: 31235963; PMCID: PMC6982533. In other embodiments, the TCR targets MR1. Crowther, M.D., Dolton, G., Legut, M. et al. Genome-wide CRISPR–Cas9 screening reveals ubiquitous T cell cancer targeting via the monomorphic MHC class I-related protein MR1. Nat Immunol 21, 178–185 (2020). https://doi.org/10.1038/s41590-019-0578-8. In other embodiments, the TCR targets E6. In other embodiments, the TCR targets E7. In other embodiments, the TCR targets KK-LC-1. In other embodiments, the TCR targets NY-ESO-1. In other embodiments, the TCR targets MAGE A3. In other embodiments, the TCR targets GD-2. In other embodiments, the TCR targets P53. In other embodiments, the TCR targets LAGE-A1. In other embodiments, the TCR targets GP100.

In any of the embodiments described herein, a modified TCR can be substituted for a CAR described herein to generate a T cell. An engineered TCR described herein can be substituted for a CAR in any of the embodiments described herein.

Chimeric Antigen Receptors (CARs) Containing LTBR Domains

The term "chimeric antigen receptor" or alternatively a "CAR" refers to a recombinant polypeptide construct comprising at least an extracellular antigen binding domain, a stalk/hinge, a

transmembrane domain, and a cytoplasmic signaling domain (also referred to as an intracellular signaling domain) comprising a functional signaling domain derived from a stimulatory molecule as defined below. See Jayaraman et al, CAR-T design: Elements and their synergistic function, eBioMedicine, 58:102931 (August 2020), which is incorporated herein by reference. In some embodiments, the stimulatory molecule is TCR zeta, FcR gamma, FcR beta, CD3 gamma, CD3 delta, CD3 epsilon, CD5, CD22, CD79a, CD79b, CD66d, 4-1BB, or CD3-zeta. In a particular embodiment, the stimulatory molecule is the zeta chain associated with the T cell receptor complex. As used herein for ease of reference, when referring to a stimulatory molecule, the term CD3ζ may be used. However, it is intended that a similar embodiment is provided in which the CD3ζ is swapped for another suitable stimulatory molecule. In one embodiment, the stimulatory molecule is 4-1BB. In one embodiment, the stimulatory molecule is CD28. In another embodiment, the stimulatory molecule is LTBR and the stimulatory signaling domain includes the LTBR intracellular domain, or variant thereof. In another embodiment, the stimulatory molecule is a gene of Table 3, and the stimulatory signaling domain includes an intracellular domain of a gene of Table 3.

In one embodiment, the cytoplasmic signaling domain further comprises one or more functional signaling domains derived from at least one costimulatory molecule as defined below (also referred to as a "costimulatory signaling domain"). In one embodiment, the costimulatory molecule is chosen from a costimulatory molecule described herein, e.g., OX40, CD27, CD28, CD30, CD40, PD-1, CD2, CD7, CD258, NKG2C, B7-H3, a ligand that binds to CD83, ICAM-1, LFA-1 (CD11a/CD18), ICOS and 4-1BB (CD137), or any combination thereof. In certain embodiments, the costimulatory molecule is LTBR, and the costimulatory signaling domain includes the LTBR intracellular domain, or variant thereof. In another embodiment, the costimulatory molecule is a gene of Table 3, and the costimulatory signaling domain includes an intracellular domain of a gene of Table 3.

As described herein, the CAR itself comprises one or more LTBR domains. The LTBR domain(s) may, in some embodiments, replace a domain from an existing CAR construct, such as those described in FIG. 19. In other embodiments, the LTBR domain(s) is/are included in addition to the domains from an existing CAR construct, such as those described in FIG. 19.

As described herein, the CAR itself comprises one or more domains from a gene of Table 3. The domain(s) from the gene of Table 3 may, in some embodiments, replace a domain from an existing CAR construct, such as those described in FIG. 19. In other embodiments, the domain(s) from the gene of Table 3 is/are included in addition to the domains from an existing CAR construct, such as those described in FIG. 19.

In certain embodiments, the stalk and the transmembrane are from the same molecule,

e.g., LTBR, CD8, or CD28. In other embodiments, the stalk and the transmembrane are from different molecules, e.g., CD8 stalk and LTBR TM, CD28 stalk and LTBR TM, etc.

In one embodiment the CAR comprises an optional leader sequence at the amino-terminus (N-ter) of the CAR fusion protein. In one embodiment, the CAR further comprises a leader sequence at the N-terminus of the extracellular antigen binding domain, wherein the leader sequence is optionally cleaved from the scFv domain during cellular processing and localization of the CAR to the cellular membrane.

In one embodiment, the CAR comprises a chimeric fusion protein comprising an extracellular antigen recognition domain, a transmembrane domain, and an intracellular signaling domain comprising a functional signaling domain derived from LTBR, or variant thereof. Without wishing to be bound by theory, T cells engineered with CARs lacking a CD3zeta chain do not induce specific cytokine secretion in the presence of CD19+ leukemia cells. However, these cells induce NFκB-induced genes (as demonstrated by CD74 expression (see FIG. 24E), and do induce IFNγ and IL2 secretion when stimulated with CD3 and CD28 antibodies (FIG. 24C and 24D).

In certain embodiments, in addition to the LTBR signaling domain, the transmembrane domain is also derived from LTBR. In certain embodiments, in addition to the LTBR signaling domain and (optionally) the transmembrane domain, the stalk is also derived from LTBR.

In one embodiment, the CAR comprises a chimeric fusion protein comprising an extracellular antigen recognition domain, a transmembrane domain, and an intracellular signaling domain comprising a functional signaling domain derived LTBR, or variant thereof.

In one embodiment, the CAR comprises a chimeric fusion protein comprising an extracellular antigen recognition domain, a transmembrane domain, an intracellular signaling domain comprising a functional cosignaling domain derived from LTBR, or variant thereof, and a functional signaling domain derived from a stimulatory molecule, e.g., CD3 zeta chain. The placement of the LTBR cosignaling domain may be varied depending on the desired function of the CAR. In certain embodiments, the LTBR cosignaling domain, or variant thereof is placed between the transmembrane domain and the signaling domain (e.g., CD3ζ). In other embodiments, the CD3ζ is placed between the transmembrane domain and the LTBR cosignaling domain, or variant thereof.

In certain embodiments, in addition to the signaling domain, the transmembrane domain is also derived from a gene of Table 3. In certain embodiments, in addition to the signaling domain and (optionally) the transmembrane domain, the stalk is also derived from a gene of Table 3.

In one embodiment, the CAR comprises a chimeric fusion protein comprising an

extracellular antigen recognition domain, a transmembrane domain, and an intracellular signaling domain comprising a functional signaling domain derived from a gene of Table 3, or variant thereof.

In one embodiment, the CAR comprises a chimeric fusion protein comprising an extracellular antigen recognition domain, a transmembrane domain, an intracellular signaling domain comprising a functional cosignaling domain derived from LTBR, or variant thereof, at least one other functional cosignaling domain, and a functional signaling domain derived from a stimulatory molecule, e.g., CD3zeta chain. The placement of the LTBR cosignaling domain may be varied depending on the desired function of the CAR. In certain embodiments, the LTBR cosignaling domain, or variant thereof is placed between the transmembrane domain and the other cosignaling domain(s) (e.g., CD28 or 4-1BB). In certain embodiments, the LTBR cosignaling domain, or variant thereof is placed between the other cosignaling domain(s) and the signaling domain (e.g., CD3ζ). In other embodiments, the LTBR cosignaling domain, or variant thereof is placed downstream of the signaling domain (e.g., CD3ζ). See, e.g., FIG. 21A and FIG. 21B.

In certain embodiments, in addition to the LTBR signaling domain, the transmembrane domain is also derived from LTBR. In certain embodiments, in addition to the LTBR signaling domain and (optionally) the transmembrane domain, the stalk is also derived from LTBR.

In one embodiment, the CAR comprises a chimeric fusion protein comprising an extracellular antigen recognition domain, a transmembrane domain, an intracellular signaling domain comprising a functional cosignaling domain derived from a gene of Table 3, or variant thereof, at least one other functional cosignaling domain, and a functional signaling domain derived from a stimulatory molecule, e.g., CD3zeta chain. The placement of the cosignaling domain may be varied depending on the desired function of the CAR. In certain embodiments, the cosignaling domain from a gene of Table 3, or variant thereof is placed between the transmembrane domain and the other cosignaling domain(s) (e.g., CD28 or 4-1BB). In certain embodiments, the cosignaling domain from a gene of Table 3, or variant thereof is placed between the other cosignaling domain(s) and the signaling domain (e.g., CD3ζ). In other embodiments, the cosignaling domain from a gene of Table 3, or variant thereof is placed downstream of the signaling domain (e.g., CD3ζ).

The present disclosure provides nucleic acid sequences, e.g., a DNA or an RNA construct, that encode any of the CARs described herein. This also refers to nucleic acid sequences encoding a known CAR such as one of those shown in FIG. 19, but modified to include an LTBR domain or variant thereof, as described herein.

The present disclosure provides nucleic acid sequences, e.g., a DNA or an RNA construct, that encode any of the CARs described herein. This also refers to nucleic acid sequences encoding a known CAR such as one of those shown in FIG. 19, but modified to include a domain of a gene of Table 3 or variant thereof, as described herein.

In certain embodiments, the CAR targets CD19. In certain embodiments, the CAR is a known CAR, such as one of those shown in FIG. 19, but modified to include an LTBR domain (or gene of Table 3) or variant thereof, as described herein. In one embodiment, the CAR is a modified axicabtagene ciloleucel. In another embodiment, the CAR is a modified Brexucabtagene autoleucel. In another embodiment, the CAR is a modified Tisagenlecleucel. In another embodiment, the CAR is a modified Lisocabtagene maraleucel. In certain embodiments, the CAR targets B-cell maturation antigen (BCMA). In another embodiment, the CAR is a modified Idecabtagene vicleucel. In one embodiment, the CAR is a modified ciltacabtagene autoleucel. In certain embodiments, the CAR targets mesothelin. In certain embodiments, the CAR targets ROR1. In certain embodiments, the CAR targets B7-H3. In certain embodiments, the CAR targets CD33. In certain embodiments, the CAR targets EGFR806. In certain embodiments, the CAR targets IL13Rα2. In certain embodiments, the CAR targets GD2. In certain embodiments, the CAR targets HER2. In certain embodiments, the CAR targets Glypican 3. In certain embodiments, the CAR targets CD7. In certain embodiments, the CAR targets NY-ESO-1. In certain embodiments, the CAR targets CD30. In certain embodiments, the CAR targets MAGE-A1. In certain embodiments, the CAR targets LMP2. In certain embodiments, the CAR targets PD1. In certain embodiments, the CAR targets mutant KRAS G12V. In certain embodiments, the CAR targets CD20. In certain embodiments, the CAR targets CD22. In certain embodiments, the CAR targets CD171. In certain embodiments, the CAR targets CD123. In certain embodiments, the CAR targets CD38. In certain embodiments, the CAR targets CD10. In certain embodiments, the CAR targets BAFFR. In certain embodiments, the CAR targets PSMA. In certain embodiments, the CAR targets mucin (TnMUC1). Posey AD Jr, et al, Engineered CAR T Cells Targeting the Cancer-Associated Tn-Glycoform of the Membrane Mucin MUC1 Control Adenocarcinoma. Immunity. 2016 Jun 21;44(6):1444-54. doi: 10.1016/j.immuni.2016.05.014. PMID: 27332733; PMCID: PMC5358667. In certain embodiments, the CAR targets CD70. See, Srinivasan et al, 1972 Investigation of ALLO-316: A Fratricide-Resistant Allogeneic CAR T Targeting CD70 As a Potential Therapy for the Treatment of AML, 62nd ASH Annual Meeting and Exposition, Dec. 5-8, 2020. In certain embodiments, the CAR targets TRIB1C. Maciocia PM, et al, Targeting the T cell receptor β-chain constant region for immunotherapy of T cell malignancies. Nat Med. 2017 Dec;23(12):1416-1423. doi: 10.1038/nm.4444. Epub 2017 Nov 13. PMID: 29131157.

Exemplary sequences for the CARs and TCRs used in the Examples are provided in the sequence listing in SEQ ID Nos: 3-54. Other exemplary antibody sequences, useful for the antigen recognition domain, are provided in the sequence listing in SEQ ID Nos: 63-83.

SEQ ID NO	Name	Type
63	synthetic anti-mesothelin monoclonal antibody HN1 VH	DNA
64	synthetic anti-mesothelin monoclonal antibody HN1 VH	AA
65	synthetic anti-mesothelin monoclonal antibody HN1 VL	DNA
66	synthetic anti-mesothelin monoclonal antibody HN1 VL	AA
67	synthetic anti-mesothelin monoclonal antibody HN2 VH	DNA
68	synthetic anti-mesothelin monoclonal antibody HN2 VH	AA
69	synthetic anti-mesothelin monoclonal antibody HN2 VL	DNA
70	synthetic anti-mesothelin monoclonal antibody HN2 VL	AA
71	AntiCD19 VH (24)	DNA
72	AntiCD19 VL (26)	DNA
73	AntiCD19 VL (40)	DNA
74	AntiCD38 hScFv (5)	DNA
75	AntiCD38 hScFv (8)	AA
76	AntiCD38 hScFv (10)	AA
77	AntiCD20 VL (156)	DNA
78	AntiCD20 VH (145)	DNA
79	AntiCD22 VL (690)	AA
80	AntiCD22 VH (680)	AA
81	AntiCD33 VL (71)	AA
82	AntiCD33 VH (62)	AA
83	AntiCD33 scFv (44)	AA

Other chimeric antigen receptors as modified herein, include those useful for treatment for autoimmune disease, such as are chimeric autoantigen receptors (CAAR). Such CAARs include DSG3-CAART and MuSK-CAART. Others may be known in the art or may be designed by the person of skill.

The present disclosure provides nucleic acid sequences, e.g., a DNA or an RNA construct, that encode any of the TCRs described herein. This also refers to nucleic acid sequences encoding a known TCR such as one of those shown in FIG. 20, but modified to include an LTBR domain (or gene of Table 3) or fragment thereof, as described herein. Various other engineered T cell receptors are known in the art or may be designed by the person of skill. Such TCRs include those currently being tested clinically, such as those identified in FIG. 20.

The expression cassettes referred to herein include a nucleic acid molecule which encodes one or more biologically useful nucleic acid sequences (e.g., a gene cDNA encoding a fusion protein, CAR, TCR, mRNA, etc.) and regulatory sequences operably linked thereto which direct

or modulate transcription, translation, and/or expression of the nucleic acid sequence(s) and its gene product(s). Operably linked sequences include both regulatory sequences that are contiguous with the nucleic acid sequence and regulatory sequences that act in trans or at a distance to control the sequence. Such regulatory sequences typically include, e.g., one or more of a promoter, an enhancer, an intron, a Kozak sequence, a polyadenylation sequence, and a TATA signal. The expression cassette may contain regulatory sequences upstream (5' to) of the gene sequence, e.g., one or more of a promoter, an enhancer, an intron, etc., and one or more of an enhancer, or regulatory sequences downstream (3' to) a gene sequence, e.g., 3' untranslated region comprising a polyadenylation site, among other elements. Thus, in addition to the coding sequences for the fusion protein, CAR, or TCR the expression cassette may also include expression control sequences.

The expression control sequences include a promoter. In some embodiments, its it is desirable to utilize a promoter having high transcriptional activity. Certain strong constitutive promoters are known in the art and include, without limitation, the CMV promoter, the EF-1α promoter, CBG promoter, CB7 promoter, etc. Alternatively, other promoters, such as regulatable (inducible) promoters [see, e.g., WO 2011/126808 and WO 2013/049493, incorporated by reference herein], or a promoter responsive to physiologic cues may be utilized. In certain embodiments, the inducible promoter is activated in response to T cell stimulation. In certain embodiments, the promoter is an NFAT, AP1, NFκB, or IRF4 promoter.

The expression cassette may also include, in certain embodiments, one or more IRES or 2A sequence(s) to allow for expression of multiple coding sequences from the same expression cassette. As exemplified herein, in one embodiment, a TCR directed to NY-ESO-1 is provided in which an LTBR intracellular domain is expressed contiguously with the TCRα (or TCRβ) chain. See, FIG. 5A, in a lentiviral vector which includes 2A sequences. Construction of such cassettes and vectors are known in the art, and are described herein in the Examples. See, e.g., Sack et al. Profound Tissue Specificity in Proliferation Control Underlies Cancer Drivers and Aneuploidy Patterns. Cell. 2018 Apr 5;173(2):499-514.e2 and Yang et al, A public genome-scale lentiviral expression library of human ORFs, Nat Methods. 2011 Aug; 8(8): 659–661, which are incorporated herein by reference.

Provided herein, in certain aspects, are compositions which include modified lymphocytes which comprise the nucleic acids and/or expression cassettes described herein. In one embodiment, the host lymphocyte is a T cell. In another embodiment, the host lymphocyte is a natural killer (NK) cell. In certain embodiments, the composition comprises a population of cells which includes a mixed population of lymphocytes (e.g., alpha beta T cells and NK T cells).

In other embodiments, the composition comprises cells which includes a population which is enriched for a particular lymphocyte population.

As used herein, the phrase "T cell" refers to a lymphocyte that expresses a T cell receptor molecule. T cells include human alpha beta (αβ) T cells and human gamma delta (γδ) T cells. T cells include, but are not limited to, naive T cells, stimulated T cells, primary T cells (e.g., uncultured), cultured T cells, immortalized T cells, helper T cells, cytotoxic T cells, memory T cells, regulatory T cells, natural killer T cells, combinations thereof, or subpopulations thereof. T cells can be CD4+, CD8+, or CD4+ and CD8+. T cells can also be CD4- , CD8-, or CD4- and CD8-. T cells can be helper cells, for example helper cells of type T_H1, T_H2, T_H3, T_H9, T_H17, or T_{FH}. T cells can be cytotoxic T cells. T cells can also be regulatory T cells. Regulatory T cells (Tregs) can be FOXP3+ or FOXP3-. T cells can be alpha/beta T cells or gamma/delta T cells. In some cases, the T cell is a $CD4+CD25^{hi}CD127^{lo}$ regulatory' T cell. In some cases, the T cell is a regulatory T cell selected from the group consisting of type 1 regulatory (Tr1), T_H3, CD8+CD28-, Treg17, and Qa-1 restricted T cells, or a combination or sub-population thereof. In some cases, the T cell is a $FOXP3^+$ T cell. In some cases, the T cell is a $CD4^+CD25^{lo}CD127^{hi}$ effector T cell. In some cases, the T cell is a $CD4^+CD25^{lo}$ $CD127^{hi}CD45RA^{hi}CD45RO$- naive T cell. In some cases, the T cell is a Vγ9Vδ2 T cell. In some embodiments, the T cell expresses a viral antigen. In other embodiments, the T cell expresses a cancer antigen. A T cell can be a recombinant T cell that has been genetically manipulated.

As used herein, the phrase "primary" in the context of a primary cell is a cell that has not been transformed or immortalized. Such primary cells can be cultured, sub-cultured, or passaged a limited number of times (e.g., cultured 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 times). In some cases, the primary cells are adapted to in vitro culture conditions. In some cases, the primary cells are isolated from an organism, system, organ, or tissue, optionally sorted, and utilized directly without culturing or sub-culturing. In some cases, the primary cells are stimulated, activated, or differentiated. For example, primary T cells can be activated by contact with (e.g., culturing in the presence of) CD3, CD28 agonists, IL-2, IFN-γ, or a combination thereof.

Methods

Methods of making modified host cells

Also provided herein are methods of making the modified cells and compositions containing modified cells as described herein. Methods of modifying cells, e.g., lymphocytes, to introduce an exogenous sequence, such as an expression cassette or expression vector comprising a coding sequence for a fusion protein, a CAR, or TCR, or more than one of these sequences, are

known in the art. For example, see, e.g., WO 2016/109410 A2, which is incorporated herein by reference. In certain embodiments, more than one exogenous sequence is introduced.

By the term "modified" as used herein, is meant a changed state or structure of a molecule or cell of the invention. Molecules may be modified in many ways, including chemically, structurally, and functionally. Cells may be modified through the introduction of nucleic acids. Modifying can refer to altering expression of a gene in a lymphocyte, for example, by introducing an exogeneous nucleic acid that encodes the gene.

The lymphocytes provided herein can be genetically modified, e.g., by transfection, transduction, or electroporation, to express a nucleic acid sequence encoding a fusion protein, TCR, or CAR, as described herein. Depending on the clinical context, e.g., patient's condition or condition to be treated, prolonged or permanent expression of the gene and/or, e.g., for robust and long-lasting CAR activity, e.g., anti-tumor activity, may be desirable. In such embodiments, the lymphocytes are genetically modified, e.g., transduced, e.g., virally transduced, using vectors comprising nucleic acid sequences encoding a gene disclosed herein to confer a desired effector function. In other embodiments, transient expression of the gene is desirable. In such embodiments, the use of, e.g., mRNA or a regulatable promoter to express the effector-enhancing gene, may be used.

Methods of introducing and expressing genes into a cell are known in the art. In the context of an expression vector, the vector can be readily introduced into a host cell, e.g., mammalian, bacterial, yeast, or insect cell by any known in the art. For example, the expression vector can be transferred into a host cell by physical, chemical, or biological means.

Physical methods for introducing a polynucleotide into a host cell include calcium phosphate precipitation, lipofection, particle bombardment, microinjection, electroporation, and the like. Methods for producing cells comprising vectors and/or exogenous nucleic acids are well-known in the art. See, for example, Sambrook et al., 2012, MOLECULAR CLONING: A LABORATORY MANUAL, volumes 1-4, Cold Spring Harbor Press, NY). A suitable method for the introduction of a polynucleotide into a host cell is calcium phosphate transfection.

Biological methods for introducing a polynucleotide of interest into a host cell include the use of DNA and RNA vectors. Viral vectors, and especially retroviral vectors, have become the most widely used method for inserting genes into mammalian, e.g., human cells. Viral vectors can be derived from lentivirus, poxviruses, herpes simplex virus I, adenoviruses, and adeno-associated viruses, and the like.

Chemical means for introducing a polynucleotide into a host cell include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes.

An exemplary colloidal system for use as a delivery vehicle in vitro and in vivo is a liposome (e.g., an artificial membrane vesicle). Other methods of targeted delivery of nucleic acids are available, such as delivery of polynucleotides with targeted nanoparticles or other suitable sub-micron sized delivery system. In the case where a non-viral delivery system is utilized, an exemplary delivery vehicle is a liposome. The use of lipid formulations is contemplated for the introduction of the nucleic acids into a host cell (in vitro, ex vivo or in vivo). In another aspect, the nucleic acid may be associated with a lipid. The nucleic acid associated with a lipid may be encapsulated in the aqueous interior of a liposome, interspersed within the lipid bilayer of a liposome, attached to a liposome via a linking molecule that is associated with both the liposome and the oligonucleotide, entrapped in a liposome, complexed with a liposome, dispersed in a solution containing a lipid, mixed with a lipid, combined with a lipid, contained as a suspension in a lipid, contained or complexed with a micelle, or otherwise associated with a lipid. Lipid, lipid/DNA or lipid/expression vector associated compositions are not limited to any particular structure in solution. For example, they may be present in a bilayer structure, as micelles, or with a "collapsed" structure. They may also simply be interspersed in a solution, possibly forming aggregates that are not uniform in size or shape. Lipids are fatty substances which may be naturally occurring or synthetic lipids. For example, lipids include the fatty droplets that naturally occur in the cytoplasm as well as the class of compounds which contain long-chain aliphatic hydrocarbons and their derivatives, such as fatty acids, alcohols, amines, amino alcohols, and aldehydes. Also contemplated are lipofectamine-nucleic acid complexes.

Regardless of the method used to introduce exogenous nucleic acids into a host cell or otherwise expose a cell to the inhibitor of the present invention, in order to confirm the presence of the recombinant nucleic acid sequence in the host cell, a variety of assays may be performed. Such assays include, for example, Southern and Northern blotting, RT-PCR and PCR, biochemical assays, such as detecting the presence or absence of a particular peptide, e.g., by immunological means (ELISAs and Western blots).

In certain embodiments, an expression vector is provided which includes the coding sequence for a fusion protein comprising an LTBR domain and a domain from a protein that is not LTBR. In other embodiments, the expression vector includes the coding sequence for one or more components of a CAR or TCR. In other embodiments, the expression vector includes the coding sequence for one or more components of a CAR or TCR that includes one or more LTBR domains. In other embodiments, the expression vector includes the coding sequence for one or more components of a CAR or TCR that includes one or more domains of a gene of Table 1. Expression vectors include all those known in the art, including cosmids, plasmids (e.g., naked or contained in liposomes) and viruses (e.g., lentiviruses, retroviruses, adenoviruses, and adeno-

associated viruses) that incorporate the recombinant polynucleotide. In one embodiment, the expression vector is a lentivirus. If more than one expression vector is utilized, each expression vector may be individually selected from amongst those known in the art.

Provided herein is a method of making a population of immune effector cells (e.g., T cells, NK cells) that are modified to express a fusion protein, TCR, or CAR as described herein. Methods for making such immune cells include introducing an exogenous nucleic acid encoding a LTBR-domain fusion protein into the cell. Also provided herein is a method of making a population of immune effector cells (e.g., T cells, NK cells) that are modified to express a CAR or TCR that includes one or more LTBR domains. Methods for making such immune cells include introducing an exogenous nucleic acid encoding the CAR or TCR into the cell. In certain embodiments, immune effector cells comprising the fusion proteins described herein are long lived and/or resistant to apoptosis.

In the examples described below, a method of making modified T cells is described for convenience. However, alternative embodiments are envisioned using other kinds of immune cells, e.g., NK T cells or NK cells. Suitable methods are known in the art.

Briefly, an exemplary method includes providing a population of immune effector cells (e.g., T cells), and optionally, removing T regulatory cells, e.g., CD25+ T cells, from the population. In one embodiment, the population of immune effector cells are autologous to the subject who the cells will be administered to for treatment. In one embodiment, the population of immune effector cells are allogeneic to the subject who the cells will be administered to for treatment. In one embodiment, the T regulatory cells, e.g., CD25+ T cells, are removed from the population using an anti-CD25 antibody, or fragment thereof, or a CD25-binding ligand, e.g., IL-2. In one embodiment, the anti-CD25 antibody, or fragment thereof, or CD25-binding ligand is conjugated to a substrate, e.g., a bead, or is otherwise coated on a substrate, e.g., a bead. In one embodiment, the anti-CD25 antibody, or fragment thereof, is conjugated to a substrate as described herein. In one embodiment, the T regulatory cells, e.g., CD25+ T cells, are removed from the population using an anti-CD25 antibody molecule, or fragment thereof. In another embodiment, CD25+ cells are not removed.

Another exemplary method includes providing a population of immune effector cells (e.g., T cells), and enriching the population for CD8+ cells and subsequently, enriching the population for CD4+ cells. In one embodiment, population is enriched for CD8+ and CD4+ T cells using an anti-CD8 and anti-CD4 antibody, or fragment thereof, or a CD8-binding ligand or CD4-binding ligand. In one embodiment, the anti-CD4 or anti-CD8 antibody, or fragment thereof, or CD4 or anti-CD8-binding ligand is conjugated to a substrate, e.g., a bead, or is

otherwise coated on a substrate, e.g., a bead. In one embodiment, the anti-CD4 antibody or anti-CD8, or fragment thereof, is conjugated to a substrate as described herein.

In one embodiment, the method further comprises transducing a cell from the population with one or more vectors comprising a nucleic acid encoding a fusion protein, CAR, or TCR as described herein. In one embodiment, the vector is selected from the group consisting of a DNA, a RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector. In one embodiment, the cell from the population of T cells is transduced with a vector once, e.g., within one day after population of immune effector cells are obtained from a blood sample from a subject, e.g., obtained by apheresis. In one embodiment, the method further comprises generating a population of RNA- engineered cells transiently expressing exogenous RNA from the population of T cells. The method comprises introducing an in vitro transcribed RNA or synthetic RNA into a cell from the population, where the RNA comprises a nucleic acid encoding an LTBR domain-containing fusion protein, a TCR, or CAR.

In another embodiment, the method further comprises transducing a cell from the population with one or more vectors comprising a nucleic acid encoding a CAR or TCR that includes one or more LTBR domains as described herein. In one embodiment, the vector is selected from the group consisting of a DNA, a RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector. In one embodiment, the cell from the population of T cells is transduced with a vector once, e.g., within one day after population of immune effector cells are obtained from a blood sample from a subject, e.g., obtained by apheresis. In one embodiment, the method further comprises generating a population of RNA- engineered cells transiently expressing exogenous RNA from the population of T cells. The method comprises introducing an in vitro transcribed RNA or synthetic RNA into a cell from the population, where the RNA comprises a nucleic acid encoding a CAR or TCR that includes one or more LTBR domains as described herein.

In one embodiment, modified cells described herein are expanded. In one embodiment, the cells are expanded in culture for a period of several hours (e.g., about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 18, 21 hours) to about 14 days (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 days). In one embodiment, the cells are expanded in culture for 3 or 4 days, and the resulting cells are more potent than the same cells expanded in culture for 9 days under the same culture conditions. Potency can be defined, e.g., by various T cell functions, e.g., proliferation, target cell killing, cytokine production, activation, migration, or combinations thereof.

Methods of Treatment

Also provided herein, in certain aspects, are methods of treating cancer in a subject. In certain embodiments, the method includes administering to the subject a cell that expresses a fusion protein as described herein such that the cancer is treated in the subject. In certain embodiments, the cell further expresses a CAR. In other embodiments, the cell further expresses a TCR. As used herein in describing the methods of treatment, LTBR is utilized as an exemplary effector-enhancing gene, for convenience. However, in alternative embodiments, the other genes of Table 3 are also utilized in modified CAR or TCR containing cells in the methods. In one embodiment, the method includes obtaining cells from a patient, modifying the cells as described herein, and administering the cells to the patient.

In certain embodiments, the method includes administering to the subject a cell that expresses a CAR or TCR that includes one or more LTBR domains as described herein such that the cancer is treated in the subject. In one embodiment, the method includes obtaining cells from a patient, modifying the cells as described herein, and administering the cells to the patient.

In certain embodiments, the method includes administering to the subject a cell that expresses a CAR or TCR that includes one or more domains from a gene of Table 3 as described herein such that the cancer is treated in the subject. In one embodiment, the method includes obtaining cells from a patient, modifying the cells as described herein, and administering the cells to the patient.

The term "cancer" as used herein refers to any disease, condition, trait, genotype or phenotype characterized by unregulated cell growth or replication. In certain embodiments, administration of the compositions disclosed herein, e.g., according to the methods disclosed herein, treats a cancer. In certain embodiments, the cancer is selected from the group consisting of adrenal cortical cancer, advanced cancer, anal cancer, aplastic anemia, bileduct cancer, bladder cancer, bone cancer, bone metastasis, brain tumors, brain cancer, breast cancer, childhood cancer, cancer of unknown primary origin, Castleman disease, cervical cancer, colon/rectal cancer, endometrial cancer, esophagus cancer, Ewing family of tumors, eye cancer, gallbladder cancer, gastrointestinal carcinoid tumors, gastrointestinal stromal tumors, gestational trophoblastic disease, Hodgkin disease, Kaposi sarcoma, renal cell carcinoma, laryngeal and hypopharyngeal cancer, acute lymphocytic leukemia, acute myeloid leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia, chronic myelomonocytic leukemia, liver cancer, hepatocellular carcinoma (HCC), non-small cell lung cancer, small cell lung cancer, lung carcinoid tumor, lymphoma of the skin, malignant mesothelioma, multiple myeloma, myelodysplastic syndrome, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-Hodgkin lymphoma, oral cavity and oropharyngeal cancer, osteosarcoma, ovarian cancer, pancreatic cancer, penile cancer, pituitary tumors, prostate cancer, retinoblastoma, rhabdomyosarcoma,

salivary gland cancer, sarcoma in adult soft tissue, basal and squamous cell skin cancer, melanoma, small intestine cancer, stomach cancer, testicular cancer, throat cancer, thymus cancer, thyroid cancer, uterine sarcoma, vaginal cancer, vulvar cancer, Waldenstrom macroglobulinemia, Wilms tumor, secondary cancers caused by cancer treatment, and any combination thereof. An example of a cancer that is treatable by the modified cell (e.g., LTBR CART or LTBR TCR-T cell, or LTBR-containing CART or TCR-T cell) is a hematological cancer. In one aspect, a hematologic cancer including but is not limited to leukemia (such as acute myelogenous leukemia, chronic myelogenous leukemia, acute lymphoid leukemia, chronic lymphoid leukemia and myelodysplastic syndrome) and malignant lymphoproliferative conditions, including lymphoma (such as multiple myeloma, non-Hodgkin's lymphoma, Burkitt's lymphoma, and small cell- and large cell-follicular lymphoma). In other embodiments, a hematologic cancer can include minimal residual disease, MRD, e.g., of a leukemia, e.g., of AML or MDS. Other cancers include breast cancer, lung cancer, prostate cancer, colorectal cancer, esophageal cancer, stomach cancer, bladder cancer, pancreatic cancer, kidney cancer, cervical cancer, liver cancer, ovarian cancer, and testicular cancer. In other embodiments, the cancer is a solid tumor cancer. In certain embodiments, the cancer is one of those listed in FIG. 19 or FIG. 20.

In certain embodiments, the CAR is selected from Axicabtagene ciloleucel (Yescarta®), Brexucabtagene autoleucel (Tecartus™), Idecabtagene vicleucel (Abecma™), Lisocabtagene maraleucel (Breyanzi®), Tisagenlecleucel (Kyrmriah®).

Autoimmune diseases are conditions arising from abnormal immune attack to the body, and they substantially increase the morbidity, mortality and healthcare costs worldwide. As T cells play a key role in the process of autoimmune diseases, engineered T-cell therapy has emerged and is also regarded as a potential approach to overcome current roadblocks in the treatment of autoimmune diseases. Either self-reactive or autoantibodies play a key role in the process of autoimmune diseases. Thus, engineering T cells to express a chimeric autoantibody receptor (CAAR) is a strategy for treatment for autoimmune disease. In one embodiment, the CAR comprises a CAAR. See, e.g., Zhang et al, Chimeric antigen receptor T-cell therapy beyond cancer: current practice and future prospects, Immunotherapy, 2020 Sep;12(13):1021-1034. doi: 10.2217/imt-2020-0009. Epub 2020 Jul 30, which is incorporated herein by reference. Autoimmune diseases include Pemphigus vulgaris (PV) (e.g., DSG3-CAAR-T) and lupus (e.g., MuSK-CAAR-T)). Other autoimmune diseases include type 1 diabetes, autoimmune thyroid disease, rheumatoid arthritis (RA), inflammatory bowel disease, colitis, systemic lupus erythematosus, and multiple sclerosis (MS). See, e.g., Chen et al, Immunotherapy Deriving from CAR-T Cell Treatment in Autoimmune Diseases, Journal of Immunology Research Volume

2019, December 31, 2019, which is incorporated herein by reference. Other conditions treatable with the compositions described herein include graft-versus-host disease (GVHD) and transplant rejection.

In another embodiment, the subject has a virally-driven cancer. In certain embodiments, the virally-driven cancer is selected from the following:

Virus	Conditions
Epstein-Barr Virus (EBV)	Burkitt's Lymphoma
Hepatitis B Virus (HBV)	Liver Cancer
Hepatitis C Virus (HCV)	Liver Cancer
Human Herpesvirus 8 (HH8)	Kaposi's Sarcoma
Human Papillomavirus (HPV)	Cervical Cancer, Head and Neck Cancers, Anal, Oral, Pharyngeal, and Penile Cancers
Human T-cell Lymphotropic Virus 1 (HTLV)	Adult T-cell Leukemia
Merkel Cell Polyomavirus	Skin Cancer (Merkel Cell Carcinoma)

In one aspect, the methods comprise administering to the subject in need thereof an effective amount of an effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell) described herein in combination with an effective amount of another therapy. Administered "in combination", as used herein, means that two (or more) different treatments are delivered to the subject during the course of the subject's affliction with the disorder, e.g., the two or more treatments are delivered after the subject has been diagnosed with the disorder and before the disorder has been cured or eliminated or treatment has ceased for other reasons. In some embodiments, the delivery of one treatment is still occurring when the delivery of the second begins, so that there is overlap in terms of administration. This is sometimes referred to herein as "simultaneous" or "concurrent delivery". In other embodiments, the delivery of one treatment ends before the delivery of the other treatment begins. In some embodiments of either case, the treatment is more effective because of combined administration. For example, the second treatment is more effective, e.g., an equivalent effect is seen with less of the second treatment, or the second treatment reduces symptoms to a greater extent, than would be seen if the second

treatment were administered in the absence of the first treatment, or the analogous situation is seen with the first treatment. In some embodiments, delivery is such that the reduction in a symptom, or other parameter related to the disorder is greater than what would be observed with one treatment delivered in the absence of the other. The effect of the two treatments can be partially additive, wholly additive, or greater than additive. The delivery can be such that an effect of the first treatment delivered is still detectable when the second is delivered.

An effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell) described herein and the at least one additional therapeutic agent can be administered simultaneously, in the same or in separate compositions, or sequentially. For sequential administration, the effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) cell described herein can be administered first, and the additional agent can be administered second, or the order of administration can be reversed.

The effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell) and/or other therapeutic agents, procedures or modalities can be administered during periods of active disorder, or during a period of remission or less active disease. The effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell) can be administered before the other treatment, concurrently with the treatment, post-treatment, or during remission of the disorder.

When administered in combination, the effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell) and the additional agent (e.g., second or third agent), or all, can be administered in an amount or dose that is higher, lower or the same than the amount or dosage of each agent used individually, e.g., as a monotherapy. In certain embodiments, the administered amount or dosage of the effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell), the additional agent (e.g., second or third agent), or all, is lower (e.g., at least 20%, at least 30%, at least 40%, or at least 50%) than the amount or dosage of each agent used individually, e.g., as a monotherapy. In other embodiments, the amount or dosage of the effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell), the additional agent (e.g., second or third agent), or all, that results in a desired effect (e.g., treatment of cancer) is lower (e.g., at least 20%, at least 30%, at least 40%, or at least 50% lower) than the amount or dosage of each agent used individually, e.g., as a monotherapy, required to achieve the same therapeutic effect.

In further aspects, a effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell) described herein may be used in a treatment regimen in combination with surgery, chemotherapy, radiation, immunosuppressive agents, such as cyclosporin, azathioprine, methotrexate, mycophenolate, and FK506, antibodies, or other immunoablative agents such as CAMPATH, anti-CD3 antibodies or other antibody therapies, cytoxan, fludarabine, cyclosporin, FK506, rapamycin, mycophenolic acid, steroids, FR901228, cytokines, irradiation, or a peptide vaccine, such as that described in Izumoto et al. 2008 J Neurosurg 108:963-971.

In certain instances, an effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell) as described herein are combined with other therapeutic agents, such as other anti-cancer agents, anti-allergic agents, anti-nausea agents (or anti-emetics), pain relievers, cytoprotective agents, and combinations thereof.

In one embodiment, an effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell) as described herein can be used in combination with a chemotherapeutic agent. Exemplary chemotherapeutic agents include an anthracycline (e.g., doxorubicin (e.g., liposomal doxorubicin)), a vinca alkaloid (e.g., vinblastine, vincristine, vindesine, vinorelbine), an alkylating agent (e.g., cyclophosphamide, decarbazine, melphalan, ifosfamide, temozolomide), an immune cell antibody (e.g., alemtuzamab, gemtuzumab, rituximab, ofatumumab, tositumomab, brentuximab), an antimetabolite (including, e.g., folic acid antagonists, pyrimidine analogs, purine analogs and adenosine deaminase inhibitors (e.g., fludarabine)), an mTOR inhibitor, a TNFR glucocorticoid induced TNFR related protein (GITR) agonist, a proteasome inhibitor (e.g., aclacinomycin A, gliotoxin or bortezomib), an immunomodulator such as thalidomide or a thalidomide derivative (e.g., lenalidomide), or a checkpoint inhibitor (e.g., a PD-1 or PD-L1 inhibitor, e.g., Pembrolizumab (Keytruda), Nivolumab (Opdivo), Cemiplimab (Libtayo), Atezolizumab (Tecentriq), Avelumab (Bavencio), Durvalumab (Imfinzi)).

General chemotherapeutic agents considered for use in combination therapies include anastrozole (Arimidex®), bicalutamide (Casodex®), bleomycin sulfate (Blenoxane®), busulfan (Myleran®), busulfan injection (Busulfex®), capecitabine (Xeloda®), N4-pentoxycarbonyl-5-deoxy-5-fluorocytidine, carboplatin (Paraplatin®), carmustine (BiCNU®), chlorambucil (Leukeran®), cisplatin (Platinol®), cladribine (Leustatin®), cyclophosphamide (Cytoxan® or Neosar®), cytarabine, cytosine arabinoside (Cytosar-U®), cytarabine liposome injection (DepoCyt®), dacarbazine (DTIC-Dome®), dactinomycin (Actinomycin D, Cosmegan), daunorubicin hydrochloride (Cerubidine®), daunorubicin citrate liposome injection

(DaunoXome®), dexamethasone, docetaxel (Taxotere®), doxorubicin hydrochloride (Adriamycin®, Rubex®), etoposide (Vepesid®), fludarabine phosphate (Fludara®), 5-fluorouracil (Adrucil®, Efudex®), flutamide (Eulexin®), tezacitibine, Gemcitabine (difluorodeoxycitidine), hydroxyurea (Hydrea®), Idarubicin (Idamycin®), ifosfamide (IFEX®), irinotecan (Camptosar®), L-asparaginase (ELSPAR®), leucovorin calcium, melphalan (Alkeran®), 6-mercaptopurine (Purinethol®), methotrexate (Folex®), mitoxantrone (Novantrone®), mylotarg, paclitaxel (Taxol®), phoenix (Yttrium90/MX-DTPA), pentostatin, polifeprosan 20 with carmustine implant (Gliadel®), tamoxifen citrate (Nolvadex®), teniposide (Vumon®), 6-thioguanine, thiotepa, tirapazamine (Tirazone®), topotecan hydrochloride for injection (Hycamptin®), vinblastine (Velban®), vincristine (Oncovin®), and vinorelbine (Navelbine®).

Treatment with a combination of a chemotherapeutic agent and an effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell) described herein can be used to treat a hematologic cancer described herein, e.g., AML. In embodiments, the combination of a chemotherapeutic agent and an effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell) is useful for targeting, e.g., killing, cancer stem cells, e.g., leukemic stem cells, e.g., in subjects with AML. In embodiments, the combination of a chemotherapeutic agent and an effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell) is useful for treating minimal residual disease (MRD). MRD refers to the small number of cancer cells that remain in a subject during treatment, e.g., chemotherapy, or after treatment. MRD is often a major cause for relapse. The present invention provides a method for treating cancer, e.g., MRD, comprising administering a chemotherapeutic agent in combination with an effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell), e.g., as described herein.

In an embodiment, the chemotherapeutic agent is administered prior to administration of the effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell). In chemotherapeutic regimens where more than one administration of the chemotherapeutic agent is desired, the chemotherapeutic regimen is initiated or completed prior to administration of the effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell). In embodiments, the chemotherapeutic agent is administered at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7

days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, 14 days, 15 days, 20 days, 25 days, or 30 days prior to administration of the effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell). In embodiments, the chemotherapeutic regimen is initiated or completed at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, 14 days, 15 days, 20 days, 25 days, or 30 days prior to administration of the effector-enhancing gene-expressing cell (e.g., LTBR CART or LTBR TCR-T cell) or LTBR-containing CAR/TCR expressing cell (LTBR-containing CART or TCR-T cell).

When "an immunologically effective amount," "an anti-tumor effective amount," "a tumor-inhibiting effective amount," or "effective amount" is indicated, the precise amount of the compositions of the present invention to be administered can be determined by a physician with consideration of individual differences in age, weight, tumor size, extent of infection or metastasis, and condition of the patient (subject). It can generally be stated that a pharmaceutical composition comprising the T cells described herein may be administered at a dosage of 10^4 to 10^9 cells/kg body weight, in some instances 10^5 to 10^6 cells/kg body weight, including all integer values within those ranges. T cell compositions may also be administered multiple times at these dosages. The cells can be administered by using infusion techniques that are commonly known in immunotherapy (see, e.g., Rosenberg et al., New Eng. J. of Med. 319:1676, 1988). As used herein, the term "effective amount" of an agent is that amount sufficient to effect beneficial or desired results, for example, clinical results, and, as such, an "effective amount" depends upon the context in which it is being applied. For example, in the context of administering an agent that treats a tumor, an effective amount of an agent is, for example, an amount sufficient to reduce or decrease a size of a tumor or to inhibit a tumor growth, as compared to the response obtained without administration of the agent. The term "effective amount" can be used interchangeably with "effective dose," "therapeutically effective amount," or "therapeutically effective dose."

Also provided herein is a method of vaccinating a subject with a combination vaccine including at least two nucleic acid sequences encoding at least one effector-enhancing gene and at least one viral protein. In one embodiment, the effector-enhancing gene is LTBR. In another embodiment, the viral protein is a coronavirus spike protein. Some embodiments provide vaccines comprising an RNA polynucleotide having an open reading frame encoding an effector-enhancing gene, an RNA polynucleotide having an open reading frame encoding an effector-enhancing gene a viral protein, and a pharmaceutically acceptable carrier or excipient, formulated within a cationic lipid nanoparticle (LNP). The vaccines described herein (e.g., LNP-encapsulated mRNA vaccines) produce prophylactically- and/or therapeutically-efficacious levels,

concentrations and/or titers of antigen-specific antibodies in the blood or serum of a vaccinated subject. See, e.g., US 2018/0311336A1, which is incorporated herein by reference in its entirety.

As used herein, the term "treatment," and variations thereof such as "treat" or "treating," refers to clinical intervention in an attempt to alter the natural course of the individual being treated and can be performed either for prophylaxis or during the course of clinical pathology. Desirable effects of treatment include, but are not limited to, preventing or reducing the occurrence or recurrence of disease, alleviation of symptoms, diminishment of any direct or indirect pathological consequences of the disease, decreasing the rate of disease progression, amelioration or palliation of the disease state, and remission or improved prognosis. In certain embodiments, compositions described herein are used to delay development of a disease or to slow the progression of a disease.

Likewise, as used herein, the term "treatment of cancer" or "treating cancer" can be described by a number of different parameters including, but not limited to, reduction in the size of a tumor in an animal having cancer, reduction in the growth or proliferation of a tumor in an animal having cancer, preventing metastasis or reducing the extent of metastasis, and/or extending the survival of an animal having cancer compared to control. In certain embodiments, treatment results in a reduced risk of distant recurrence or metastasis.

With regard to the description of the inventions provided herein, it is intended that each of the compositions described, is useful, in another embodiment, in the methods of the invention. In addition, it is also intended that each of the compositions herein described as useful in the methods, is, in another embodiment, itself an embodiment of the invention.

The following examples are provided for the purpose of illustration only and the invention should in no way be construed as being limited to this example but rather should be construed to encompass any and all variations that become evident as a result of the teachings provided herein.

EXAMPLES

Example 1: Materials and Methods

Isolation and culture of primary human T cells

Standard buffy coats containing peripheral blood from de-identified healthy donors were collected by and purchased from the New York Blood Center under an IRB-exempt protocol. All donors provided informed consent. Peripheral blood mononuclear cells (PBMC) were isolated from buffy coats using Lymphoprep (Stemcell) gradient centrifugation. For most assays, $CD8^+$ and $CD4^+$ were isolated sequentially from the same donor. First, $CD8^+$ T cells were isolated by magnetic positive selection using the EasySep Human CD8 Positive Selection Kit II (Stemcell).

Then, $CD4^+$ T cells were isolated from the resulting flowthrough by negative magnetic selection using the EasySep Human $CD4^+$ T cell Isolation Kit (Stemcell). γδ T cells were isolated by magnetic negative selection using the EasySep Human Gamma/Delta T cell Isolation Kit (Stemcell). Immediately after isolation, T cells were resuspended in T cell medium, which consisted of Immunocult-XF T cell Expansion Medium (Stemcell) supplemented with 10 ng ml^{-1} recombinant human IL-2 (Stemcell).

Activation of T cells was performed with Immunocult Human CD3/CD28 T cell Activator (Stemcell) using 25 µl per 10^6 cells per ml. Typically, T cells were transduced with concentrated lentivirus 24 h after isolation. For some experiments, T cells were electroporated with in-vitro-transcribed mRNA 24 h after isolation or with Cas9 protein 48 h after isolation. At 72 h after isolation, lentivirally transduced T cells were selected with 2 µg ml^{-1} puromycin.

Every 2–3 days, T cells were either split or had the medium replaced to maintain a cell density of 1×10^6–2×10^6 cells per ml. Lentivirally transduced T cells were maintained in medium containing 2 µg ml^{-1} puromycin for the duration of culture. T cells were used for phenotypic or functional assays between 14 and 21 days after isolation, or cryopreserved in Bambanker Cell Freezing Medium (Bulldog Bio). γδ T cells were further purified before functional assays using anti-Vγ9 PE antibody (Biolegend) and anti-PE microbeads (Miltenyi Biotec) according to the manufacturer's recommendations, in the presence of dasatinib, a protein kinase inhibitor, to prevent activation-induced cell death resulting from TCR cross-linking[42]. PBMCs from patients with diffuse large B cell lymphoma were obtained from the Perlmutter Cancer Center under a protocol approved by the Perlmutter Cancer Center Institutional Review Board (S14-02164).

Vector design and molecular cloning

All vectors used were cloned using Gibson Assembly (NEB). For the experiments shown in FIG. 1A – FIG. 1D, we used the lentiviral backbone from the pHAGE plasmid[14]. For all other experiments, the backbone from lentiCRISPRv2 (Addgene 52961) was used. ORFs were PCR-amplified for cloning from the genome-scale library used in the screen.

After adding Gibson overhangs by PCR, ORFs and P2A-puro were inserted into XbaI- and EcoRI-cut lentiCRISPRv2. The sgRNA cassette was removed from lentiCRISPRv2 using PacI and NheI digest. For *LTBR* overexpression and knockout experiments, the sgRNA cassette was not removed. CARs were synthesized as gBlocks (IDT). For CAR-ORF cloning, CAR-P2A-puro-T2A(partial) were first inserted into XbaI- and EcoRI-cut lentiCRISPRv2. For subsequent ORF insertion, the plasmid was cut with HpaI located within the partial T2A and EcoRI. The following vectors were deposited to Addgene: pOT_01 (lenti-EFS-LTBR-2A-puro, Addgene 181970), pOT_02 (lenti-EFS-tNGFR-2A-puro, Addgene 181971), pOT_03 (lenti-EFS-FMC6.3-

28z-2A-puro-2A-LTBR, Addgene 181972), pOT_04 (lenti-EFS-FMC6.3-BBz-2A-puro-2A-LTBR, Addgene 181973), pOT_05 (lenti-EFS-FMC6.3-28z-2A-puro-2A-tNGFR, Addgene 181974) and pOT_06 (lenti-EFS-FMC6.3-BBz-2A-puro-2A-tNGFR, Addgene 181975).

Nuclease and CRISPR guide RNA design

All sgRNAs were designed using the GUIDES webtool[43]. We selected guides that target initial protein-coding exons (with the preference for targeting protein family domains enabled in GUIDES) as well as minimizing off-target and maximizing on-target scores. For Cas9 nuclease nucleofection, we used purified sNLS-SpCas9-sNLS nuclease (Aldevron).

Preparation of ORF library plasmids for paired-end sequencing

We re-amplified a previously described genome-scale ORF library[14] using Endura electrocompetent cells (Lucigen). The identity of ORFs and matched barcodes was confirmed by paired-end sequencing. In brief, the plasmid was first linearized with I-SceI meganuclease, which cuts downstream of the barcode. Then, the linearized plasmid was tagmented using TnY transposase[44]. Then, the fragmented plasmid was amplified in a PCR reaction, using a forward primer binding to a handle introduced by TnY and a reverse primer binding to a sequence downstream of the barcode. All transposons and PCR primer oligonucleotides were synthesized by IDT. The resulting amplicon was sequenced on a NextSeq 500. The forward read (containing the ORF) was mapped to GRCh38.101 CDS transcriptome annotations using STAR v.2.7.3a (map quality ≥ 10)[45]. Using the paired-end read, we also captured the 24 nucleotide barcode downstream of the constant plasmid sequence. We tabulated ORF–barcode combinations and further curated this table by eliminating any spurious pairs that might be due to sequencing or PCR error. Specifically, a permutation test was performed to identify the maximum number of ORF–barcode combinations expected by random chance, after which we only kept ORF–barcode combinations with a count that exceeded this maximum number. We excluded all non-coding elements from the reference and then collapsed barcodes that were within a Levenshtein distance less than 2.

Cell culture

HEK293FT cells were obtained from Thermo Fisher Scientific and cultured in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% Serum Plus-II (Thermo Fisher Scientific). Nalm6, Jurkat and BxPC3 cells were obtained from ATCC and cultured in RPMI-1640 supplemented with 10% Serum Plus-II. Capan-2 cells were obtained from ATCC and cultured in McCoy's medium supplemented with 10% Serum Plus-II. For γδ co-incubation

experiments, cell lines were pre-treated with 50 μM zoledronic acid (Sigma) for 24 h. Cell lines were routinely tested for mycoplasma using MycoAlert PLUS (Lonza) and found to be negative. Cell lines were not authenticated in this study.

Lentivirus production

We produced lentivirus by co-transfecting third-generation lentiviral transfer plasmids together with packaging plasmid psPAX2 (Addgene 12260) and envelope plasmid pMD2.G (Addgene 12259) into HEK293FT cells, using polyethyleneimine linear MW 25000 (Polysciences). After 72 h, we collected the supernatants, filtered them through a 0.45-μm Steriflip-HV filter (Millipore) and concentrated the virus using Lentivirus Precipitation Solution (Alstem). Concentrated lentivirus was resuspended in T cell medium containing IL-2 and stored at -80 C°.

Pooled ORF library screening

For pooled ORF library screening, $CD4^+$ and $CD8^+$ T cells were isolated from a minimum of 500×10^6 PBMCs from 3 healthy donors. The amount of lentivirus used for transduction was titrated to result in 20–30% transduction efficiency, to minimize the probability of multiple ORFs being introduced into a single cell. The cells were maintained in T cell medium containing 2 μg ml−1 puromycin and counted every 2–3 days to maintain a cell density of $1 \times 10^6 – 2 \times 10^6$ cells per ml. On day 14 after isolation, T cells were collected, counted, labelled with 5 μM CFSE (Biolegend) and stimulated with CD3/CD28 Activator (Stemcell) at 1.56 μl per 1×10^6 cells. An aliquot of cells representing 1,000× coverage of the library was frozen down at this step to be used as a pre-stimulation control. After 4 days of stimulation, cells were collected and an aliquot of cells representing 1,000× coverage of the library was frozen down to be used as a pre-sort control. The remaining cells were stained with LIVE/DEAD Violet cell viability dye (Thermo Fisher Scientific), and $CFSE^{low}$ cells (corresponding to the bottom 15% of the distribution) were sorted using a Sony SH800S cell sorter. Genomic DNA was isolated, and two rounds of PCR to amplify ORF barcodes and add Illumina adaptors were performed[46].

Pooled ORF screen analysis

For most of the analyses, equal numbers of reads from all three donors were combined per bin before trimming and alignment. The barcodes were mapped to the reference library after adaptor trimming with Cutadapt v.1.13 (-m 24 -e 0.1 --discard-untrimmed) using Bowtie v.1.1.2 (-v 1 -m 1 --best --strata)[47,48]. All subsequent analyses were performed in RStudio v.1.1.419 with R 4.0.0.2. To calculate individual barcode enrichment, barcode counts were normalized to the

total number of reads per sample (with pseudocount added) and $\log_2$-transformed. To calculate ORF enrichment, raw barcode counts were first collapsed by genes before normalization and $\log_2$ transformation.

We performed enrichment analyses at both the barcode and gene level. Statistical analysis on barcode enrichment was performed using MAGeCK[49], comparing $CFSE^{low}$ samples to corresponding inputs (pre-stimulation), using $CD4^+$ and $CD8^+$ as replicates. Statistical analysis on ORF enrichment was performed using DESeq2[50]. We obtained raw gene counts by collapsing barcodes into corresponding genes. $CFSE^{low}$ samples were compared to corresponding inputs (both pre-stimulation and pre-sort), using $CD4^+$ and $CD8^+$ as replicates. GO enrichment (biological process) on genes passing DESeq2 criteria ($\log_2$-transformed fold change > 0.5, $P_{adj} < 0.05$) was performed using the topGO package[51]. For the genes enriched in the $CFSE^{low}$ screen (DESeq2 analysis), we overlapped these genes with differentially expressed genes after CD3/CD28 stimulation using data from the Database of Immune Cell eQTLs, Expression, Epigenomics (DICE; https://dice-database.org/)[41]. For differentially expressed genes, we used the following DICE datasets: 'T cell, CD4, naive' versus 'T cell, CD4, naive [activated]', 'T cell, CD8, naive' versus 'T cell, CD8, naive [activated]'. Significant differential expression was as given in the DICE dataset ($P_{adj} < 0.05$).

Proliferation assays

Transduced T cells were collected at day 14 after isolation, counted and plated at 2.5×10^4 cells per well in a round bottom 96-well plate, in 2 sets of triplicate wells per transduction. One set of triplicate wells was cultured in Immunocult-XF T cell Expansion Medium supplemented with 10 ng ml^{-1} IL-2 and another set of triplicate wells was further supplemented with 1.56 µl CD3/CD28 Activator per 1 ml of medium. The cells were cultured for 4 days, and then were collected and stained with LIVE/DEAD Violet cell viability dye. Before flow cytometric acquisition, the cells were resuspended in D-PBS with 10% v/v Precision Counting Beads (Biolegend). For quantification, the number of viable cell events was normalized to the number of bead events per sample. Then, for each ORF the normalized number of viable cells in wells supplemented with CD3/CD28 Activator was divided by the mean number of viable cells in control wells to quantify T cell proliferation. To enable comparisons between donors and $CD4^+/CD8^+$ T cells, the proliferation of T cells transduced with a given ORF was finally normalized to the proliferation of a matched tNGFR control.

In addition to the counting beads assay, we also measured proliferation using a dye dilution assay. For this assay, transduced T cells were collected at day 14 after isolation, washed with D-PBS and then labelled with 5 µM CellTrace Yellow (CTY) in D-PBS for 20 min at room

temperature. The excess dye was removed by washing with a fivefold excess of RPMI-1640 supplemented with 10% Serum Plus-II. The labelled cells were then plated at 2.5×10^4 cells per well on a round bottom 96-well plate. One set of triplicate wells was cultured in supplemented Immunocult-XF T cell Expansion Medium (that is, without IL-2) and another set of triplicate wells was supplemented with 10 ng ml^{-1} IL-2 and 1.56 µl CD3/CD28 Activator per 1 ml of medium. The cells were cultured for 4 days, and then were collected and stained with LIVE/DEAD Violet cell viability dye. For quantification of the proliferation index, events were first gated on viable T cells in FlowJo (Treestar) and exported for further analysis in R/RStudio using the flowFit and flowCore packages[52]. Unstimulated cells were used to determine the parent population size and position to account for differences in staining intensity between different samples. These fitted parent population parameters were then used to fit the CTY profiles of matched stimulated samples, modelled as Gaussian distributions assuming log_2-distanced peaks as a result of cell division and dye dilution. Fitted CTY profiles were inspected visually for concordance with the original CTY profiles and used to calculate the proliferation index. The proliferation index is defined as the sum of cells in all generations divided by the computed number of parent cells present at the beginning of the assay.

Flow cytometry for cell-surface and intracellular markers

For CD25 (IL2RA) and CD154 (CD40L) quantification, T cells were restimulated with CD3/CD28 Activator (6.25 µl per 10^6 cells) for 6 h (CD154 staining in $CD8^+$) or for 24 h before staining (CD25 staining in both $CD4^+$ and $CD8^+$, and CD154 staining in $CD4^+$). For Ki-67 and 7-amino-actinomycin D (7-AAD) staining, T cells were rested overnight in Immunocult-XF T cell Expansion Medium without IL-2 and then activated with CD3/CD28 Activator (25 µl per 10^6 cells) for 24 h. In other cases, T cells were stained without stimulation. For detection of secreted proteins, T cells were stimulated for 24 h with CD3/CD28 Activator (25 µl per 10^6 cells) (LTA, LIGHT), and protein transport inhibitors brefeldin A (5 µg ml^{-1}) and monensin (2 µM) were included for the last 6 h of stimulation (IL12B, LTA, LIGHT).

First, the cells were collected, washed with D-PBS and stained with LIVE/DEAD Violet cell viability dye for 5 min at room temperature in the dark, followed by surface antibody staining for 20 min on ice. After surface antibody staining (where applicable) the cells were washed with PBS and acquired on a Sony SH800S cell sorter or taken for intracellular staining. For intracellular staining, the cells were resuspended in an appropriate fixation buffer. The following fixation buffers were used for specific protein detection: Fixation Buffer (Biolegend) for IL12B and MS4A3 staining; True-Nuclear Transcription Factor Fix (Biolegend) for BATF, TCF1 and FLAG staining; and FoxP3/Transcription Factor Fixation Reagent, (eBioscience) for Ki-67. After

resuspension in the fixation buffer, cells were incubated at room temperature in the dark for 1 h. Following the incubation, the cells were washed twice in the appropriate permeabilization buffer. The following permeabilization buffers were used: Intracellular Staining Permeabilization Wash Buffer (Biolegend) for IL12B and MS4A3 staining; True-Nuclear Perm Buffer (Biolegend) for BATF, TCF1 and FLAG staining; and FoxP3/Transcription Factor Permeabilization Buffer (eBioscience) for Ki-67. After permeabilization, the cells were stained with the specific antibody or isotype control for 30 min in the dark at room temperature. Finally, the cells were washed twice in the appropriate permeabilization buffer and acquired on a Sony SH800S flow cytometer. For cell-cycle analysis, the cells were further stained with 0.5 μg ml^{-1} 7-AAD for 5 min immediately before acquisition. Gating was performed using appropriate isotype, fluorescence minus one and biological controls. Typically, 5,000–10,000 live events were recorded per sample.

Flow cytometry detection of phosphorylated proteins

T cells were rested for 24 h in in Immunocult-XF T cell Expansion Medium without IL-2 before detection of phosphorylated proteins. The rested cells were stimulated with CD3/CD28 Activator (25 μl per 10^6 cells) for the times indicated in the corresponding figure. Immediately after the stimulation period, the cells were fixed with a 1:1 volume ratio of the pre-warmed Fixation Buffer (Biolegend) for 15 min at 37 °C and washed twice with the cell staining buffer (D-PBS + 2% FBS). As per the manufacturer's protocol, the cells were resuspended in the residual volume and permeabilized in 1 ml of pre-chilled True-Phos Perm Buffer (Biolegend) while vortexing. The cells were incubated in the True-Phos Perm Buffer for 60 min at –20 °C. After permeabilization the cells were washed twice with the cell staining buffer and stained with anti-CD4, anti-CD8, anti-RELA and anti-phospho-RELA antibodies (or isotype controls) for 30 min at room temperature. After staining, the cells were washed twice in the cell staining buffer and acquired on a Sony SH800S cell sorter. Gating was performed on $CD4^+$ or $CD8^+$ cells, and the levels of RELA and phospho-RELA were determined using appropriate isotype and biological controls.

Western blot detection of proteins and phosphorylated proteins

T cells expressing tNGFR or LTBR, resting or stimulated for 15 min with CD3/CD28 Activator (25 μl per 10^6 cells), were collected, washed with 1× D-PBS and lysed with TNE buffer (10 mM Tris-HCl, pH 7.4, 150 mM NaCl, 1 mM EDTA, 1% Nonidet P-40) in the presence of a protease inhibitor cocktail (Bimake B14001) and a phosphatase inhibitor cocktail (Cell Signaling Technologies 5872S) for 1 h on ice. Cell lysates were spun for 10 min at 10,000g, and the protein concentration was determined with the BCA assay (Thermo Fisher Scientific). Equal amounts of

cell lysates (25 mg) were denatured in Tris-Glycine SDS Sample buffer (Thermo Fisher Scientific) and loaded on a Novex 4–12 or 4–20 % Tris-Glycine gel (Thermo Fisher Scientific). The PageRuler pre-stained protein ladder (Thermo Fisher Scientific) was used to determine the protein size. The gel was run in 1× Tris-Glycine-SDS buffer (IBI Scientific) for about 120 min at 120 V. Proteins were transferred on a nitrocellulose membrane (BioRad)in the presence of prechilled 1× Tris-Glycine transfer buffer (Thermo Fisher Scientific) supplemented with 20% methanol for 100 min at 100 V.

Immunoblots were blocked with 5% skimmed milk dissolved in 1× PBS with 1% Tween-20 (PBST) and incubated overnight at 4 °C separately with the following primary antibodies: rabbit anti-GAPDH (0.1 mg ml^{-1}, Cell Signaling, 2118S), mouse anti-IKKα (1:1,000 dilution, Cell Signaling, 3G12), rabbit anti-IKKβ (1:1,000 dilution, Cell Signaling, D30C6), rabbit anti-NF-κB p65 (1:1,000 dilution, Cell Signaling, D14E12), rabbit anti-phospho-NF-κB p65 Ser536 (1:1,000 dilution, Cell Signaling, 93H1), mouse anti-IκBα (1:1,000 dilution, Cell Signaling, L35A5), rabbit anti-phospho-IκBα Ser32 (1:1,000 dilution, Cell Signaling, 14D4), rabbit anti-NF-κB p100/p52 (1:1,000 dilution, Cell Signaling, 4882) and rabbit anti-RELB (1:1,000 dilution, Cell Signaling, C1E4). After the primary antibody, the blots were incubated with IRDye 680RD donkey anti-rabbit (0.2 mg ml^{-1}, LI-COR 926–68073) or with IRDye 800CW donkey anti-mouse (0.2 mg ml^{-1}, LI-COR 926–32212). The blots were imaged using Odyssey CLx (LI-COR) and quantified using ImageJ v.1.52.

Quantification of cytokine secretion

For measurement of secreted IFNγ and IL-2, T cells were first collected and rested for 24 h in medium without IL-2. Then, they were counted, plated at 2.5×10^4 cells per well in a round bottom 96-well plate and incubated in medium without IL-2, with or without CD3/CD28 Activator (25 µl per 10^6 cells) for 24 h. Then, cell supernatants were collected, diluted and used for cytokine quantification with an enzyme-linked immunosorbent assay (Human IL-2 or IFNγ DuoSet, R&D Systems), using an Infinite F200 Pro (Tecan) plate reader. Multiplexed quantification of secreted cytokines and chemokines in resting or stimulated T cells was performed using the Human Cytokine/Chemokine 48-Plex Discovery Assay Array (Eve Technologies).

T cell killing assays

$CD19^+$ Nalm6 cells were first transduced with a lentiviral vector encoding EGFPd2PEST-NLS and a puromycin resistance gene[53]. The transduced cells were kept in puromycin selection throughout the culture, to maintain stable EGFP expression, and puromycin was only removed

from the medium before the killing assay. T cells were transduced with a vector encoding a CAR specific for CD19, using either a CD28 stalk, CD28 transmembrane and CD28 signaling domain or CD8 stalk and CD8 transmembrane domain with 4-1BB signaling domain, and CD3ζ signaling domain[54]. Fourteen days after transduction, transduced T cells were combined with 5×10^4 Nalm6 GFP$^+$ cells in triplicate at indicated effector:target ratios in a flat 96-well plate pre-coated with 0.01% poly-l-ornithine (EMD Millipore) in Immunocult medium without IL-2. The wells were then imaged using an Incucyte SX1, using 20× magnification and acquiring 4 images per well every 2 h for up to 120 h. For each well, the integrated GFP intensity was normalized to the 2 h time point, to allow the cells to fully settle after plating.

In vitro mRNA preparation

The template for in vitro transcription was generated by PCR from a plasmid encoding LTBR or tNGFR with the resulting amplicon including a T7 promoter upstream of the ORF. The purified template was then used for in vitro transcription with capping and poly-A tailing using the HiScribe T7 ARCA mRNA Kit with Capping (NEB).

Primary T cell nucleofection

Activated T cells were nucleofected with in-vitro-transcribed mRNA at 24 h after activation or with Cas9 protein at 48 h after activation. The cells were collected, washed twice in PBS and resuspended in P3 Primary Cell Nucleofector Solution (Lonza) at 5×10^5 cells per 20 µl. Immediately after resuspension, 1 µg mRNA or 10 µg Cas9 (Aldevron) were added (not exceeding 10% v/v of the reaction) and the cells were nucleofected using the E0–115 program on a 4D-Nucleofector (Lonza). After nucleofection the cells were resuspended in pre-warmed Immunocult medium with IL-2 and recovered at 37 °C with 5% CO2 for 20 min. After recovery, the cells were plated at 1×10^6 cells per ml and used in downstream assays.

OverCITE-seq sample preparation and sequencing

For single-cell sequencing, CD8$^+$ T cells were individually transduced with ORFs and kept, separately, under puromycin selection for 14 days. Then, transduced cells were combined and split into two conditions: one was cultured for 24 h only in the presence of IL-2; the other was further supplemented with 6.25 µl CD3/CD28 Activator per 10^6 cells. After stimulation, the cells were collected, counted and resuspended in staining buffer (2% BSA + 0.01% Tween-20 in PBS) at 2×10^7 cells per ml. Then, 10% (v/v) Human TruStain FcX Fc Receptor Blocking Solution (Biolegend) was added, and the cells were incubated at 4 °C for 10 min. After Fc receptor blocking, the cell concentration was adjusted to 5×10^6 cells per ml and the stimulated

and unstimulated cells were split into 4 conditions each. Each condition received a different oligonucleotide-conjugated (barcoded) cell hashing antibody to allow for pooling of different conditions in the same 10x Genomics Chromium lane[23]. After 20 min co-incubation on ice, the cells were washed 3 times with staining buffer and counted using Trypan blue exclusion. Cell viability was typically around 95%.

Then, cells stained with different hashing antibodies were pooled together at equal numbers and stained with the following oligonucleotide-conjugated (barcoded) antibodies for quantification of cell surface antigens: CD11c (0.1 μg), CD14 (0.2 μg), CD16 (0.1 μg), CD19 (0.1 μg), CD56 (0.2 μg), CD3 (0.2 μg), CD45 (0.01 μg), CD45RA (0.2 μg), CD45RO (0.2 μg), CD4 (0.1 μg), CD8 (0.1 μg), CD25 (0.25 μg), CD69 (0.25 μg) and NGFR (0.25 μg) (TotalSeq-C, Biolegend). The cells were stained for 30 min on ice, washed 3 times with staining buffer, resuspended in PBS and filtered through a 40-μm cell strainer. The cells were then counted and the concentration was adjusted to 1×10^6 ml^{-1}. For loading into the 10x Genomics Chromium, 3×10^4 cells were combined with Chromium Next GEM Single Cell 5′ v2 Master Mix (10x Genomics) supplemented with a custom reverse primer binding to the puromycin resistance cassette for boosting ORF transcript capture at the reverse transcription stage. The custom reverse primer was added at a 1:3 ratio to the poly-dT primer included in the Master Mix.

For cDNA amplification, additive primers for amplification of sample hashing and surface antigen barcodes were included[23], as well as a nested reverse primer binding to the puromycin resistance cassette downstream of the ORF. Following cDNA amplification, SPRI beads were used for size selection of resulting PCR products: small-size (fewer than 300 bp) sample hashing and surface antigen barcodes were physically separated from larger cDNA and ORF amplicons for downstream processing. Sample hashing and surface antigen barcodes were also processed[22]. Amplified cDNA was then separated into three conditions, for construction of the gene expression library, αβ TCR library and ORF library. The ORF library was processed similarly to the αβ TCR library, using nested reverse primers binding downstream of the ORF. The quality of produced libraries was verified on BioAnalyzer using the High Sensitivity DNA kit (Agilent). The libraries were sequenced on a NextSeq 500. For the gene expression library, more than 25,000 reads per cell were generated. For other libraries, more than 5,000 reads per cell were generated.

OverCITE-seq data analysis

Gene expression unique molecular identifier (UMI) count matrices and TCR clonotypes were derived using 10x Genomics Cell Ranger 3.1.0. Hashtag oligo (HTO) and antibody UMI count matrices were generated using kallisto v.0.46.0[55] and bustools v.0.39.3[56]. ORF reads were

first aligned to plasmid references using Bowtie2 v.2.2.8[57] and indexed to the associated ORF, after which kallisto and bustools were used to generate UMI count matrices. All modalities were normalized using a centred log ratio (CLR) transformation. Cell doublets and negatives were identified using the HTODemux[58] function and then excluded from downstream analysis. The UMI cut-off quantile for HTODemux was optimized to maximize singlet recovery using grid search with values between 0 and 1. ORF singlets were identified using MULTIseqDemux[59].We then excluded cells with low-quality gene expression metrics and removed cells with fewer than 200 unique RNA features or greater than 5% of reads mapping to the mitochondrial transcriptome.

Count matrices were then loaded into and analyzed with Seurat v.4.0.1[60]. Cell cycle correction and scaling of gene expression data was performed using the CellCycleScoring function with default genes, followed by scaling the data using the ScaleData function. Principal component (PC) optimization of the scaled and corrected data was then performed using JackStraw[61], in which we selected all PCs up to the first non-significant PC to use in clustering. Clustering of cells was performed using a shared nearest neighbor (SNN)-based clustering algorithm and visualized using UMAP dimensional reduction[62] to project cluster PCs into 2D space. Cluster marker analysis was performed using the FindAllMarkers function with the hypothesis set defined as positive and negative markers present in at least 25% of cluster cells and with a $\log_2$-transformed fold change threshold of 0.25 as compared to non-cluster cells. Differential expression analysis of ORFs was performed using DESeq2[50] to identify genes up and downregulated in ORF-expressing cells as compared to NGFR (control) cells, with differential expression defined as those with $q < 0.1$ calculated using the Storey method[63].

Bulk RNA-seq and analysis

$CD4^+$ and $CD8^+$ LTBR- or tNGFR-transduced T cells were stimulated for 24 h with CD3/CD28 Activator (25 µl per 10^6 cells) or left unstimulated ($n = 3$ biological replicates). Total RNA was extracted using the Direct-zol RNA purification kit (Zymo). The 3′-enriched RNA-seq library was prepared as described before[64]. In brief, RNA was reverse-transcribed using SMARTScribe Reverse Transcriptase (Takara Bio) and a poly(dT) oligo containing a partial Nextera handle. The resulting cDNA was then PCR-amplified for 3 cycles using OneTaq polymerase (NEB) and tagmented for 5 min at 55 °C using homemade transposase TnY[44]. Immediately afterwards, the tagmented DNA was purified on a MinElute column (Qiagen) and PCR-amplified using OneTaq polymerase and barcoded primers for 12 cycles. The PCR product was purified using a dual (0.5×–0.8×) SPRI clean-up (Agencourt) and the size distribution was determined using Tapestation (Agilent). Samples were sequenced on a NextSeq 500 (Illumina)

using a v2.5 75-cycle kit (paired end). Paired-end reads were aligned to the transcriptome (human Ensembl v.96 reference[65]) using kallisto v.0.46.0[55] and loaded into RStudio 1.1.419 with R 4.0.0.2 using the tximport package[66]. Differential gene expression analysis was performed using DESeq2[50]. GO enrichment (biological process) on genes passing DESeq2 criteria (log_2-transformed fold change > 1, *P*adj < 0.05) was performed using the topGO package[51].

ATAC-seq library preparation

$CD8^+$ LTBR and tNGFR T cells were stimulated for 24 h with CD3/CD28 Activator (25 µl per 10^6 cells) or left unstimulated ($n = 2$ biological replicates). We performed bulk ATAC-seq as previously described[44]. In brief, cell membranes were lysed in the RSB buffer (10mM Tris-HCL pH 7.4, 3 mM $MgCl_2$, 10 mM NaCl) with 0.1% IGEPAL freshly added. After pipetting up and down, nuclei were isolated by centrifugation at 500*g* for 5 min at 4 °C. After discarding the supernatant, the nuclei were resuspended in the Tagmentation DNA (TD) Buffer[44] with homemade transposase TnY protein[44] and incubated at 37 °C for 30 min. After purification on a MinElute column (Qiagen), the tagmented DNA was PCR-amplified using a homemade Pfu X7 DNA polymerase[44] and barcoded primers for 12 cycles. The PCR product was purified via a 1.5×SPRI clean-up (Agencourt) and checked for a characteristic nucleosome banding pattern using TapeStation (Agilent). Samples were sequenced on a NextSeq 500 (Illumina) using the v2.5 75-cycle kit (single end).

ATAC-seq analysis

Single-end reads were aligned to the Gencode hg38 primary assembly[67] using Bowtie2 v.2.4.4[57]. We then used SAMtools v.1.9[68] to filter out alignments with low-mapping quality (MAPQ < 30) and subsequently to sort and index the filtered BAM files[68]. Read duplicates were removed using Picard v.4.1.8.1[69]. Peaks were called using MACS3 v.3.0.0[70] with default parameters (-g 2.7e9 -q 0.05).

To construct the union feature space ('union peaks') used for much of the downstream analyses, we began by performing intersections on pairs of biological replicate narrowPeak files using BEDTools v.2.29.0 (using bedtools intersect), keeping only those peaks found in both replicates[71]. After marking the shared peaks between replicates, we used bedtools merge to consolidate the biological replicates at each shared peak (at least 1 bp overlap). In this new peak BED file, each shared peak includes all sequence found under the peak in either of the biological replicates. Next, we took the union of each of these peak files (LTBR resting, LTBR stimulated, tNGFR resting, tNGFR stimulation); we combined any peaks with at least 1 bp overlap. Using the union peaks, we generated a peak read count matrix (union peaks × ATAC samples), in which

each entry in the matrix corresponds to the number of reads overlapping that peak in the specified sample—we term this the per-peak ATAC matrix. The overlapping reads are taken directly from the BAM files (converted to BED) that provide an alignment for each sample. Thus, the matrix includes a column for each biological replicate. Although samples had minimal differences in aligned reads, we normalized each entry in the matrix by the number of reads that overlapped the TSS regions in each sample. In this manner, any difference in read or alignment depth between samples would be normalized appropriately. In addition to the per-peak ATAC matrix, we also constructed a per-gene ATAC matrix as follows: we assigned a gene's total ATAC reads as the sum of normalized reads from the per-peak ATAC matrix for all peaks within 3 kb of a gene's start or end coordinates.

We imported these two ATAC matrices (per-peak and per-gene) into R v.4.1.1 for gene and peak enrichment analysis using DESeq2 v.1.32.0. For comparison between ATAC-seq and RNA-seq, we used a statistical threshold of adjusted P value < 0.05 and either $\log_2$-transformed fold change > 0 (for increases in ATAC or RNA) or $\log_2$-transformed fold change < 0 (for decreases in ATAC or RNA). For transcription factor-motif analysis we used Chrom-VAR v.1.14.072 as follows: For each of the test versus control conditions, we constructed Summarized Experiment objects using column and sample subsets of the per-peak matrix and the union feature space. We used the matchMotifs function to annotate transcription factormotifs. We computed enrichment deviations between test and control conditions using the computeDeviations function.

To produce read pile-up tracks at specific genomic loci, we pooled de-duplicated reads from biological replicates (BAM) using samtools merge. We converted these pooled-replicate BAM files to bigWig files by using the bamCoverage function from deeptools v.3.4.2 and setting the scaleFactor to the relative number of TSSs found in the pooled biological replicates compared to all other sample aggregates73. Using the bigWig files, read pileups were plotted with pyGenomeTracks v.3.6[74].

Finally, we performed k-means clustering on ATAC peaks near genes with increased chromatin accessibility. First, using DEseq2 on the ATAC per-gene matrix, we identified genes with $\log_2$-transformed fold change > 1 and adjusted P value < 0.05 (that is, genes with increased chromatin accessibility) in either of two comparisons: (1) LTBR stimulated versus tNGFR stimulated; (2) LTBR resting versus tNGFR resting. After identifying these genes, we isolated all accessibility peaks in the per-peak ATAC matrix within 3 kb of the gene body; this subset of peaks from the per-peak ATAC matrix was used as input for the clustering. Then, using deeptools (computeMatrix and plotHeatmap functions) on this subset of ATAC peaks, we performed k-means clustering with $k = 4$ clusters and 6 kb read windows.

Statistical analysis

Data between two groups were compared using a two-tailed unpaired Student's *t*-test or the Mann–Whitney test as appropriate for the type of data (depending on the normality of the distribution). Unless otherwise indicated, a *P* value less than or equal to 0.05 was considered statistically significant for all analyses, and not corrected for multiple comparisons. In cases in which multiple comparison corrections were necessary, we adjusted the *P* value using the Benjamini–Hochberg method. All group results are represented as mean ± s.e.m., if not stated otherwise. Statistical analyses were performed in Prism (GraphPad) and RStudio (Rstudio PBC). Flow cytometry data were analyzed using FlowJo v.10.7.1 (Treestar).

Example 2: Genome-scale screen for synthetic drivers of T-cell proliferation

We performed a genome-scale gain-of-function screen in primary human $CD4^+$ and $CD8^+$ T cells, using a lentiviral library of barcoded human ORFs. We show that T cells with the strongest proliferation phenotypes are enriched for both known and unknown regulators of the immune response, many of which are not typically expressed by peripheral T cells. We validate top-ranked ORFs in cells from screen-independent donors and further demonstrate that these ORFs not only drive T cell proliferation but also increase the expression of activation markers and the secretion of key proinflammatory cytokines. To gain more comprehensive insight into the mechanism of action of these genes, we develop a single-cell sequencing approach coupled with direct ORF capture. We identify LTBR – one of the top-ranked ORFs not expressed by lymphocytes – as a key driver of profound transcriptional and epigenetic remodeling through increased NF-κB signaling, which results in a marked increase in the secretion of proinflammatory cytokines and resistance to apoptosis. Finally, we show that top-ranked ORFs potentiate antigen-specific T cell functions, in the context of CD19-directed CAR T cells and broadly tumor-reactive γδ T cells from healthy donors and patients with blood cancer.

Genome-scale ORF screen in T cells

To avoid relying on constitutive expression of large bacterial proteins or chromatin accessibility in the vicinity of target genes[13], we decided to use a lentiviral library of human ORFs; this library contains nearly 12,000 full-length genes, with around 6 barcodes per gene[14] (FIG. 1A, FIG. 6A – FIG. 6G). Previously, genome-scale loss-of-function screens in human T cells have focused on either $CD4^+$ or $CD8^+$ T cells. However, both $CD4^+$ and $CD8^+$ T cells are required for durable tumor control in adoptive therapies[15,16], as further exemplified by FDA approvals of anti-CD19 CAR T cells with a defined 1:1 $CD4^+$ and $CD8^+$ ratio[1]. Thus, we decided

to use the ORF library to discover genes that boost the proliferation of both $CD4^+$ and CD8+ T cells in response to T cell receptor (TCR) stimulation (FIG. 1A, FIG. 6H – FIG. 6J).

We transduced the lentiviral ORF library into $CD4^+$ and $CD8^+$ T cells from three healthy donors, and after a brief period in culture (14 days) we restimulated the cells to identify drivers of proliferation in response to TCR stimulation. We were able to capture the majority of individual ORF barcodes, and nearly all ORFs, including the largest ones (FIG. 6K, FIG. 6L). Comparing the relative frequencies of genes in the most highly proliferative cells to unsorted cells, we found an enrichment of genes that are known to participate in immune processes among the top-ranked ORFs (FIG. 6M, FIG. 6N). We identified *MAPK3* (encoding ERK1), a critical mediator of T cell functions[17], the co-stimulatory molecule CD59[18], the transcription factor BATF, and cytokines that are known to promote T cell proliferation, such as IL12B and IL23A[19]. In fact, two recent studies showed that overexpression of IL12B and BATF boosts proliferation, cytotoxicity and cytokine secretion in CAR T cells[19,20].

Each ORF in the library is linked to an average of six DNA barcodes (FIG. 6B). To increase confidence in our top-ranked ORFs from the pooled screen, we assessed the enrichment of individual barcodes corresponding to a given ORF in proliferating $CD4^+$ and $CD8^+$ cells (FIG. 6B, FIG. 6C, FIG. 6O). For the majority of ORFs, multiple individual barcodes for each gene were enriched in the highly proliferating population, thus suggesting that the observed enrichment does not stem from spurious clonal outgrowth or PCR bias. Surprisingly, the most significantly enriched gene was lymphotoxin-β receptor (*LTBR*), a gene that is broadly expressed in stromal and myeloid cells but completely absent in lymphocytes.

Overall, the enriched ORFs spanned a range of diverse biological processes. Among the top-enriched Gene Ontology (GO) biological processes were lymphocyte proliferation, interferon-γ (IFNγ) production and NF-κB signaling (FIG. 6P). We observed that enriched ORFs showed only a slight preference for genes endogenously upregulated by T cells during stimulation with CD3 and CD28 (CD3/CD28), and in fact were represented in all classes of differential expression (FIG. 6Q). This result highlights the capacity of the pooled ORF screen to discover genes that enable T cell proliferation but that are not expressed normally during CD3/CD28-mediated activation and proliferation. For subsequent validation, we decided to test a broad range of ORFs that function in diverse pathways of relevance to T cell fitness, and that showed different modes of endogenous regulation (FIG. 1E).

Top ORFs enhance T cell functions

To validate the top-ranked ORFs and understand their effect on other relevant aspects of T cell function, we subcloned 33 ORFs from the library into a vector co-expressing a P2A-linked puromycin resistance gene from the same promoter. We chose a truncated nerve growth factor receptor (tNGFR), lacking its intracellular domain, as a control that has no effect on T cell phenotype[21]. $CD4^+$ and $CD8^+$ populations were separately isolated from several screen-independent healthy donors and transduced with individual ORFs (FIG. 2A). Using flow cytometry on representative ORFs, we confirmed that they were stably and uniformly expressed in both subsets of T cells for the duration of the experiment (FIG. 7A, FIG. 7B).

Fourteen days after isolation, we restimulated the cells and measured the relative increase in cell numbers. We found that 16 tested ORFs significantly improved cell proliferation compared with tNGFR, and that proliferation was well correlated between $CD4^+$ and $CD8^+$ cells (Spearman's $r = 0.61$, $P = 0.002$) (FIG. 2B, FIG. 2C, FIG. 7C – FIG. 7H). Having established that the top ORFs improve T cell proliferation, we next tested whether there is also a change in other T cell phenotypes and functions, such as increased cell cycle entry, expression of the activation markers IL2RA (CD25) and CD40L (CD154), and cytokine secretion. Most of the ORFs tested showed no difference in cycling (FIG. 2I, FIG. 2J), but showed higher expression of both CD25 and CD154 in T cells after stimulation (FIG. 2D, FIG. 8A), further corroborating their effect in improving the magnitude of T cell responses.

Finally, we measured the secretion of the cytokines interleukin-2 (IL-2) and IFNγ after restimulation with CD3/CD28 (FIG. 2E, FIG. 8B – FIG. 8E). Although our screen was not designed to identify genes that modulate cytokine secretion, several ORFs could both improve T cell proliferation and boost IL-2 or IFNγ secretion (FIG. 2F). The strongest effect was observed for LTBR, which increased the secretion of both these cytokines in $CD4^+$ and $CD8^+$ T cells by more than fivefold.

Single-cell analysis of ORF phenotypes

Building on our quantification of how each ORF affects proliferation, activation and cytokine release, we next sought to better understand the underlying mechanisms that drive these changes in cell state. To gain a more comprehensive view of the mechanisms of action of individual ORFs, and to provide a multidimensional characterization of the phenotypic changes they induce, we developed a single-cell sequencing strategy with direct ORF capture. This approach, OverCITE-seq (Overexpression-compatible Cellular Indexing of Transcriptomes and Epitopes by Sequencing) extends previous approaches that we have developed for quantifying surface antigens[22] and CRISPR perturbations[23], and allows for high-throughput, single-cell analysis of a pool of T cells with different ORFs. In brief, mRNA from lentivirally integrated

ORFs is reverse-transcribed by a primer binding to a constant sequence of the transcript downstream of the ORF and barcoded, along with the cell transcriptome, during template switching. The resulting cDNA pool is then split for separate construction of gene expression and ORF expression libraries (FIG. 3A, FIG. 3B, FIG. 9A).

We optimized and applied OverCITE-seq to a pool of around 30 ORFs transduced into $CD8^+$ T cells from a healthy donor. The cell pool was either left unstimulated ('resting') or stimulated with CD3/CD28 antibodies to mimic TCR activation. To gain confidence in how well ORFs are assigned to each single cell, we leveraged the fact that the protein produced by the control gene, tNGFR, is expressed on the cell surface and can thus be captured with a DNA-barcoded antibody[23]. The proportion of cells designated as tNGFR positive was consistent when measured by CITE-seq or flow cytometry (FIG. 3C). An analysis of the entire ORF pool showed that single cells assigned with a given ORF had overall the strongest expression of the corresponding gene (FIG. 9B – FIG. 9D), indicating that our ORF capture strategy reliably assigned a genetic perturbation to each single cell.

Unsupervised clustering showed clear separation for stimulated and resting T cells. Within these activation-driven super-clusters we could observe individual clusters associated with a particular cell state or function, such as cell cycle (clusters 1 and 9), macromolecule biosynthesis (cluster 2), type I IFN signaling (cluster 3), cytotoxicity (cluster 6), T cell activation and proliferation (cluster 10), and stress response and apoptosis (cluster 11) (FIG. 3D). Although in many cases several ORFs contributed to a given cluster phenotype (FIG. 9E), we observed a notable enrichment of two ORFs, CDK1 and CLIC1, in cluster 1, characterized by the increased expression of genes that are responsible for chromosome condensation in preparation for cell cycle (FIG. 3E). An even stronger enrichment was observed for cluster 10, which was almost exclusively composed of cells expressing LTBR.

To investigate the mechanisms of genetic perturbations with the strongest transcriptional changes, we looked at the transcriptomic profiles of CD3/CD28-stimulated ORF T cells compared to unstimulated control T cells (FIG. 9F – FIG. 9I). This approach allowed us to identify gene modules that are shared between perturbations or that are perturbation-specific. For example, LTBR and CDK1 showed the strongest enrichment of genes involved in RNA metabolism and cell cycle (*CDK4*, *HSPA8* and *BTG3*), as well as in the tumor necrosis factor (TNF) signaling pathway (*TNFAIP3*, *TRAF1* and *CD70*). FOSB appeared to drive an opposite program to LTBR in terms of genes involved in TCR signaling (*CD3D*, *CD3E*, *LAPTM5* and *LAT*), cytokine responses (*GATA3* and *TNFRSF4*) and the NF-κB pathway (*NFKB2*, *NFKBIA* and *UBE2N*). Finally, we determined that the observed phenotypes were a result of a genetic perturbation rather than an outgrowth of a single clone because virtually every single cell

expressed a unique TCR clonotype (FIG. 9J). This result highlights the utility of OverCITE-seq's multimodal capture approach, yielding each T cell's transcriptome, clonotype, cell surface proteome, cell hashing (for treatment or stimulation conditions) and lentiviral ORF identity.

LTBR improves multiple T cell functions

Having identified LTBR as a strong driver of proinflammatory cytokine secretion (FIG. 2E) and profound transcriptional remodeling (FIG. 3D, FIG. 3E), we decided to investigate its mechanisms of action in more detail. LTBR belongs to the tumor necrosis factor receptor superfamily (TNFRSF) and is expressed on a variety of non-immune cell types and on immune cells of myeloid origin, but is absent from lymphocytes (FIG. 10A, FIG. 10B). Using bulk RNA sequencing (RNA-seq), we compared global gene expression between LTBR- and tNGFR-transduced cells, with or without TCR stimulation (FIG. 4A, FIG. 4B, FIG. 10C). In addition to upregulation of MHC-I and II genes (*HLA-C*, *HLA-B*, *HLA-DPB1*, *HLA-DPA1* and *HLA-DRB6*) and transcription factors necessary for MHC-II expression (*RFX5* and *CIITA*), LTBR cells also expressed the MHC-II invariant chain (encoded by *CD74*). Notably, CD74 has been shown in B cells to activate the pro-survival NF-κB pathway, in particular through upregulation of the anti-apoptotic genes *TRAF1* and *BIRC3* (both of which are also upregulated in LTBR-overexpressing cells)[24]. Similarly, LTBR cells strongly upregulated *BATF3*, which has been shown to promote the survival of $CD8^+$ T cells[25]. We also observed upregulation of *JUNB*, a transcription factor involved in IL-2 production[26], and *TCF7* (encoding TCF1), a key transcription factor responsible for T cell self-renewal[27]. We confirmed the RNA-seq results at the protein level (FIG. 10D – FIG. 10I). LTBR cells were also more resistant to activation-induced cell death and retained greater functionality after repeated stimulations (FIG. 4C, FIG. 4D, FIG. 10J – FIG. 10M).

LTBR signaling in its endogenous context (in myeloid cells) is triggered either by a heterotrimer of lymphotoxin-α (LTA) and lymphotoxin-β (LTB) or by LIGHT (encoded by the *TNFSF14* gene). As LTA, LTB and LIGHT are expressed by activated T cells, we sought to elucidate whether addition of exogenous LTA or LIGHT could modulate the cytokine secretion, differentiation or proliferation of CD3/CD28-stimulated LTBR-overexpressing T cells; however, we found no effect of exogenous ligands on LTBR T cell function (FIG. 11A – FIG. 11E). Thus, although LTBR could potentiate the TCR-driven T cell response, it does not drive activation on its own – which would be a potential safety issue and result in loss of antigen specificity of the engineered T cell response. We also determined that constitutive expression of LTBR is required for maintenance of its phenotype but that there is a substantial lag time between loss of detectable LTBR expression and loss of phenotype (FIG. 11F – FIG. 11I), indicating that transient expression of LTBR may be a safe avenue into a therapeutic application.

Finally, to identify the key domains of the LTBR protein that drive its activity in T cells, we designed a series of point or deletion mutants of LTBR (FIG. 4E, FIG. 11J). In general, we found that the N terminus of LTBR was less sensitive to deletions than the C terminus. Similarly, a partial reduction of the LTBR phenotype was achieved by introducing three alanine point mutations in the key residues for LTA and LTB binding[28], or by removal of the signal peptide. Using our C-terminal deletions, we found that a mutant version of LTBR that lacks residues 393–435 showed no difference compared with full-length LTBR, whereas the deletion of residues 377–435 completely abrogated the LTBR phenotype, despite being expressed at a comparable – if not higher – level (FIG. 11K), probably owing to the loss of a binding site for TRAF2, TRAF3 or TRAF5[29]. Moreover, a deletion of the self association domain[30] (324–377) also completely abrogated the phenotype.

LTBR acts through canonical NF-κB in T cells

LTBR overexpression was shown to induce broad transcriptomic changes in T cells, accompanied by changes in T cell function (FIG. 4A, FIG. 4B). Thus, we sought to determine whether the perturbations in gene expression in LTBR cells were accompanied by epigenetic alterations, leveraging the assay for transposase-accessible chromatin by sequencing (ATAC-seq) (FIGF. 12A – FIG. 12G). Comparing the enrichments of specific transcription factor motifs in differentially accessible chromatin regions, we identified NF-κB p65 (RELA) as the most enriched transcription factor in LTBR cells (FIG. 12H, FIG. 12I). Of note, NF-κB p65 and NFAT–AP-1 were the two most enriched transcription factors in open chromatin in stimulated versus resting T cells (both LTBR and tNGFR), in line with their well-established role in T cell activation[31], but only NF-κB p65 showed strong enrichment in LTBR cells, with and without stimulation (FIG. 4F). This result suggests that LTBR induces a partial T cell activation state but still requires signal 1 (TCR stimulation) for full activation.

We then decided to investigate changes in protein expression and/or phosphorylation of the members of the NF-κB signaling pathway. We observed a more rapid phosphorylation of p65 (RELA) and a strong increase in phosphorylation of an NF-κB inhibitor, IκBα, targeting IκBα for degradation; both of these effects enhance NF-κB activation or transcription (FIG. 4G, FIG. 4H, FIG. 13A – FIG. 13C). In addition to changes in the canonical NF-κB pathway, we also detected an upregulation of key mediators of the non-canonical NF-κB pathway, RELB and NF-κB p52 (FIG. 4I, FIG. 13B, FIG. 13C).

Having established that LTBR activates both the canonical and the non-canonical NF-κB pathways, we sought to determine the molecular basis of this phenomenon by perturbing key genes in the LTBR and NF-κB pathways by co-delivery of LTBR or tNGFR and CRISPR

constructs that target 11 genes involved in the LTBR signaling pathway[32] (FIG. 4J, FIG. 13D – FIG. 13O). Knockout of *LTB*, *TRAF2* and *NIK* (also known as *MAP3K14*) significantly reduced the secretion of IFNγ from LTBR cells but not (or to a lesser extent) from control (tNGFR) cells, whereas perturbations of *LIGHT* (also known as *TNFSF14*), *ASK1* (also known as *MAP3K5*) and *RELA* had a stronger effect on control cells than on LTBR cells. The effect of LTB loss on T cell activation in LTBR cells supports the observation that alanine mutagenesis of key residues involved in LTA or LTB binding (FIG. 4E) partially reduced the LTBR phenotype. Notably, we observed that loss of either TRAF2 or TRAF3 boosted IFNγ secretion in tNGFR cells only, in line with previous findings that T cells from TRAF2, dominant negative mice are hyperresponsive to TCR stimulation[33].

To investigate the potential roles of canonical versus non-canonical NF-κB signaling in LTBR T cells, we decided to analyze the global effects of RELA or RELB loss on the LTBR-driven gene expression profiles. Using bulk RNA-seq on T cells overexpressing LTBR or tNGFR, we discovered that only the loss of RELA significantly downregulated the expression of 'core' LTBR genes, whereas loss of RELB had no effect (FIG. 4K, FIG. 13P).

ORFs enhance antigen-specific responses

Thus far we have shown that top-ranked genes from the ORF screen improve T cell function using a non-specific, pan-TCR stimulation. We next sought to determine whether a similar improvement could be observed using antigen-specific stimulation (FIG. 5A). To that end, we co-expressed several top-ranked genes with two FDA-approved CARs that target CD19, a B cell marker (FIG. 14A – FIG. 14D). Using LTBR as an example, we demonstrated that ORF expression is achievable with this tricistronic vector (FIG. 14E – FIG. 14I).

Since both CARs use different costimulatory domains, from CD28 or 4-1BB, we wanted to determine whether top-ranked genes that were selected using CD28 co-stimulation could also work in the context of 4-1BB co-stimulation. Nearly all of the top-ranked genes tested, with the exception of *AKR1C4*, improved upregulation of CD25 and antigen-specific cytokine secretion, with no major differences in the differentiation or exhaustion phenotype (FIG. 5B, FIG. 5C, FIG. 14J – FIG. 14P, FIG. 15A – FIG. 15D).

Although production of IL-2 and IFNγ is crucial for the clonal expansion and antitumor activity of T cells, another vital component of tumor immunosurveillance is direct cytotoxicity. Top-ranked genes had an overall stronger effect on the cytotoxicity of CD28 CAR T cells than 4-1BB CAR T cells (FIG. 5D – FIG. 5F, FIG. 15E, FIG. 15F). Notably, we observed that CAR T cells co-expressing LTBR tended to form large cell clusters; these clusters were typically absent in wells with control cells but are consistent with the overall higher expression of adhesion

molecules such as ICAM-1 in LTBR-expressing cells (FIG. 15G). Another important feature of effective antitumor T cells is the ability to maintain functionality despite chronic antigen exposure. In line with our previous findings in the context of LTBR alone (FIG. 4D), CAR T cells expressing LTBR showed a better functionality than matched CAR T cells expressing tNGFR after repeated challenge with target cells (FIG. 5G, FIG. 15H – FIG. 15J).

T cells from healthy donors are relatively easy to engineer and rarely show signs of dysfunction in culture, whereas autologous T cells in patients with cancer are often dysfunctional, showing limited proliferation and effector functions[34]. To investigate whether top-ranked genes can improve CAR T cell response not only in healthy T cells but also in potentially dysfunctional T cells derived from patients, we transduced CD19 CARs co-expressed with LTBR or a control gene into peripheral blood mononuclear cells (PBMCs) from patients with diffuse large B cell lymphoma. After co-incubation with $CD19^+$ target cells, we observed a similar increase in the secretion of IL-2 and IFNγ from LTBR CAR T cells to that seen in healthy donors, indicating that identified ORFs can be successfully used to engineer T cells from patients with lymphoma ex vivo (FIG. 5H, FIG. 15K). Of note, there was no secretion of cytokines in response to $CD19^-$ cells, indicating that overexpression of LTBR does not induce a spurious, antigen-independent response.

The screen and subsequent validations were performed in αβ T cells, the predominant subset of T cells in human peripheral blood. Although immunotherapy based on αβ T cells has shown considerable potential in the clinic, γδ T cells present an attractive alternative, owing to their lack of MHC restriction, ability to target broadly expressed stress markers in a cancer-type-agnostic manner and more innate-like characteristics[5]. We therefore sought to determine whether the top genes validated in αβ T cells translated to γδ T cells. After co-incubation with leukemia or pancreatic ductal adenocarcinoma cancer cells, we observed an increase in IL-2 and IFNγ secretion from γδ T cells that were transduced with top-ranked genes (FIG. 5I, FIG. 15L – FIG. 15P). Thus, top-ranked genes from our screen can act on signaling pathways that are conserved between even highly divergent T cell subsets, highlighting their broad applicability for cancer immunotherapy.

Discussion

In summary, here we developed a genome-scale gain-of-function screen in primary human T cells, in which we examined the effects of nearly 12,000 full-length genes on TCR-driven proliferation in a massively parallel manner. The largest – to our knowledge – previously published gain-of-function study in primary T cells involved 36 constructs, including full-length

genes and synthetic receptors[35]. That approach relied on construct delivery via donor DNA and Cas9-mediated targeted insertion. Although using donor DNA for target gene delivery allows for more flexibility in terms of construct design, especially for engineering synthetic receptors, that method is less scalable and less accessible in terms of cost and complexity than the lentiviral library that we used here. Thus, ORF-based gain-of-function screens are readily applicable to a plethora of T cell phenotypes and settings, and that they offer the opportunity for clinical translation. In fact, all FDA-approved CAR therapies already rely on lentiviral or retroviral integration of a CAR transgene, and therefore an addition of an ORF to this system should pose no major manufacturing or regulatory challenges. The use of ORF-encoding mRNA delivered to CAR T cells before infusion is another translational route, especially if there are safety concerns about the mode of action of a particular ORF.

Gain-of-function screens have the potential to uncover regulators that are tightly controlled, restricted to a specific developmental stage or expressed only in certain circumstances. As shown here, LTBR is canonically absent from cells of lymphoid origin, but, owing to the intact signaling pathway, it can have a synthetic role when introduced to T cells. Although constitutive activation of other TNFRSF members might result in a similar phenotype, one of the features that distinguishes LTBR (and plausibly led to its enrichment, but not that of other TNFRSF members, in the screen) is the formation of an autocrine loop whereby the receptor and its ligands are present in the same cell. It is particularly noteworthy that expression of LTBR boosts IL-2 secretion, as this cytokine is produced exclusively by T cells and not by cell types that endogenously express LTBR. In addition to boosting cytokine secretion, overexpression of LTBR promoted stemness (expression of TCF1) and decreased activation-induced apoptosis, as well as offered a level of protection against phenotypic and functional hallmarks of T cell exhaustion – all of which are features not recapitulated by cell types that endogenously express LTBR. Previous work using overexpression of LTBR in cell lines showed that LTBR has a pro-apoptotic role[36], in direct contrast to the phenotype that we observed in primary T cells. Transcript- and protein-level analyses revealed that LTBR drives the constitutive activation of both canonical and non-canonical NF-κB pathways. However, using epigenomic profiling and CRISPR-based functional perturbations we showed that the phenotypic and functional changes resulting from LTBR expression are mediated primarily through activation of the canonical NF-κB pathway, whereas changes in the non-canonical pathway may not be essential for the observed phenotypes – in contrast to the well-established role of non-canonical NF-κB activation in cells that endogenously express LTBR37.

Gene overexpression has been used for pre-clinical enhancement of CAR T cell therapies in numerous studies. For example, armoring CAR T cells with cytokines such as IL-12 or IL-18,

which are not typically produced by T cells but are known to improve T cell function when secreted by other cell types, was shown to improve their antitumor activity[38,39]. Notably, a previous study found that CAR T cell exhaustion can be alleviated by overexpression of c-JUN, a transcription factor identified by RNA-seq as specifically depleted in exhausted cells[40]. Future studies that adapt genome-wide gain-of-function screens to relevant models of immunotherapy will lead to advanced target selection for engineering synthetic cellular therapies that can overcome the immunosuppressive tumor microenvironment and eradicate established cancers.

Example 3: Improved CAR solid tumor responses

We have shown that LTBR and several other top-ranked genes (ORFs, open reading frames) identified in the screen boost the antitumor response of anti-CD19 CARs in context of a B cell leukemia. Here we tested whether a similar improvement of activity can be seen in conjunction with two clinically-tested anti-mesothelin CARs (using either 4-1BB or CD28 costimulatory domains) in the context of pancreatic cancers. We tested T cells co-expressing a CAR and an ORF against Capan-2, a pancreatic cancer line expressing high levels of mesothelin, the CAR target, and BxPC3, a pancreatic cancer line expressing low levels of mesothelin (FIG. 16A).

Following overnight co-incubation, we determined that all but one ORF tested (that is, AHNAK, BATF, IFNL2, IL12B, and LTBR) boosted antigen-specific secretion of IFNγ, when used with either CAR (either 41BB or CD28) against a mesothelin-high cell line Capan-2 (FIG. 16B). In terms of boosting IL-2 secretion, we observed a striking improvement over the negative (tNGFR) control when using LTBR, and to lesser extent AHNAK (FIG. 16C). In terms of reactivity against mesothelin-low line BxPC3, an improvement over the negative control was observed predominantly in T cells overexpressing IL12B or LTBR (FIG. 16D).

Cytokine secretion is one of the aspects of a productive antitumor response - another one is direct cytotoxicity. Therefore, we tested the ability of CAR T cells co-expressing top genes to kill GFP+ Capan2 or BxPC3 cells (FIG. 16E, FIG. 16F). While increased cytotoxicity against mesothelin-high Capan-2 exhibited by CAR T cells overexpressing any of the six top genes tested (including GPD1) was expected given the improvement in cytokine secretion, we also observed increased cytotoxicity against BxPC3 cells. Therefore, we concluded that the top-ranked genes identified in our screen (including but not limited to AHNAK, BATF, GPD1, IFNL2, IL12B, and LTBR) could boost reactivity of diverse CARs (anti-CD19 shown previously, anti-mesothelin shown here) using different costimulatory domains (CD28 or 4-1BB), in different cancer types (including liquid tumors such as B cell leukemia and solid tumors such as pancreatic cancer), and at different target antigen densities (mesothelin-high and mesothelin-low cell lines).

Example 4: Improved activity of a TCR in solid tumor

T cell therapies can rely on redirecting the cells to a given tumor target using either a CAR or a TCR. The former has the advantage of being able to target tumors in different patients, regardless of their HLA haplotype, while the latter can also target antigens that are intracellular (since epitopes from all cellular proteins are sampled by and displayed on the HLA molecules). Here we used a clinically-tested TCR directed against an epitope from NY-ESO-1, commonly expressed in many cancer histologies, including but not limited to melanoma, multiple myeloma, sarcoma, lung cancer. Due to size restrictions we delivered the TCR and the gene (ORF, open reading frame) on two separate lentiviruses that were used to co-transduce T cells (FIG. 17A). Then, the dual-transduced T cells were selected using puromycin (only T cells transduced with the ORF lentivirus would survive) and using antibody-based selection of NY-ESO-1 TCR positive cells (in presence of dasatinib to prevent T cell activation and thus activation-induced cell death during the selection process).

We then tested the engineered CD8+ T cells against an HLA-A2+ NY-ESO-1+ melanoma line A375. Most genes tested increased the secretion one or both of cytokines IFNγ and IL2 (FIG. 17B, FIG. 17C). We also measured direct cytotoxicity against A375 cells and demonstrated that all genes tested showed superior cytotoxicity than the TCR-transduced T cells co-expressing the negative control gene tNGFR (FIG. 17D). Therefore, we concluded that the top-ranked genes identified in our screen (including but not limited to AHNAK, BATF, GPD1, IFNL2, IL12B, and LTBR) could boost reactivity of T cells engineered with a cancer-specific TCR.

Example 5: Intracellular signaling domain from LTBR potentiates CAR T cell activity

We have demonstrated that LTBR overexpression in T cells, in conjunction with anti-CD19 CARs utilizing either CD28 or 4-1BB costimulatory domains in addition to CD3z signaling domain, increases cytokine (IFNγ and IL-2) secretion and target cell killing (B cell leukemia cell line Nalm6). We have also demonstrated that CAR T cells co-expressing LTBR have an increased expression of core genes that are activated by LTBR, for instance an adhesion molecule ICAM-1(also known as CD54) and CD74, an invariant part of the MHC-II complex with proposed anti-apoptotic roles. Finally, we have shown that T cells overexpressing LTBR, with or without a CAR, show a less differentiated, "younger" phenotype (predominantly central memory [CM], with reduced frequency of terminally differentiated effector cells) which is beneficial in context of cellular therapies.

Here, we inserted the intracellular part of LTBR (https://www.uniprot.org/uniprot/P36941, amino acids 249-435) within the intracellular domains of most commonly used CAR constructs to see if: 1) this insertion does not disrupt the CAR; 2) this insertion bestows similar phenotypic and functional benefit as expressing a full length LTBR as a separate gene in a multicistronic construct, and 3) this insertion boosts CAR activity above that of the CAR and LTBR delivered together but as separate proteins. To that effect we first engineered 3 constructs whereby the intracellular domain of LTBR is inserted into various position in a CAR construct identical to the one used in the FDA-approved axicabtagene ciloleucel (here denoted as 19-28-z), specifically: 1) downstream of the CD28 stalk and transmembrane domains but upstream of CD28 signaling and CD3z signaling domains; 2) downstream of the CD28 signaling domain but upstream of CD3z signaling domain; and 3) downstream of both CD28 and CD3z signaling domains (FIG. 21A). These three constructs were then transduced into CD4+ and CD8+ T cells from a healthy donor and compared to a full-length CAR expressed separately with a control gene tNGFR (19-28-z + tNGFR) or LTBR (19-28-z + LTBR). We also engineered two additional constructs whereby the intracellular domain of LTBR is inserted into various position in a CAR construct identical to the one used in the FDA-approved tisagenlecleucel (here denoted as 19-BB-z), specifically: 1) downstream of the 4-1BB signaling domain but upstream of CD3z signaling domain; and 2) downstream of both the 4-1BB and CD3z signaling domains (FIG. 21B). These two constructs were then transduced into CD4+ and CD8+ T cells from a healthy donor and compared to a full-length CAR expressed separately with a control gene tNGFR (19-BB-z + tNGFR) or LTBR (19-BB-z + LTBR).

SEQ ID NO	Name	Type
3	19-28-z + LTBR protein	AA
4	19-28-z + LTBR protein	DNA
5	19-28-z + NGFR protein	AA
6	19-28-z + NGFR protein	DNA
7	19-BB-z + LTBR	AA
8	19-BB-z + LTBR	DNA
9	19-BB-z + tNGFR	AA
10	19-BB-z + tNGFR	DNA
11	19-LTBR-28-z protein	AA
12	19-LTBR-28-z protein	DNA
13	19-28-LTBR-z	AA
14	19-28-LTBR-z	DNA
15	19-28-z-LTBR	AA
16	19-28-z-LTBR	DNA
17	19-BB-LTBR-z	AA

18	19-BB-LTBR-z	DNA
19	19-BB-z-LTBR	AA
20	19-BB-z-LTBR	DNA

We first verified that the surface CAR expression is similar between these constructs, thus indicating that inserting LTBR intracellular domain did not have a profound effect on expression or protein stability of the CAR, and that the observed functional effects were not due to the expression level of the CAR (FIG. 21C, FIG. 21D). Since full-length LTBR induced higher expression of a wide range of genes beneficial for cell therapy, including CD54 and CD74, we tested whether inclusion of the intracellular LTBR domain in the CAR phenocopies the effect of the full length LTBR. In fact, we observed an even higher upregulation of these two markers in cells expressing LTBR as the second or third component in the intracellular CAR domain, namely 19-28-LTBR-z, 19-28-z-LTBR, 19-BB-LTBR-z, and 19-BB-z-LTBR (FIG. 21E, FIG. 21F). This suggests that inclusion of just the signaling domain of LTBR into the CAR may have a more profound effect on T cell state than expressing the whole protein. We also observed an increase in central memory (CM) and decrease in effector phenotype in cells expressing LTBR as the second or third component in the intracellular CAR domain, to a higher extent than in cells expressing full-length LTBR (FIG. 21G, FIG. 21H).

Having established that some of the tested constructs not only phenotypically replicate the effects of full-length LTBR but are in fact superior, we then sought to determine if they also improve antigen-specific response of CAR T cells against CD19+ cancer cells. In terms of cytokine secretion, we observed that the 19-LTBR-28-z construct generally performed worse than the control ("regular" CAR T cells, i.e. 19-28-z + tNGFR) while 19-28-LTBR-z showed similar performance to the control. Most importantly, 19-28-zLTBR outperformed T cells expressing (separately) the CAR and full-length LTBR in terms of IFNg secretion and showed an improvement over control CAR T cells in terms of IL2 secretion (FIG. 21I, FIG. 21J). In cases of CARs utilizing the 4-1BB domain, the construct containing LTBR in the second position (19-BBLTBR-z) showed overall an improvement over the control CAR T cells and similar performance to CAR T-cells co-expressing full-length LTBR – while the construct containing LTBR in the third position outperformed even the CAR + full length LTBR in all cases tested (FIG. 21K, FIG. 21K).

While cytokine secretion (IFNg, IL2) is crucial for T cells to remodel the tumor microenvironment and stimulate T cell proliferation, another key aspect of anticancer activity is direct cytotoxicity, performed predominantly by CD8+ T cells. Therefore, we tested the ability of engineered T cells to kill CD19+ cancer cells. Interestingly, all CD28 LTBR constructs showed

an improvement over control CAR at high T cell dose. More importantly, the 19-28-z-LTBR construct was also able to efficiently kill tumor cells at a low T cell dose, where T cells expressing 19-28-z CAR and full-length LTBR provided only a slim benefit over a regular CAR (FIG. 21M). Similarly in cases of 4-1BB CARs: both constructs tested showed an improvement over a regular CAR at high T cell dose but only the 19-BB-z-LTBR construct was more cytotoxic at a low T cell dose (FIG. 21N). This is of particular importance for three reasons: 1) clinical efficacy: other than infusing more T cells, there is no possibility to clinically control how many CAR T cells will encounter tumor cells so they should be able to destroy the cancer cells with as much efficacy as possible, 2) safety: if the bulk of the disease is eliminated rapidly, that reduces the chances of severe adverse events, in particular cytokine release syndrome – especially if this disease debulking can be achieved at a lower T cell number, and 3) manufacturing: due to exhaustion/dysfunction, T cells from some patients fail to expand sufficiently ex vivo prior to re-infusion to achieve the recommended cell dose – if the recommended cell does can be scaled down due to superior efficacy, that may make more patients eligible to receive the therapy.

Example 6: Intracellular LTBR as an alternative to CD28 or 4-1BB in 2nd generation CARs

1st generation CAR constructs contained only the CD3z signaling domain attached to the target recognition modality. These 1st generation receptors were not efficient in vitro and especially in vivo because of lack of a costimulatory signal, thus necessitating the provision of costimulation via inclusion of CD28 or 4-1BB signaling domains in 2nd generation CARs (currently FDA approved). We wanted to assess if the presence of LTBR could improve the response of 1st generation CARs.

Thus, we designed constructs that possessed only the target recognition domain and transmembrane part of a CAR (generation 0) as well as constructs that also contained the intracellular CD3z signaling domain (1st generation) and compared them to 2nd generation CARs utilizing the 4-1BB costimulatory domain (FIG. 22A). Each generation CAR was co-expressed with either tNGFR (negative control) or full-length LTBR.

SEQ ID NO	Name	Type
21	19 + tNGFR	AA
22	19 + tNGFR	DNA
23	19 + LTBR	AA
24	19 + LTBR	DNA
25	19-z + tNGFR	AA
26	19-z + tNGFR	DNA
27	19-z + LTBR	AA

28	19-z + LTBR	DNA

When co-incubated with CD19+ leukemia cell line Nalm6, generation 0 CARs showed no response in terms of cytokine (IFNγ, IL2) secretion (FIG. 22B, FIG. 22C). T cells expressing the 1st generation CAR together with tNGFR showed a weaker response than a 2nd generation CAR, as expected. Interestingly, when a 1st generation CAR was co-expressed with LTBR, the response was in all cases stronger compared to a regular 2nd generation CAR (19-BB-z + tNGFR) and in some cases similar to the 2nd generation CAR co-expressed with LTBR. Thus, a CAR containing CD3z and LTBR signaling domain could offer an attractive alternative to conventional 2nd generation CARs (i.e., containing CD28 or 4-1BB derived costimulatory domains). This is further supported by the results described in Example 5.

SEQ ID NO	Name	Type
29	LTBR-28-z	AA
30	LTBR-28-z	DNA
31	NGFR-28-z	AA
32	NGFR-28-z	DNA
33	LTBR-28TM-28-z	AA
34	LTBR-28TM-28-z	DNA
35	NGFR-28TM-28-z	AA
36	NGFR-28TM-28-z	DNA

Example 7: Usage of the extracellular domain of LTBR

We have previously shown that LTBR overexpression improves T cell phenotype and function via ligand dependent and independent mechanisms. We wanted to assess whether the extracellular domains of LTBR can provide additional T cell activation via the same mechanisms (ligand binding or tonic signaling) when linked to signaling domains derived from 2nd generation CAR T cells.

To that effect we generated constructs that express the full-length extracellular domain of LTBR (LTBR: https://www.uniprot.org/uniprot/P36941, amino acids 1-248) including the transmembrane part, or utilize the stalk and transmembrane part from FDA-approved CARs - that is, CD28 stalk and transmembrane or CD8 stalk and transmembrane (LTBR: https://www.uniprot.org/uniprot/P36941, amino acids 1-227). In some cases, the extracellular domain of LTBR was linked to CD28 and CD3z or 4-1BB and CD3z signaling domains, as in FDA-approved CARs. In all iterations of the constructs, a matched NGFR fragment was used as a negative control (FIG. 23A).

SEQ ID NO	Name	Type
37	LTBR-CD8-BB-z	AA
38	LTBR-CD8-BB-z	DNA
39	NGFR-CD8-BB-z	AA
40	NGFR-CD8-BB-z	DNA
41	19-CD8-LTBR	AA
42	19-CD8-LTBR	DNA
43	19-CD8-LTBR(TM)	AA
44	19-CD8-LTBR(TM)	DNA
45	19-28-LTBR	AA
46	19-28-LTBR	DNA
47	19-28-LTBR(TM)	AA
48	19-28-LTBR(TM)	DNA

We observed no cytokine (IFNγ, IL2) secretion when the T cells were incubated alone, indicating that ligand availability or tonic signaling mediated by LTBR were not sufficient to activate the cells. However, when the T cells were activated via their T cell receptor (CD3 and CD28 antibodies), we observed a strong increase in secretion of both IFNg and IL2 by T cells expressing a construct that contains the extracellular part of LTBR fused to the CD8 stalk and transmembrane domain, and 4-1BB and CD3z signaling domains (LTBR-CD8-BB-z) (FIG. 23B, FIG. 23C). This result indicates that the extracellular domain of LTBR fused to a CAR in place of or in addition to a targeting moiety (typically derived from an scFv antibody fragment) may be a useful approach to potentiating T cell function.

Example 8: Usage of the extracellular domain of LTBR

We have previously shown that LTBR overexpression improves T cell phenotype and function via ligand dependent and independent mechanisms. We wanted to assess whether the extracellular domains of LTBR can provide additional T cell activation via the same mechanisms (ligand binding or tonic signaling) when linked to signaling domains derived from 2nd generation CAR T cells.

To that effect we generated constructs that express the full-length extracellular domain of LTBR (LTBR: https://www.uniprot.org/uniprot/P36941, amino acids 1-248) including the transmembrane part, or utilize the stalk and transmembrane part from FDA-approved CARs - that is, CD28 stalk and transmembrane or CD8 stalk and transmembrane (LTBR: https://www.uniprot.org/uniprot/P36941, amino acids 1-227). In some cases, the extracellular domain of LTBR was linked to CD28 and CD3z or 4-1BB and CD3z signaling domains, as in FDA-approved CARs. In all iterations of the constructs, a matched NGFR fragment was used as a

negative control (FIG. 24A).

We observed no cytokine (IFNg, IL2) secretion when the T cells were incubated alone, indicating that ligand availability or tonic signaling mediated by LTBR were not sufficient to activate the cells. However, when the T cells were activated via their T cell receptor (CD3 and CD28 antibodies), we observed a strong increase in secretion of both IFNg and IL2 by T cells expressing a construct that contains the extracellular part of LTBR fused to the CD8 stalk and transmembrane domain, and 4-1BB and CD3z signaling domains (LTBR-CD8-BB-z) (FIG. 24B, FIG. 24C). This result indicates that the extracellular domain of LTBR fused to a CAR in place of or in addition to a targeting moiety (typically derived from an scFv antibody fragment) may be a useful approach to potentiating T cell function.

Example 9: Modified TCR complexes

The intracellular signaling domain of LTBR (https://www.uniprot.org/uniprot/P36941, amino acids 249-435*) fused to different components of the TCR complex. FIG. 25A shows the existing design that improved T cell function (i.e. NY-ESO-1 TCR and LTBR expressed separately, see Example 4) as well as fusing LTBR signaling domain to different components of the TCR-CD3 complex, specifically at the C-terminal end of the intracellular domains of CD3epsilon (https://www.uniprot.org/uniprot/P07766), CD3gamma (https://www.uniprot.org/uniprot/P09693), CD3delta (https://www.uniprot.org/uniprot/P04234) , and CD247 (also known as CD3zeta, https://www.uniprot.org/uniprot/P20963). The LTBR signaling domain can also be fused to the C-terminal ends of TCR-α or TCR-β chains.

In a similar manner as with using LTBR intracellular domain to modify αβ TCR complex, γδTCR complex can be modified too (FIG. 25B). As shown in FIG. 5I, expression of full-length LTBR boosts γδ T cell functions.

αβ T cells use CD4 to co-receive antigens presented by MHC-II (HLA-DR, HLA-DP, HLA-DQ) or CD8 (composed of CD8a and CD8b chains) to co-receive antigens presented by MHC-I (HLA-A, HLA-B, HLA-C). Thus, intracellular LTBR can be fused to the C-terminal intracellular tail of CD4 or to C-terminal intracellular tails of CD8a or CD8b to improve T cell function (FIG. 25C).

Example 10: LTBR co-delivery potentiates antitumor functions of a B7-H3 targeting CAR

We have previously shown that co-delivery of LTBR with an anti-CD19 CARs into primary T cells boosts their activity against hematological cancers. See, e.g., Legut et al, Nature, (2022). We have shown similar results with co-delivery of LTBR with an anti-mesothelin CARs to boost T cell activity against a range of solid tumors. We have now expanded this application of

LTBR co-delivery to an anti-B7-H3 CAR which is being tested clinically against a range of solid tumors, including but not limited to pediatric cancers, brain tumors, sarcomas and melanoma. See, e.g., Theruvath et al, Nature Medicine (2020).

When LTBR was co-delivered to primary human T cells together with an anti-B7-H3 CAR (MGA271-28-z), we observed (as before in cases of CD19 and mesothelin CARs) that LTBR had a positive impact on CAR T cell phenotype. Specifically, LTBR CAR T cells showed a predominantly central memory phenotype with practically no terminally differentiated effector cells, in contrast with CAR T cells co-expressing a control gene tNGFR (FIG. 26A). LTBR CAR T cells also strongly upregulated markers of LTBR activity, CD54 and CD74 (FIG. 26B, FIG. 26C).

In terms of antitumor efficacy, LTBR CAR T cells, both CD4 and CD8, showed a much stronger response to cancer cells expressing B7-H3 (including two atypical teratoid rhabdoid tumor lines BT12 and BT16, as well as a melanoma line A375) than control CAR T cells while remaining inert to a B7-H3-negative leukemia line Nalm6 (FIG. 26D - FIG. 26G). This improvement of antitumor response was observed across all T cell functions tested, including secretion of key cytokines IFNγ and IL2, as well as direct cell killing.

Finally, we assessed the efficacy and safety of LTBR CAR T cells in a mouse xenograft models. We implanted A375 tumor into the flank of NSG mice and allowed it to grow for two weeks to be reminiscent of advanced solid tumors in human (FIG. 26H). When monitoring body weight, we observed no meaningful body weight loss in mice treated with CAR T cells, with or without LTBR, indicating that LTBR did not result in any overt toxicities (FIG. 26I). When measuring the tumor size, we observed that LTBR CAR T cells resulted in overall lower tumor burden, at both doses tested, than mice treated with control CAR T cells or untransduced T cells, indicating that LTBR improved the CAR T cell efficacy in this model (FIG. 26J, FIG. 26K). Due to rapid progression in this advanced solid tumor model, the study was terminated 12 days after T cell injection, preventing us from monitoring the long-term effect of LTBR T cells on tumor regression and survival.

Example 11: Identification of the minimal intracellular domain of LTBR that drives its function in T cells

We have previously shown that fusion of the intracellular tail of LTBR to the C-terminus of CD19-targeting CARs, either utilizing CD28 or 4-1BB design (FMC6.3-28-z-LTBR or FMC6.3-BB-z-LTBR) results in CAR T cells that show superior antitumor potency and LTBR-driven phenotype than when the full-length CAR and full-length LTBR are co-expressed as separate molecules. Here we wanted to determine if truncations (either N- or C-terminal) of the

LTBR signaling tail could result in a smaller but equally or more potent CAR construct than one incorporating the full-length LTBR signaling tail.

Construct	LTBR amino acids (Uniprot: P36941)	Included in SEQ ID NO
Full length	249:435	84, 85
V1	249:396	86, 87
V2	249:393	88, 89
V3	249:387	90, 91
V4	249:377	92, 93
V5	262:435	94, 95
V6	297:435	96, 97
V7	324:435	98, 99
V8	345:435	100, 101
V9	358:435	102, 103

We began by annotating the LTBR intracellular tail based on the literature to identify key functional domains (FIG. 27A). We then designed a series of 4 N-terminal truncation and 5 C-terminal truncations of the LTBR tail, for a stepwise removal of unannotated parts (which we presumed not to play any biological role) and extending into key signaling domains that were previously annotated (FIG. 27B). We then fused the resulting truncation mutants to the C-terminus of a CD28-based CD19 CAR and compared them with either a CD28-based CAR incorporating the full-length LTBR signaling tail (19-28-z-LTBR) or regular CAR (19-28-z) co-expressed with LTBR or control gene tNGFR. The sequences are shown in SEQ ID Nos: 84-103. Each sequence includes 19-28-z (SEQ ID NO: 134, 135), LTBR variant as indicated above, P2A, puromycin.

All CAR-LTBR fusions resulted in similar levels of CAR surface expression (FIG. 27C).

In terms of differentiation status of T cells, the LTBR truncation fusions showed a range of phenotypes, with certain variants (e.g., V7) resembling full length LTBR very closely while certain other variants (e.g., V4) more reminiscent of regular CAR T cells not expressing LTBR (FIG. 27D). Similarly, full-length LTBR fusion as well as most truncation mutants, with the exception of V3 and V4, resulted in a stronger expression of TCF1, a key transcription factor governing T cell stemness and self-renewal (FIG. 27E). Another indication of the successful induction of the LTBR program, which involves differential expression of hundreds of genes critical for the immune response (See, e.g., Legut et al, Nature (2022)), is surface expression of CD54 and CD74 markers. While certain truncation variants, such as V3, V4 and V9, failed to

upregulate CD54 and CD74, the remaining variants showed similar activity to full-length LTBR fusion (FIG. 27F).

In addition to phenotypic measurements, we also assayed the antigen-specific antitumor response by co-incubating T cells expressing anti-CD19 CARs, with or without LTBR fusion, with CD19+ leukemia cells. To quantify that response, we measured the secretion of key antitumor cytokines IFNγ and IL2 (FIG. 27G). In line with the CD54 and CD74 quantification, we observed a similar boost over "regular" CAR (19-28-z + tNGFR) with V5-V7 variants as with full-length LTBR fusion. V1 and V2 showed no improvement of cytokine secretion over "regular" CAR, despite increased levels of CD54 and CD74, while V3 and V4 showed hardly any cytokine secretion, showing that those designs interfered with the CAR itself. Interestingly, V8 variant resulted in greatest upregulation of CD54 and CD74 but an inferior cytokine secretion while V9 showed mild upregulation of CD54 and CD74 but strong boost of antitumor activity. This suggests that phenotypic effects of LTBR (CD54, CD74) can be de-coupled from functional effects (IL2, IFNγ).

Example 12: LTBR signaling tail fusion to a mesothelin targeting CAR

We have previously shown that co-expression of full-length LTBR together with mesothelin-targeting CARs, utilizing both the 4-1BB and CD28 designs, boosts antitumor reactivity of CAR T cells as well as that fusing the intracellular tail of LTBR to CD19-targeting CARs, utilizing both the 4-1BB and CD28 designs, results in superior phenotype and function than co-expression of a regular CD19-targeting CAR and LTBR as two independent molecules.

To extend that observation, we fused the intracellular tail of LTBR to mesothelin-targeting CARs (see FIG. 28A for schematic representations of the CAR-LTBR fusion designs). Specifically, we selected the C-terminus of the meso-28-z CAR for LTBR fusion, based on the optimal LTBR positioning within the CAR construct determined in the CD19 system. We also investigated replacing the CD28 costimulatory domain with LTBR, placing it either upstream or downstream of CD3z, testing whether LTBR can be used instead of CD28 to provide costimulation.

SEQ ID NO	Name	Type
104	Meso-28-z-LTBR-P2A-puroR	DNA
105	Meso-28-z-LTBR-P2A-puroR	AA
106	Meso-BB-z-LTBR-P2A-puroR	DNA
107	Meso-BB-z-LTBR-P2A-puroR	AA
108	Meso-LTBR-z-P2A-puroR (CD28 stalk	DNA
109	Meso-LTBR-z-P2A-puroR (CD28 stalk	AA

110	Meso-LTBR-z-P2A-puroR (CD8 stalk)	DNA
111	Meso-LTBR-z-P2A-puroR (CD8 stalk)	AA
112	Meso-z-LTBR-P2A-puroR (CD28 stalk)	DNA
113	Meso-z-LTBR-P2A-puroR (CD28 stalk)	AA
114	Meso-z-LTBR-P2A-puroR (CD8 stalk)	DNA
115	Meso-z-LTBR-P2A-puroR (CD8 stalk)	AA

When looking at the surface expression of the CAR, we observed, in contrast to our data in the CD19 system, that fusing the LTBR tail in any position within the mesothelin CAR resulted in a markedly decreased surface expression of the CAR (FIG. 28B).

To assess the functional impact of the reduced CAR expression upon fusion with LTBR, we measured key functional outputs of CAR-driven response to mesothelin-positive cancer cells: T cell proliferation, direct cancer cell killing, and secretion of key cytokines. In terms of antigen-driven proliferation, co-expression of the full-length LTBR resulted in the strongest expansion but CAR-LTBR fusions still outperformed the regular, unmodified CAR (FIG. 28C). In terms of cancer cell killing, a CAR design lacking CD28 but containing LTBR tail downstream of CD3z (Meso-z-LTBR) showed similar killing to the regular CAR co-expressed with full-length LTBR (FIG. 28D). Surprisingly, despite better or comparable functional activity of mesothelin CAR-LTBR fusions in terms of proliferation and killing, two out of three constructs tested (Meso-28-z-LTBR and Meso-LTBR-z) showed barely any activity when measuring cytokine secretion (FIG. 28E). Meso-z-LTBR T cells were capable of producing cytokines upon co-incubation with mesothelin+ cancer cells but to lesser extent than regular Meso-28-z CAR T cells.

Given that CAR-specific functions were reduced upon fusion with the LTBR tail, we were wondering about the LTBR-specific functions of those constructs. When looking at key markers of LTBR activity, that is, surface expression of CD54 and CD74 (FIG. 28F), as well as intracellular/nuclear expression of the transcription factor TCF1 (FIG. 28G), we observed that all three CAR-LTBR fusion constructs drive a stronger LTBR program than co-expression of the CAR and full-length LTBR. This phenomenon was observed in both the CD28 and 4-1BB designs. Therefore, we hypothesized that mesothelin CAR-LTBR fusions may be suboptimal to act as a CAR but are superior, non-natural versions of LTBR. To test that further, we stimulated the engineered T cells through their endogenous T cell receptors, as an alternative to providing them with signal 1 than using CAR-mesothelin binding. Supporting our hypothesis, we observed in that context, where CAR-LTBR fusions were needed only to provide LTBR-like signal 2 costimulation without the need to provide CAR-like signal 1 stimulation, CAR-LTBR fusion T cell functional response was superior to that in T cells expressing CAR and LTBR as two independent molecules (FIG. 28H).

To demonstrate the utility of using CAR-LTBR fusion as a superior LTBR-like molecule to be used in conjunction with an independent antigen receptor, we co-delivered natural LTBR or Meso-z-LTBR together with Meso-28-z CAR T to T cells (FIG. 28I). All constructs tested showed the same CAR expression on the surface (FIG. 28J); also, co-delivery of CAR and LTBR on separate viruses resulted in strong surface expression of LTBR, similar to that in T cells transduced only with the LTBR virus but not the CAR virus – highlighting the potential of LTBR delivery on a separate lentivirus as an alternative to co-expressing from the same lentiviral cassette as an antigen receptor (FIG. 28K).

In this co-delivery setting, CAR + Meso-z-LTBR T cells upregulated LTBR marker genes CD54 and CD74 to the similar extent as CAR + LTBR T cells (FIG. 28L). CAR + Meso-z-LTBR T cells also showed superior antigen-specific response to mesothelin+ cancer cells to that of CAR only T cells and even outperformed CAR + natural LTBR T cells in terms of IFNγ secretion (FIG. 28M, FIG. 28N). Taken together, we have shown utility of Meso-z-LTBR synthetic fusion receptor as an alternative to naturally occurring full length LTBR.

Example 13: LTBR signaling tail fusion to the members of the TCR-CD3 complex.

We have previously shown that co-expression of full-length LTBR together with an NY-ESO-1 targeting αβ TCR boosts antitumor reactivity of engineered T cells as well as that fusing the intracellular tail of LTBR to CD19-targeting CARs, utilizing both the 4-1BB and CD28 designs, results in superior phenotype and function than co-expression of a regular CD19-targeting CAR and LTBR as two independent molecules.

To extend this observation, we fused the intracellular tail of LTBR to α or β chains of the TCR heterodimer, or δ, ε, γ or ζ chains of the CD3 complex. CD3 constitutively associates with the TCR and is required for its surface expression and downstream signaling (https://www.pnas.org/doi/10.1073/pnas.1420936111).

To first test whether LTBR signaling tail can boost TCR activity as a direct fusion, we generated constructs that included LTBR intracellular tail attached to the C-terminus of the short intracellular tail of TCRα or TCRβ (FIG. 29A) and tested them alongside an unmodified TCR co-expressed with either a full length LTBR or an irrelevant gene tNGFR.

SEQ ID NO	Name	Type
116	TCRa:LTBR-P2A-TCRb	DNA
117	TCRa:LTBR-P2A-TCRb	AA
118	TCRa-P2A-TCRb:LTBR	DNA
119	TCRa-P2A-TCRb:LTBR	AA
120	CD3D:LTBR-P2A-puroR	DNA

121	CD3D:LTBR-P2A-puroR	AA
122	CD3E:LTBR-P2A-puroR	DNA
123	CD3E:LTBR-P2A-puroR	AA
124	CD3G:LTBR-P2A-puroR	DNA
125	CD3G:LTBR-P2A-puroR	AA
126	CD3Z:LTBR-P2A-puroR	DNA
127	CD3Z:LTBR-P2A-puroR	AA

We first looked at whether LTBR fusion affects surface expression of the TCR. We noticed that LTBR fusion to TCR-β, but not TCR-α, strongly reduced its surface expression (FIG. 29B). We then examined the key phenotypic hallmarks of LTBR activity, that is surface expression of CD54 and CD74. Only LTBR-TCR-β, but not LTBR-TCR-α, resulted in an increased expression of CD54 and CD74, albeit to a lesser extent than full length LTBR (FIG. 29C). In terms of antigen-specific activity, both LTBR-TCR-α and LTBR-TCR-β fusions were proven to be non-functional, resulting in a similar level of cytokine secretion as untransduced cells upon co-incubation with NY-ESO-1+ melanoma cell line A375 (FIG. 29D). Therefore, we concluded that direct LTBR tail fusion to TCR chains results in disruption of expression and/or function of the TCR.

CD3 molecules are necessary for mediating TCR signaling. Therefore, we engineered fusions of all four CD3 polypeptides with LTBR signaling tail (FIG. 29E) and sequentially transduced the CD3-LTBR fusions, or unmodified CD3 genes, together with the NY-ESO-1 TCR into T cells (FIG. 29F). In terms of TCR surface expression, there were no major differences between different conditions, as expected given that T cells already express all CD3 genes (FIG. 29G). Looking at phenotypic hallmarks of LTBR activity, we observed that CD3-LTBR fusions resulted in an overall higher expression of CD54 and CD74 than matched unmodified CD3 constructs (FIG. 29H). In terms of antigen-specific response upon co-incubation with NY-ESO-1+ melanoma line A375, CD3-LTBR fusions failed to boost the activity of TCR engineered T cells above the control level (FIG. 29I). Interestingly, overexpression of unmodified CD3ε or CD3ζ resulted in a small but significant increase in the antigen-specific response, albeit to the lesser extent than overexpression of full length LTBR. Overall, LTBR-CD3 fusions have failed to outperform natural, full length LTBR across phenotypic and functional assays, presumably due to competition with endogenous, highly expressed components of the CD3 complex.

Example 14: LTBR signaling tail fusion to the members of the CD8 complex.

We have shown that co-expression of full-length LTBR together with an NY-ESO-1 targeting αβ TCR boosts antitumor reactivity of engineered T cells (WO 2023/279049) as well as

that fusing the intracellular tail of LTBR to CD19-targeting CARs, utilizing both the 4-1BB and CD28 designs, results in superior phenotype and function than co-expression of a regular CD19-targeting CAR and LTBR as two independent molecules.

To extend this observation, we fused the intracellular tail of LTBR to CD8α or CD8β molecules (FIG. 30A). CD8α-CD8β heterodimer is critical for productive engagement of a TCR (such as an NY-ESO-1 targeting αβ TCR used here) with a peptide antigen (in this case an NY-ESO-1 derived peptide SLLMWITQC) presented by an MHC-I molecule (in this case HLA-A2).

SEQ ID NN	Name	Type
128	CD8a:LTBR-P2A-puroR	DNA
129	CD8a:LTBR-P2A-puroR	AA
130	CD8b:LTBR-P2A-puroR	DNA
131	CD8b:LTBR-P2A-puroR	AA

In this experiment, CD8 T cells, expressing an endogenous CD8α-CD8β heterodimer, were sequentially transduced with an NY-ESO-1 targeting TCR as well as a modifier gene to be overexpressed: a control gene tNGFR, a full-length LTBR, CD8α (wild-type or fused with the LTBR signaling tail) or CD8β (wild-type or fused with the LTBR signaling tail) (FIG. 30B).

We first measured the surface expression of markers of LTBR activity, CD54 and CD74, as well as intracellular expression of a key transcription factor TCF1. As expected, NY-ESO-1 TCR-transduced T cells co-expressing LTBR exhibited a marked increase of expression of both surface markers and the transcription factor, compared with the control gene tNGFR (FIG. 30C – FIG. 30E). T cells transduced with the CD8-LTBR fusions showed slight increase in CD54 and CD74 expression, but not TCF1, compared with the wild-type counterparts, indicating that the LTBR signaling was at least partially active in these constructs.

Finally, we tested the impact of the CD8-LTBR fusion on the functional response of engineered T cells. NY-ESO-1 antigen is expressed on a variety of tumor types (Thomas et al, NY-ESO-1 Based Immunotherapy of Cancer: Current Perspectives, Front. Immunol., 01 May 2018, Sec. Cancer Immunity and Immunotherapy, Volume 9 – 2018). To test the sensitivity and magnitude of response of LTBR engineered T cells to this antigen, we pulsed an HLA-A2+ cell line with different concentrations of the immunodominant peptide epitope derived from the NY-ESO-1 protein, SLLMWITQC. T cell response was measured as secretion of two key cytokines, IFNγ and IL2, after 24 h co-incubation of T cells with the peptide-presenting cell line (FIG. 30F, FIG. 30G). As expected, co-expression of full-length LTBR induced a much stronger T cell response to the antigen than a matched control, tNGFR, even at peptide concentrations as low as 10^{-7} M. LTBR transduced T cells also showed >3-fold increase in sensitivity to the peptide

concentration (IC_{50} for IFNγ secretion of 6 x 10^{-7} M for LTBR, 2 x 10^{-6} M for tNGFR). Importantly, CD8-LTBR fusions also increased the magnitude of response, for both cytokines measured, over the matched controls. Thus, we demonstrated the functionality and utility of the synthetic CD8-LTBR fusions as an alternative to the full-length natural LTBR.

Example 15: ORF library vector engineering to improve transduction efficiency

We have previously shown that a pooled, barcoded lentiviral library containing >12,000 human genes can be used to discover new modulators of key T cell functions (See, e.g., Legut et al, Nature 2022). Here we show that engineering of the lentiviral vector backbone drastically boosts the functional titer of the library virus, improving the scalability of the approach. The improved ORF library vector (SEQ ID NO: 132) showed >5X increase over the original vector in terms of the transduction efficiency, making it possible to reach ~30% transduction rate (which is desirable for pooled screening) with as little as 50 ul lentivirus (FIG. 31). As expected, the engineered vector backbone without the ORF library showed an even higher transduction efficiency, due to its smaller size.

References

1. Abramson, J. S. et al. Transcend NHL 001: immunotherapy with the CD19-directed CAR T-cell product JCAR017 results in high complete response rates in relapsed or refractory B-cell non-Hodgkin lymphoma. *Blood* 128, 4192–4192 (2016).
2. Shifrut, E. et al. Genome-wide CRISPR screens in primary human T cells reveal key regulators of immune function. *Cell* 175, 1958–1971 (2018).
3. Dong, M. B. et al. Systematic immunotherapy target discovery using genome-scale in vivo CRISPR screens in CD8 T cells. *Cell* 178, 1189–1204 (2019).
4. Chen, Z. et al. In vivo CD8+ T cell CRISPR screening reveals control by Fli1 in infection and cancer. *Cell* 184, 1262–1280 (2021).
5. Kabelitz, D., Serrano, R., Kouakanou, L., Peters, C. & Kalyan, S. Cancer immunotherapy with γδ T cells: many paths ahead of us. *Cell. Mol. Immunol.* 17, 925–939 (2020).
6. Munshi, N. C. et al. Idecabtagene vicleucel in relapsed and refractory multiple myeloma. *N. Engl. J. Med.* 384, 705–716 (2021).
7. Fraietta, J. A. et al. Determinants of response and resistance to CD19 chimeric antigen receptor (CAR) T cell therapy of chronic lymphocytic leukemia. *Nat. Med.* 24, 563–571 (2018).
8. Singer, M. et al. A distinct gene module for dysfunction uncoupled from activation in tumor-infiltrating T cells. *Cell* 166, 1500–1511 (2016).
9. Gurusamy, D. et al. Multi-phenotype CRISPR–Cas9 screen identifies p38 kinase as a target for adoptive immunotherapies. *Cancer Cell* 37, 818–833 (2020).
10. Legut, M., Dolton, G., Mian, A. A., Ottmann, O. G. & Sewell, A. K. CRISPR-mediated TCR replacement generates superior anticancer transgenic T cells. *Blood* 131, 311–322 (2018).
11. Ren, J. et al. Multiplex genome editing to generate universal CAR T cells resistant to PD1 inhibition. *Clin. Cancer Res.* 23, 2255–2266 (2017).
12. Wagner, D. L. et al. High prevalence of *Streptococcus pyogenes* Cas9-reactive T cells within the adult human population. *Nat. Med.* 25, 242–248 (2019).

13. Wu, X. et al. Genome-wide binding of the CRISPR endonuclease Cas9 in mammalian cells. *Nat. Biotechnol.* 32, 670–676 (2014).
14. Sack, L. M. et al. Profound tissue specificity in proliferation control underlies cancer drivers and aneuploidy patterns. *Cell* 173, 499–514 (2018).
15. Yuan, J. et al. CTLA-4 blockade enhances polyfunctional NY-ESO-1 specific T cell responses in metastatic melanoma patients with clinical benefit. *Proc. Natl Acad. Sci. USA* 105, 20410–20415 (2008).
16. Sommermeyer, D. et al. Chimeric antigen receptor-modified T cells derived from defined CD8+ and CD4+ subsets confer superior antitumor reactivity in vivo. *Leukemia* 30, 492–500 (2016).
17. Fischer, A. M., Katayama, C. D., Pagès, G., Pouysségur, J. & Hedrick, S. M. The role of Erk1 and Erk2 in multiple stages of T cell development. *Immunity* 23, 431–443 (2005).
18. Lipp, A. M. et al. Lck mediates signal transmission from CD59 to the TCR/CD3 pathway in Jurkat T cells. *PLoS One* 9, e85934 (2014).
19. Ma, X. et al. Interleukin-23 engineering improves CAR T cell function in solid tumors. *Nat. Biotechnol.* 38, 448–459 (2020).
20. Seo, H. et al. BATF and IRF4 cooperate to counter exhaustion in tumor-infiltrating CAR T cells. *Nat. Immunol.* 22, 983–995 (2021).
21. Jamali, A. et al. Highly efficient and selective CAR-gene transfer using CD4- and CD8-targeted lentiviral vectors. *Mol. Ther. Methods Clin. Dev.* 13, 371–379 (2019).
22. Stoeckius, M. et al. Simultaneous epitope and transcriptome measurement in single cells. *Nat. Methods* 14, 865–868 (2017).
23. Mimitou, E. P. et al. Multiplexed detection of proteins, transcriptomes, clonotypes and CRISPR perturbations in single cells. *Nat. Methods* 16, 409–412 (2019).
24. Gil-Yarom, N. et al. CD74 is a novel transcription regulator. *Proc. Natl Acad. Sci. USA* 114, 562–567 (2017).
25. Ataide, M. A. et al. BATF3 programs CD8+ T cell memory. *Nat. Immunol.* 21, 1397–1407 (2020).
26. Katagiri, T., Kameda, H., Nakano, H. & Yamazaki, S. Regulation of T cell differentiation by the AP-1 transcription factor JunB. *Immunol. Med.* 44, 197–203 (2021).
27. Zhao, X., Shan, Q. & Xue, H.-H. TCF1 in T cell immunity: a broadened frontier. *Nat. Rev. Immunol.* https://doi.org/10.1038/s41577-021-00563-6 (2021).
28. Sudhamsu, J. et al. Dimerization of LTβR by LTα1β2 is necessary and sufficient for signal transduction. *Proc. Natl Acad. Sci USA* 110, 19896–19901 (2013).
29. Li, C. et al. Structurally distinct recognition motifs in lymphotoxin-β receptor and CD40 for tumor necrosis factor receptor-associated factor (TRAF)-mediated signaling. *J. Biol. Chem.* 278, 50523–50529 (2003).
30. Wu, M.-Y., Wang, P.-Y., Han, S.-H. & Hsieh, S.-L. The cytoplasmic domain of the lymphotoxin-β receptor mediates cell death in HeLa cells. *J. Biol. Chem.* 274, 11868–11873 (1999).
31. Macian, F. NFAT proteins: key regulators of T-cell development and function. *Nat. Rev. Immunol.* 5, 472–484 (2005).
32. Dejardin, E. et al. The lymphotoxin-β receptor induces different patterns of gene expression via two NF-κB pathways. *Immunity* 17, 525–535 (2002).
33. Saoulli, K. et al. CD28-independent, TRAF2-dependent costimulation of resting T cells by 4-1BB ligand. *J. Exp. Med.* 187, 1849–1862 (1998).
34. Thommen, D. S. & Schumacher, T. N. T cell dysfunction in cancer. *Cancer Cell* 33, 547–562 (2018).
35. Roth, T. L. et al. Pooled knockin targeting for genome engineering of cellular immunotherapies. *Cell* 181, 728–744 (2020).
36. VanArsdale, T. L. et al. Lymphotoxin- receptor signaling complex: role of tumor necrosis

factor receptor-associated factor 3 recruitment in cell death and activation of nuclear factor B. *Proc. Natl Acad. Sci. USA* 94, 2460–2465 (1997).
37. Yılmaz, Z. B. et al. Quantitative dissection and modeling of the NF-κB p100-p105 module reveals interdependent precursor proteolysis. *Cell Rep.* 9, 1756–1769 (2014).
38. Hu, B. et al. Augmentation of antitumor immunity by human and mouse CAR T cells secreting IL-18. *Cell Rep.* 20, 3025–3033 (2017).
39. Yeku, O. O., Purdon, T. J., Koneru, M., Spriggs, D. & Brentjens, R. J. Armored CAR T cells enhance antitumor efficacy and overcome the tumor microenvironment. *Sci. Rep.* 7, 10541 (2017).
40. Lynn, R. C. et al. c-Jun overexpression in CAR T cells induces exhaustion resistance. *Nature* 576, 293–300 (2019).
41. Schmiedel, B. J. et al. Impact of genetic polymorphisms on human immune cell gene expression. *Cell* 175, 1701–1715 (2018).
42. Legut et al, A genome-scale screen for synthetic drivers of T cell proliferation. *Nature* 603, 728-723 (March 2022).
43. Theruvath et al, Locoregionally administered B7-H3-targeted CAR T cells for treatment of atypical teratoid/rhaboid tumors. *Nature Medicine* 26, 712-719 (April 2020).

All publications cited in this specification are incorporated herein by reference. US Provisional Patent Application No. 63/320,100 filed March 15, 2022 is incorporated herein by reference. While the invention has been described with reference to particular embodiments, it will be appreciated that modifications can be made without departing from the spirit of the invention. Such modifications are intended to fall within the scope of the appended claims.

What is claimed is:

1. A lymphocyte genetically modified to express a chimeric antigen receptor (CAR), wherein the CAR comprises:

a) an antigen binding domain;

b) a transmembrane domain; and

c) a signaling domain;

wherein at least one domain comprises an LTBR domain.

2. The modified lymphocyte according to claim 1, wherein the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof.

3. The modified lymphocyte according to claim 2, wherein the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or a fragment, deletion, or variant thereof.

4. The modified lymphocyte according to claim 2 or 3, wherein the LTBR intracellular domain has a deletion in at least amino acids 393 to 435.

5. The modified lymphocyte according to any one of claims 1 to 4, wherein the transmembrane domain is an LTBR domain.

6. The modified lymphocyte according to any one of claims 1 to 5, wherein the extracellular domain is an LTBR domain.

7. The modified lymphocyte according to any one of claims 1 to 6, wherein the lymphocyte is a T cell.

8. The modified lymphocyte according to any one of claims 1 to 7, wherein the lymphocyte is an alpha beta T cell or gamma delta T cell, optionally a Vγ9Vδ2 T cell.

9. The modified lymphocyte according to any one of claims 1 to 6, wherein the lymphocyte is an NK cell or NK T cell.

10. The modified lymphocyte according to any one of claims 1 to 9, wherein the LTBR intracellular domain is positioned between the co-stimulatory signaling domain of and the signaling domain of (c).

11. The modified lymphocyte according to any one of claims 1 to 9, wherein the LTBR domain is positioned after the signaling domain of (c).

12. A lymphocyte genetically modified to express a chimeric antigen receptor (CAR), wherein the CAR comprises:

a) an antigen binding domain;

b) a transmembrane domain;

c) a co-stimulatory signaling domain; and

d) a signaling domain;

wherein at least one domain comprises an LTBR domain.

13. The modified lymphocyte according to claim 12, wherein the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof.

14. The modified lymphocyte according to claim 13, wherein the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or a fragment, deletion, or variant thereof.

15. The modified lymphocyte according to claim 13 or 14, wherein the LTBR intracellular domain has a deletion in at least amino acids 393 to 435.

16. The modified lymphocyte according to any one of claims 12 to 15, wherein the transmembrane domain is an LTBR domain.

17. The modified lymphocyte according to any one of claims 12 to 16, wherein the extracellular domain is an LTBR domain.

18. The modified lymphocyte according to any one of claims 12 to 17, wherein the lymphocyte is a T cell.

19. The modified lymphocyte according to any one of claims 12 to 18, wherein the lymphocyte is an alpha beta T or gamma delta T cell, optionally a Vγ9Vδ2 T cell.

20. The modified lymphocyte according to any one of claims 12 to 18, wherein the lymphocyte is an NK cell or NK T cell.

21. The modified lymphocyte according to any one of claims 12 to 20, wherein the LTBR intracellular domain is positioned between the transmembrane domain of (b) and the co-stimulatory signaling domain of (c).

22. The modified lymphocyte according to any one of claims 1 to 20, wherein the LTBR intracellular domain is positioned between the co-stimulatory signaling domain of (c) and the signaling domain of (d).

23. The modified lymphocyte according to any one of claims 1 to 20, wherein the LTBR domain is positioned after the signaling domain of (c).

24. The modified lymphocyte according to any one of claims 1 to 23, wherein the CAR is selected from Axicabtagene ciloleucel (Yescarta®), Brexucabtagene autoleucel (Tecartus™), Idecabtagene vicleucel (Abecma™), Lisocabtagene maraleucel (Breyanzi®), Tisagenlecleucel (Kymriah®), or one of those found in FIG. 19, modified to include an LTBR domain.

25. A nucleic acid molecule comprising a sequence that encodes a chimeric antigen receptor (CAR), wherein the CAR comprises:

a) an antigen binding domain;

b) a transmembrane domain; and

c) a signaling domain;

wherein at least one domain comprises an LTBR domain.

26. The nucleic acid molecule according to claim 25, wherein the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof.

27. The nucleic acid molecule according to claim 26, wherein the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or a fragment, deletion, or variant thereof.

28. The nucleic acid molecule according to claim 26 or 27, wherein the LTBR intracellular domain has a deletion in at least amino acids 393 to 435.

29. The nucleic acid molecule according to any one of claims 25 to 28, wherein the transmembrane domain is an LTBR domain.

30. The nucleic acid molecule according to any one of claims 25 to 29, wherein the extracellular domain is an LTBR domain.

31. The nucleic acid molecule according to any one of claims 25 to 30, wherein the LTBR intracellular domain is positioned between the co-stimulatory signaling domain of and the signaling domain of (c).

32. The nucleic acid molecule according to any one of claims 25 to 30, wherein the LTBR domain is positioned after the signaling domain of (c).

33. A nucleic acid molecule comprising a sequence that encodes a chimeric antigen receptor (CAR), wherein the CAR comprises:

a. an antigen binding domain;

b. a transmembrane domain;

c. a co-stimulatory signaling domain; and

d. a signaling domain;

wherein at least one domain comprises an LTBR domain.

34. The nucleic acid molecule according to claim 33, wherein the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof.

35. The nucleic acid molecule according to claim 34, wherein the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or a fragment, deletion, or variant thereof.

36. The nucleic acid molecule according to claim 34 or 35, wherein the LTBR intracellular domain has a deletion in at least amino acids 393 to 435.

37. The nucleic acid molecule according to any one of claims 33 to 36, wherein the transmembrane domain is an LTBR domain.

38. The nucleic acid molecule according to any one of claims 33 to 37, wherein the extracellular domain is an LTBR domain.

39. The nucleic acid molecule according to any one of claims 33 to 38, wherein the LTBR intracellular domain is positioned between the transmembrane domain of (b) and the co-stimulatory signaling domain of (c).

40. The nucleic acid molecule according to any one of claims 33 to 39, wherein the LTBR intracellular domain is positioned between the co-stimulatory signaling domain of (c) and the signaling domain of (d).

41. The nucleic acid molecule according to any one of claims 33 to 40, wherein the LTBR domain is positioned after the signaling domain of (c).

42. The nucleic acid molecule according to any one of claims 25 to 41, wherein the CAR is selected from Axicabtagene ciloleucel (Yescarta®), Brexucabtagene autoleucel (Tecartus™), Idecabtagene vicleucel (Abecma™), Lisocabtagene maraleucel (Breyanzi®), Tisagenlecleucel (Kyrmriah®), or one of those found in FIG. 19, modified to include an LTBR domain.

43. An expression cassette comprising the nucleic acid molecule according to any one of claims 25 to 42.

44. The expression cassette according to claim 43, further comprising an expression control sequence.

45. The expression cassette according to claim 44, wherein the expression control sequence comprises a promoter.

46. The expression cassette according to claim 45, wherein the promoter is a constitutive promoter or an inducible promoter.

47. A modified lymphocyte comprising the nucleic acid molecule according to any one of claims 25 to 42 or the expression cassette according to any one of claims 43 to 46.

48. A method of producing a modified lymphocyte comprising introducing the nucleic acid molecule according to any one of claims 25 to 42 or the expression cassette according to any one of claims 43 to 46 into the lymphocyte.

49. A method of treating cancer in a subject in need thereof, the method comprising administering a composition comprising the modified lymphocyte according to any one of claims 1 to 24 or 47 to the subject.

50. The method according to claim 49, wherein the subject has lymphoma, optionally B cell lymphoma, follicular lymphoma, and mantle cell lymphoma.

51. The method according to claim 49, wherein the subject has a solid tumor cancer.

52. The method according to claim 49, wherein the subject has leukemia.

53. The method according to claim 49, wherein the subject has multiple myeloma.

54. The method according to claim 49, wherein the subject has a virally-driven cancer.

55. The method according to claim 54, wherein the subject has HPV.

56. The method according to claim 54, wherein the subject has a cancer selected from Burkitt's lymphoma, liver cancer, Kaposi's sarcoma, cervical cancer, head cancer, neck cancer,

anal cancer, pancreatic cancer, melanoma, oral cancer, pharyngeal cancer, penile cancer, adult T-cell lymphoma, and merkel cell carcinoma.

57. A method of treating a viral disease in a subject in need thereof, the method comprising administering a composition comprising the modified lymphocyte according to any one of claims 1 to 24 or 47 to the subject.

58. The method according to claim 57, wherein the disease is HIV or HPV.

59. A method of treating an autoimmune in a subject in need thereof, the method comprising administering a composition comprising the modified lymphocyte according to any one of claims 1 to 24 or 47 to the subject.

60. The method according to claim 29, wherein the disease is an autoimmune disorder.

61. A method of increasing proliferation, or T cell effector function including cytokine production and/or secretion, the method comprising administering a composition comprising the modified lymphocyte according to any one of claims 1 to 24 or 47 to the subject.

62. The method according to claim 61, wherein the T cell is obtained from a human prior to treating the T cell to overexpress LTBR, and the treated T cell is reintroduced into a human.

63. A fusion protein comprising an LTBR domain and at least one domain from a second protein, that is not LTBR.

64. The fusion protein according to claim 63, wherein the second protein is CD4.

65. The fusion protein according to claim 63, wherein the second protein is CD8A or CD8B.

66. The fusion protein according to claim 63, wherein the second protein is CD3E.

67. The fusion protein according to claim 63, wherein the second protein is CD3D.

68. The fusion protein according to claim 63, wherein the second protein is CD3G.

69. The fusion protein according to claim 63, wherein the second protein is CD3Z.

70. The fusion protein according to any one of claims 63-69, wherein the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof.

71. The fusion protein according to claim 70, wherein the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or a fragment, deletion, or variant thereof.

72. The fusion protein according to claim 70 or 71, wherein the LTBR intracellular domain has a deletion in at least amino acids 393 to 435.

73. A nucleic acid molecule comprising a sequence that encodes the fusion protein according to any one of claims 63 to 72.

74. A host cell comprising the nucleic acid molecule according to claim 73.

75. The host cell according to claim 74, which is a lymphocyte.

76. The host cell according to claim 75, which is a T cell.

77. A lymphocyte genetically modified to express a T cell receptor (TCR), wherein the TCR comprises an alpha chain fused to an LTBR intracellular domain.

78. A lymphocyte genetically modified to express a T cell receptor (TCR), wherein the TCR comprises a beta chain fused to an LTBR intracellular domain.

79. A lymphocyte genetically modified to express a T cell receptor (TCR), wherein the TCR comprises a gamma chain fused to an LTBR intracellular domain.

80. A lymphocyte genetically modified to express a T cell receptor (TCR), wherein the TCR comprises a delta chain fused to an LTBR intracellular domain.

81. The modified lymphocyte according to any one of claims 77 to 80, wherein the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof.

82. The modified lymphocyte according to claim 81, wherein the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or a fragment, deletion, or variant thereof.

83. The modified lymphocyte according to claim 81 or 82, wherein the LTBR intracellular domain has a deletion in at least amino acids 393 to 435.

84. The modified lymphocyte according to any one of claims 77 to 83, wherein the lymphocyte is a T cell.

85. The modified lymphocyte according to any one of claims 77 to 84, wherein the lymphocyte is an alpha beta T cell or gamma delta T cell, a Vγ9Vδ2 T cell.

86. The modified lymphocyte according to any one of claims 77 to 83, wherein the lymphocyte is an NK cell or NK T cell.

87. The modified lymphocyte according to any one of claims 77 to 86, wherein the TCR is tebentafusp-tebn (Kimmtrak®) or one of those found in FIG. 20, modified to include an LTBR domain.

88. A nucleic acid molecule comprising a sequence that encodes a chimeric antigen receptor (CAR), wherein the CAR comprises:

a. an antigen binding domain;

b. a transmembrane domain; and

c. a signaling domain;

wherein at least one domain comprises an LTBR domain.

89. The nucleic acid molecule according to claim 88, wherein the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof.

90. The nucleic acid molecule according to claim 89, wherein the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or a fragment, deletion, or variant thereof.

91. The nucleic acid molecule according to claim 88 or 89, wherein the LTBR intracellular domain has a deletion in at least amino acids 393 to 435.

92. An expression cassette comprising the nucleic acid molecule according to any one of claims 88 to 91.

93. The expression cassette according to claim 92, further comprising an expression control sequence.

94. The expression cassette according to claim 93, wherein the expression control sequence comprises a promoter.

95. The expression cassette according to claim 94, wherein the promoter is a constitutive promoter or an inducible promoter.

96. A modified lymphocyte comprising the nucleic acid molecule according to any one of claims 88 to 91 or the expression cassette according to any one of claims 92 to 95.

97. A method of producing a modified lymphocyte comprising introducing the nucleic acid molecule according to any one of claims 88 to 91 or the expression cassette according to any one of claims 92 to 95 into the lymphocyte.

98. A method of treating cancer in a subject in need thereof, the method comprising administering a composition comprising the modified lymphocyte according to any one of claims 77 to 87 or 96 to the subject.

99. The method according to claim 98, wherein the subject has lymphoma, optionally B cell lymphoma, follicular lymphoma, and mantle cell lymphoma.

100. The method according to claim 99, wherein the subject has a solid tumor cancer.

101. The method according to claim 98, wherein the subject has leukemia.

102. The method according to claim 98, wherein the subject has multiple myeloma.

103. The method according to claim 98, wherein the subject has multiple uveal melanoma.

104. The method according to claim 98, wherein the subject has a virally-driven cancer.

105. The method according to claim 98, wherein the subject has HPV.

106. The method according to claim 104, wherein the subject has a cancer selected from Burkitt's lymphoma, liver cancer, Kaposi's sarcoma, cervical cancer, head cancer, neck cancer, anal cancer, oral cancer, pharyngeal cancer, penile cancer, adult T-cell lymphoma, and merkel cell carcinoma.

107. A method of increasing proliferation, or T cell effector function including cytokine production and/or secretion, the method comprising administering a composition comprising the modified lymphocyte according to any one of claims 77 to 87 or 96 to the subject.

108. The method according to claim 107, wherein the T cell is obtained from a human prior to modifying the lymphocyte, and the modified lymphocyte is reintroduced into a human.

109. The nucleic acid molecule according to XX, wherein the CAR targets CD19, mesothelin, ROR1, B7-H3, IL13Rα2, GD2, Her2, Glypican 3, CD7, NY-ESO-1, CD30, MAGE-A1, LMP2, PD1, KRAS G12V, CD20, CD22, CD171, CD123, CD38, CD10, BAFFR, PSMA, or mucin.

110. A fusion protein comprising:

a. an antigen binding domain;

b. LTBR;

c. and at least one domain from a second protein that is not LTBR.

111. The fusion protein according to claim 110, wherein the second protein is CD4.

112. The fusion protein according to claim 110, wherein the second protein is CD8A or CD8B.

113. The fusion protein according to claim 110, wherein the second protein is CD3E.

114. The fusion protein according to claim 110, wherein the second protein is CD3D.

115. The fusion protein according to claim 110, wherein the second protein is CD3G.

116. The fusion protein according to claim 110, wherein the second protein is CD3Z.

117. The fusion protein according to any one of claims 110-116, wherein the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof.

118. A nucleic acid molecule comprising a sequence that encodes the fusion protein according to any one of claims 110 to 117.

119. A modified lymphocyte comprising the nucleic acid molecule according to claim 118.

120. A modified lymphocyte comprising the nucleic acid molecule according to claim 118 and further comprising a nucleic acid molecule that encodes a CAR.

121. The modified lymphocyte according to claim 120, wherein the CAR and the antigen binding domain both target mesothelin.

122. A lymphocyte genetically modified to express a T cell receptor (TCR) and a CD8 alpha chain fused to an LTBR intracellular domain.

123. A lymphocyte genetically modified to express a T cell receptor (TCR) and a CD8 beta chain fused to an LTBR intracellular domain.

124. The modified lymphocyte according to claim 122 or 123, wherein the LTBR domain is an LTBR intracellular domain, or fragment or variant thereof.

125. The modified lymphocyte according to claim 124, wherein the LTBR intracellular domain comprises amino acids 249 to 435 of SEQ ID NO: 2, or a fragment, deletion, or variant thereof.

126. The modified lymphocyte according to claim 124 or 125, wherein the LTBR intracellular domain has a deletion in at least amino acids 393 to 435.

127. The modified lymphocyte according to any one of claims 122 to 126, wherein the lymphocyte is a T cell.

128. The modified lymphocyte according to any one of claims 122 to 127, wherein the lymphocyte is an alpha beta T cell or gamma delta T cell, a Vγ9Vδ2 T cell.

129. The modified lymphocyte according to any one of claims 122 to 126, wherein the lymphocyte is an NK cell or NK T cell.

130. The modified lymphocyte according to any one of claims 122 to 129, wherein the TCR is tebentafusp-tebn (Kimmtrak®) or one of those found in FIG. 20.

131. An engineered lentiviral vector comprising the sequence of SEQ ID NO: 132, or a sequence sharing at least 90% identity with SEQ ID NO: 132, optionally with an open reading frame (ORF) for a gene of interest and/or a barcode inserted within the sequence.

132. The engineered vector of claim 131, wherein the ORF and/or barcode are inserted after nucleotide 3291 of SEQ ID NO: 132.

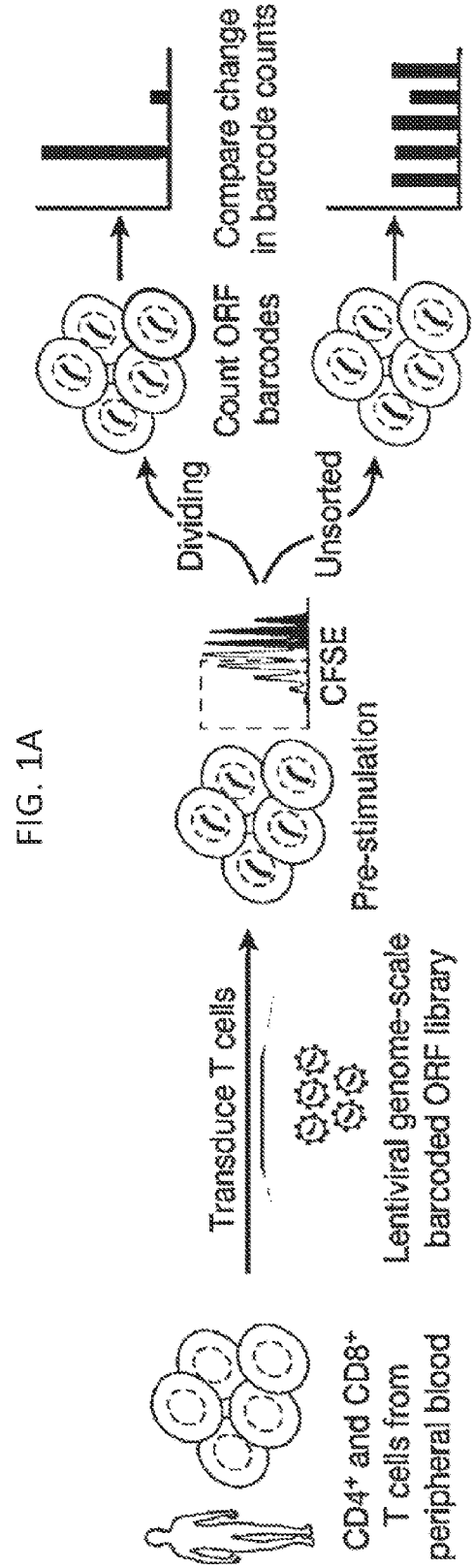


FIG. 1A

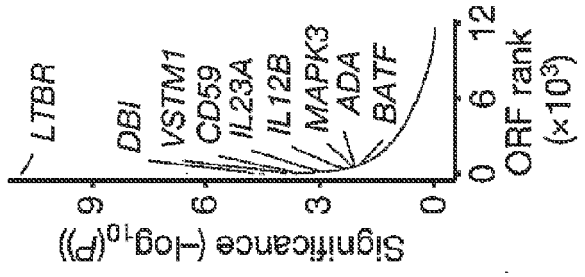


FIG. 1C

FIG. 1B

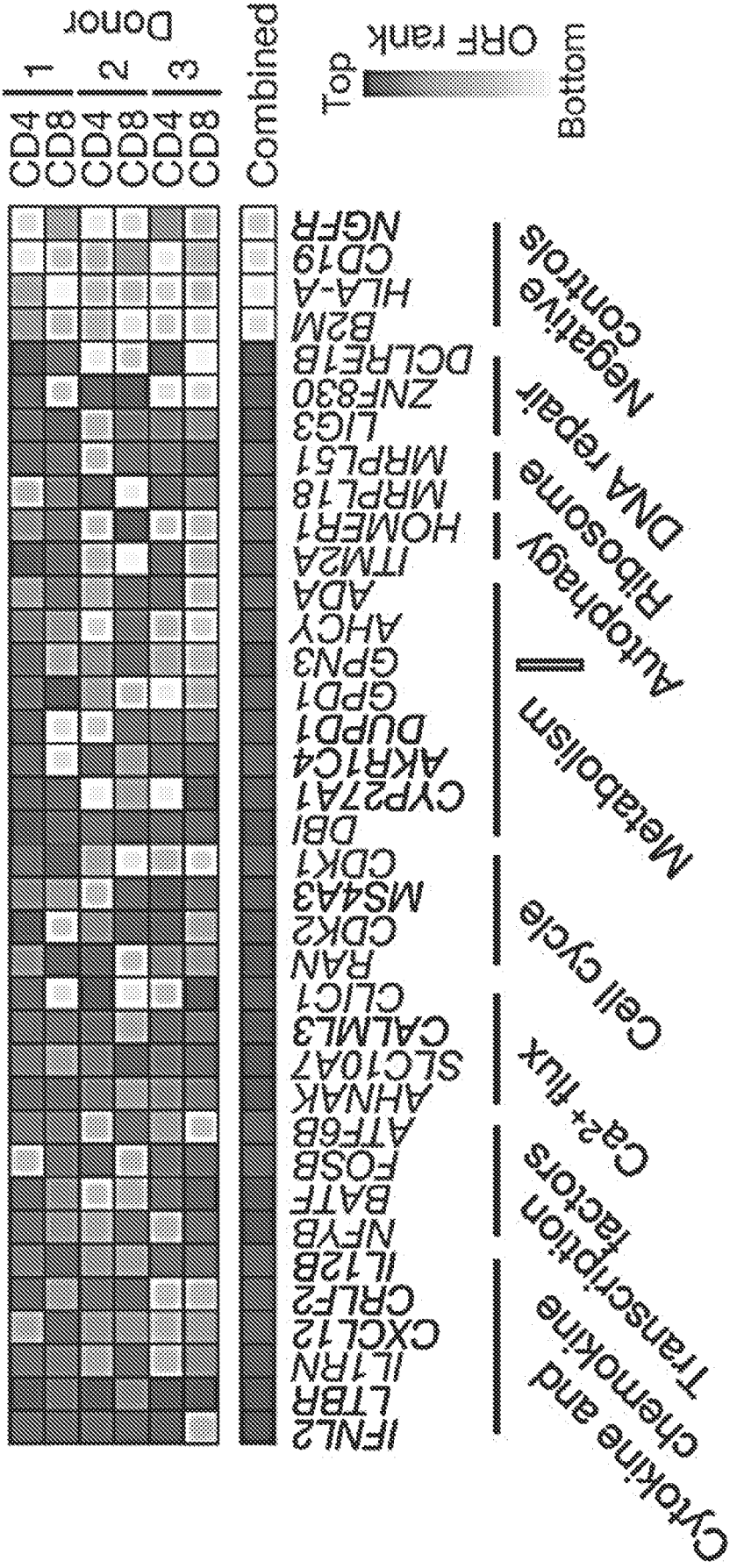
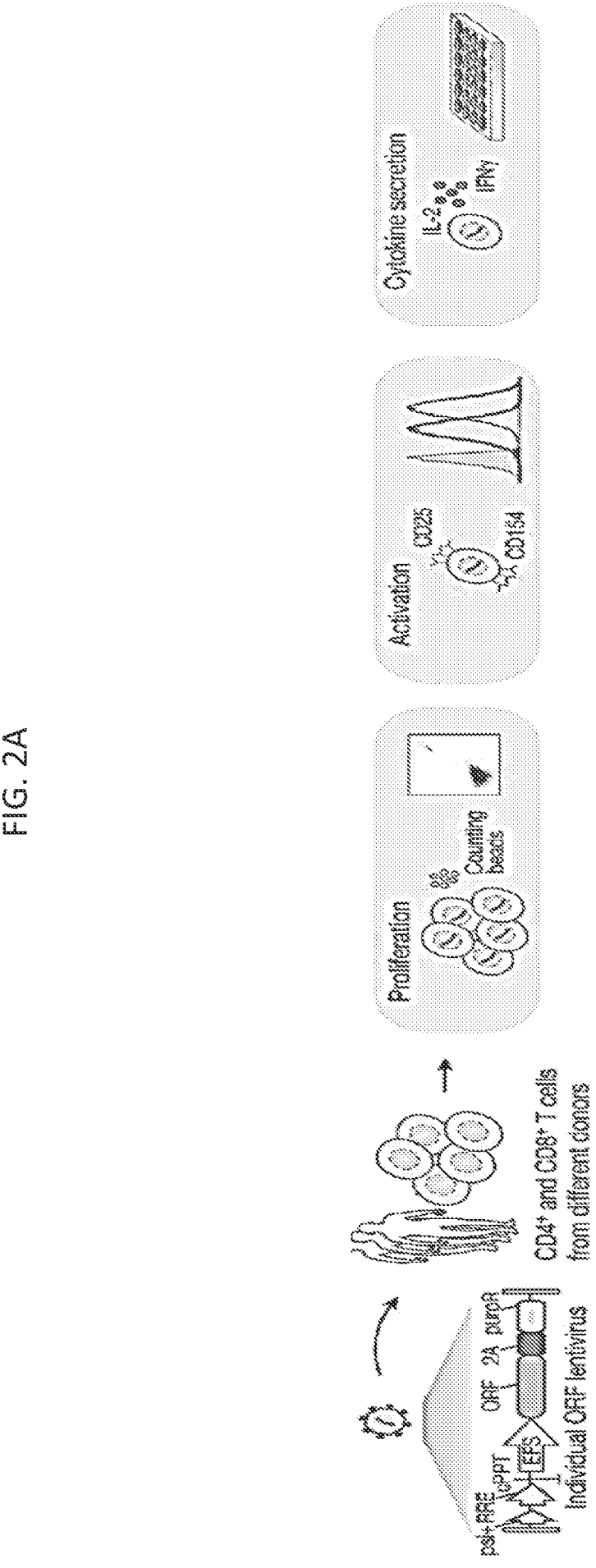

Donor
1
2
3
CD4
CD8
Combined
Top
ORF rank
Bottom
IFNL2
LTBR
IL1RN
CXCL12
CRLF2
IL12B
NFYB
BATF
FOSB
ATF6B
AHNAK
SLC10A7
CALML3
CLIC1
RAN
CDK2
MS4A3
CDK1
DBI
CYP27A1
AKR1C4
DUPD1
GPD1
GPN3
AHCY
ADA
ITM2A
HOMER1
MRPL18
MRPL51
LIG3
ZNF830
DCLRE1B
B2M
HLA-A
CD19
NGFR
Cytokine and chemokine
Transcription factors
Ca2+ flux
Cell cycle
Metabolism
Autophagy
Ribosome
DNA repair
Negative controls

FIG. 1D

FIG. 2A


Cytokine secretion
IL-2
IFNγ
Activation
CD25
CD154
Proliferation
Counting beads
CD4+ and CD8+ T cells from different donors
Individual ORF lentivirus
psi+ RRE
cPPT
EF5
ORF
2A
puro

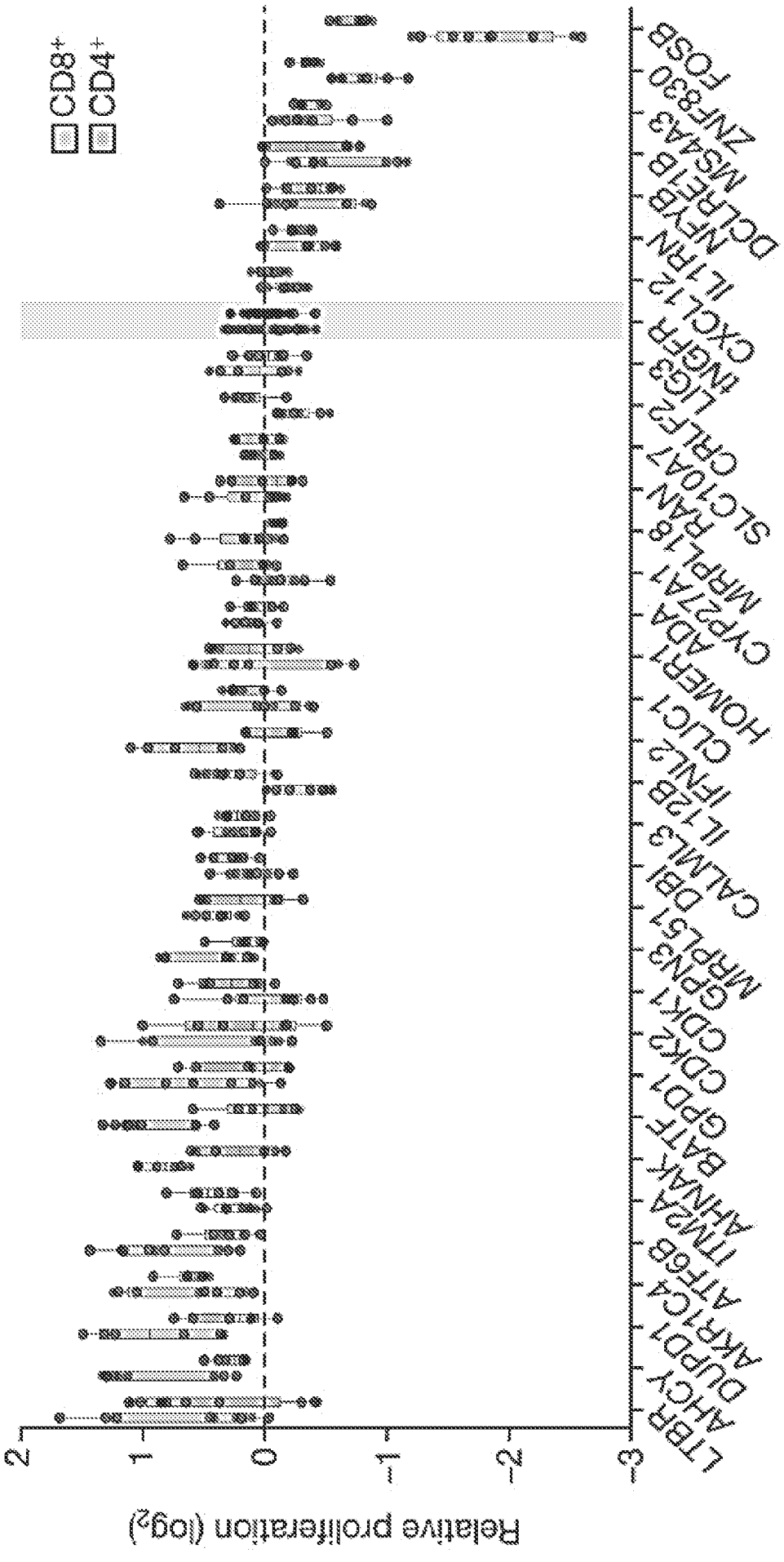

CD8+
CD4+
Relative proliferation (log2)
2
1
0
-1
-2
-3
LTBR
AHCY
DUPD1
AKR1CA
ATF6B
TMEM2A
AHNAK
BAIAP
GPD1
CDK2
CDK1
GPN3
MRPL51
DBI
CALML3
IL12B
IFNL2
CLIC1
HOMER1
ADA
CYP27A1
MRPL18
RAN
SLC10A7
CRLF3
LIG3
NGFR
CXCL12
IL1RN
NFYB
DCLRE1B
MSA43
ZNF830
FOSB

FIG. 2B

FIG. 2C

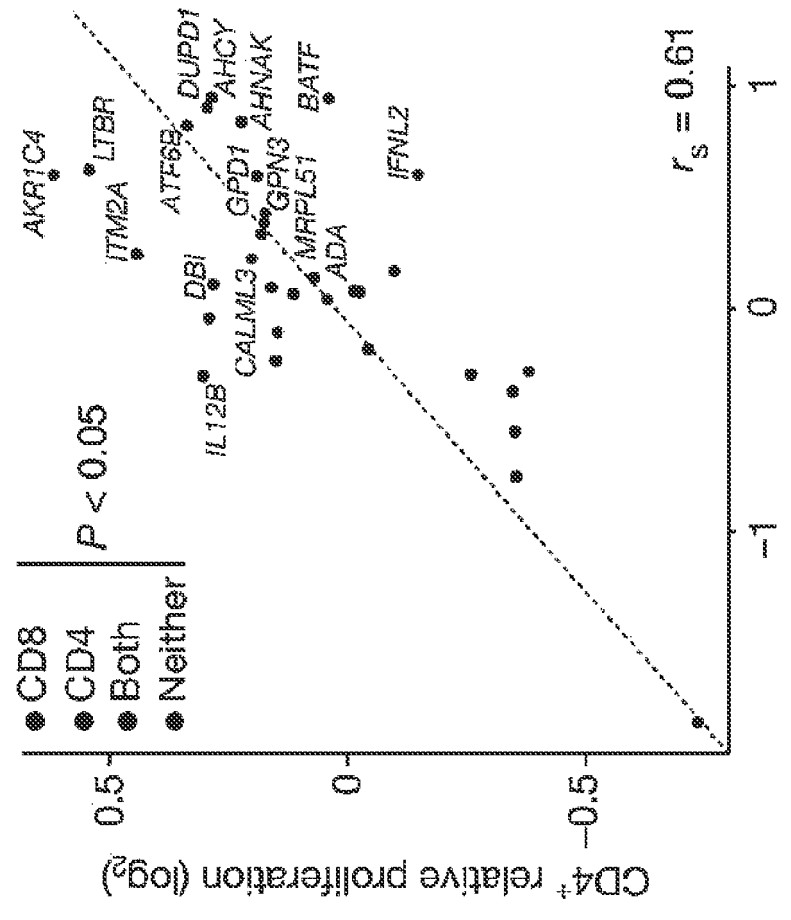

CD8
CD4
Both
Neither
P < 0.05
AKR1C4
LTBR
ITM2A
ATF6B
DUPD1
AHCY
DBI
GPD1
AHNAK
IL12B
CALML3
GPN3
MRPL51
BATF
ADA
IFNL2
$r_S = 0.61$
CD4+ relative proliferation (log2)
CD8+ relative proliferation (log2)
0.5
0
−0.5
−1
0
1

FIG. 2D

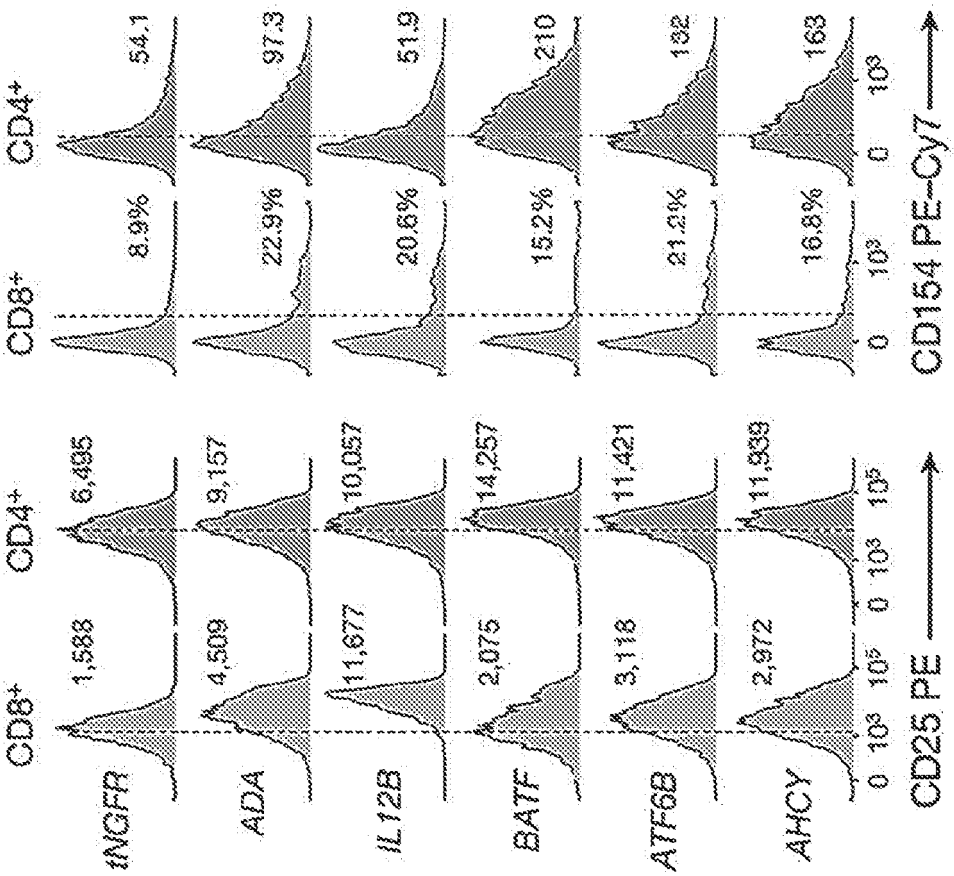

CD8+
CD4+
tNGFR
1,588
6,495
8.9%
54.1
ADA
4,509
9,157
22.9%
97.3
IL12B
11,677
10,057
20.6%
51.9
BATF
2,075
14,257
15.2%
210
ATF6B
3,118
11,421
21.2%
132
AHCY
2,972
11,939
16.8%
163
0 10³ 10⁵
CD25 PE
CD154 PE–Cy7

FIG. 2F

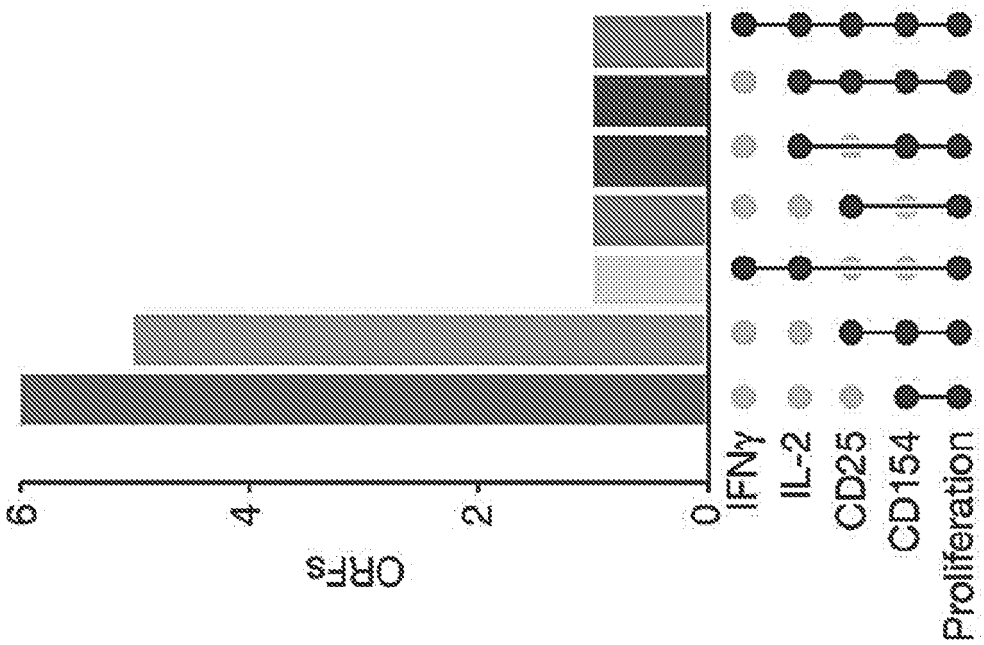
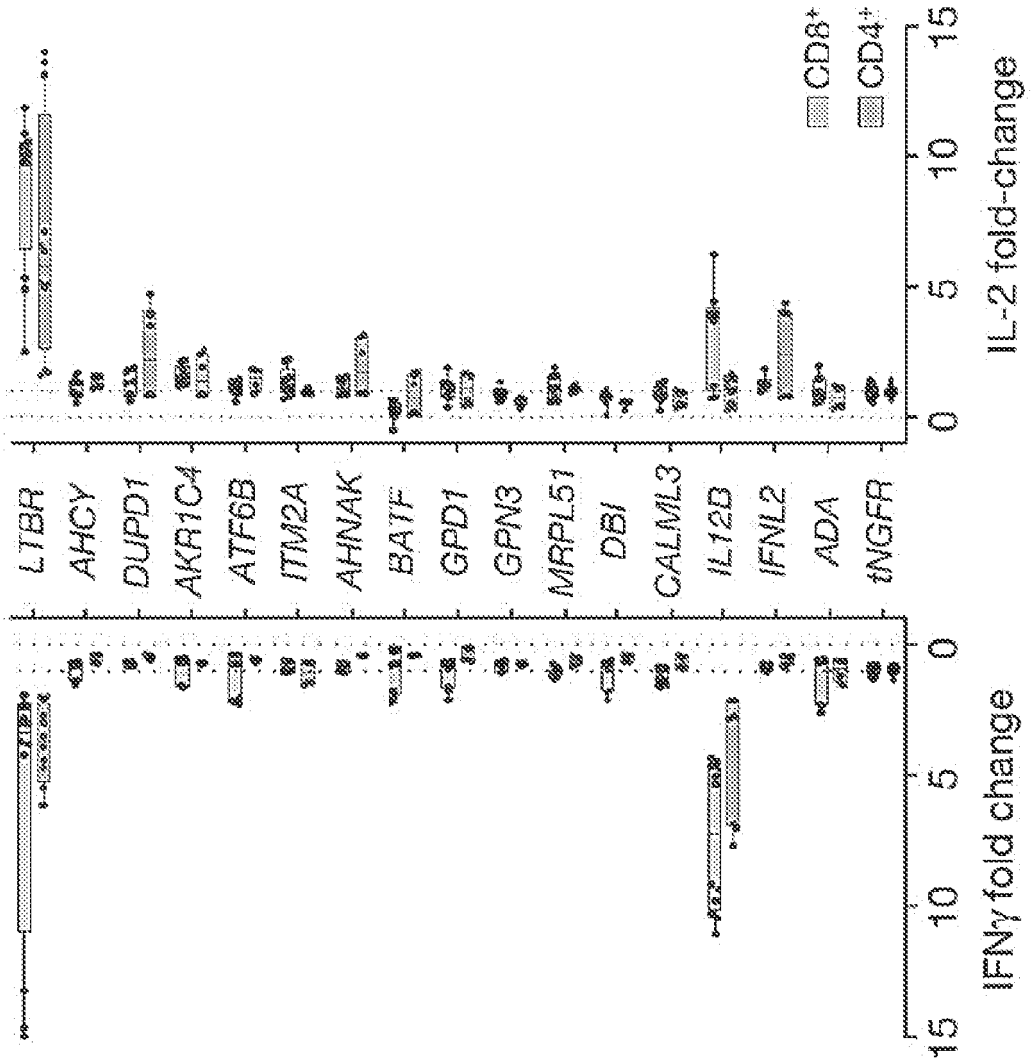

OR
6
4
2
0
IFNγ
IL-2
CD25
CD154
Proliferation

FIG. 2E


LTBR
AHCY
DUPD1
AKR1C4
ATF6B
ITM2A
AHNAK
BATF
GPD1
GPN3
MRPL51
DBI
CALML3
IL12B
IFNL2
ADA
tNGFR
CD8+
CD4+
0
5
10
15
IL-2 fold-change
IFNγ fold change

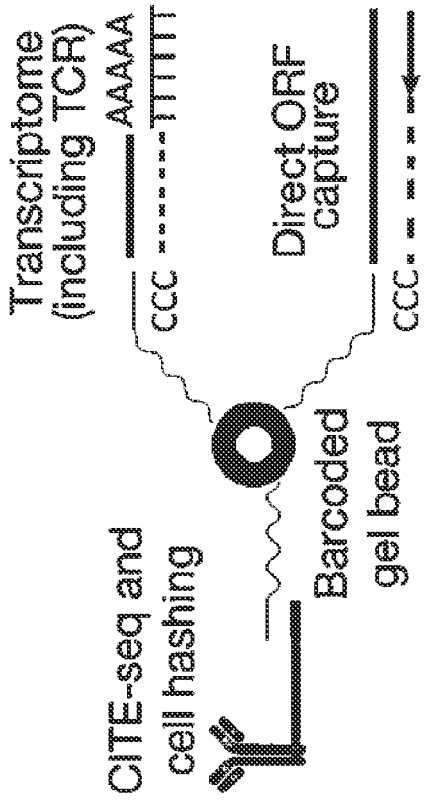


FIG. 3A

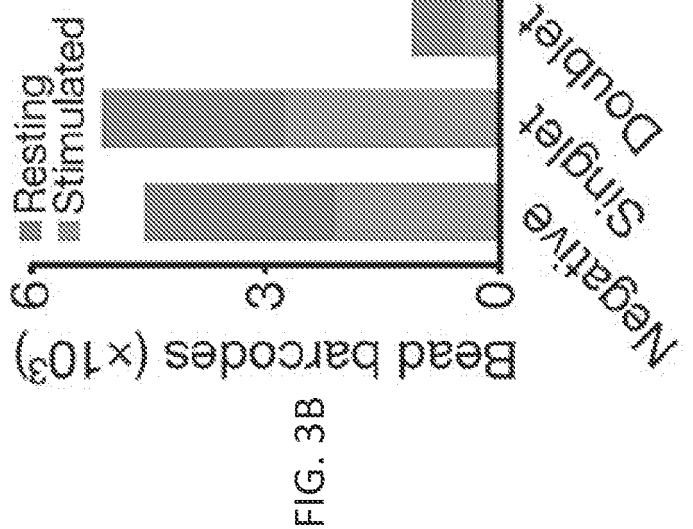


FIG. 3B

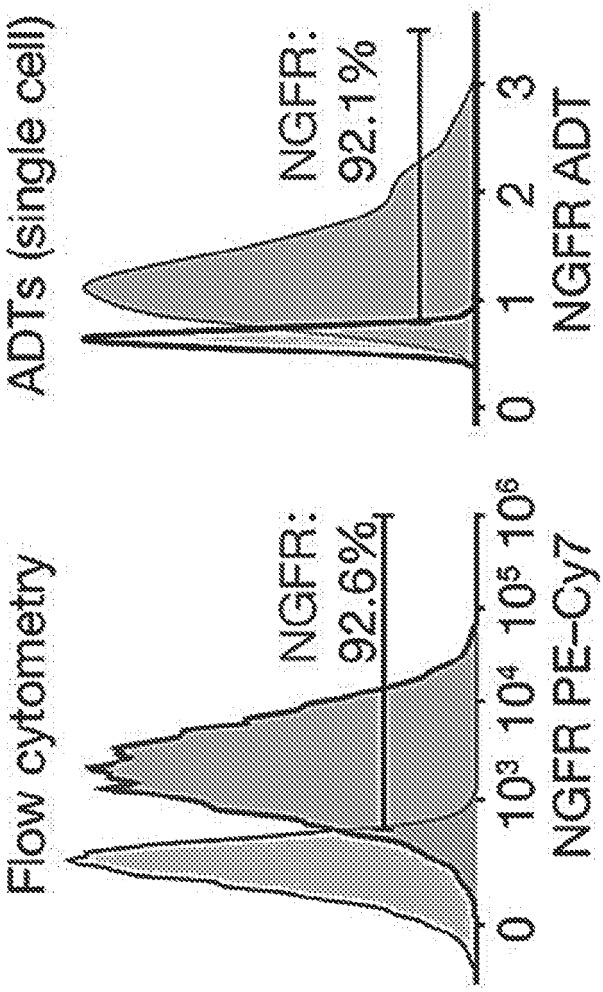


FIG. 3C

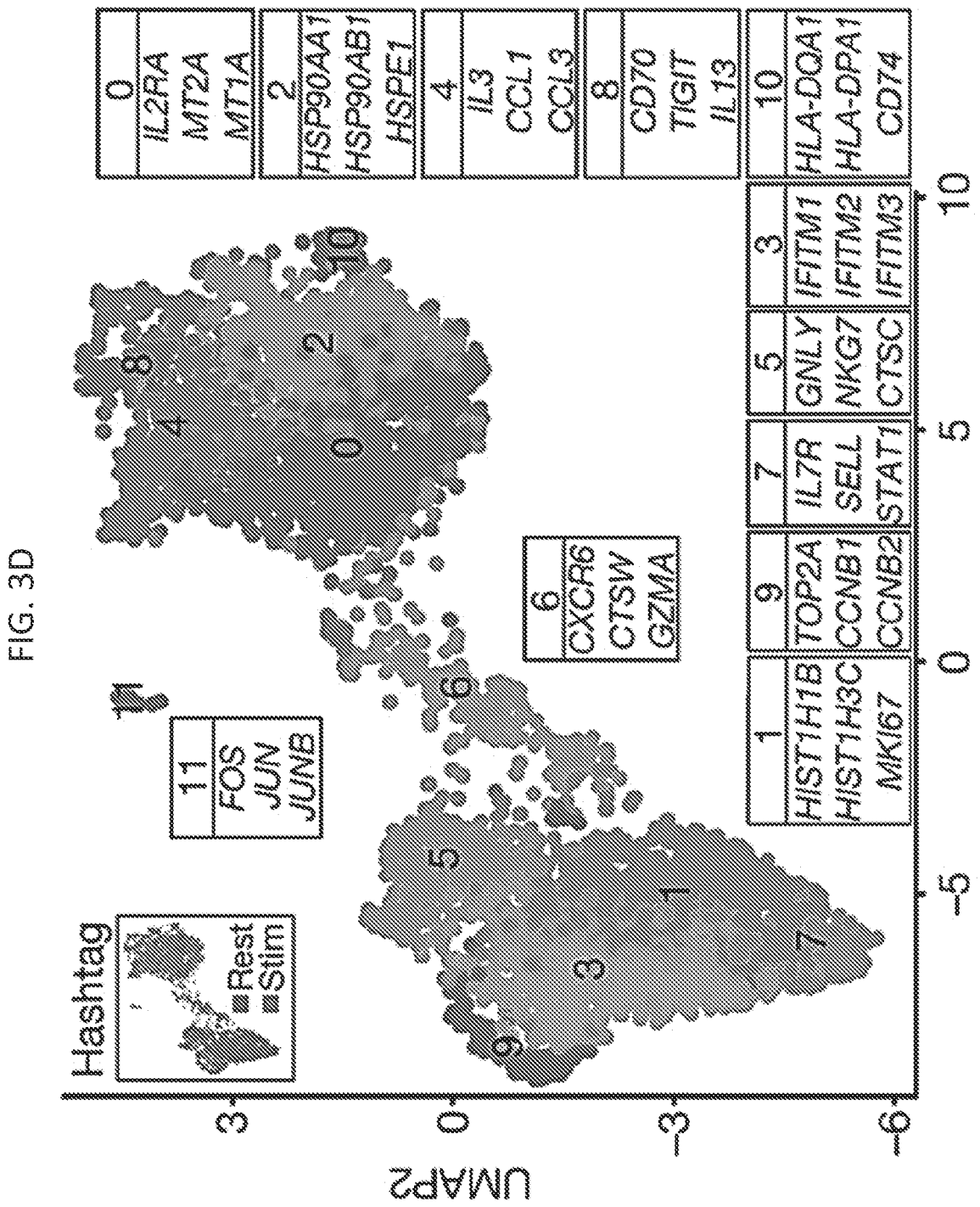

0
IL2RA
MT2A
MT1A
2
HSP90AA1
HSP90AB1
HSPE1
4
IL3
CCL1
CCL3
8
CD70
TIGIT
IL13
10
HLA-DQA1
HLA-DPA1
CD74
3
IFITM1
IFITM2
IFITM3
5
GNLY
NKG7
CTSC
7
IL7R
SELL
STAT1
9
TOP2A
CCNB1
CCNB2
1
HIST1H1B
HIST1H3C
MKI67
6
CXCR6
CTSW
GZMA
11
FOS
JUN
JUNB
Hashtag
Rest
Stim
UMAP1
UMAP2
−5
0
5
10
3
0
−3
−6

FIG. 3D

FIG. 3E

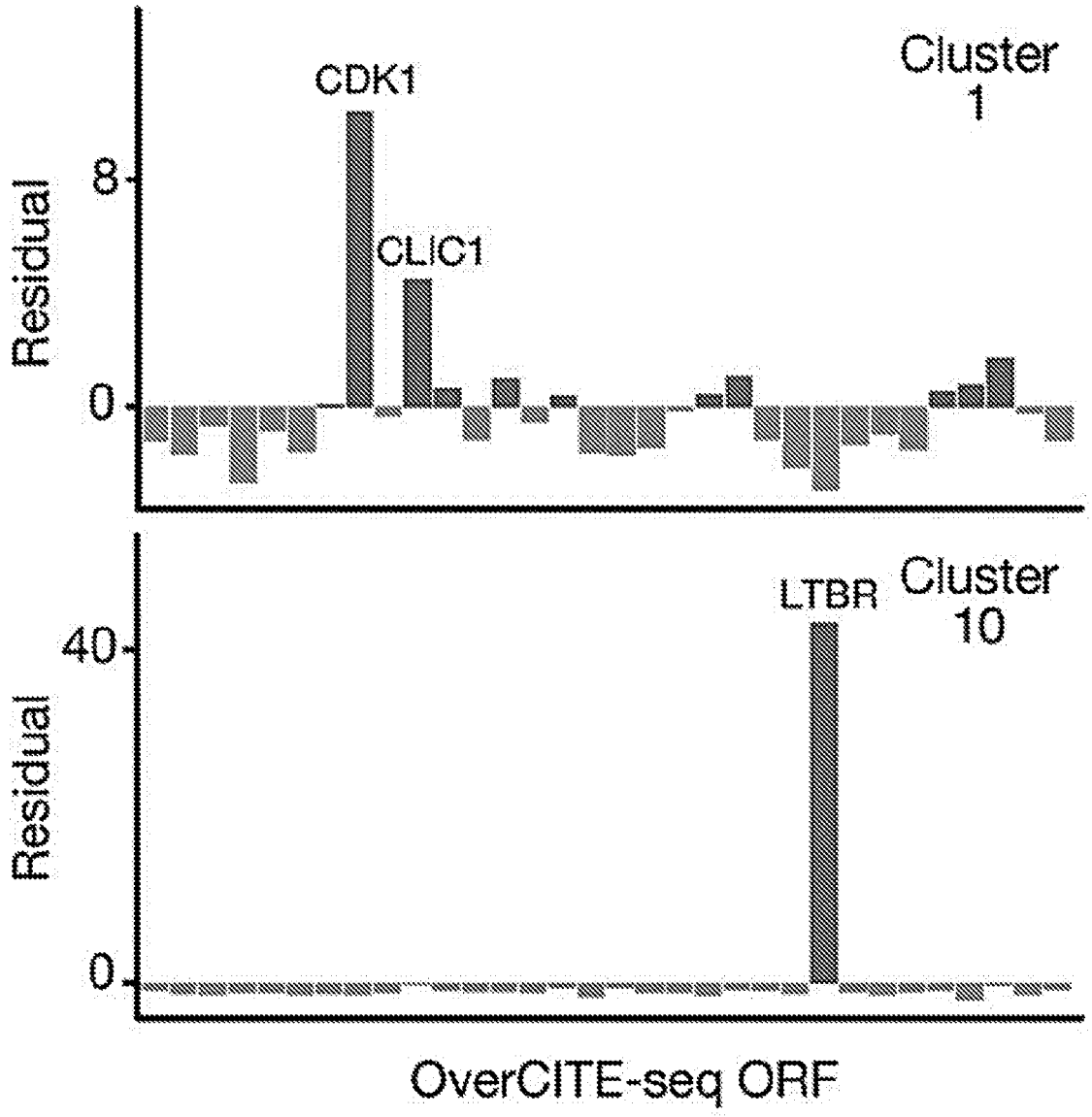

Cluster
1
CDK1
CLIC1
8
0
Residual
Cluster
10
LTBR
40
0
Residual
OverCITE-seq ORF

FIG. 4A

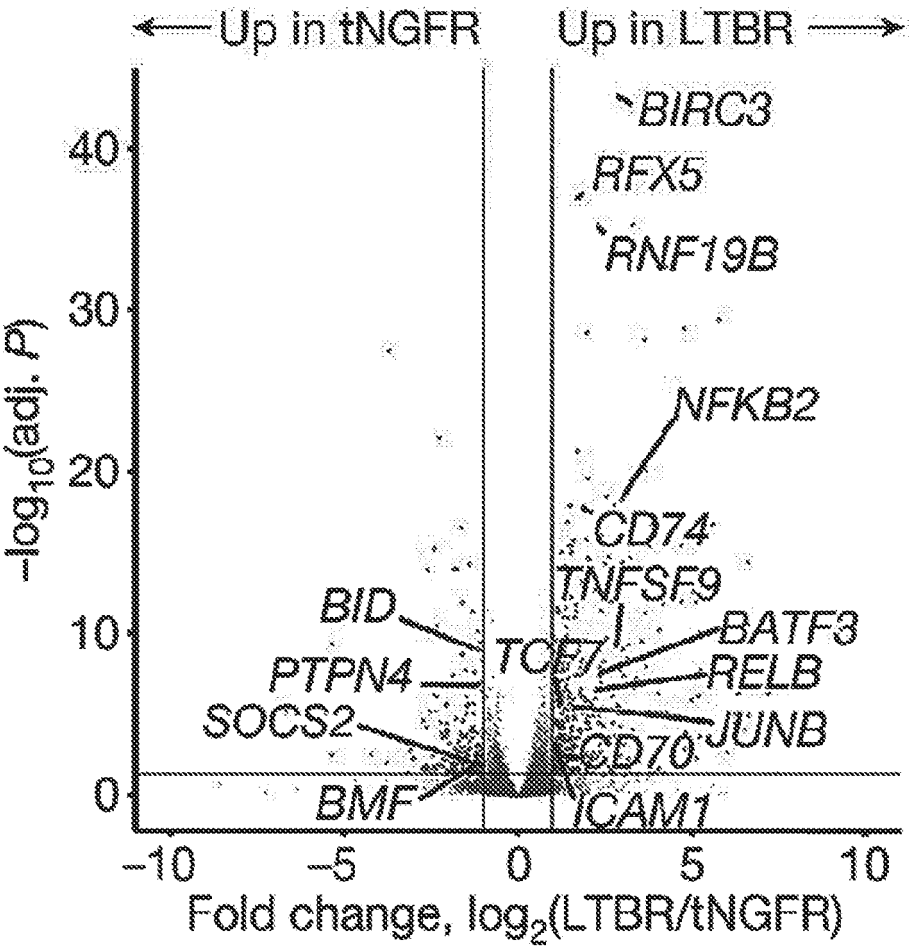

Up in tNGFR
Up in LTBR
BIRC3
RFX5
RNF19B
NFKB2
CD74
TNFSF9
BID
TCF7
BATF3
PTPN4
RELB
SOCS2
JUNB
CD70
BMF
ICAM1
40
30
20
10
0
−10
−5
0
5
10
−log10(adj. P)
Fold change, log2(LTBR/tNGFR)

FIG. 4B

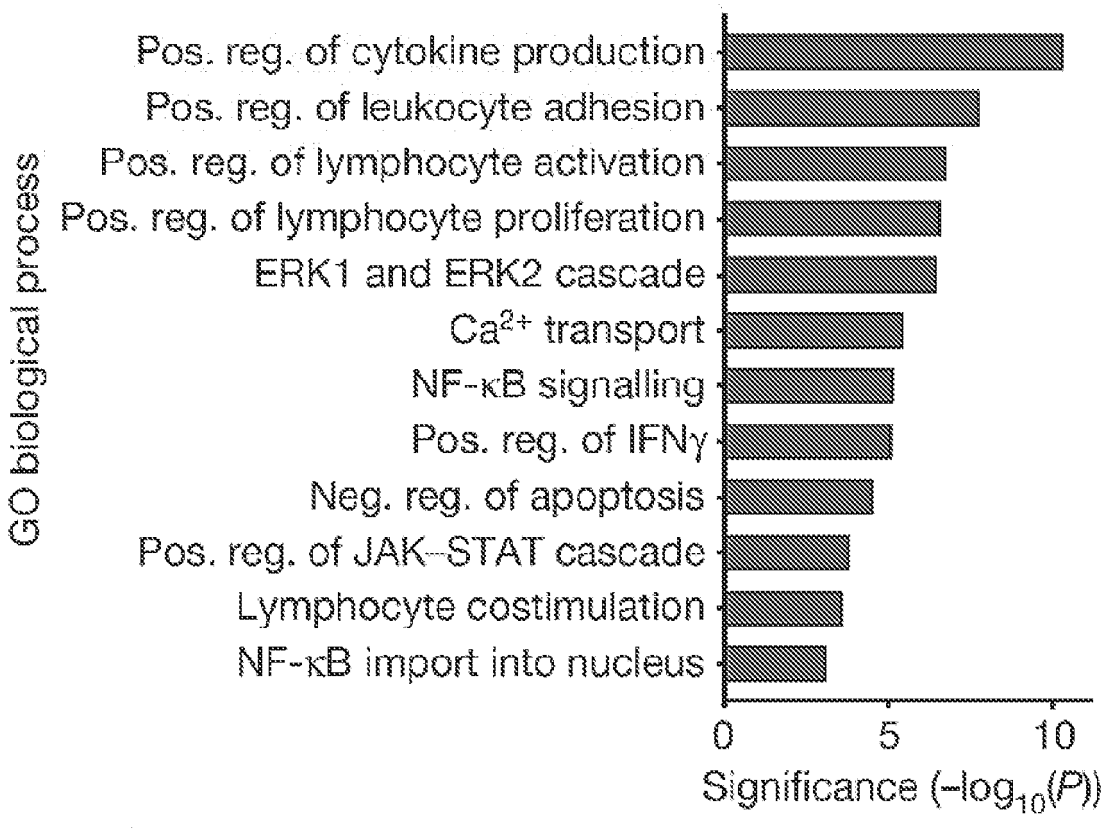

Pos. reg. of cytokine production
Pos. reg. of leukocyte adhesion
Pos. reg. of lymphocyte activation
Pos. reg. of lymphocyte proliferation
ERK1 and ERK2 cascade
Ca2+ transport
NF-κB signalling
Pos. reg. of IFNγ
Neg. reg. of apoptosis
Pos. reg. of JAK–STAT cascade
Lymphocyte costimulation
NF-κB import into nucleus
GO biological process
0
5
10
Significance (−log10(P))

FIG. 4C

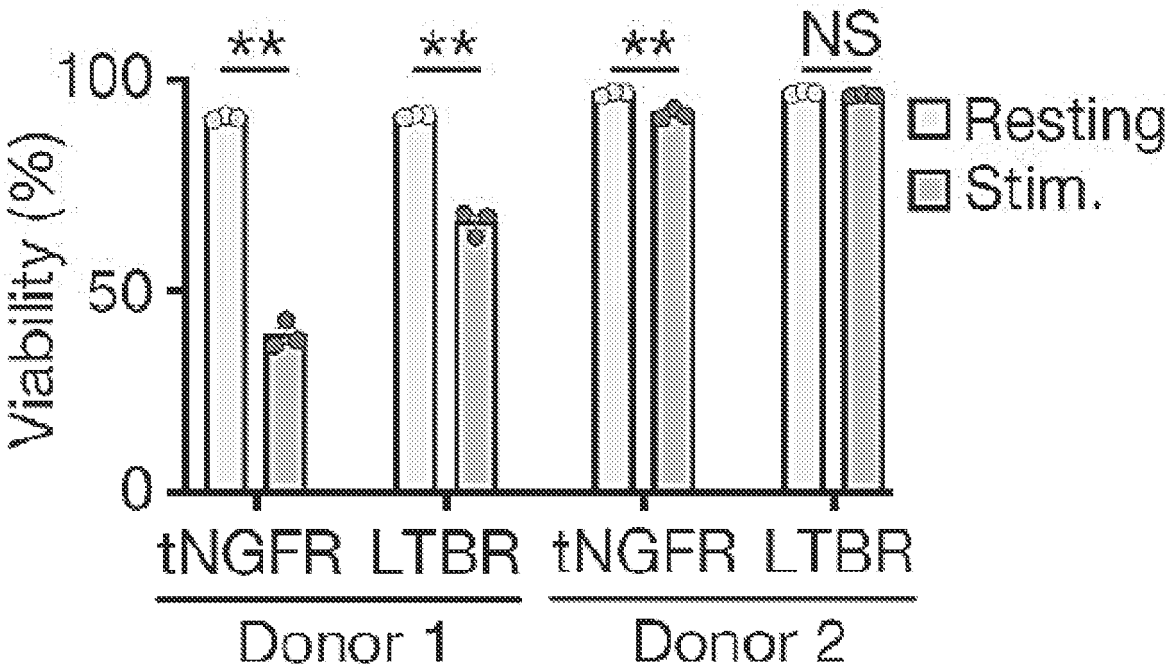

**
**
**
NS
100
50
0
Viability (%)
Resting
Stim.
tNGFR LTBR tNGFR LTBR
Donor 1
Donor 2

FIG. 4D

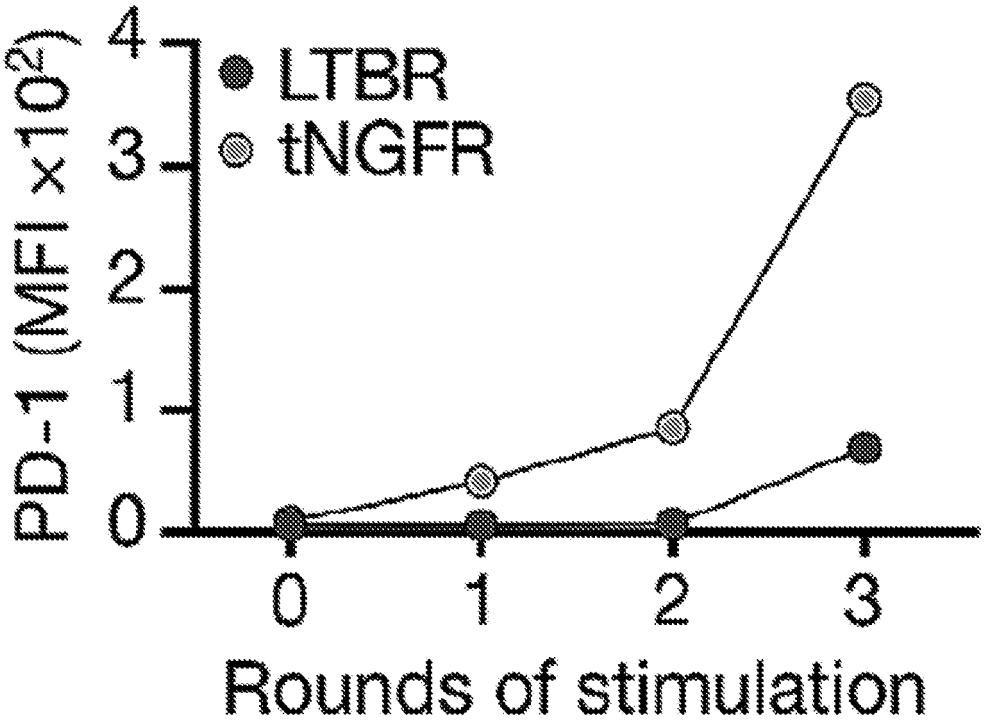
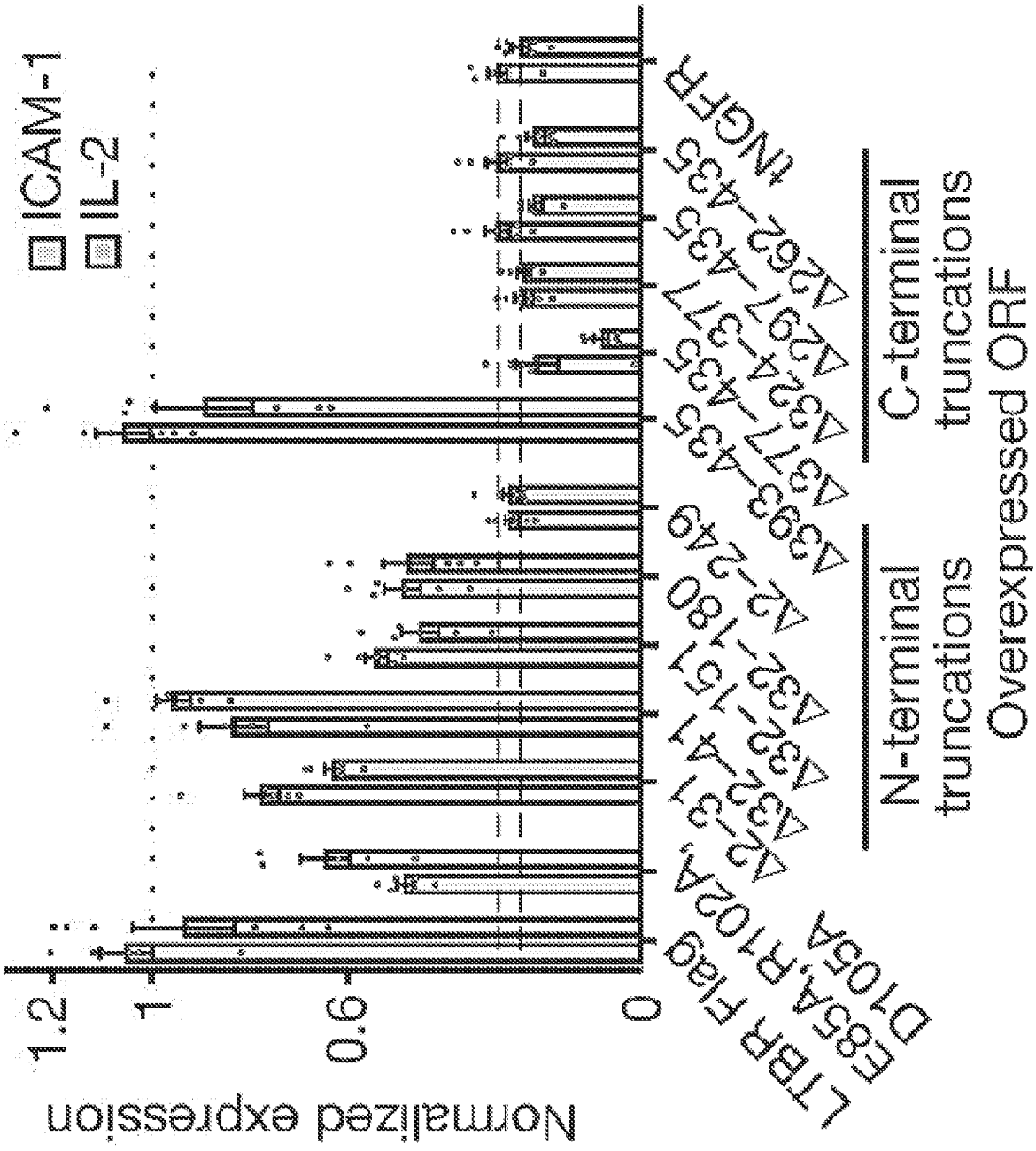

PD-1 (MFI x10²)
4
3
2
1
0
LTBR
tNGFR
0
1
2
3
Rounds of stimulation

FIG. 4E


ICAM-1
IL-2
Normalized expression
1.2
1
0.6
0
LTBR Flag
E85A,R102A
D105A
Δ2-131
Δ32-171
Δ32-180
Δ2-229
Δ32-151
Δ393-435
Δ371-435
Δ324-435
Δ291-371
Δ262-435
mGFR
N-terminal truncations
C-terminal truncations
Overexpressed ORF

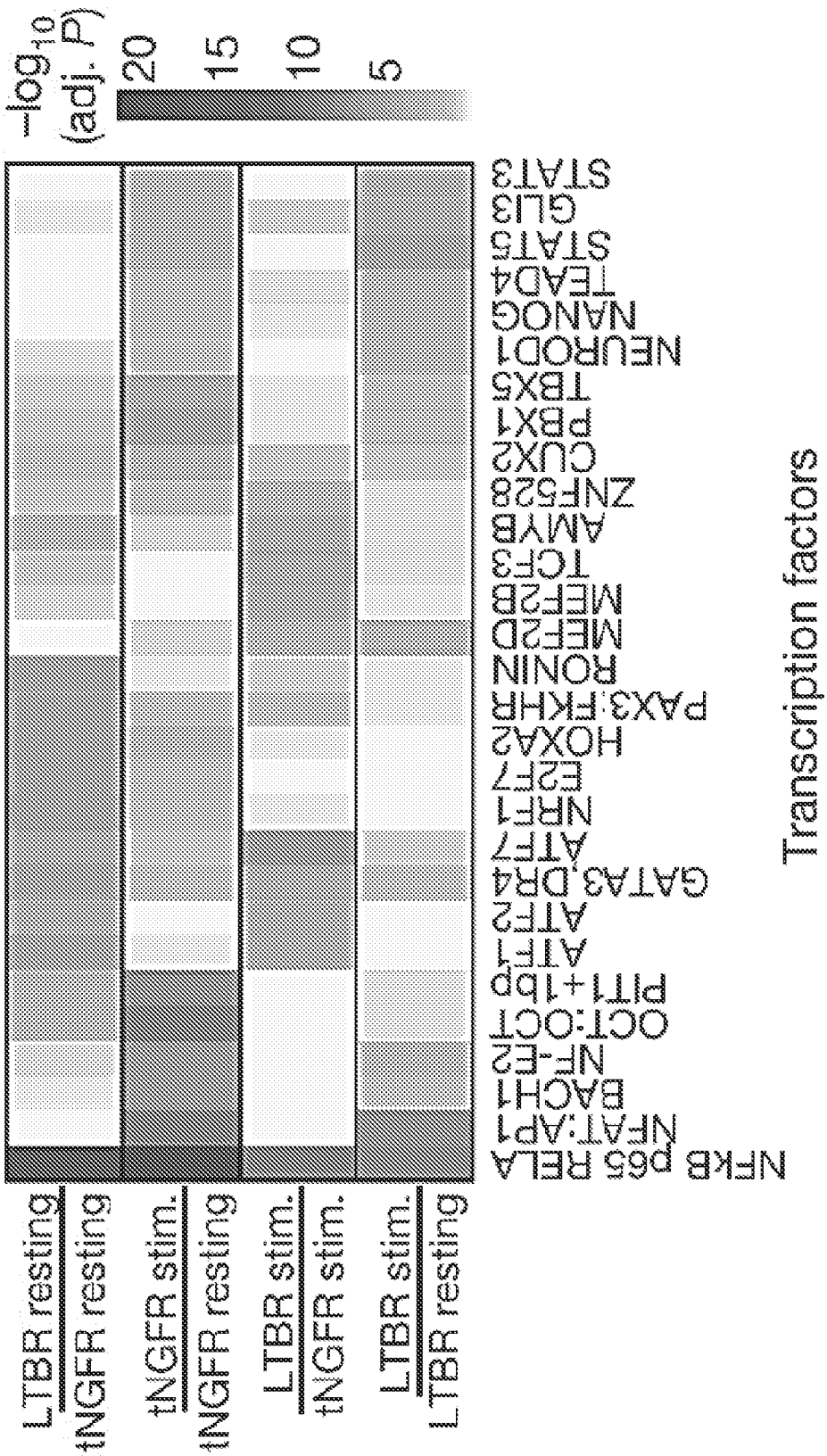

−log10 (adj. P)
20
15
10
5
Transcription factors
NFKB p65 RELA
NFAT:AP1
BACH1
NF-E2
OCT:OCT
PIT1+1bp
ATF1
ATF2
GATA3,DR4
ATF7
NRF1
E2F7
HOXA2
PAX3:FKHR
RONIN
MEF2D
MEF2B
TCF3
AMYB
ZNF528
CUX2
PBX1
TBX5
NEUROD1
NANOG
TEAD4
STAT5
GLI3
STAT3
LTBR resting
tNGFR resting
tNGFR stim.
tNGFR resting
LTBR stim.
tNGFR stim.
LTBR stim.
LTBR resting

FIG. 4F

FIG. 4G

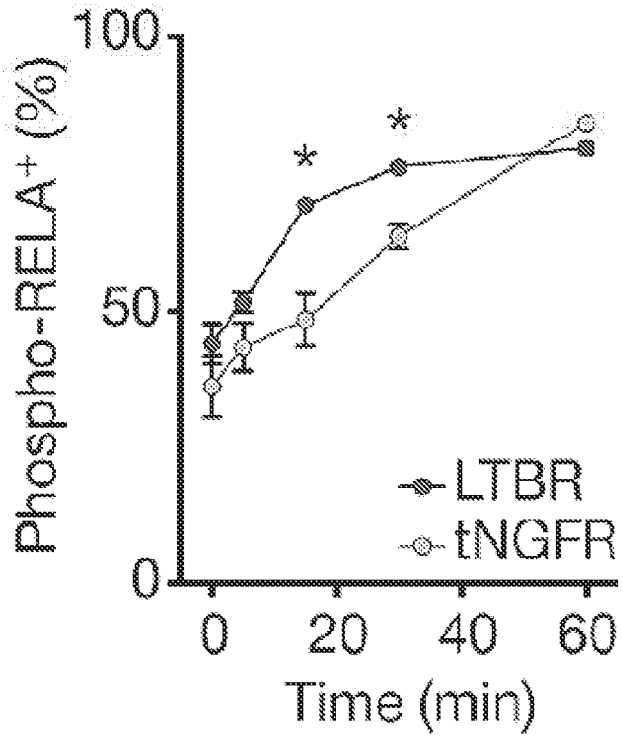


FIG. 4H

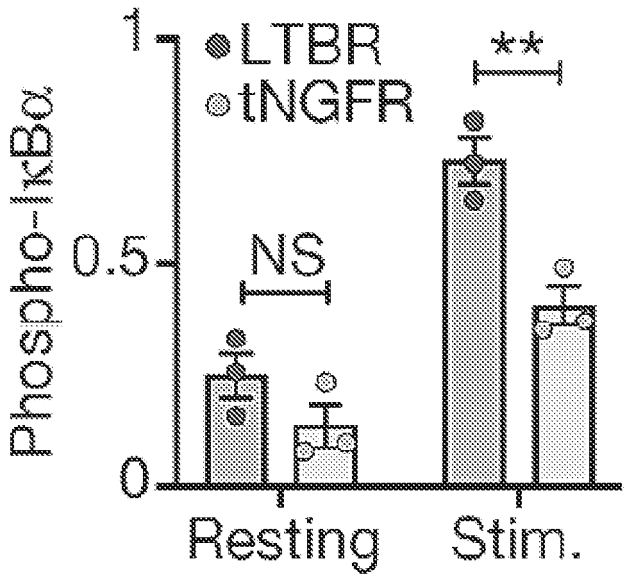
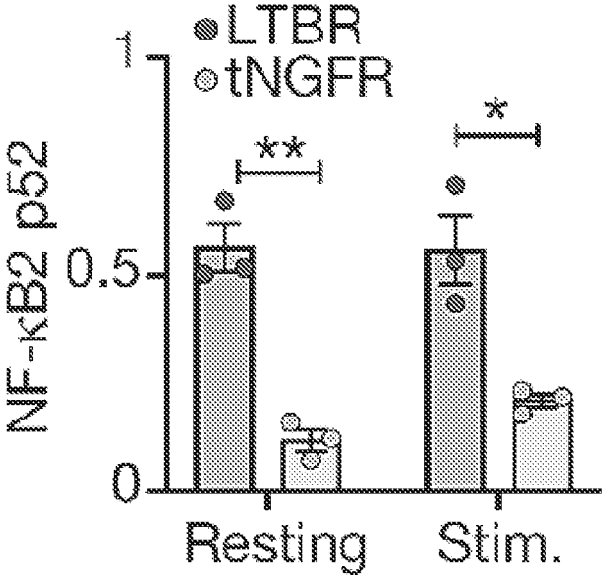


FIG. 4I



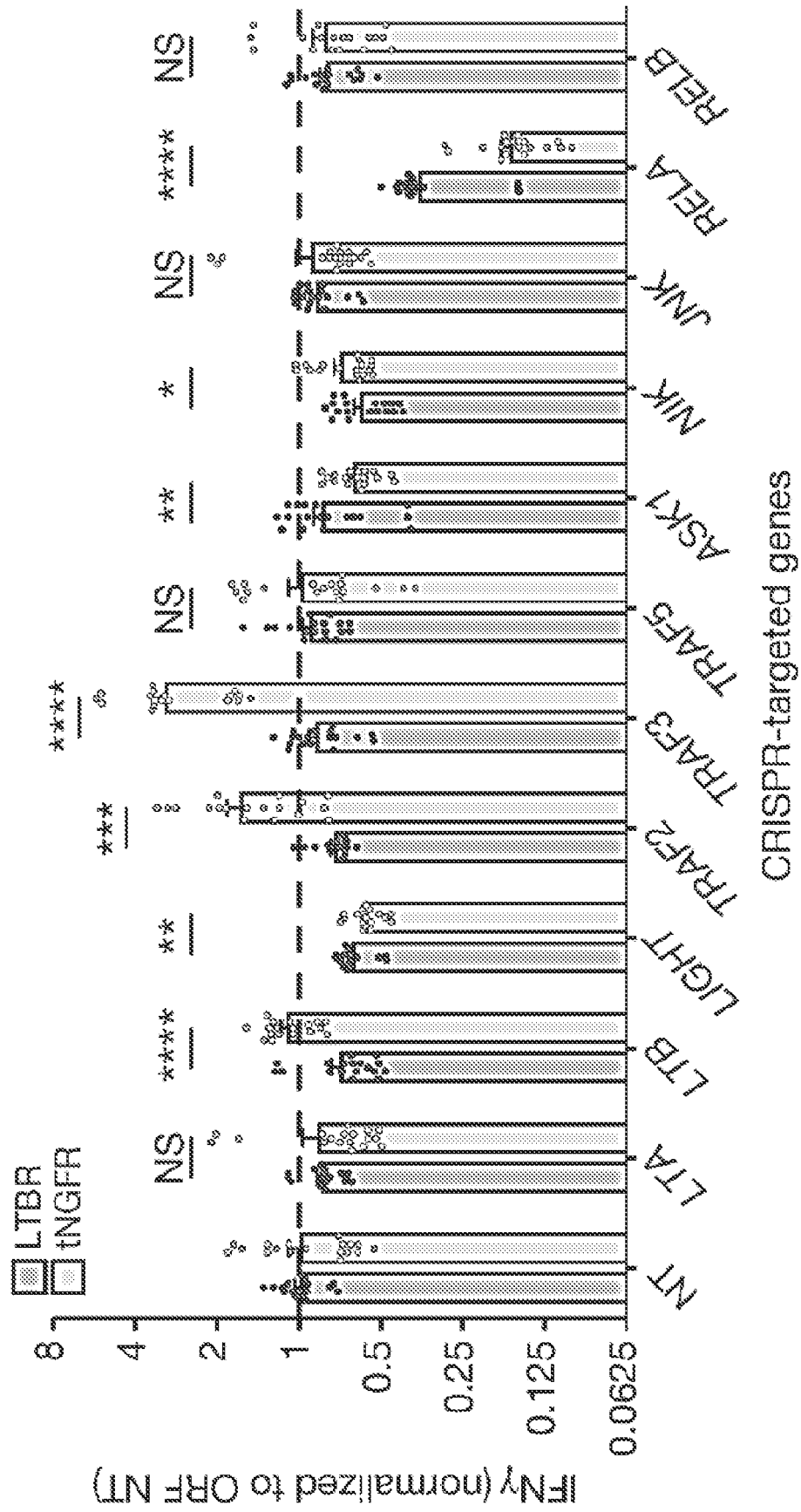

LTBR
tNGFR
IFNγ (normalized to ORF NT)
8
4
2
1
0.5
0.25
0.125
0.0625
NT
LTA
LTB
LIGHT
TRAF2
TRAF3
TRAF5
ASK1
Nik
JNK
RELA
RELB
NS
****
***
**
*
CRISPR-targeted genes

FIG. 4J

FIG. 4K

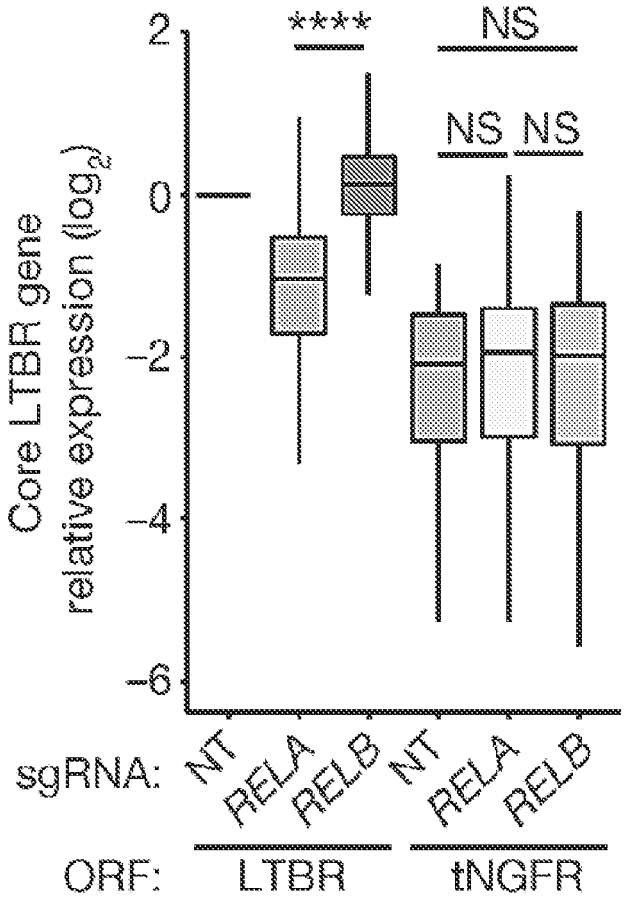

Core LTBR gene relative expression (log_2)
2
0
−2
−4
−6
****
NS
NS NS
sgRNA:
NT
RELA
RELB
NT
RELA
RELB
ORF:
LTBR
tNGFR

FIG. 5A

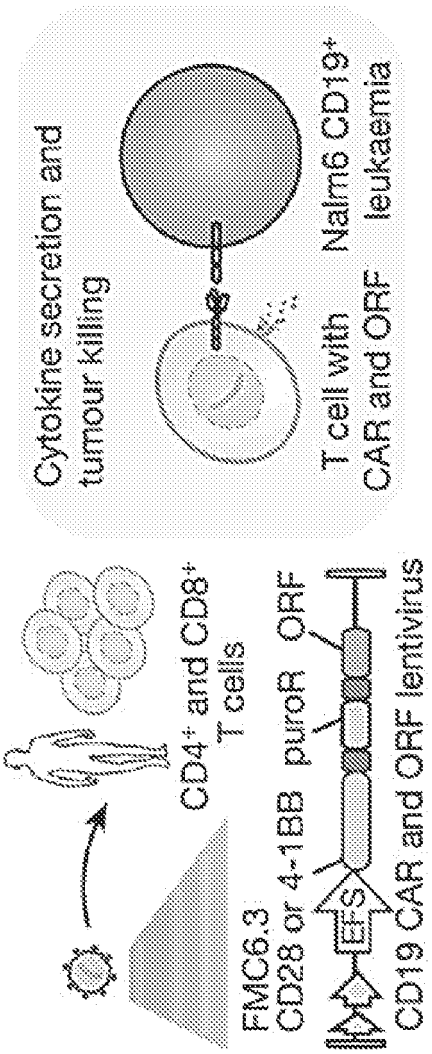


FIG. 5B

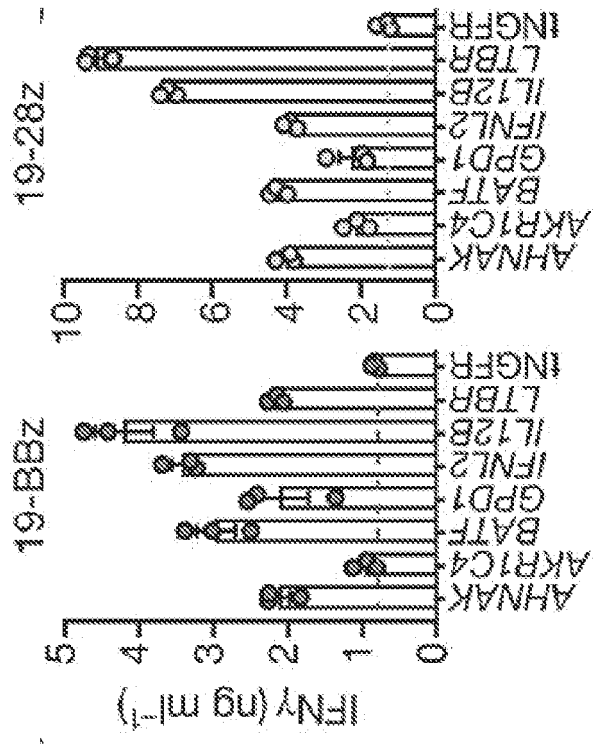
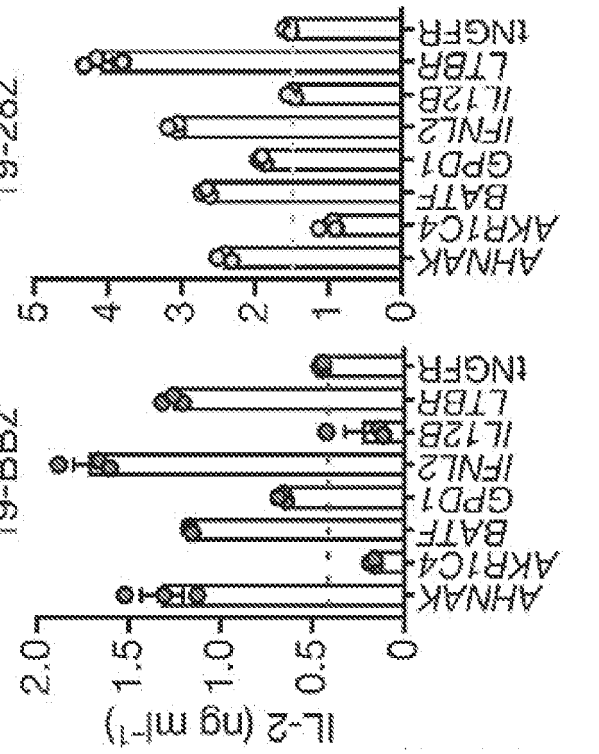


FIG. 5C



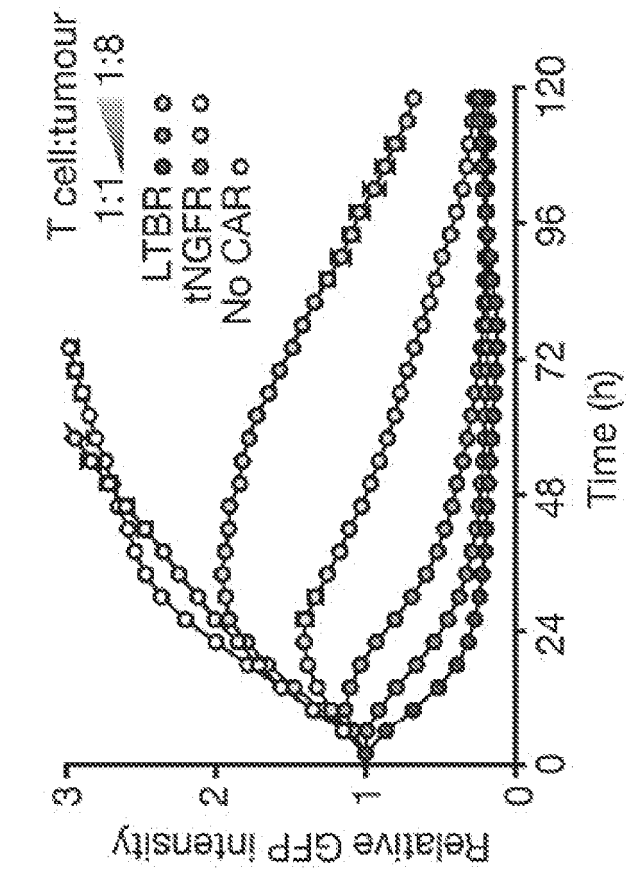


FIG. 5E

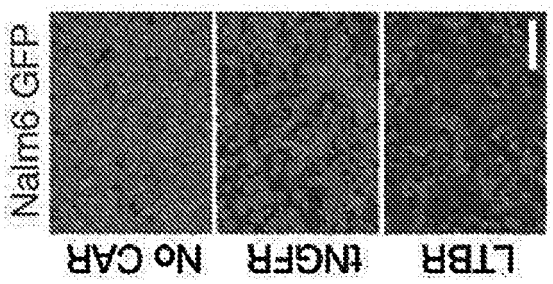


FIG. 5D

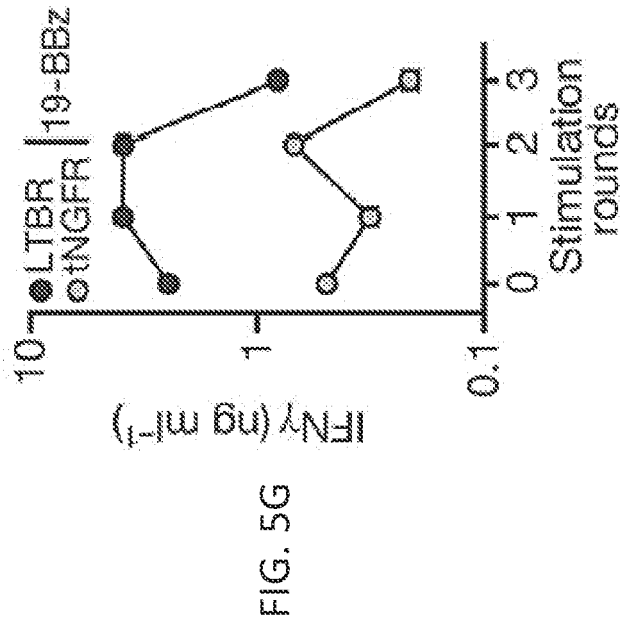


FIG. 5G

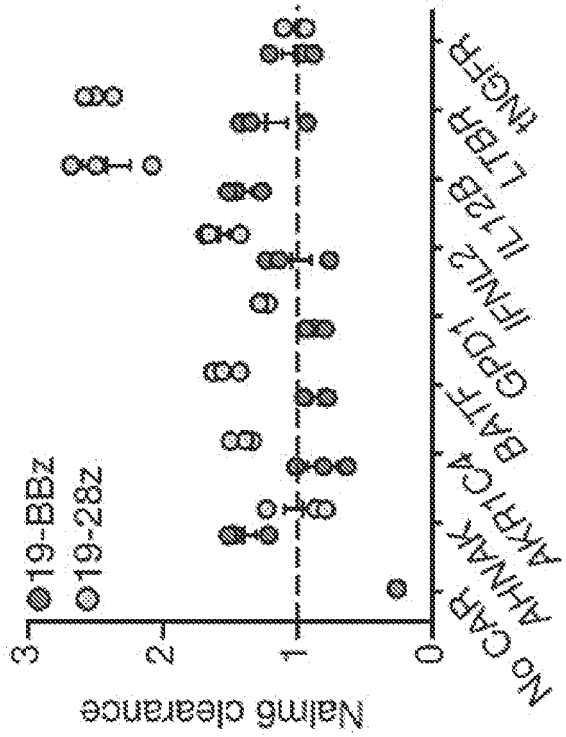


FIG. 5F

FIG. 5H

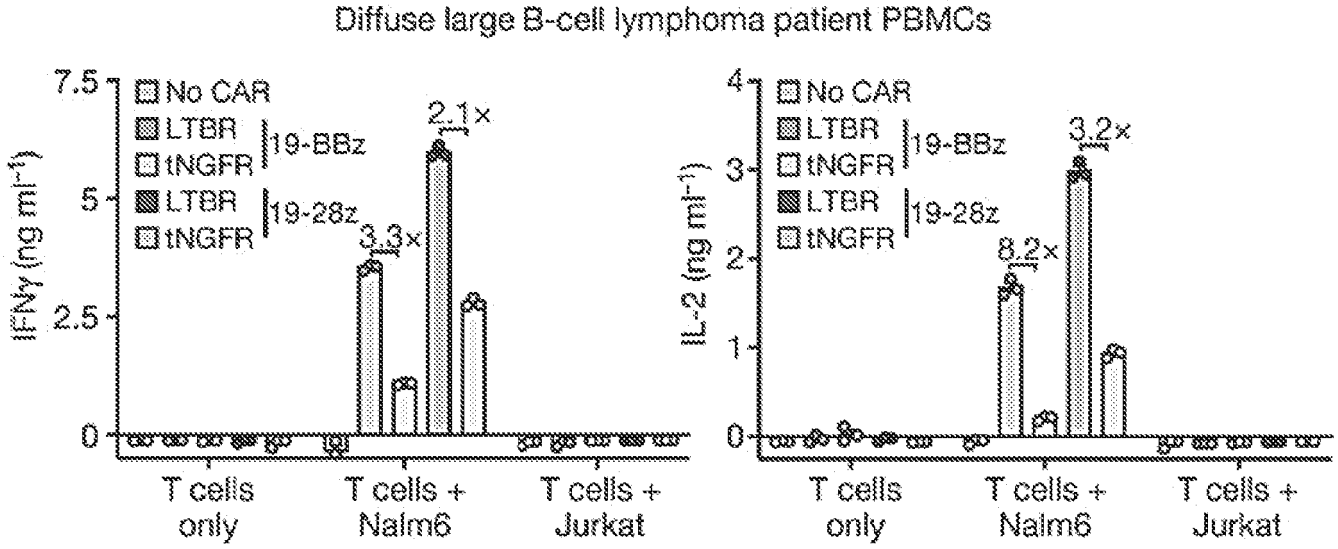
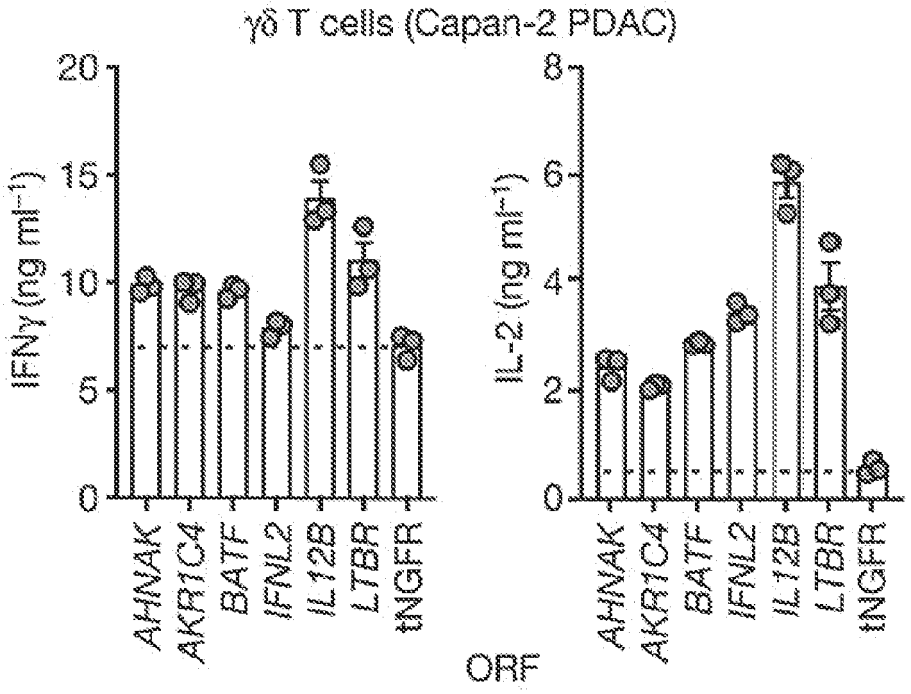

Diffuse large B-cell lymphoma patient PBMCs
IFNγ (ng ml-1)
IL-2 (ng ml-1)
No CAR
LTBR
tNGFR
19-BBz
LTBR
tNGFR
19-28z
3.3×
2.1×
8.2×
3.2×
T cells only
T cells + Nalm6
T cells + Jurkat

FIG. 5I


γδ T cells (Capan-2 PDAC)
IFNγ (ng ml-1)
IL-2 (ng ml-1)
AHNAK
AKR1C4
BATF
IFNL2
IL12B
LTBR
tNGFR
ORF

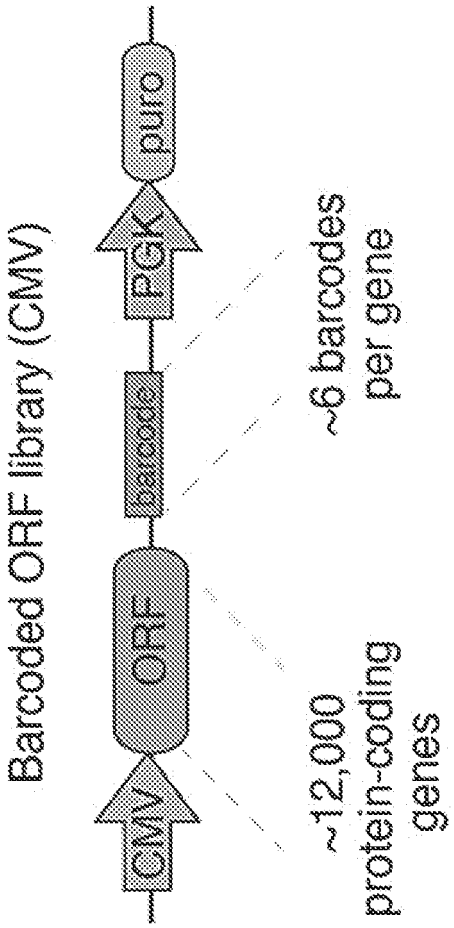


FIG. 6A

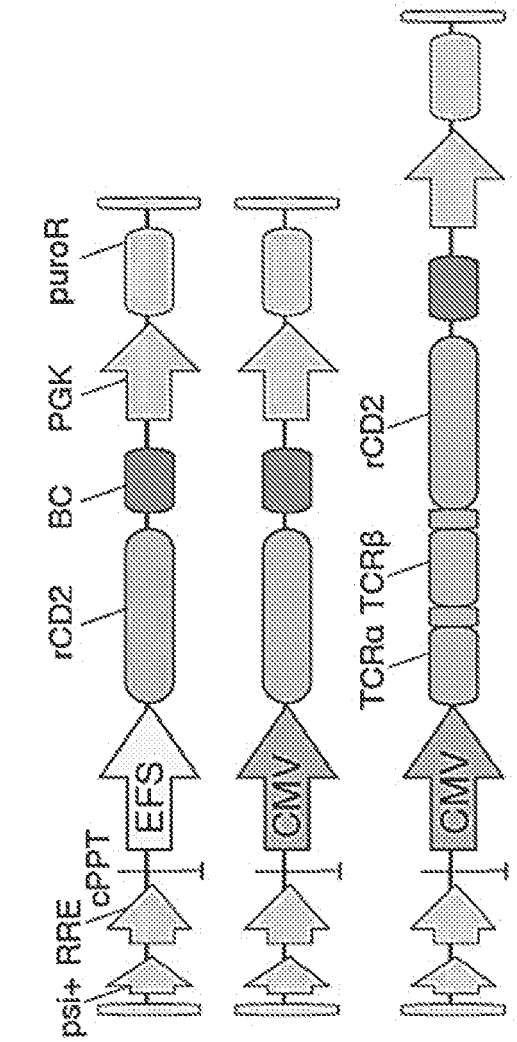


FIG. 6C

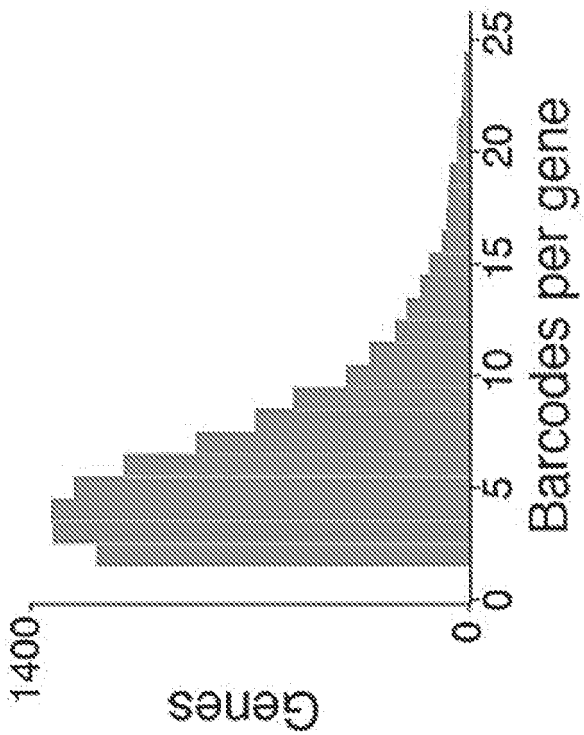


FIG. 6B

FIG. 6D

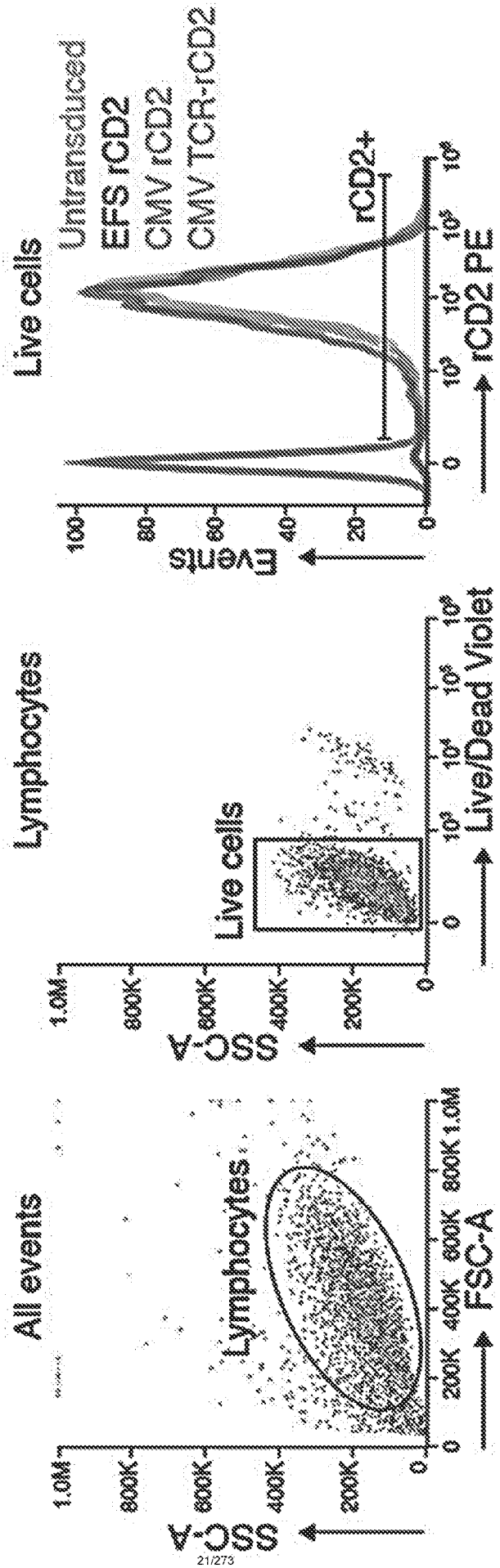

All events
Lymphocytes
SSC-A
FSC-A
Lymphocytes
Live cells
Live/Dead Violet
Untransduced
EFS rCD2
CMV rCD2
CMV TCR-rCD2
rCD2+
Events
rCD2 PE

FIG. 6E

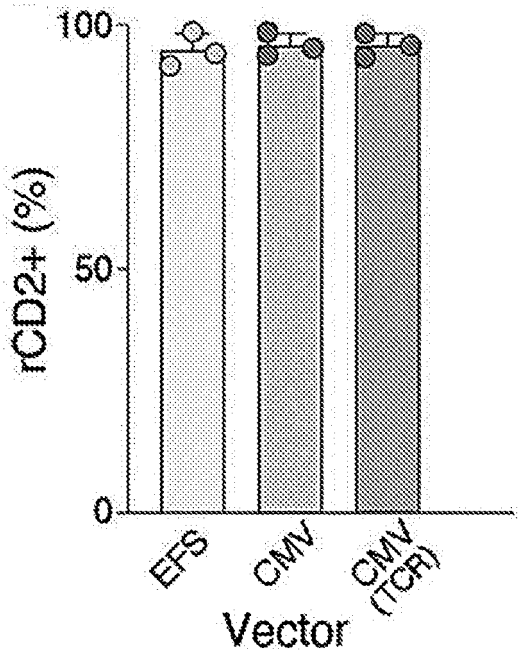


FIG. 6F

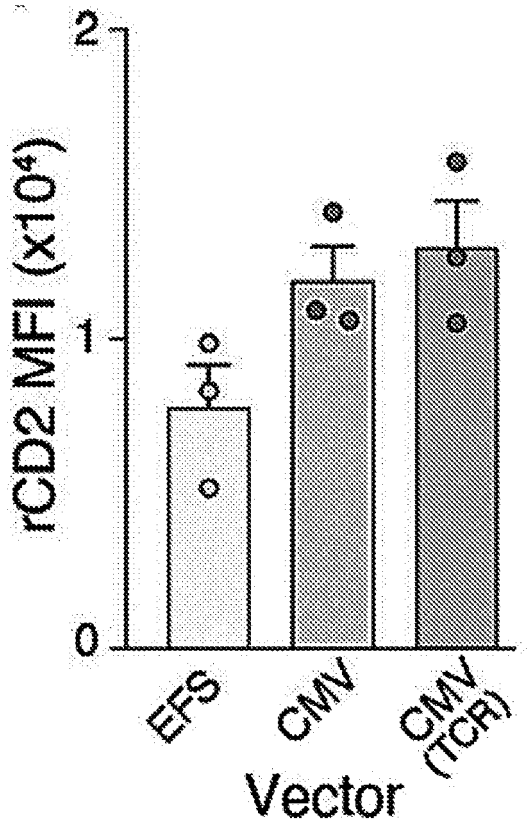


FIG. 6G

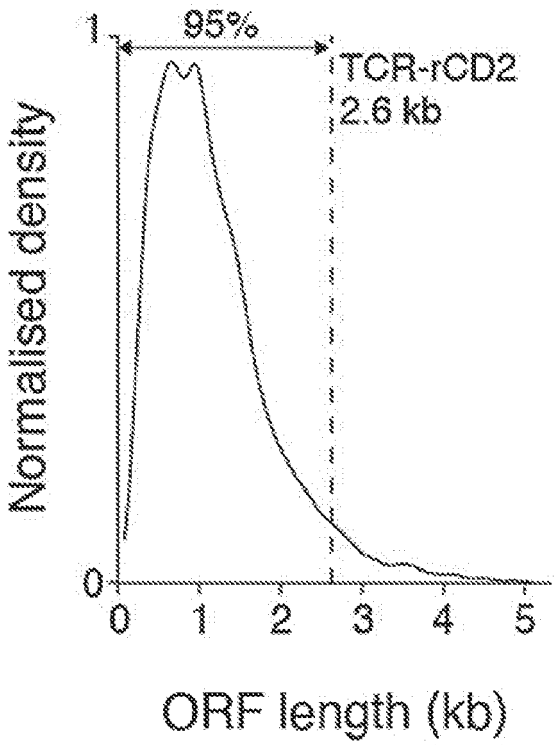


FIG. 6H

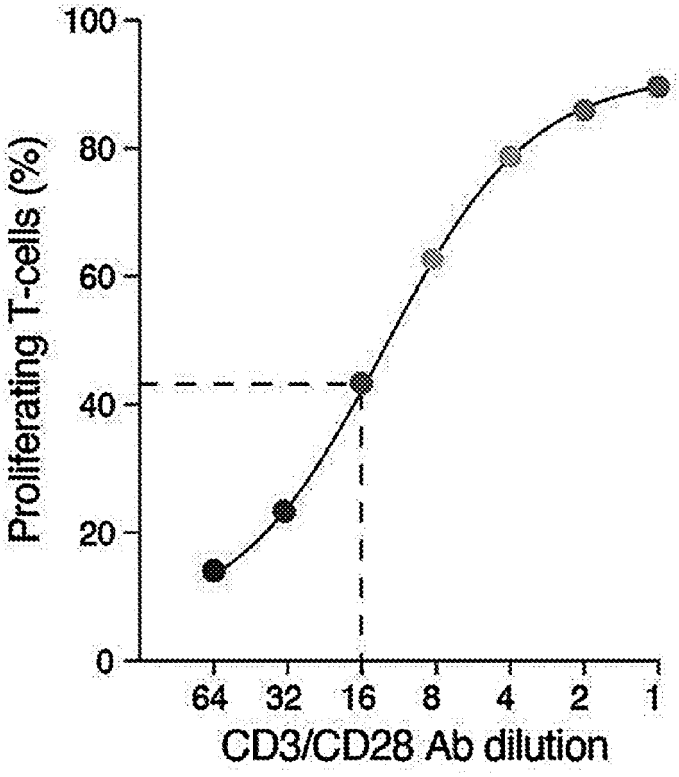

Proliferating T-cells (%)
100
80
60
40
20
0
64
32
16
8
4
2
1
CD3/CD28 Ab dilution

FIG. 6I

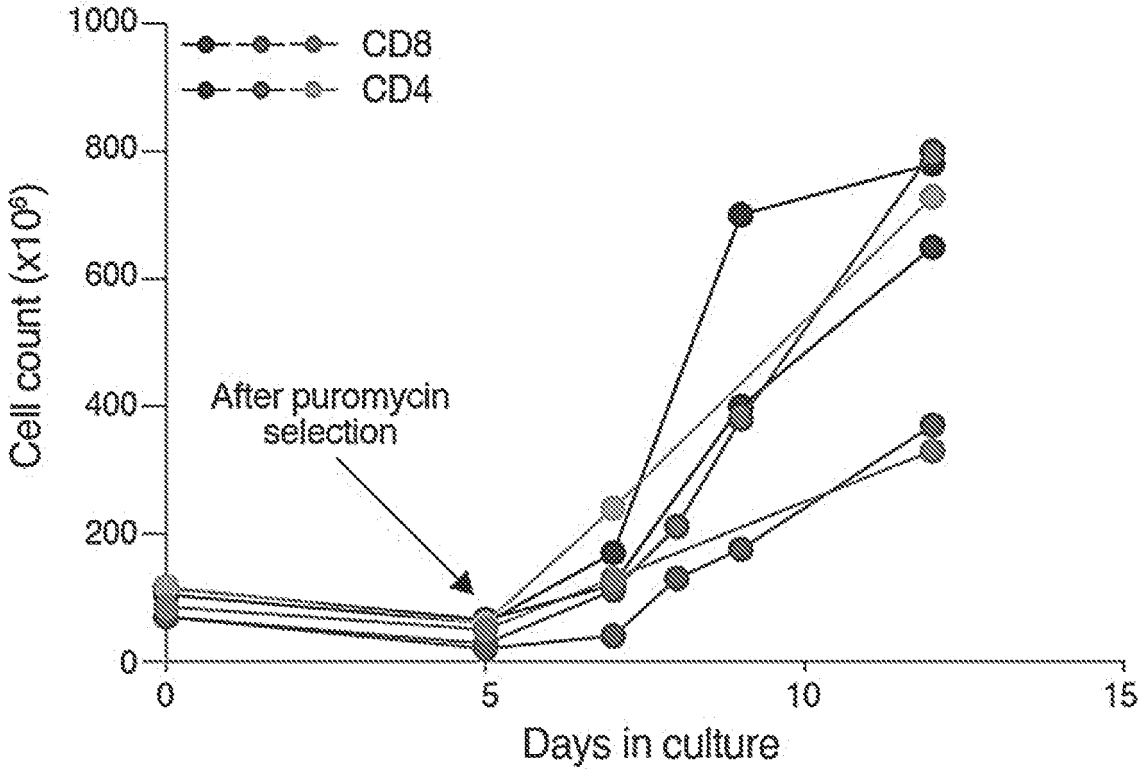

Cell count (x10⁶)
1000
800
600
400
200
0
CD8
CD4
After puromycin selection
0
5
10
15
Days in culture

FIG. 6J

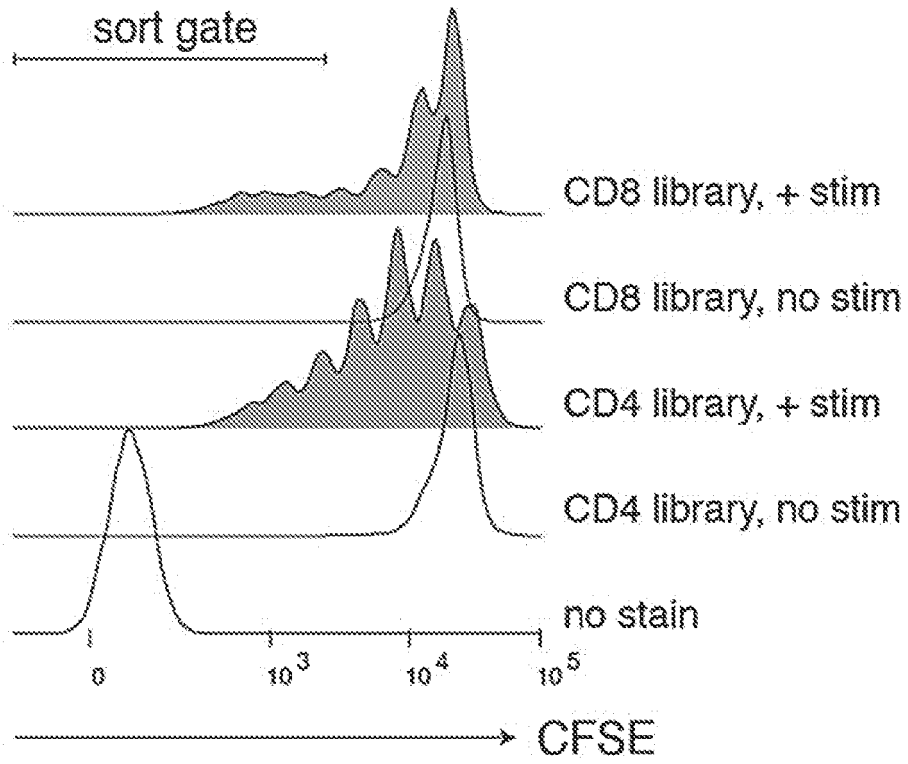

sort gate
CD8 library, + stim
CD8 library, no stim
CD4 library, + stim
CD4 library, no stim
no stain
0
10^3
10^4
10^5
CFSE

FIG. 6K

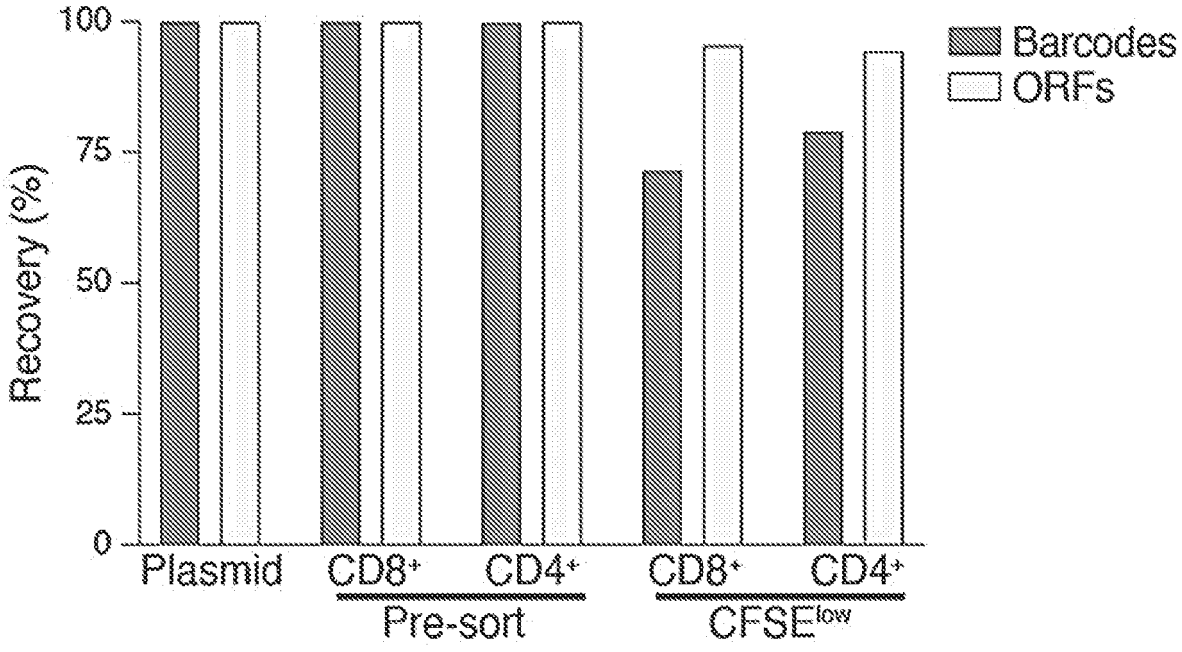

100
75
50
25
0
Recovery (%)
Barcodes
ORFs
Plasmid
CD8+
CD4+
CD8+
CD4+
Pre-sort
CFSE^low

FIG. 6L

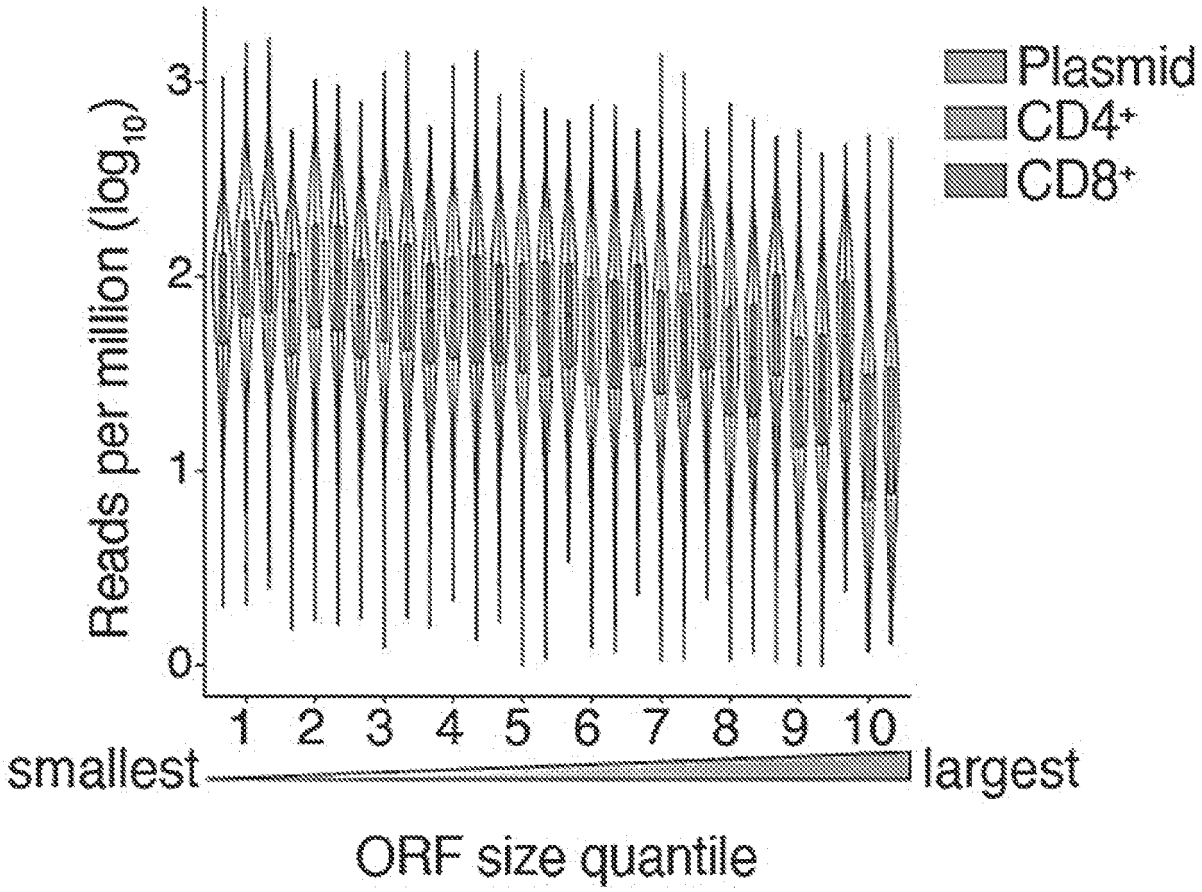

Plasmid
CD4+
CD8+
Reads per million (log10)
0
1
2
3
1 2 3 4 5 6 7 8 9 10
smallest
largest
ORF size quantile

FIG. 6M

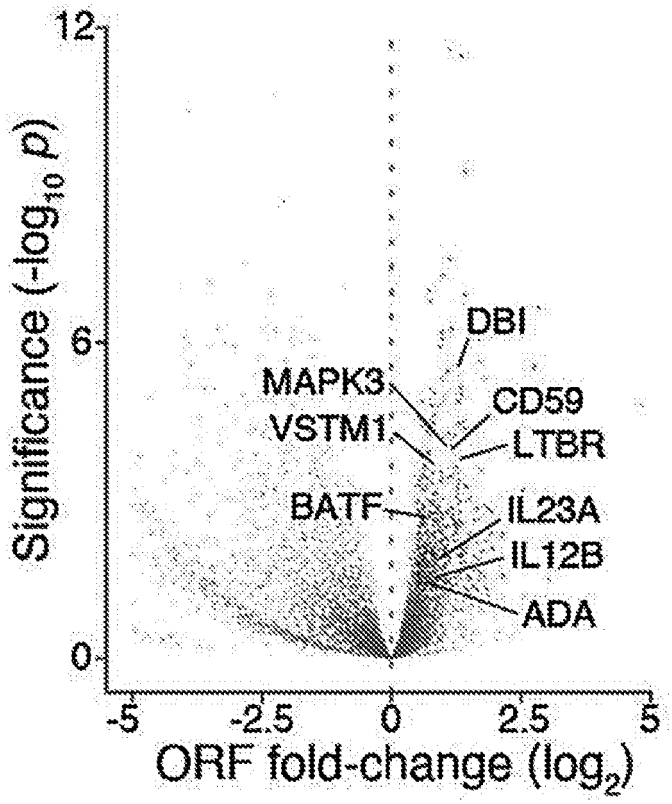

12
6
0
Significance (-log10 p)
DBI
MAPK3
CD59
VSTM1
LTBR
BATF
IL23A
IL12B
ADA
-5
-2.5
0
2.5
5
ORF fold-change (log2)

FIG. 6N

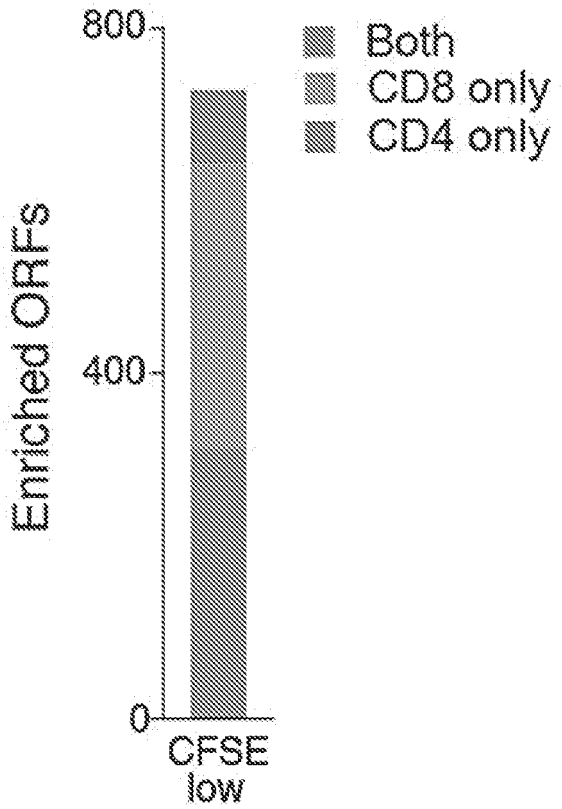

800
400
0
Enriched ORFs
Both
CD8 only
CD4 only
CFSE
low

FIG. 6O

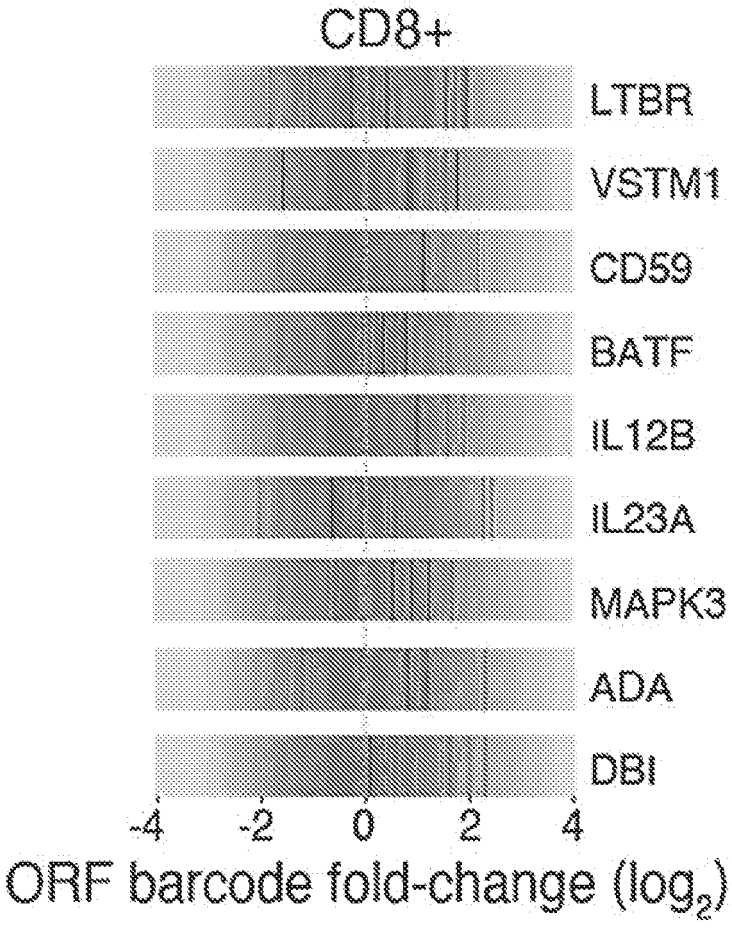

CD8+
LTBR
VSTM1
CD59
BATF
IL12B
IL23A
MAPK3
ADA
DBI
-4
-2
0
2
4
ORF barcode fold-change (log2)

FIG. 6Q

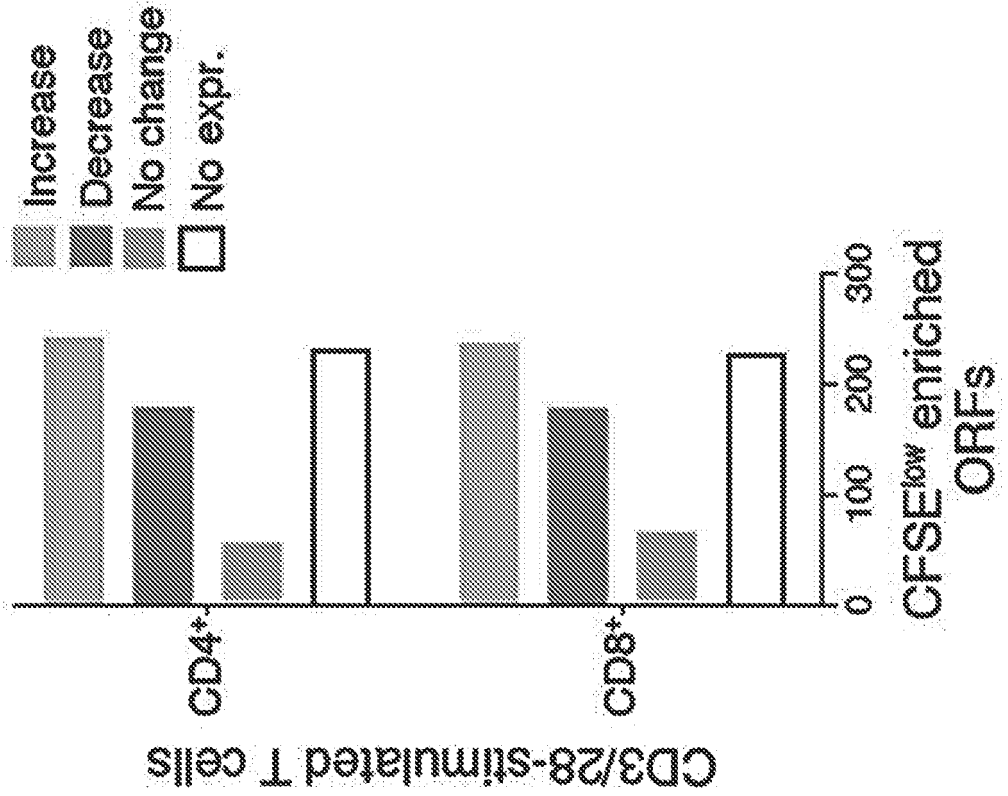

Increase
Decrease
No change
No expr.
CD4+
CD8+
CD3/28-stimulated T cells
0
100
200
300
CFSE^low enriched ORFs

FIG. 6P

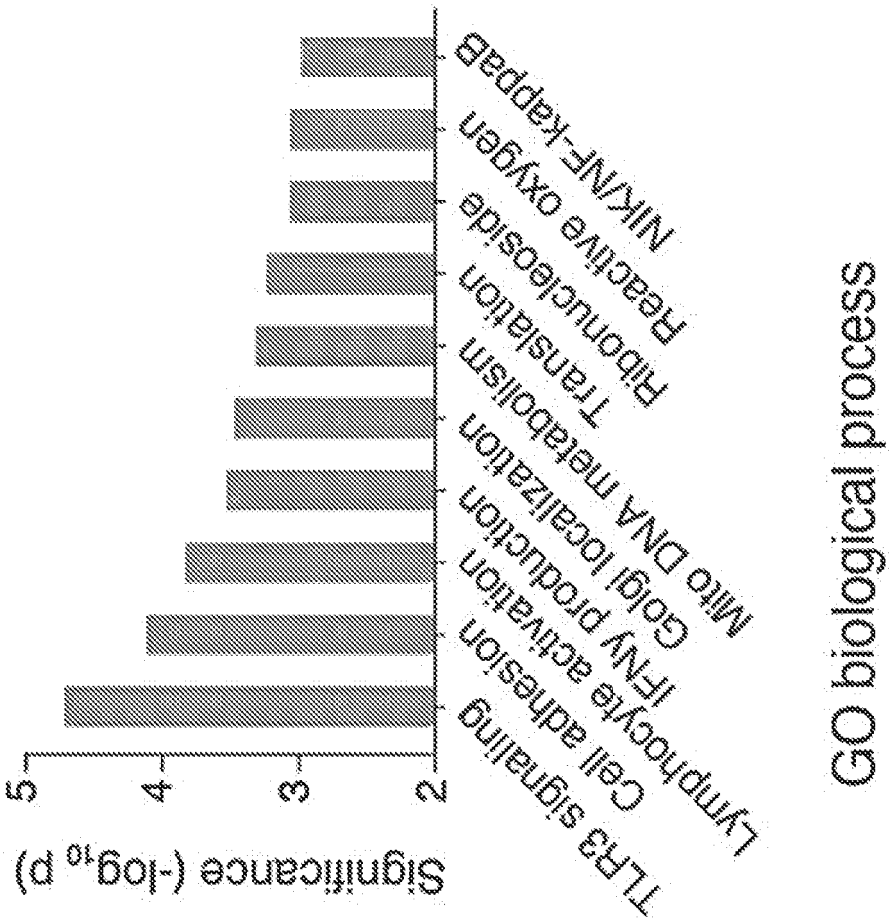

TLR3 signaling
Cell adhesion
Lymphocyte activation
IFNγ production
Golgi localization
Mito DNA metabolism
Translation
Ribonucleoside
Reactive oxygen
NIK/NF-kappaB
2
3
4
5
Significance (-log10 p)
GO biological process

FIG. 7A

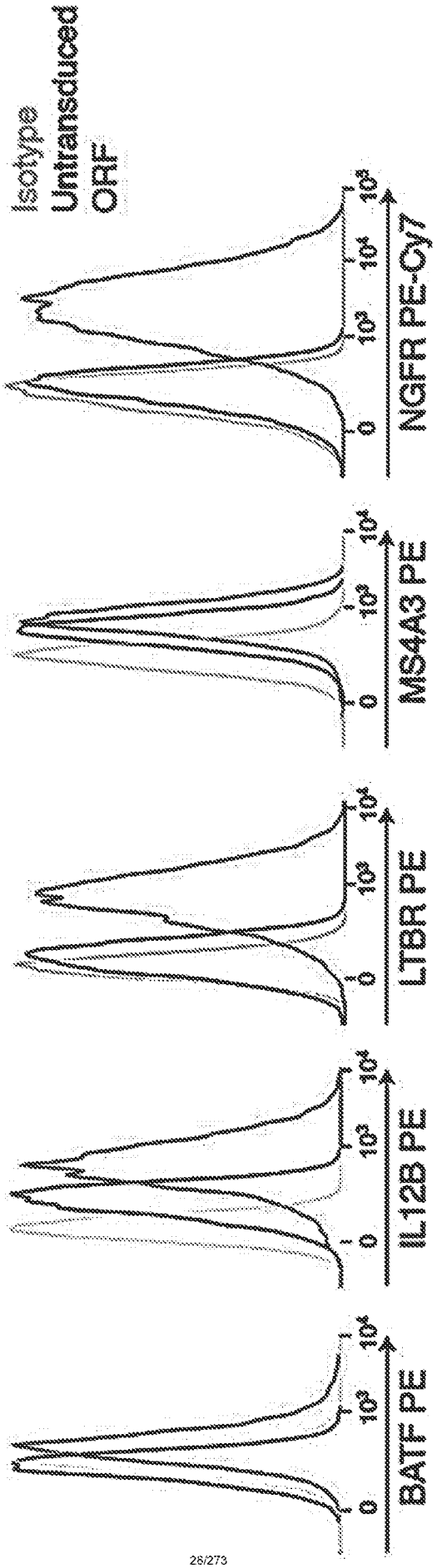

Isotype
Untransduced
ORF
0
10³
10⁴
10⁵
BATF PE
IL12B PE
LTBR PE
MS4A3 PE
NGFR PE-Cy7

FIG. 7B

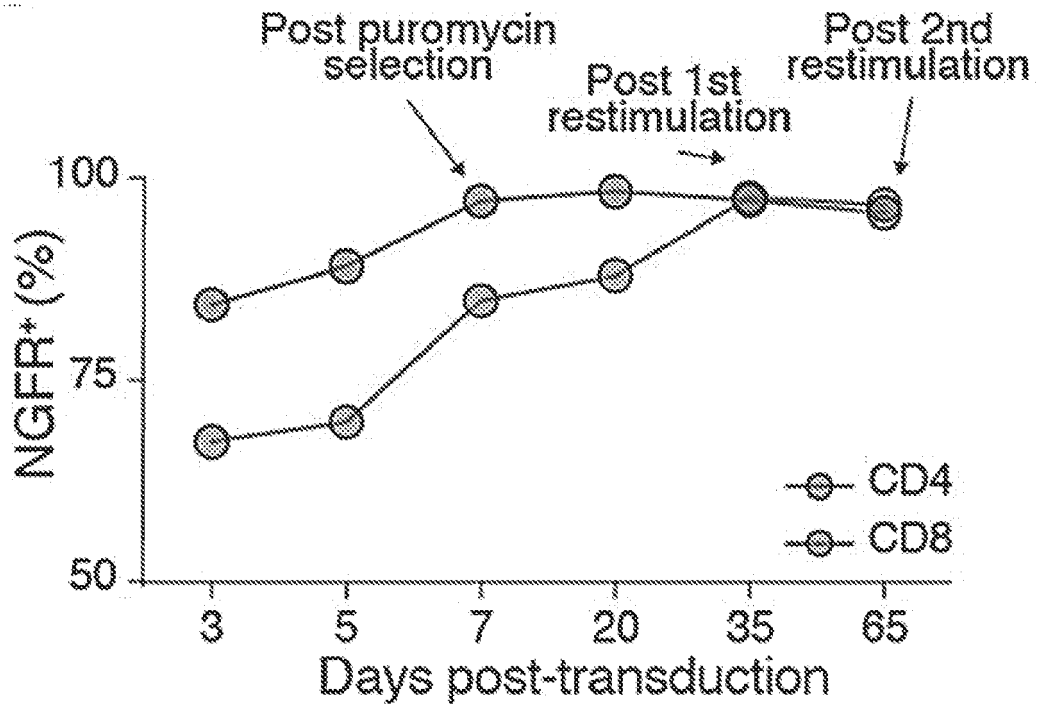
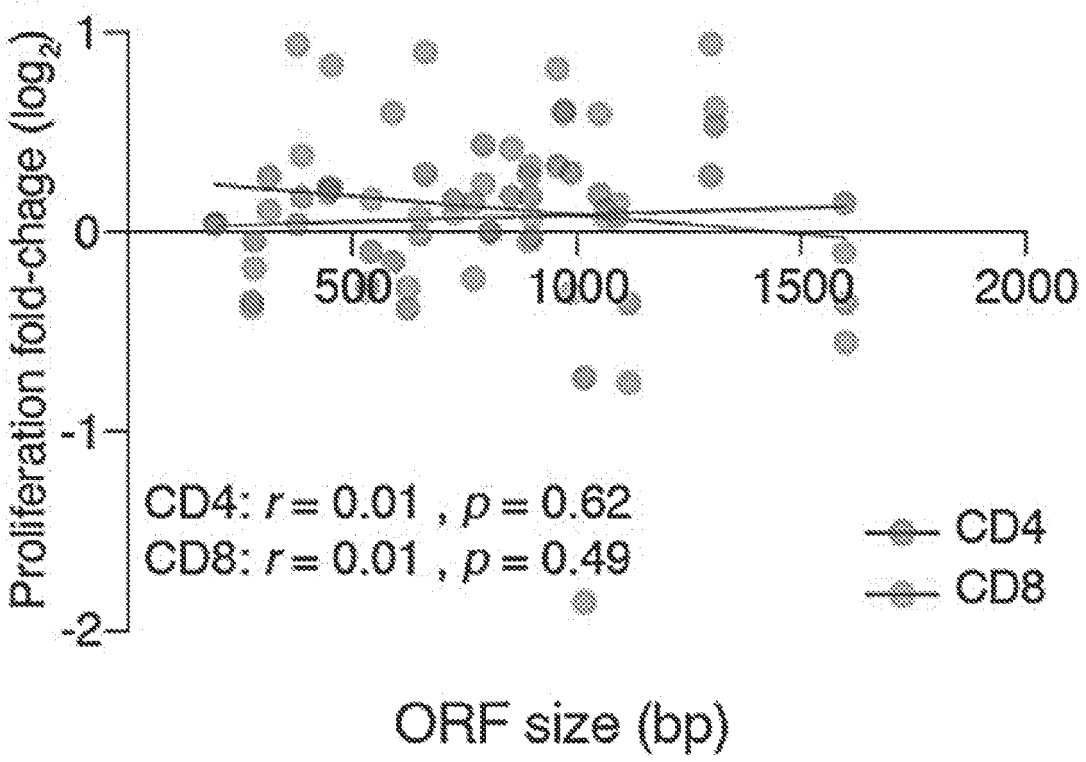

Post puromycin selection
Post 1st restimulation
Post 2nd restimulation
100
75
50
NGFR+ (%)
CD4
CD8
3
5
7
20
35
65
Days post-transduction

FIG. 7C


1
0
-1
-2
Proliferation fold-chage (log2)
500
1000
1500
2000
CD4: r = 0.01 , p = 0.62
CD8: r = 0.01 , p = 0.49
CD4
CD8
ORF size (bp)

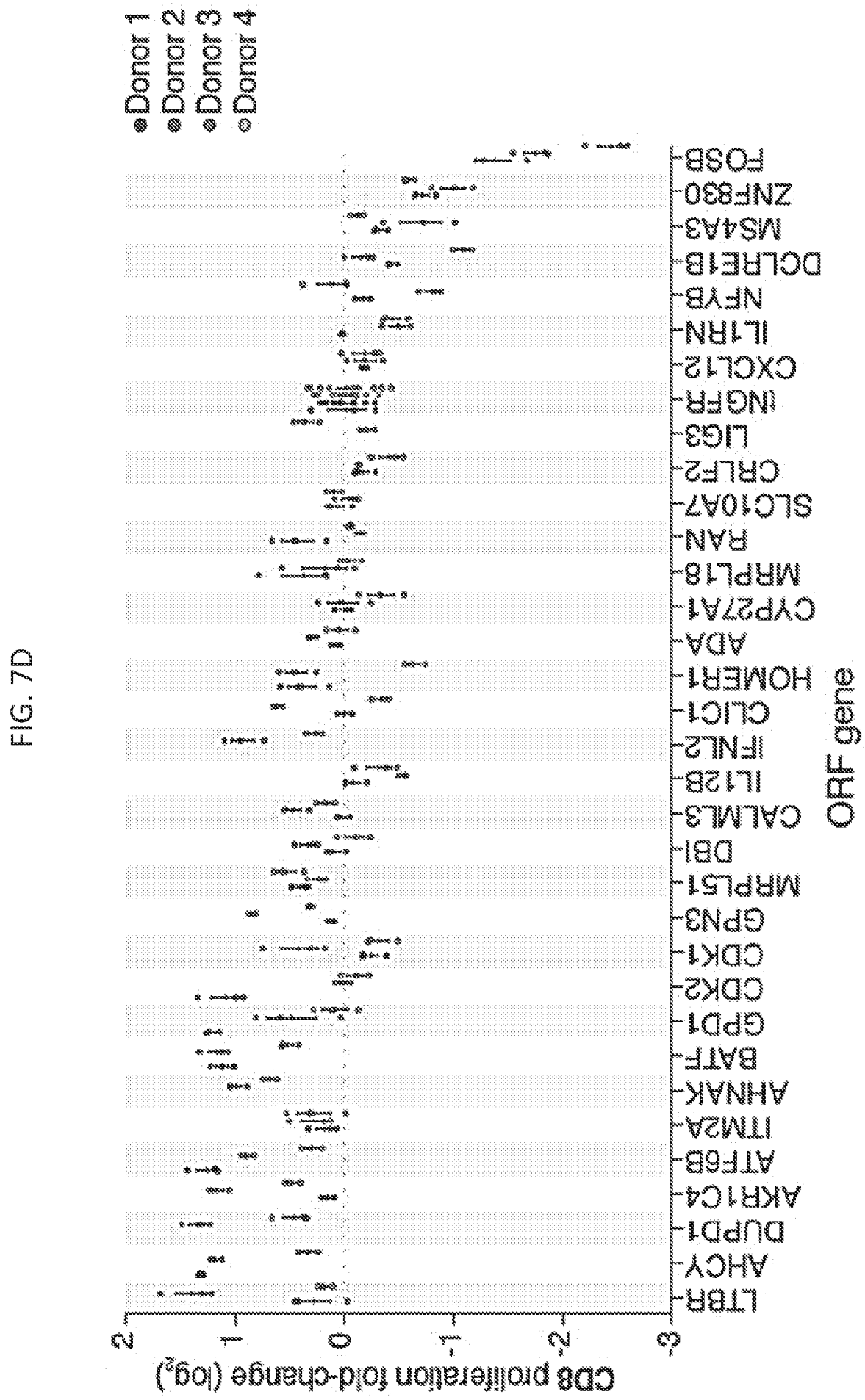

Donor 1
Donor 2
Donor 3
Donor 4
CD8 proliferation fold-change (log2)
2
1
0
-1
-2
-3
ORF gene
LTBR
AHCY
DUPD1
AKR1C4
ATF6B
ITM2A
AHNAK
BATF
GPD1
CDK2
CDK1
GPN3
MRPL51
DBI
CALML3
IL12B
IFNL2
CLIC1
HOMER1
ADA
CYP27A1
MRPL18
RAN
SLC10A7
CRLF2
LIG3
ING FR
CXCL12
IL1RN
NFYB
DCLRE1B
MS4A3
ZNF830
FOSB

FIG. 7D

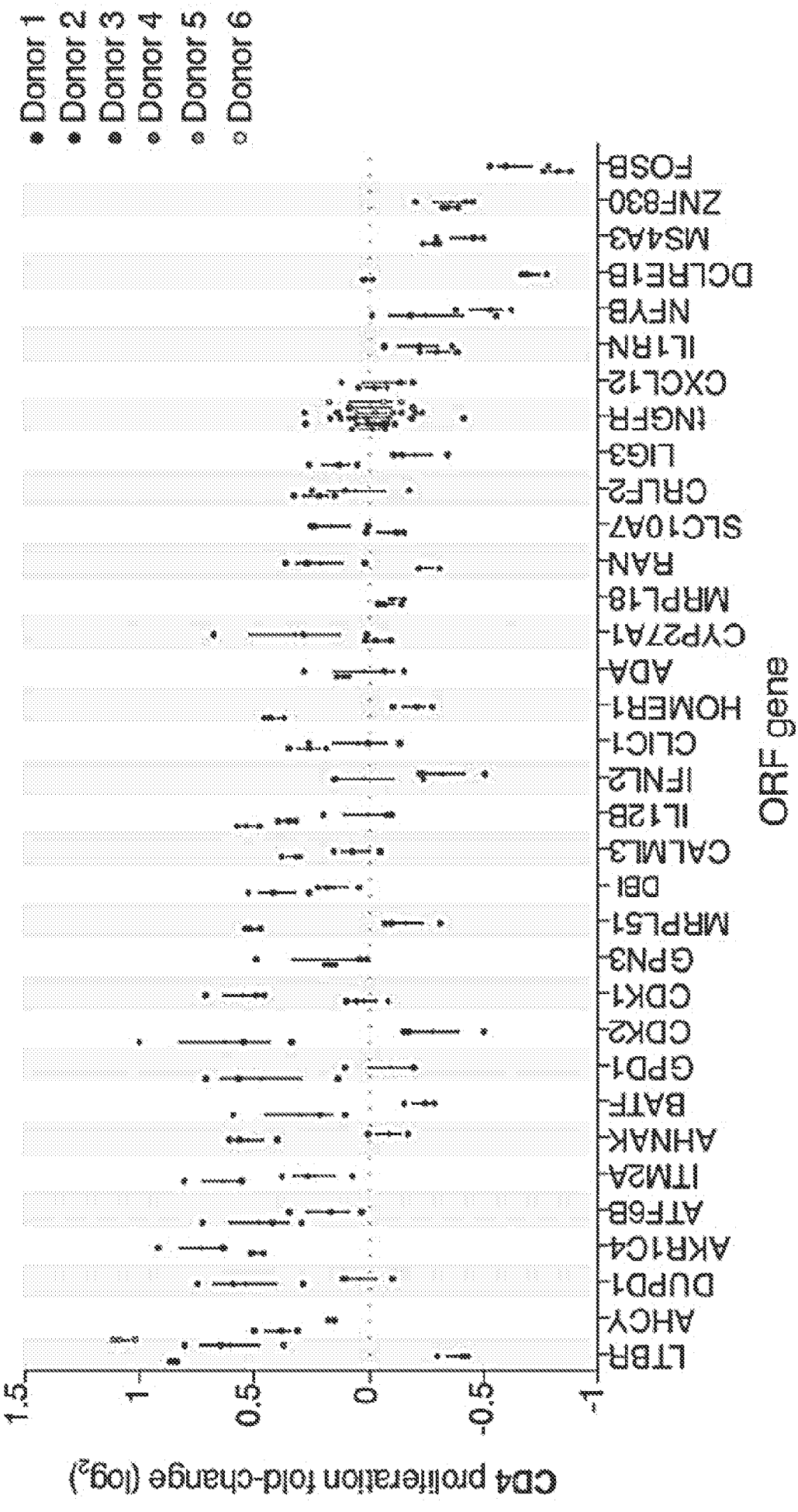

Donor 1
Donor 2
Donor 3
Donor 4
Donor 5
Donor 6
CD4 proliferation fold-change (log2)
1.5
1
0.5
0
-0.5
-1
ORF gene
LTBR
AHCY
DUPD1
AKR1C4
ATF6B
ITM2A
AHNAK
BATF
GPD1
CDK2
CDK1
GFN3
MRPL51
DBI
CALML3
IL12B
IFNL2
CLIC1
HOMER1
ADA
CYP27A1
MRPL18
RAN
SLC10A7
CRLF2
LIG3
INGFR
CXCL12
IL1RN
NFYB
DCLRE1B
MS4A3
ZNF830
FOSB

FIG. 7E

FIG. 7F

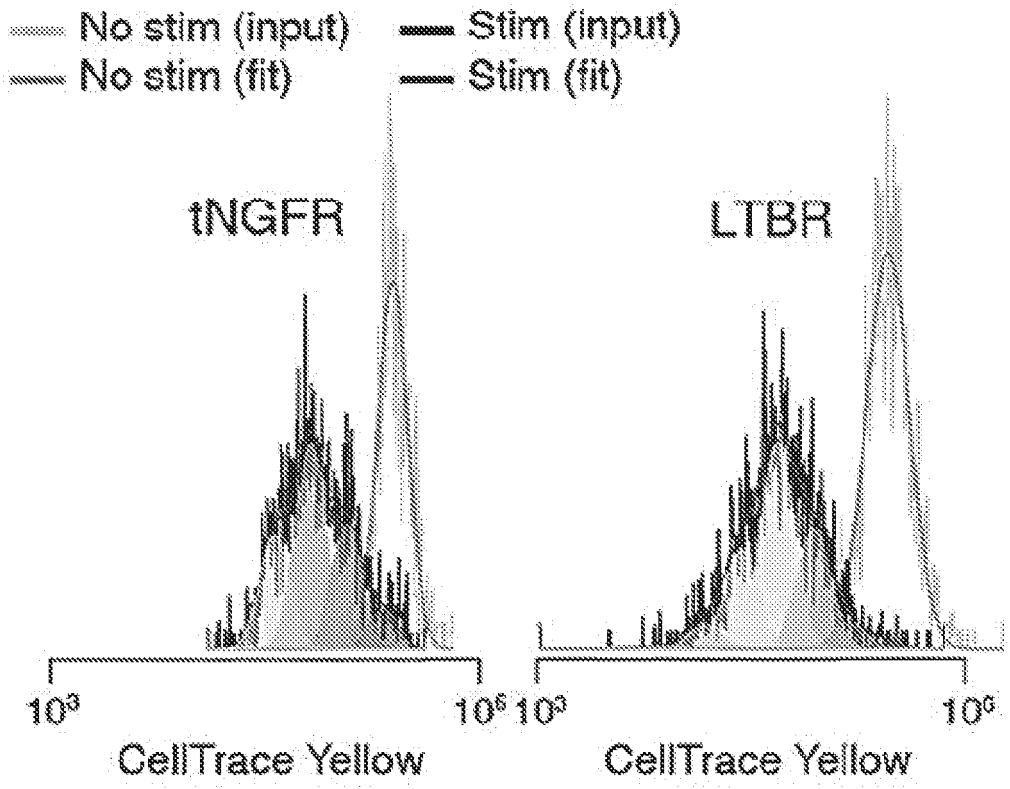
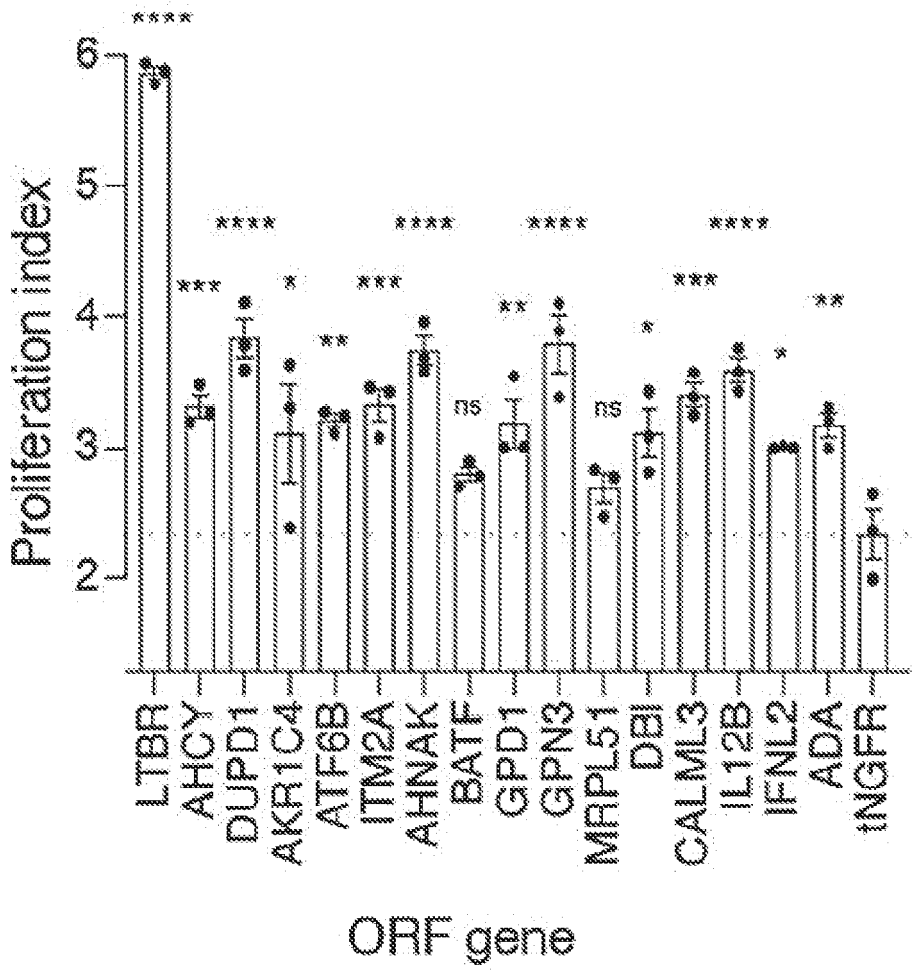

No stim (input)
No stim (fit)
Stim (input)
Stim (fit)
tNGFR
LTBR
10^3
10^6
CellTrace Yellow
10^3
10^6
CellTrace Yellow

FIG. 7G


Proliferation index
2
3
4
5
6
LTBR
AHCY
DUPD1
AKR1C4
ATF6B
ITM2A
AHNAK
BATF
GPD1
GPN3
MRPL51
DBI
CALML3
IL12B
IFNL2
ADA
tNGFR
ORF gene

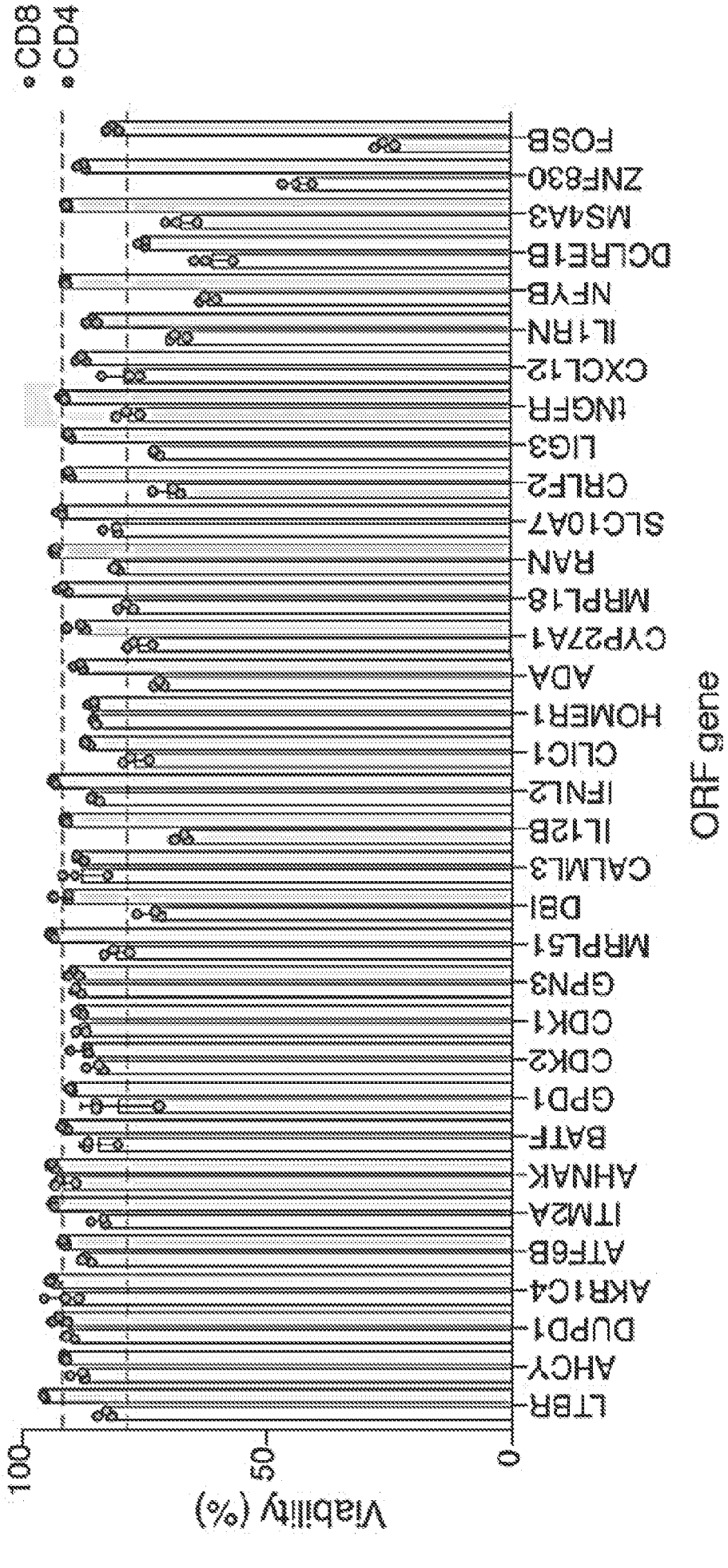

CD8
CD4
Viability (%)
100
50
0
ORF gene
LTBR
AHCY
DUPD1
AKR1C4
ATF6B
ITM2A
AHNAK
BATF
GPD1
CDK2
CDK1
GPN3
MRPL51
DBI
CALML3
IL12B
IFNL2
CLIC1
HOMER1
ADA
CYP27A1
MRPL18
RAN
SLC10A7
CRLF2
LIG3
tNGFR
CXCL12
IL1RN
NFYB
DCLRE1B
MS4A3
ZNF830
FOSB

FIG. 7H

FIG. 7I

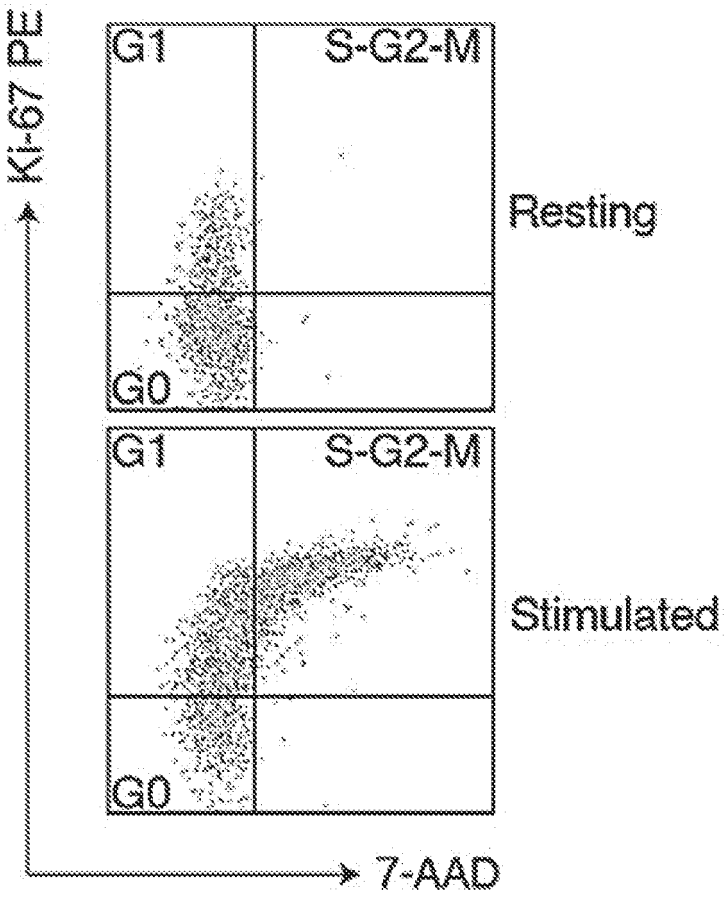

Ki-67 PE
G1
S-G2-M
Resting
G0
G1
S-G2-M
Stimulated
G0
7-AAD

FIG. 7J

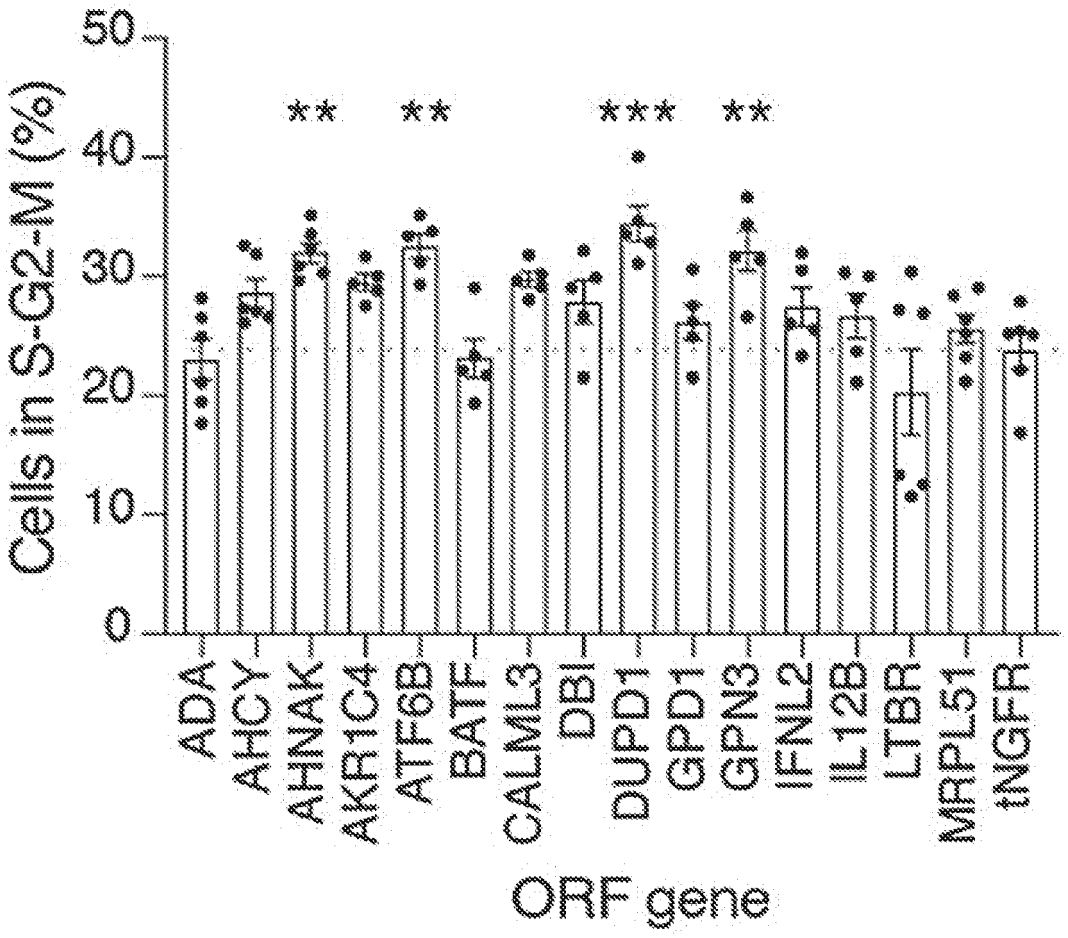

Cells in S-G2-M (%)
50
40
30
20
10
0
**
**
***
**
ADA
AHCY
AHNAK
AKR1C4
ATF6B
BATF
CALML3
DBI
DUPD1
GPD1
GPN3
IFNL2
IL12B
LTBR
MRPL51
tNGFR
ORF gene

FIG. 8A

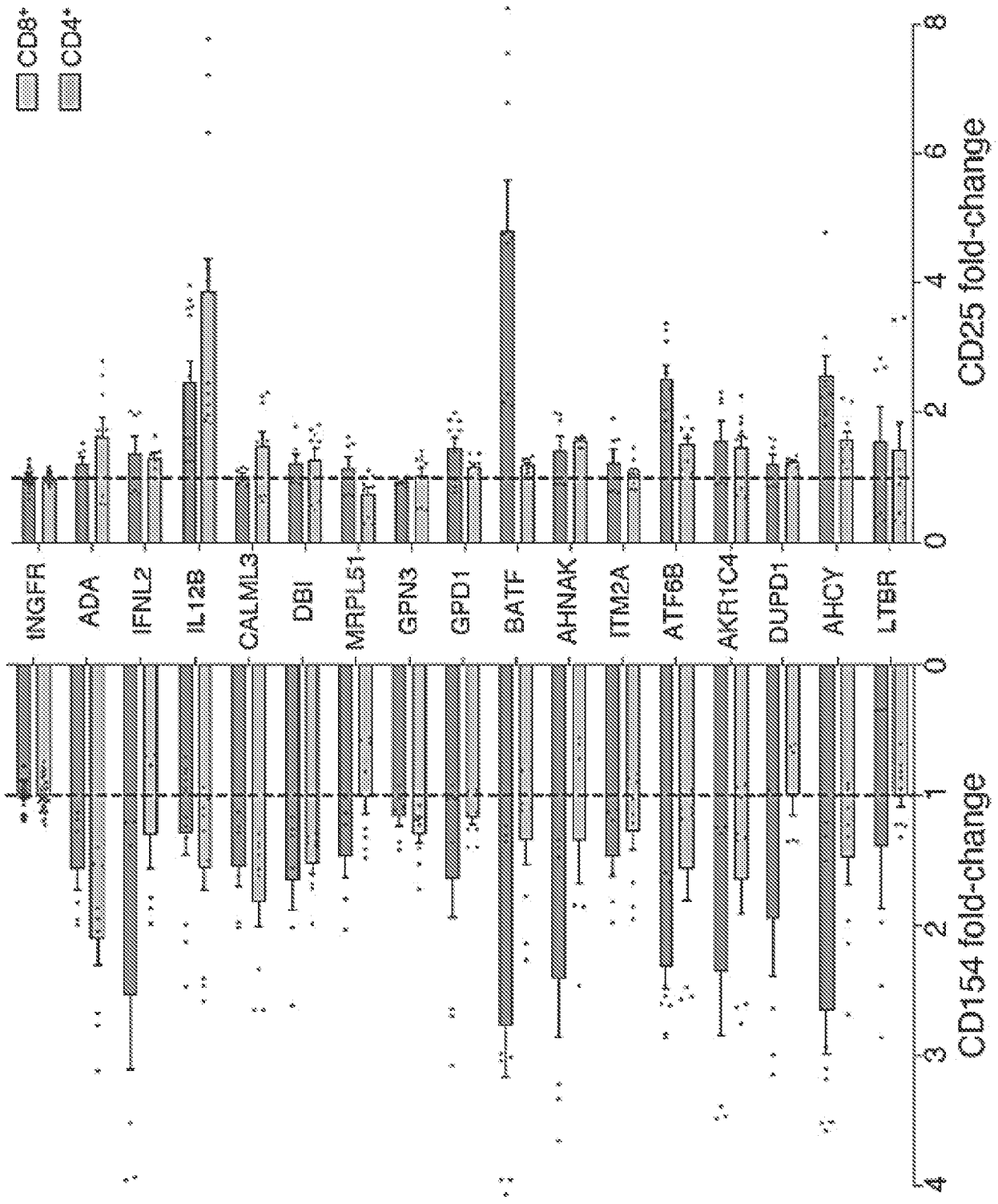

CD8+
CD4+
INGFR
ADA
IFNL2
IL12B
CALML3
DBI
MRPL51
GPN3
GPD1
BATF
AHNAK
ITM2A
ATF6B
AKR1C4
DUPD1
AHCY
LTBR
CD25 fold-change
CD154 fold-change
0
2
4
6
8
0
1
2
3
4

FIG. 8B

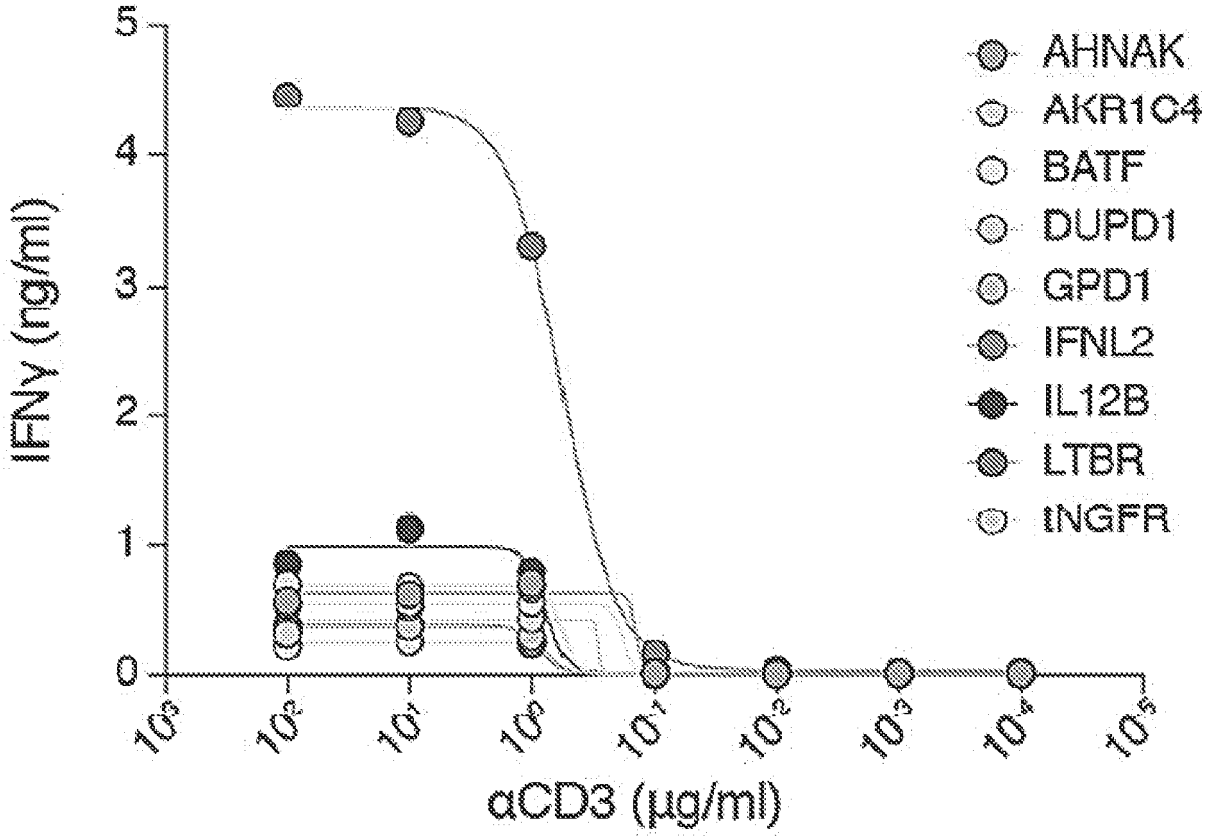
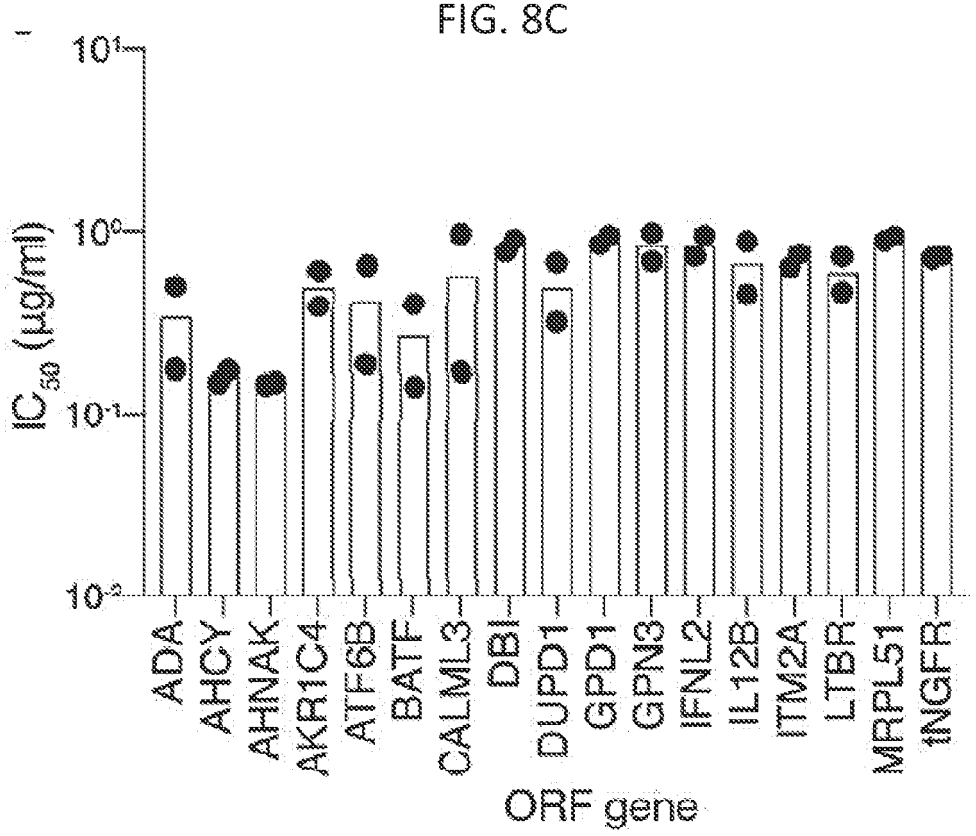

IFNγ (ng/ml)
5
4
3
2
1
0
10^{-3}
10^{-2}
10^{-1}
10^{0}
10^{1}
10^{2}
10^{3}
10^{4}
10^{5}
αCD3 (μg/ml)
AHNAK
AKR1C4
BATF
DUPD1
GPD1
IFNL2
IL12B
LTBR
INGFR

FIG. 8C


IC_{50} (μg/ml)
10^{1}
10^{0}
10^{-1}
10^{-2}
ADA
AHCY
AHNAK
AKR1C4
ATF6B
BATF
CALML3
DBI
DUPD1
GPD1
GPN3
IFNL2
IL12B
ITM2A
LTBR
MRPL51
tNGFR
ORF gene

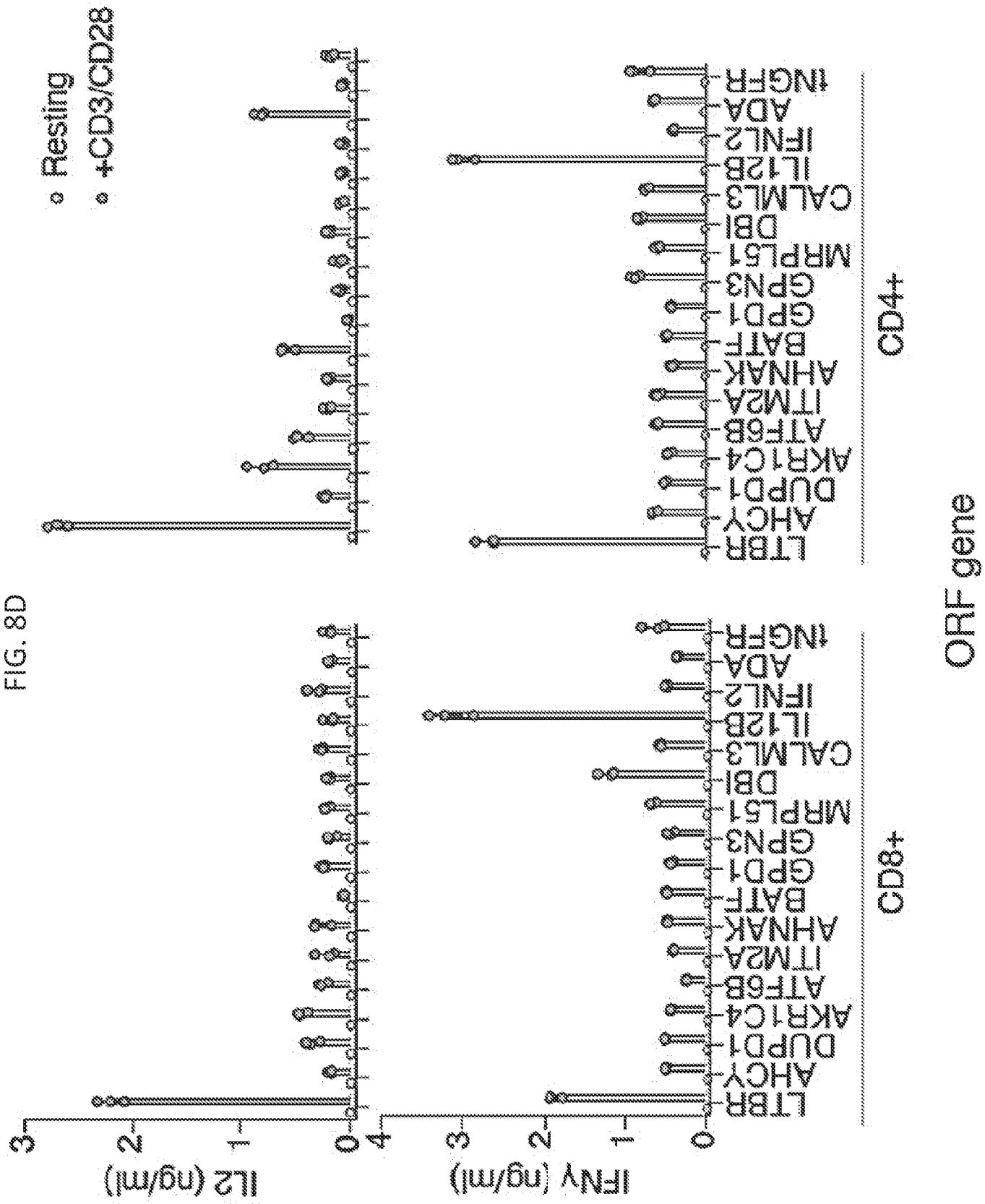

Resting
+CD3/CD28
IL2 (ng/ml)
IFNγ (ng/ml)
CD8+
CD4+
LTBR
AHCY
DUPD1
AKR1C4
ATF6B
ITM2A
AHNAK
BATF
GPD1
GPN3
MRPL51
DBI
CALML3
IL12B
IFNL2
ADA
tNGFR
ORF gene

FIG. 8D

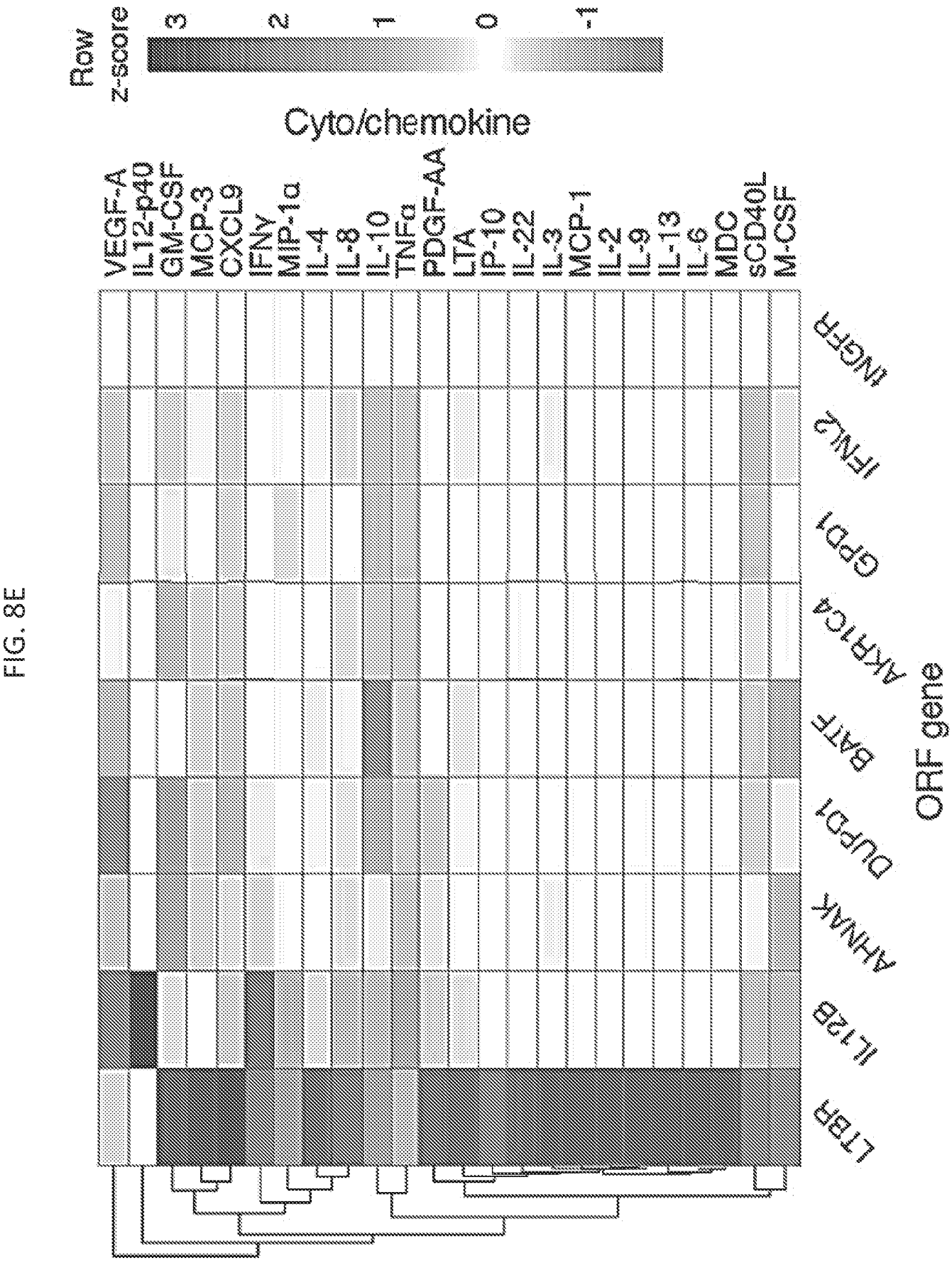

Row z-score
3
2
1
0
-1
Cyto/chemokine
VEGF-A
IL12-p40
GM-CSF
MCP-3
CXCL9
IFNγ
MIP-1α
IL-4
IL-8
IL-10
TNFα
PDGF-AA
LTA
IP-10
IL-22
IL-3
MCP-1
IL-2
IL-9
IL-13
IL-6
MDC
sCD40L
M-CSF
LTBR
IL12B
AHNAK
DUPD1
BATF
AKR1C4
GPD1
IFNL2
NGFR
ORF gene

FIG. 8E

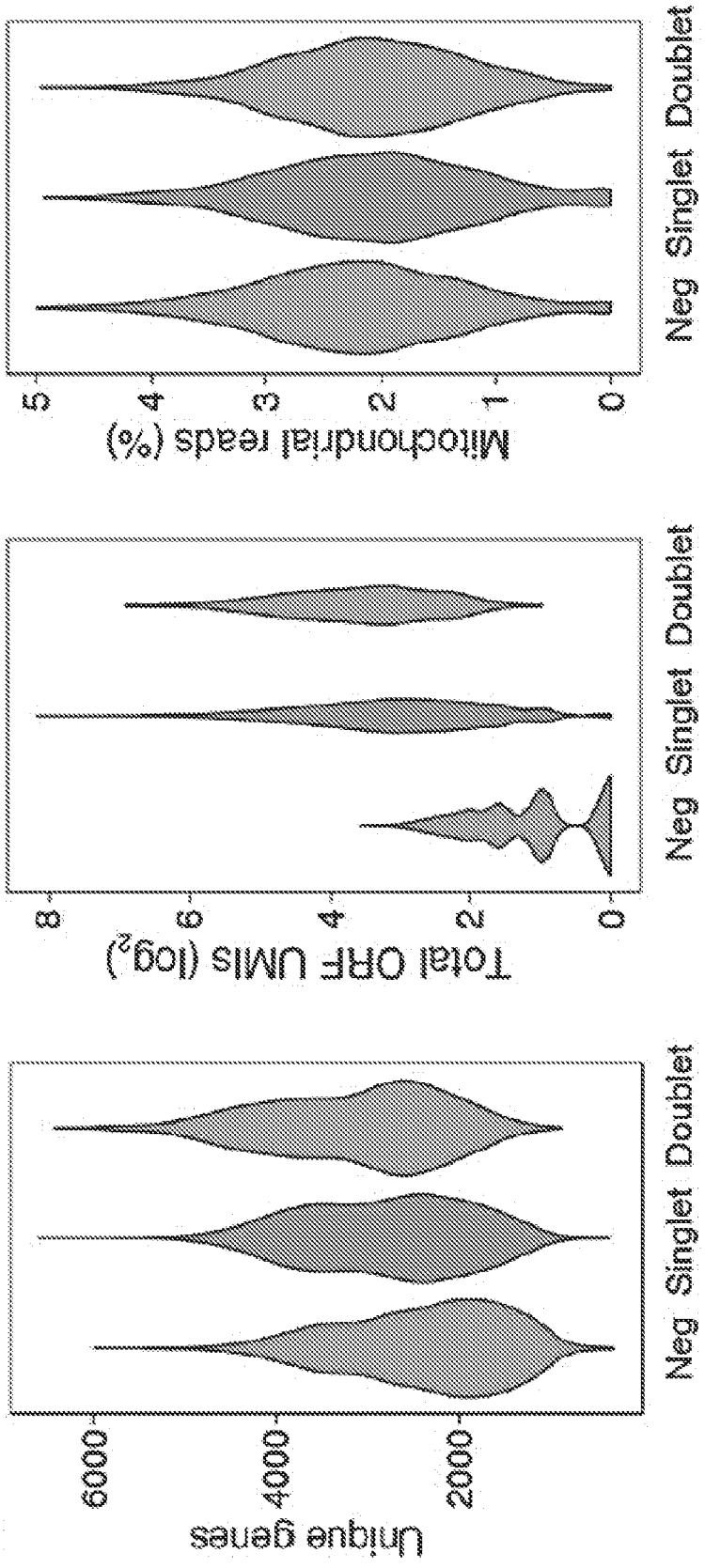

Unique genes
6000
4000
2000
Neg Singlet Doublet
Total ORF UMIs (log2)
8
6
4
2
0
Neg Singlet Doublet
Mitochondrial reads (%)
5
4
3
2
1
0
Neg Singlet Doublet

FIG. 9A

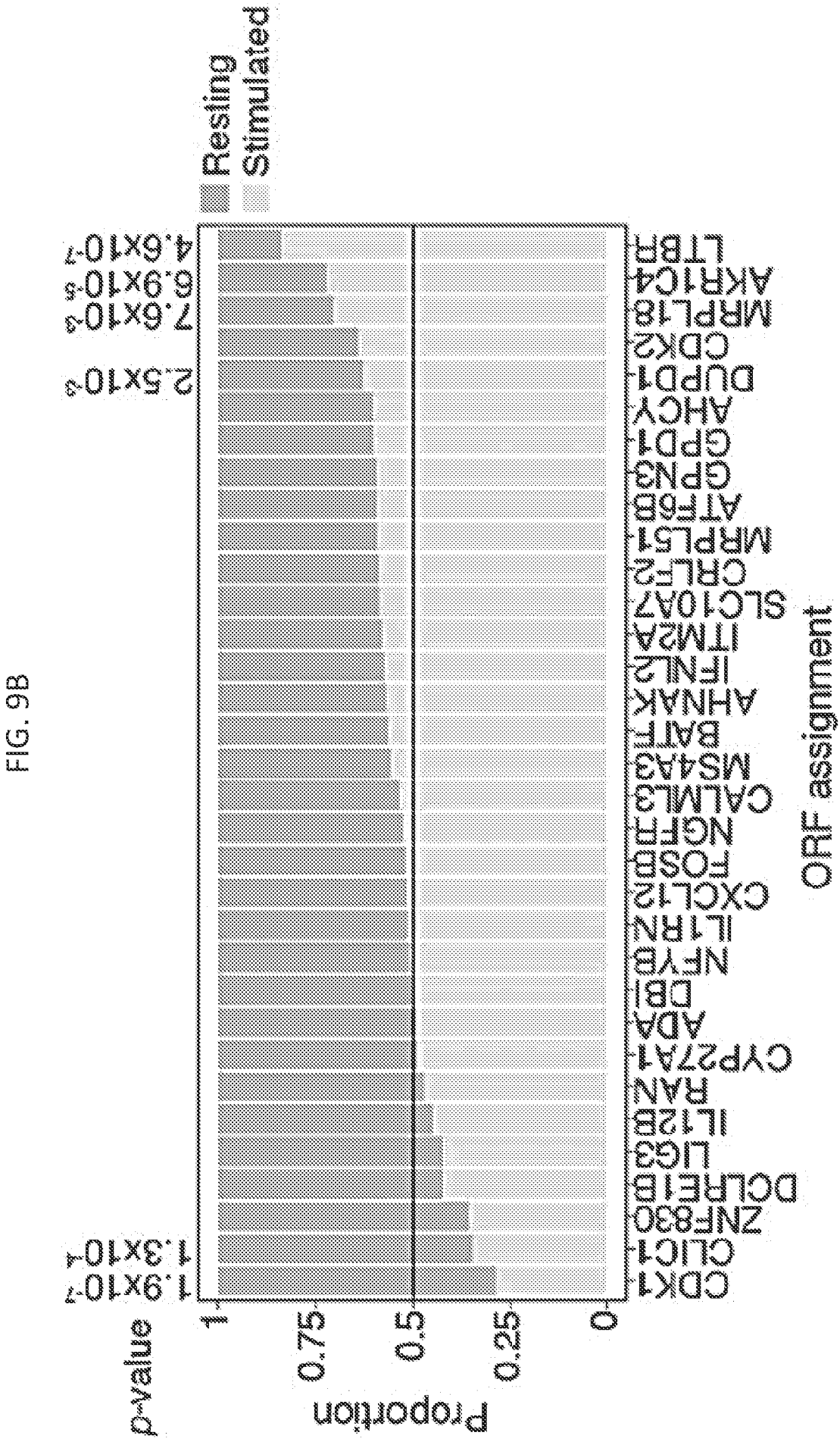
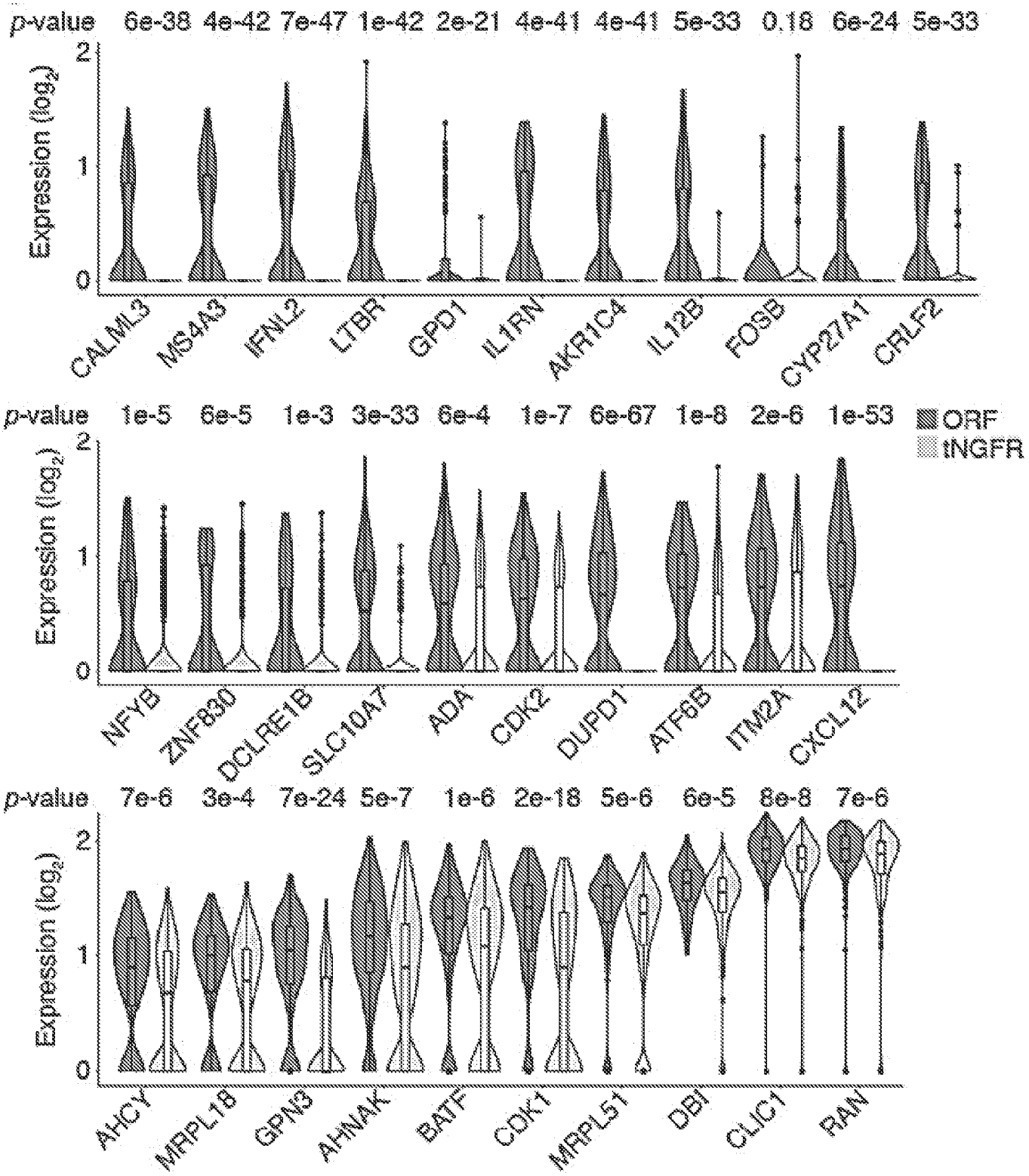

Resting
Stimulated
Proportion
1
0.75
0.5
0.25
0
p-value
1.9X10-7
1.3X10-4
2.5X10-3
7.6X10-3
6.9X10-3
4.6X10-7
CDK1
CLIC1
ZNF830
DCLRE1B
LIG3
IL12B
RAN
CYP27A1
ADA
DBI
NFYB
IL1RN
CXCL12
FOSB
NGFR
CALML3
MS4A3
BATF
AHNAK
IFNL2
ITM2A
SLC10A7
CRLF2
MRPL51
ATF6B
GPN3
GPD1
AHCY
DUPD1
CDK2
MRPL18
AKR1C4
LTBR
ORF assigment

FIG. 9B

FIG. 9C


p-value 6e-38 4e-42 7e-47 1e-42 2e-21 4e-41 4e-41 5e-33 0.18 6e-24 5e-33
Expression (log2)
CALML3
MS4A3
IFNL2
LTBR
GPD1
IL1RN
AKR1C4
IL12B
FOSB
CYP27A1
CRLF2
p-value 1e-5 6e-5 1e-3 3e-33 6e-4 1e-7 6e-67 1e-8 2e-6 1e-53
ORF
tNGFR
NFYB
ZNF830
DCLRE1B
SLC10A7
ADA
CDK2
DUPD1
ATF6B
ITM2A
CXCL12
p-value 7e-6 3e-4 7e-24 5e-7 1e-6 2e-18 5e-6 6e-5 8e-8 7e-6
AHCY
MRPL18
GPN3
AHNAK
BATF
CDK1
MRPL51
DBI
CLIC1
RAN

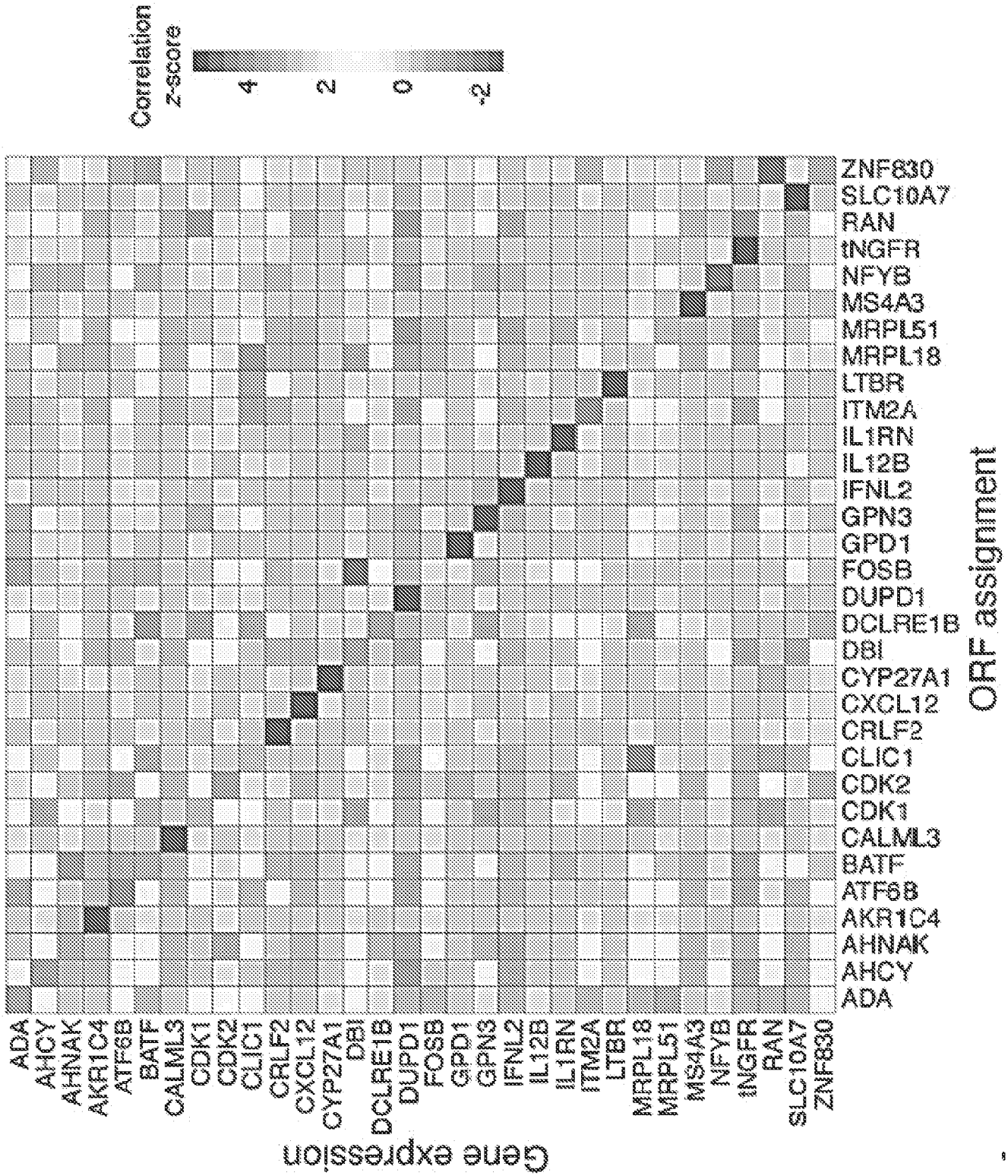

Correlation
z-score
4
2
0
-2
ZNF830
SLC10A7
RAN
tNGFR
NFYB
MS4A3
MRPL51
MRPL18
LTBR
ITM2A
IL1RN
IL12B
IFNL2
GPN3
GPD1
FOSB
DUPD1
DCLRE1B
DBI
CYP27A1
CXCL12
CRLF2
CLIC1
CDK2
CDK1
CALML3
BATF
ATF6B
AKR1C4
AHNAK
AHCY
ADA
ADA
AHCY
AHNAK
AKR1C4
ATF6B
BATF
CALML3
CDK1
CDK2
CLIC1
CRLF2
CXCL12
CYP27A1
DBI
DCLRE1B
DUPD1
FOSB
GPD1
GPN3
IFNL2
IL12B
IL1RN
ITM2A
LTBR
MRPL18
MRPL51
MS4A3
NFYB
tNGFR
RAN
SLC10A7
ZNF830
Gene expression
ORF assigment

FIG. 9D

FIG. 9E

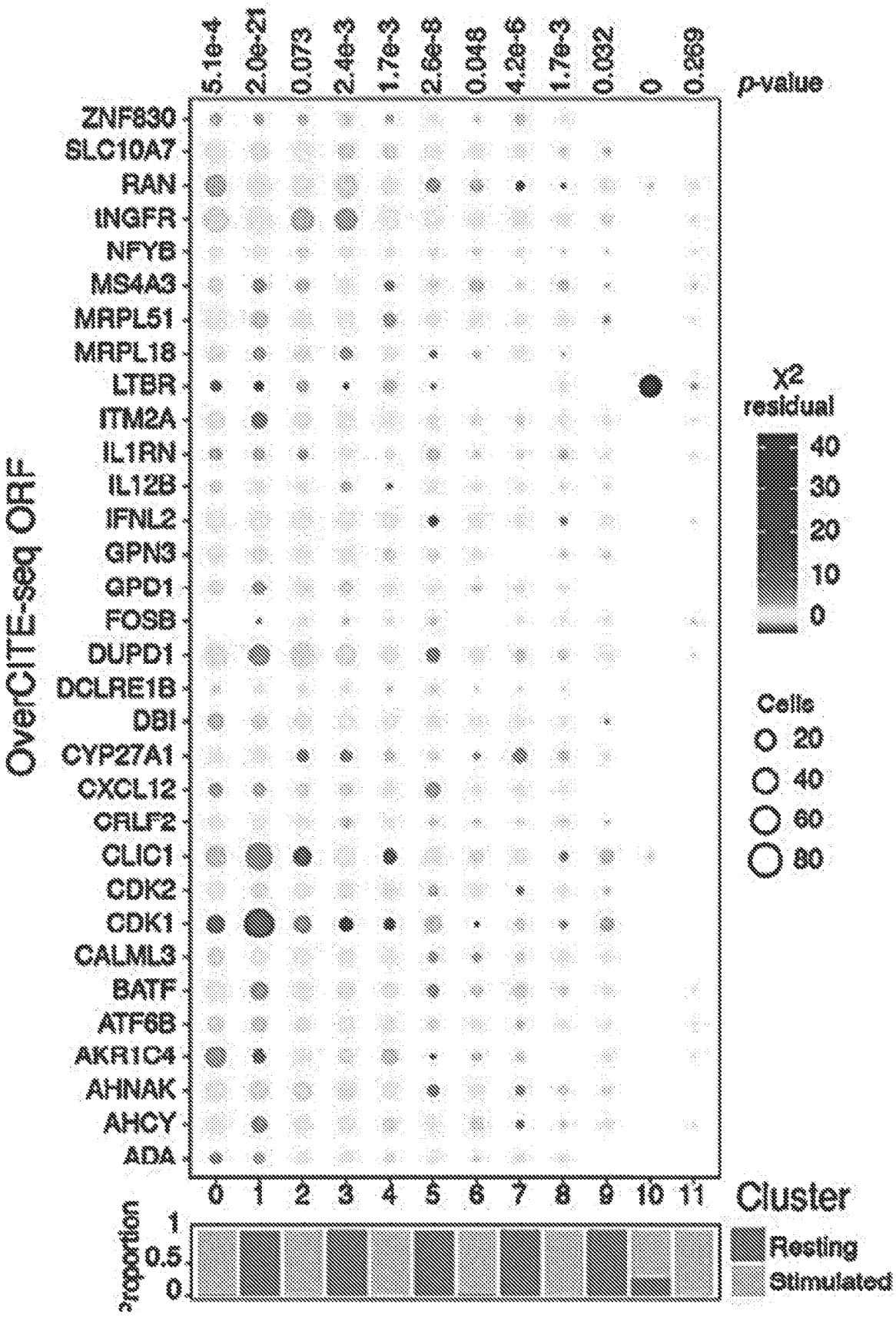

5.1e-4
2.0e-21
0.073
2.4e-3
1.7e-3
2.6e-8
0.048
4.2e-6
1.7e-3
0.032
0
0.269
p-value
ZNF830
SLC10A7
RAN
INGFR
NFYB
MS4A3
MRPL51
MRPL18
LTBR
ITM2A
IL1RN
IL12B
IFNL2
GPN3
QPD1
FOSB
DUPD1
DCLRE1B
DBI
CYP27A1
CXCL12
CRLF2
CLIC1
CDK2
CDK1
CALML3
BATF
ATF6B
AKR1C4
AHNAK
AHCY
ADA
OverCITE-seq ORF
X2 residual
40
30
20
10
0
Cells
20
40
60
80
0 1 2 3 4 5 6 7 8 9 10 11
Cluster
proportion
1
0.5
0
Resting
Stimulated

FIG. 9F

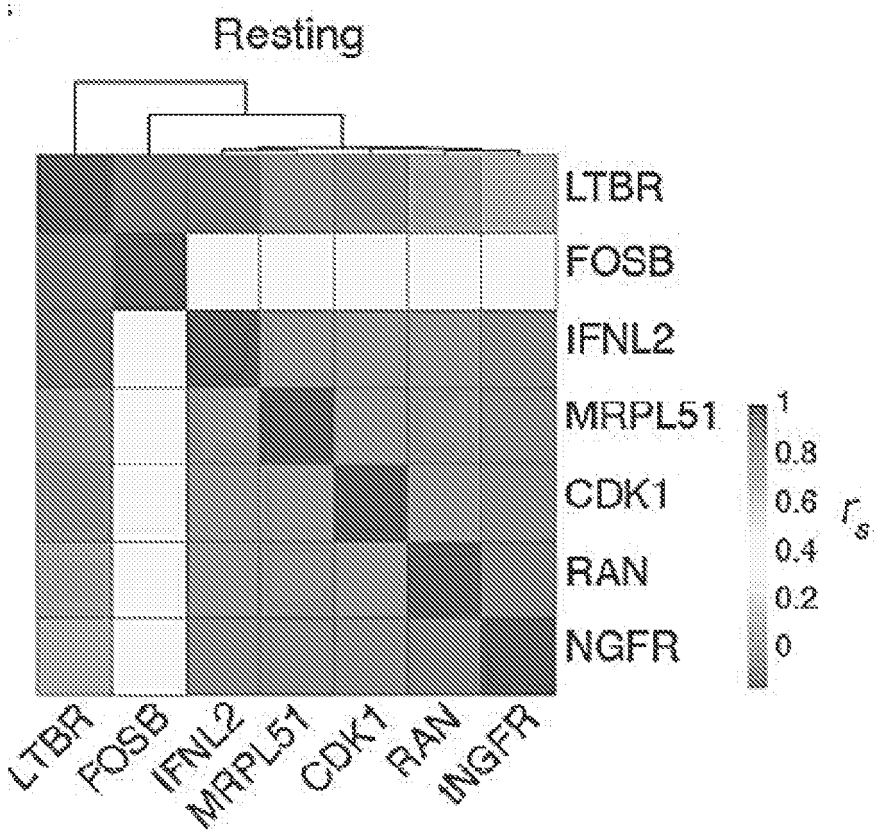
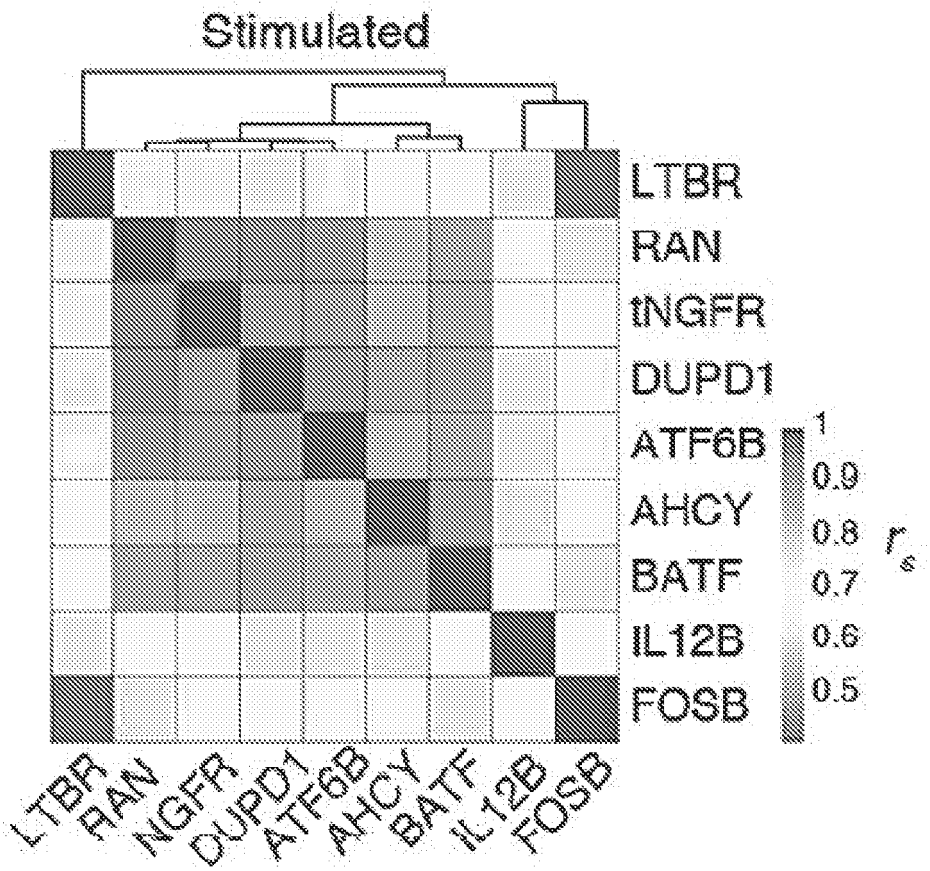

Resting
LTBR
FOSB
IFNL2
MRPL51
CDK1
RAN
NGFR
1
0.8
0.6
0.4
0.2
0
r_s
LTBR
FOSB
IFNL2
MRPL51
CDK1
RAN
tNGFR

FIG. 9G


Stimulated
LTBR
RAN
tNGFR
DUPD1
ATF6B
AHCY
BATF
IL12B
FOSB
1
0.9
0.8
0.7
0.6
0.5
r_s
LTBR
RAN
NGFR
DUPD1
ATF6B
AHCY
BATF
IL12B
FOSB

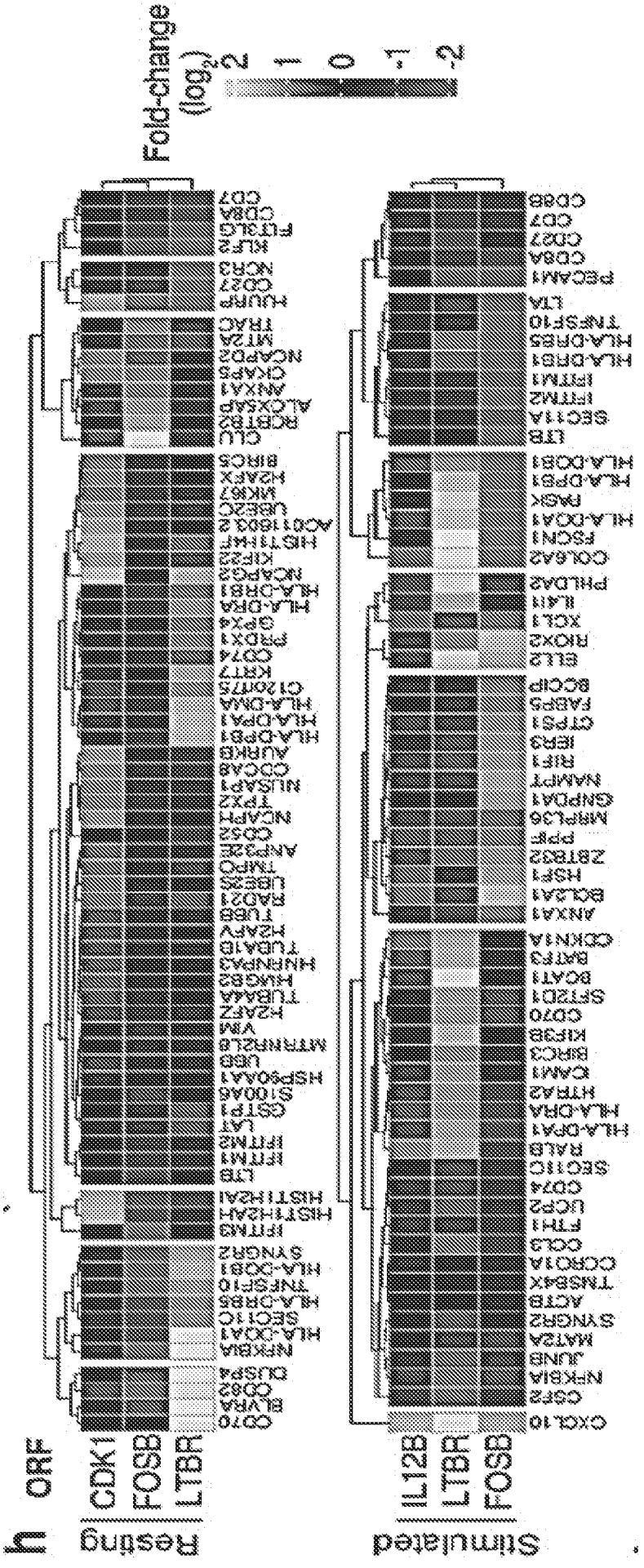

h
ORF
Resting
CDK1
FOSB
LTBR
Stimulated
IL12B
LTBR
FOSB
Fold-change
(log2)
2
1
0
-1
-2

FIG. 9H

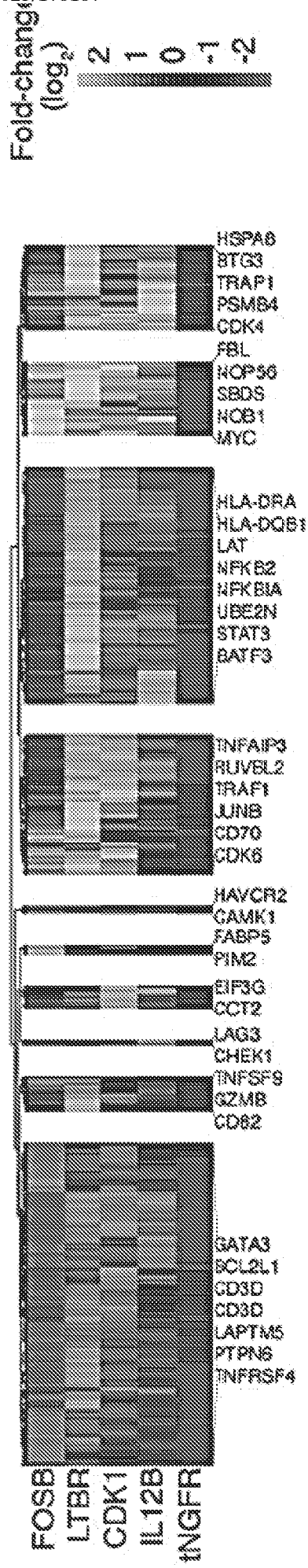

Fold-change (log2)
2
1
0
-1
-2
HSPA8
BTG3
TRAP1
PSMB4
CDK4
FBL
NOP56
SBDS
NOB1
MYC
HLA-DRA
HLA-DQB1
LAT
NFKB2
NFKBIA
UBE2N
STAT3
BATF3
TNFAIP3
RUVBL2
TRAF1
JUNB
CD70
CDK6
HAVCR2
CAMK1
FABP5
PIM2
EIF3G
CCT2
LAG3
CHEK1
TNFSF9
GZMB
CD82
GATA3
BCL2L1
CD3D
CD3D
LAPTM5
PTPN6
TNFRSF4
FOSB
LTBR
CDK1
IL12B
tNGFR

FIG. 9I

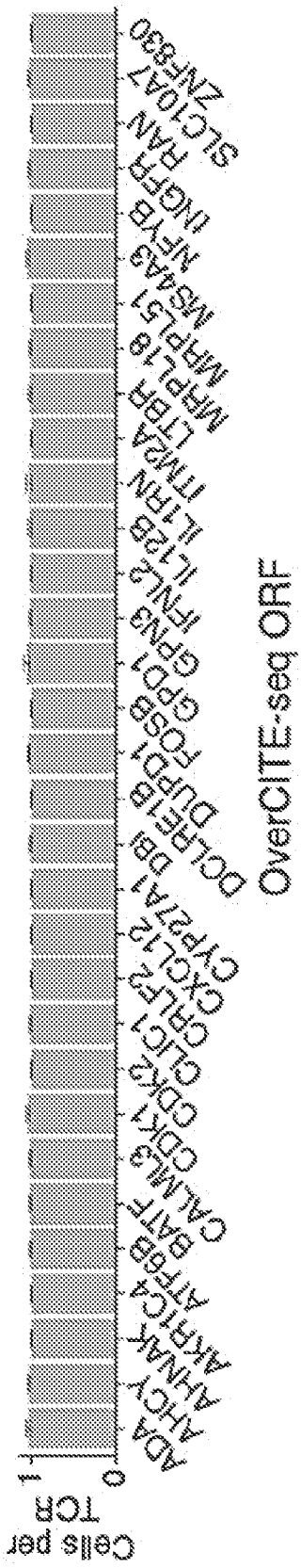

Cells per TCR
1
0
ADA
AHCY
AHNAK
AKR1C4
ATP8B
BATF
CALM3
CDK1
CDK2
CLIC1
CRLF3
CXCL12
CYP27A1
DBI
DCLRE1B
DUSP1
FOSB
GPD1
GPN3
IFNLR1
IL12B
IL1RN
ITM2A
LTBR
MRPL18
MRPL51
MS4A3
NFYB
NGFRAP1
SLC10A7
ZNF830
OverOITE-seq ORF

Fig. 9J

FIG. 10A

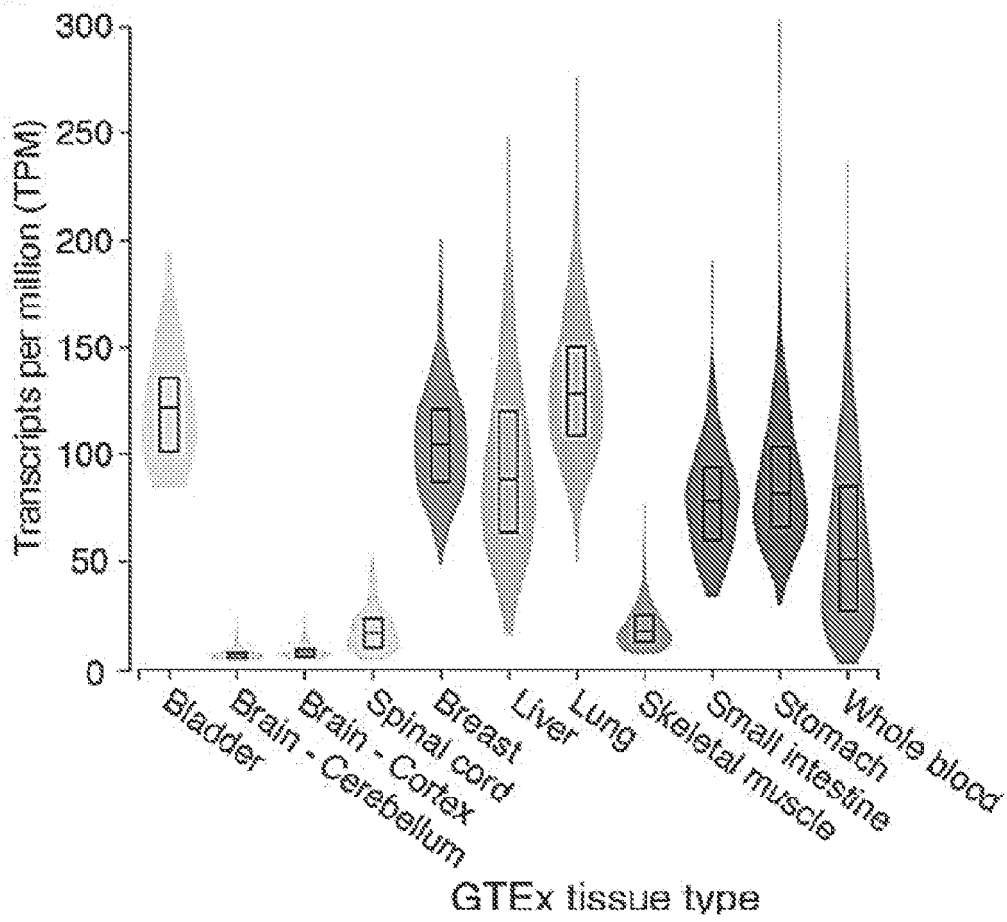


FIG. 10B

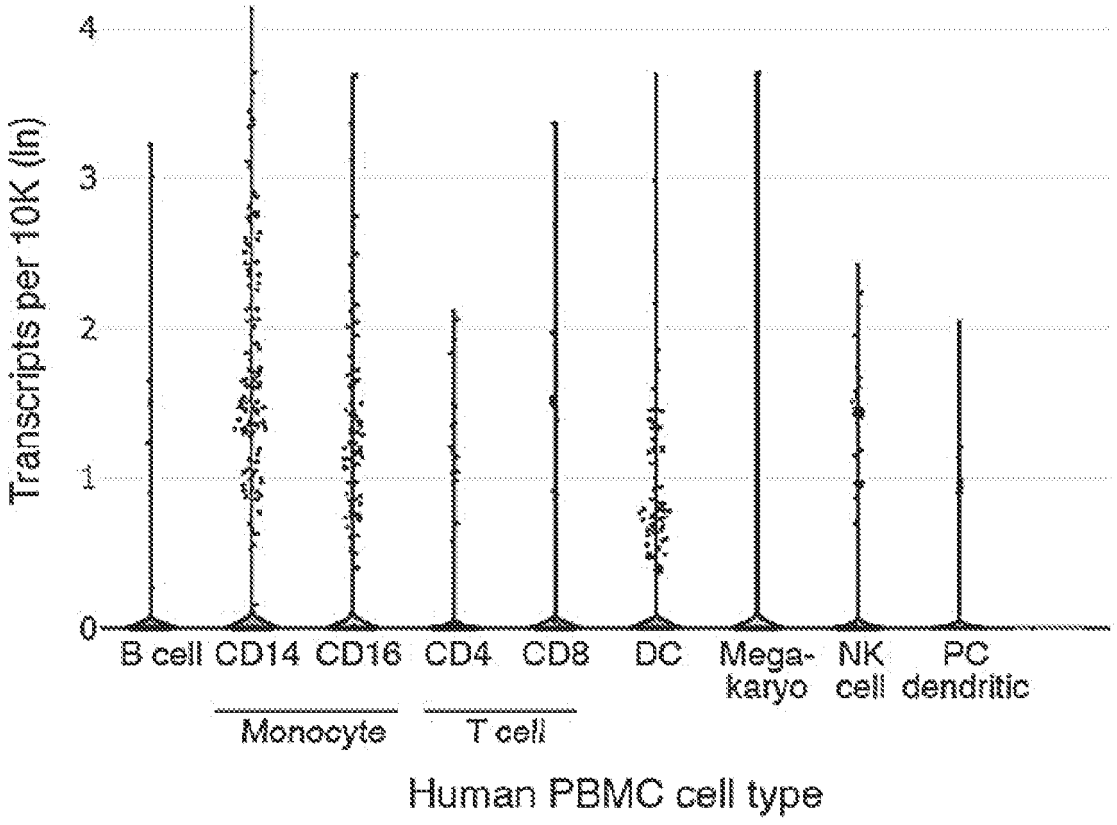


Fig. 10C

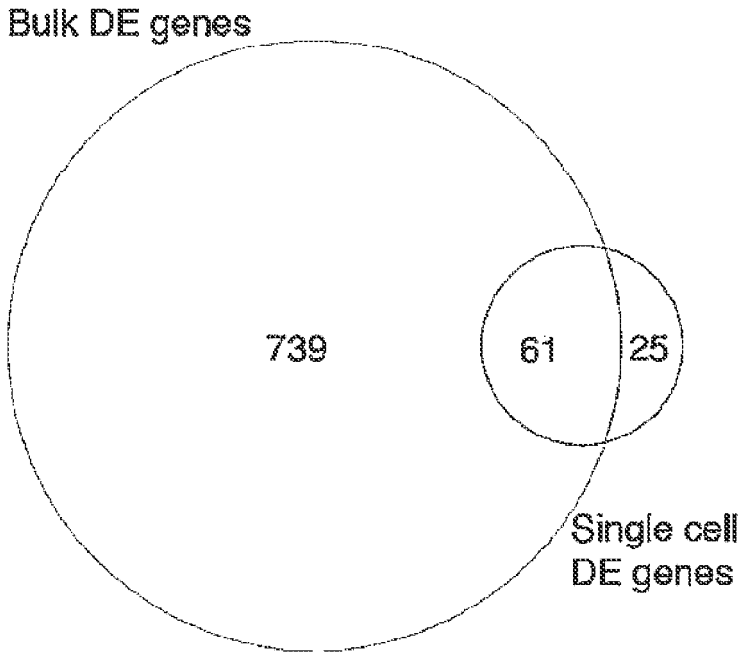


Fig. 10D

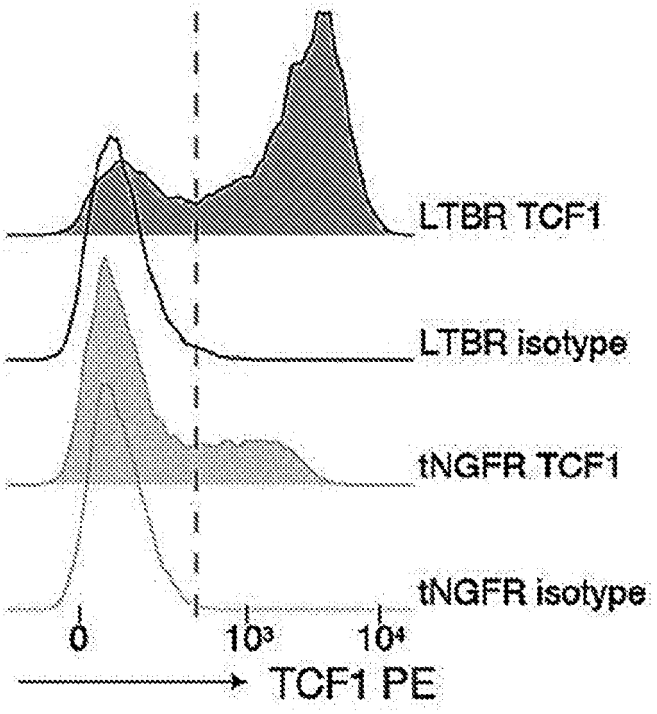


Fig. 10E

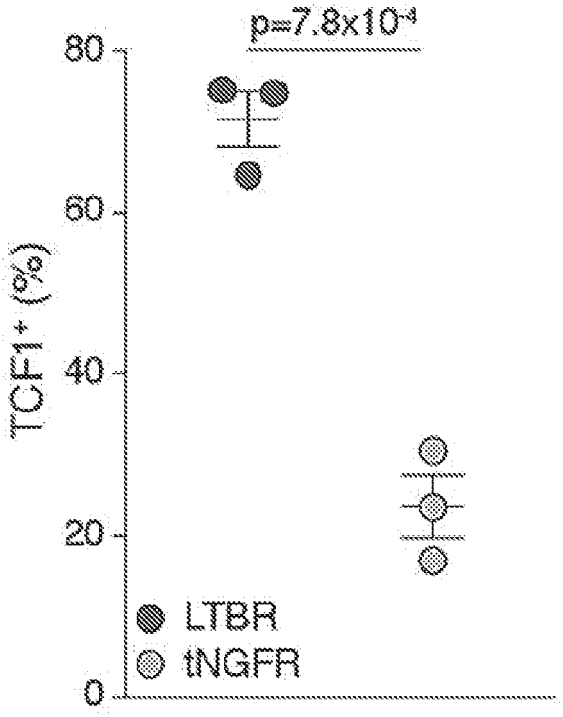


FIG. 10F

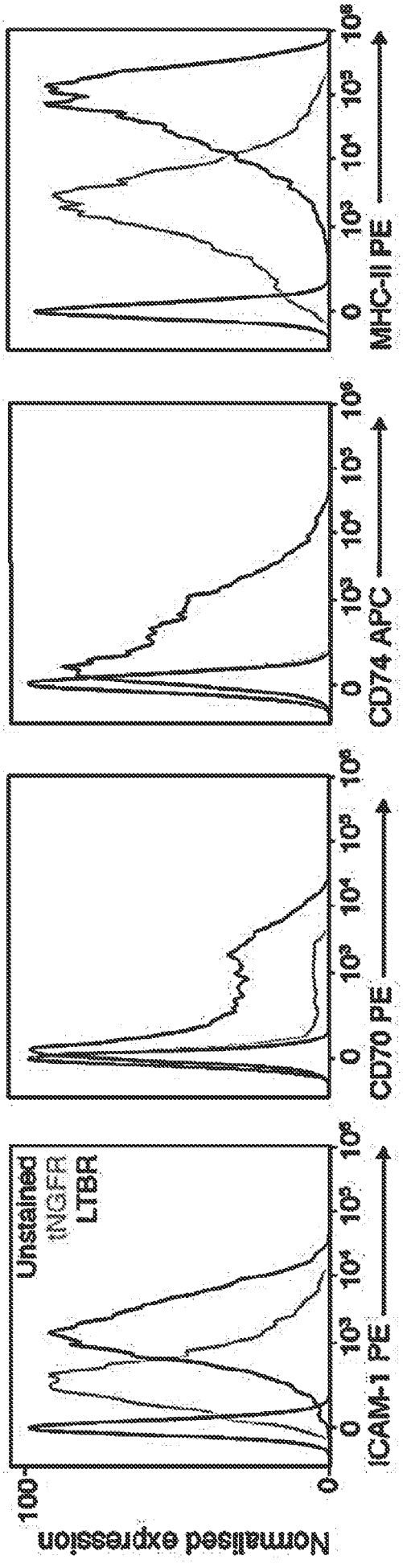

Normalised expression
100
0
Unstained
tNGFR
LTBR
ICAM-1 PE
CD70 PE
CD74 APC
MHC-II PE
0
10³
10⁴
10⁵
10⁶

FIG. 10G

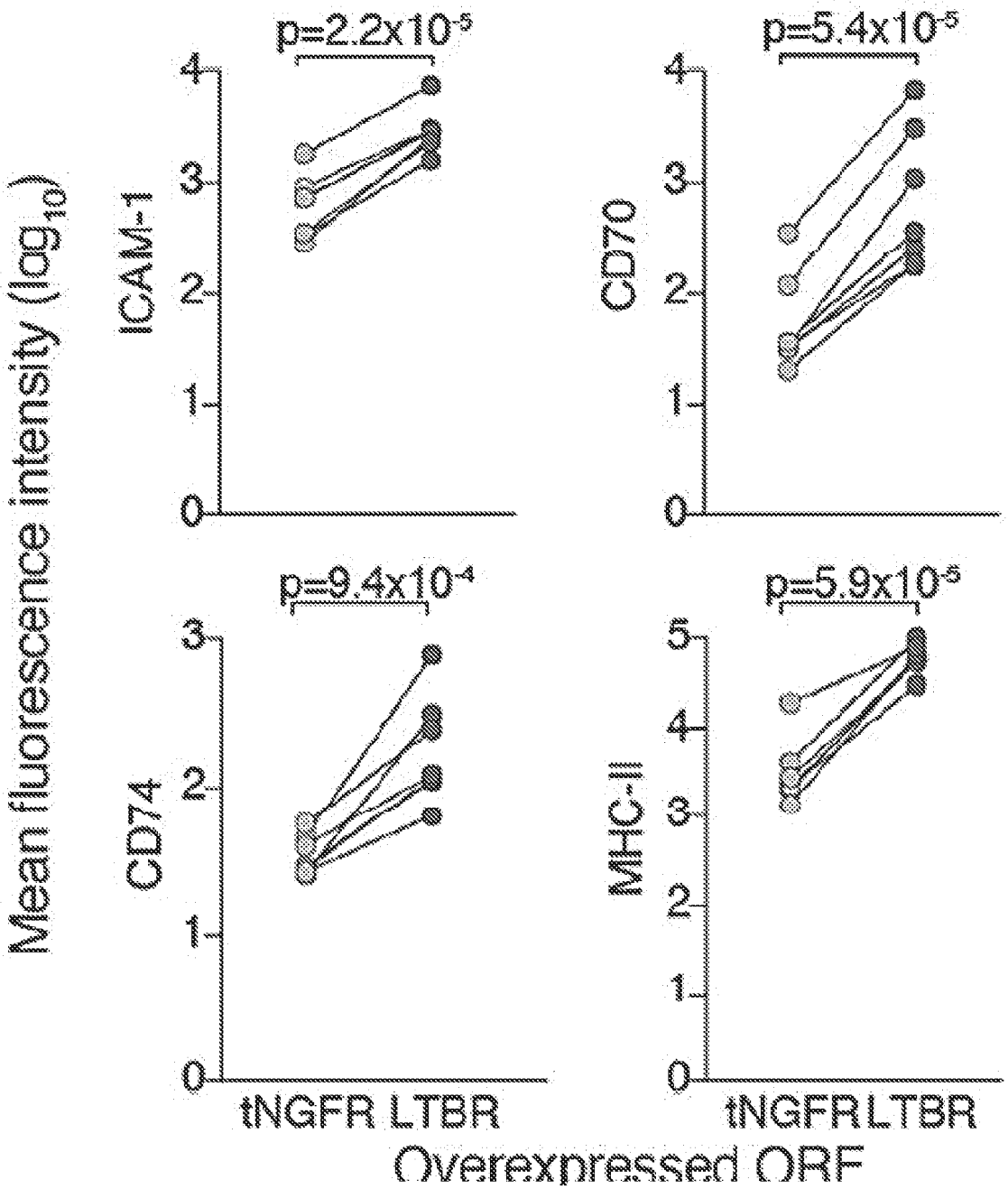

Mean fluorescence intensity (log_{10})
ICAM-1
p=2.2x10^{-5}
CD70
p=5.4x10^{-5}
CD74
p=9.4x10^{-4}
MHC-II
p=5.9x10^{-5}
tNGFR LTBR
tNGFR LTBR
Overexpressed ORF

FIG. 10H

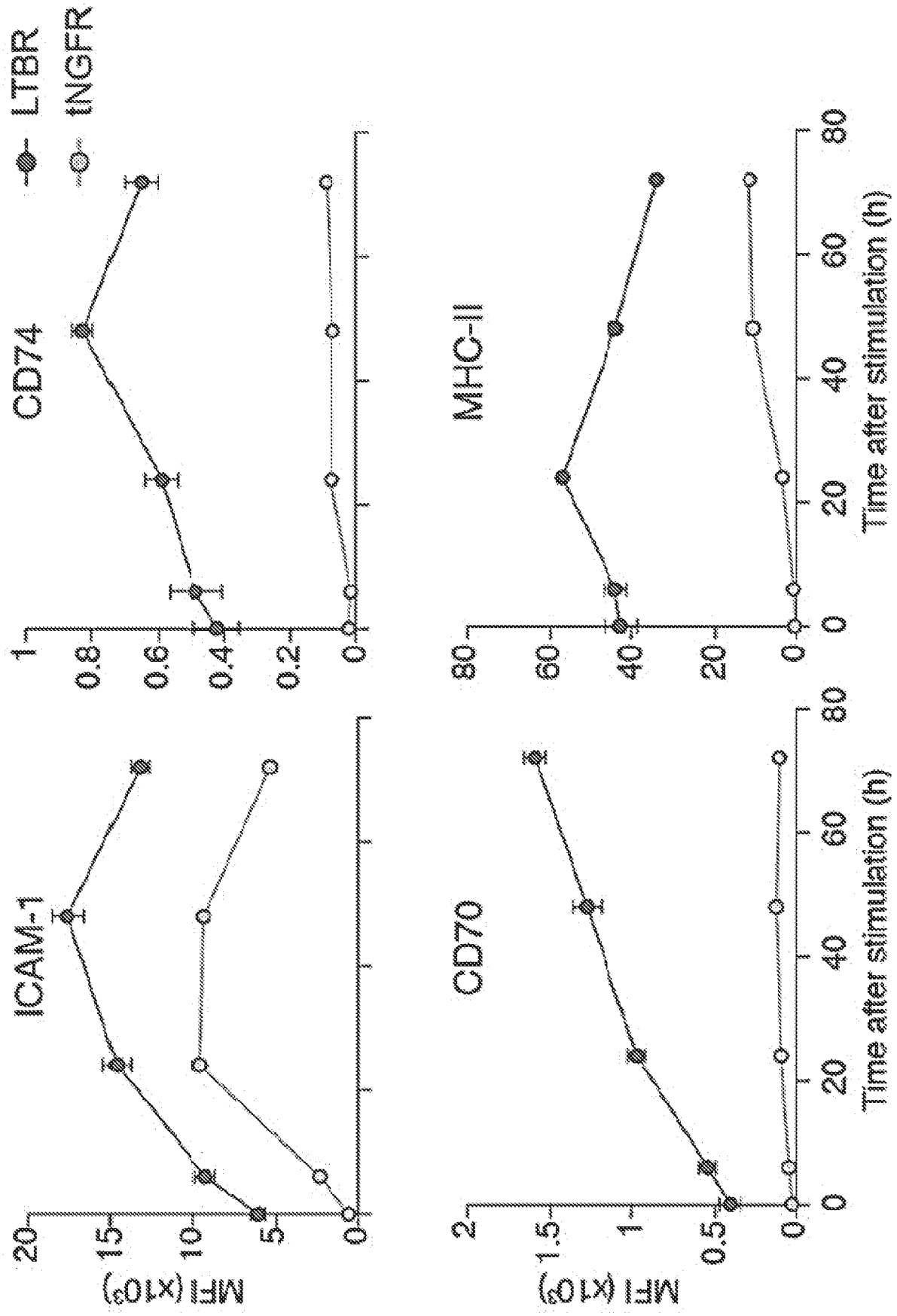

LTBR
tNGFR
CD74
MHC-II
ICAM-1
CD70
MFI (x10³)
Time after stimulation (h)
0
0.2
0.4
0.6
0.8
1
20
40
60
80
5
10
15
20
0.5
1
1.5
2

FIG. 10I

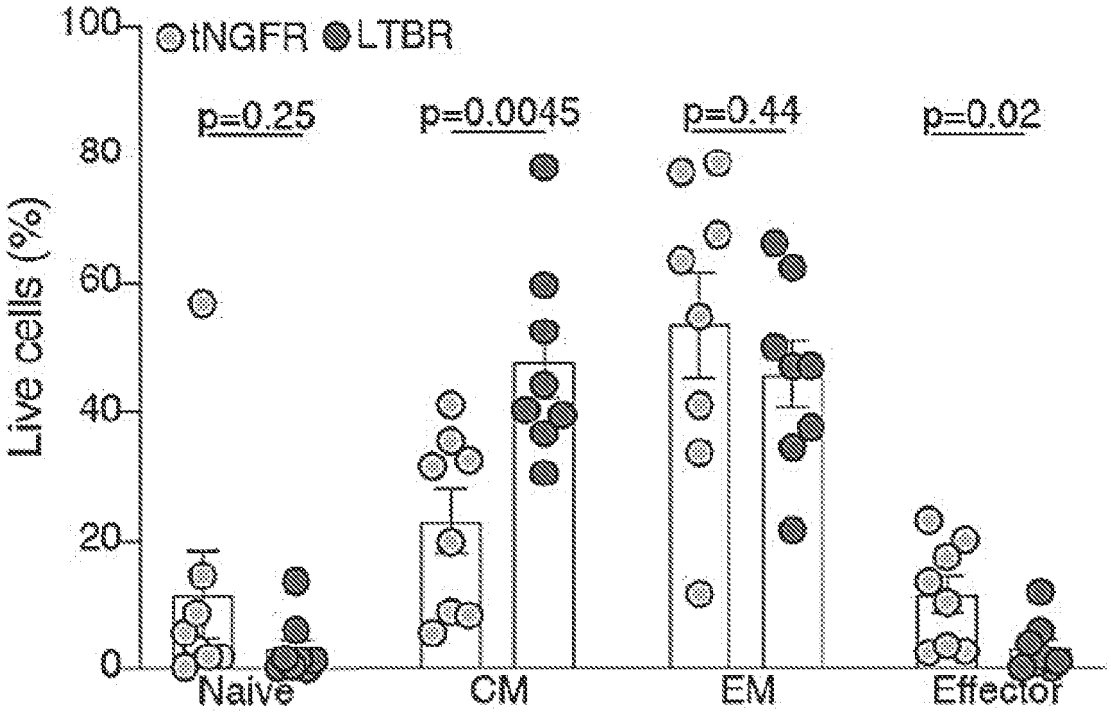


FIG. 10J

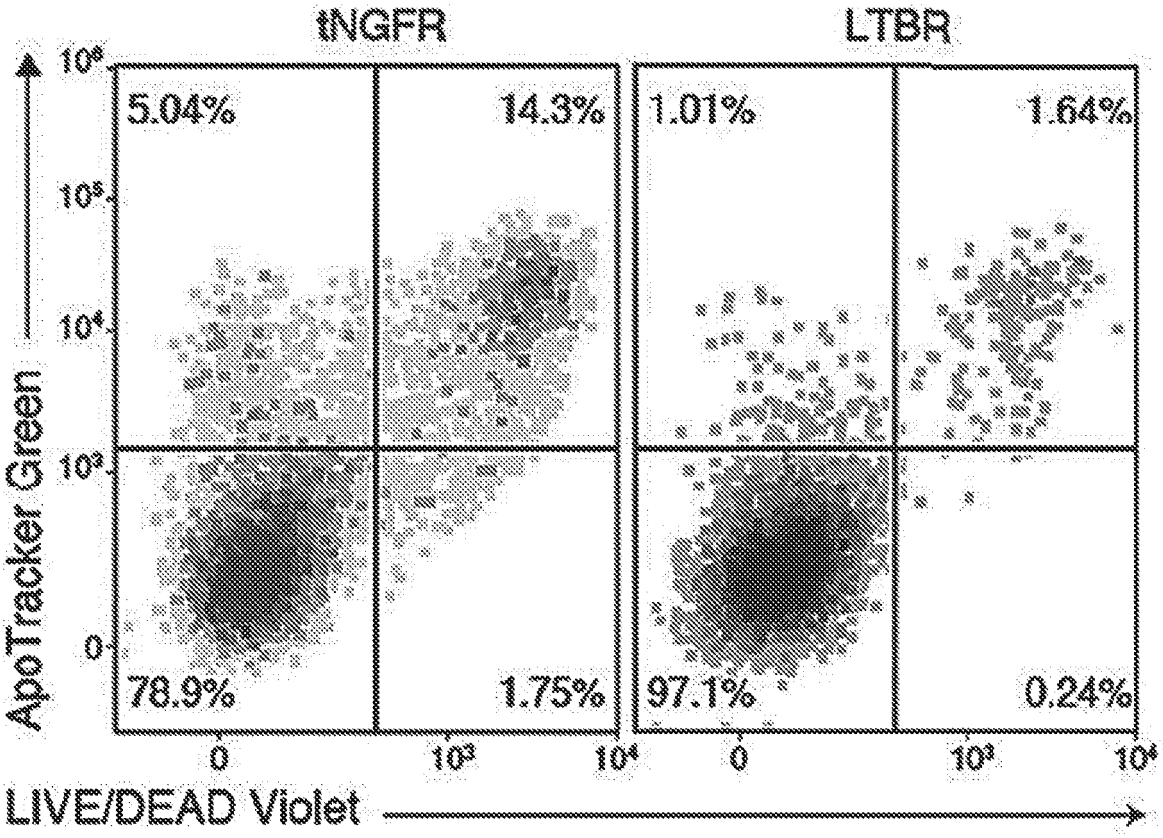


FIG. 10K

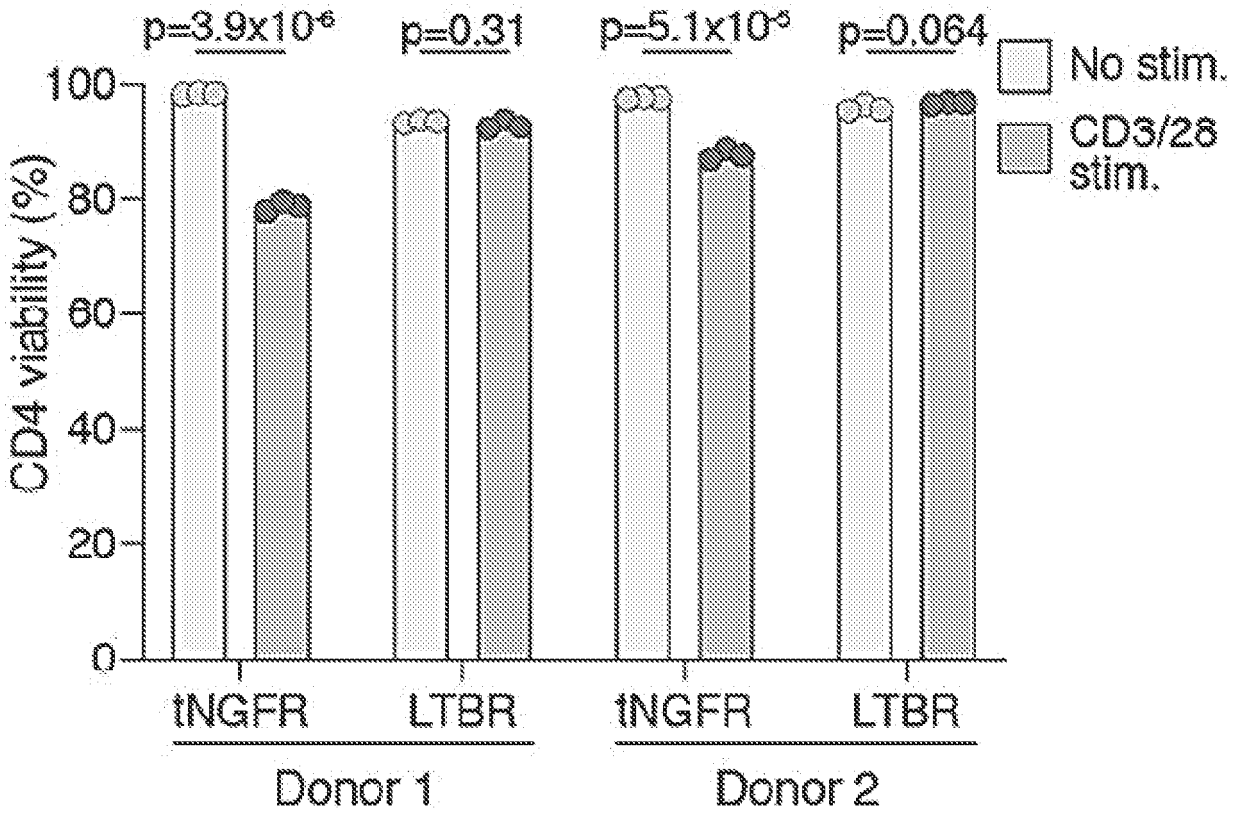
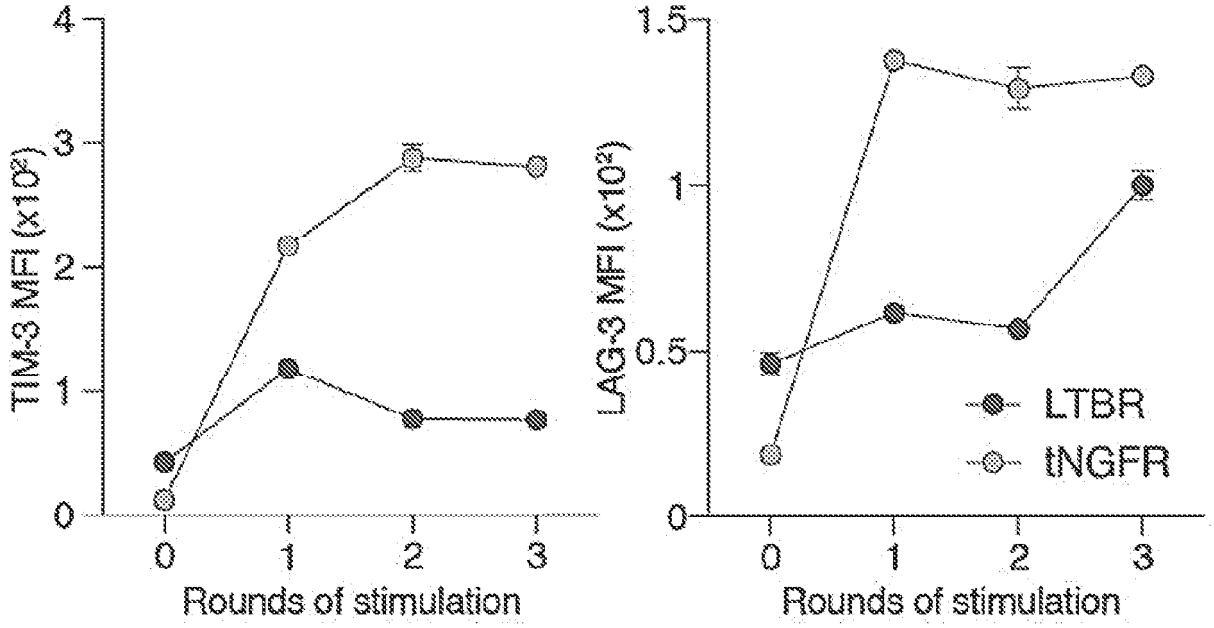


FIG. 10L



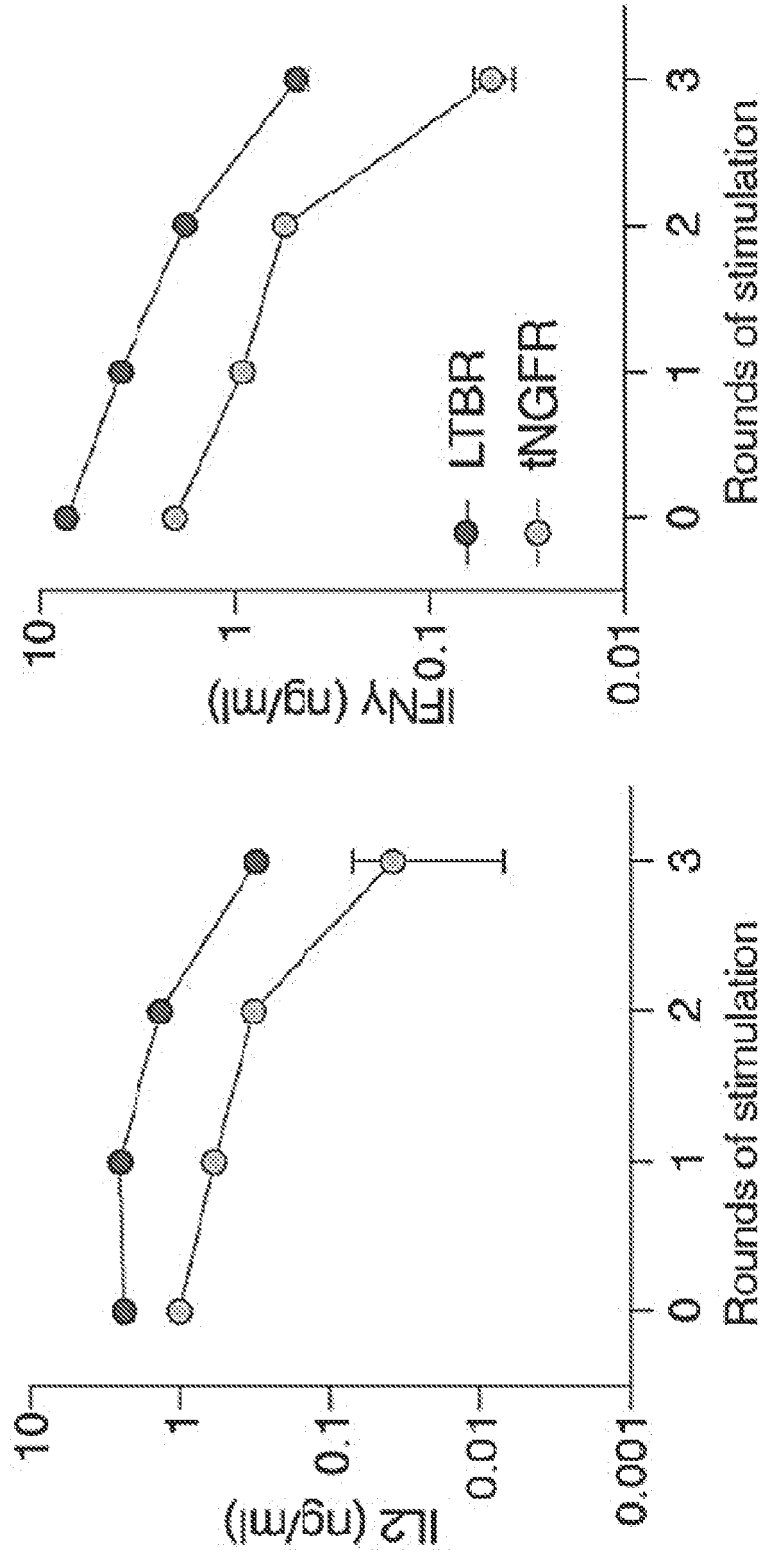

IFNγ (ng/ml)
10
1
0.1
0.01
LTBR
tNGFR
0
1
2
3
Rounds of stimulation
IL2 (ng/ml)
10
1
0.1
0.01
0.001
0
1
2
3
Rounds of stimulation

FIG. 10M

FIG. 11A

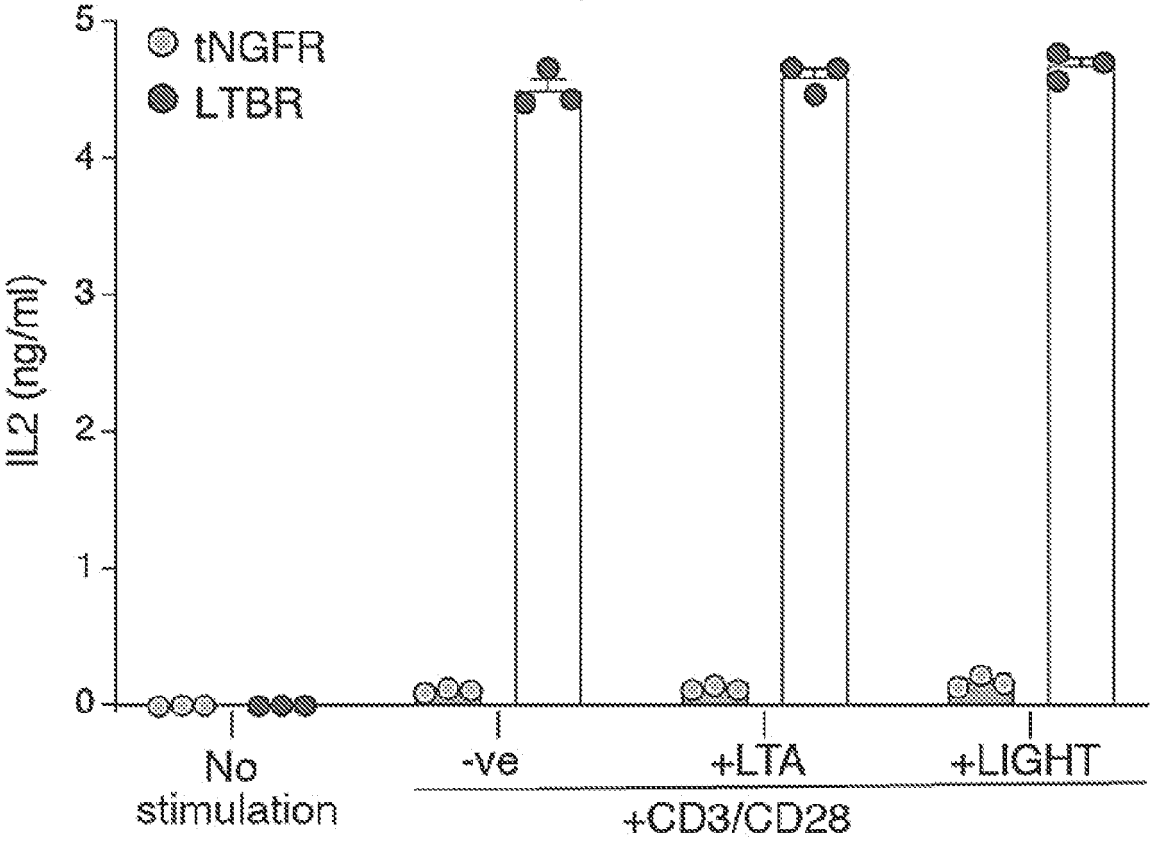
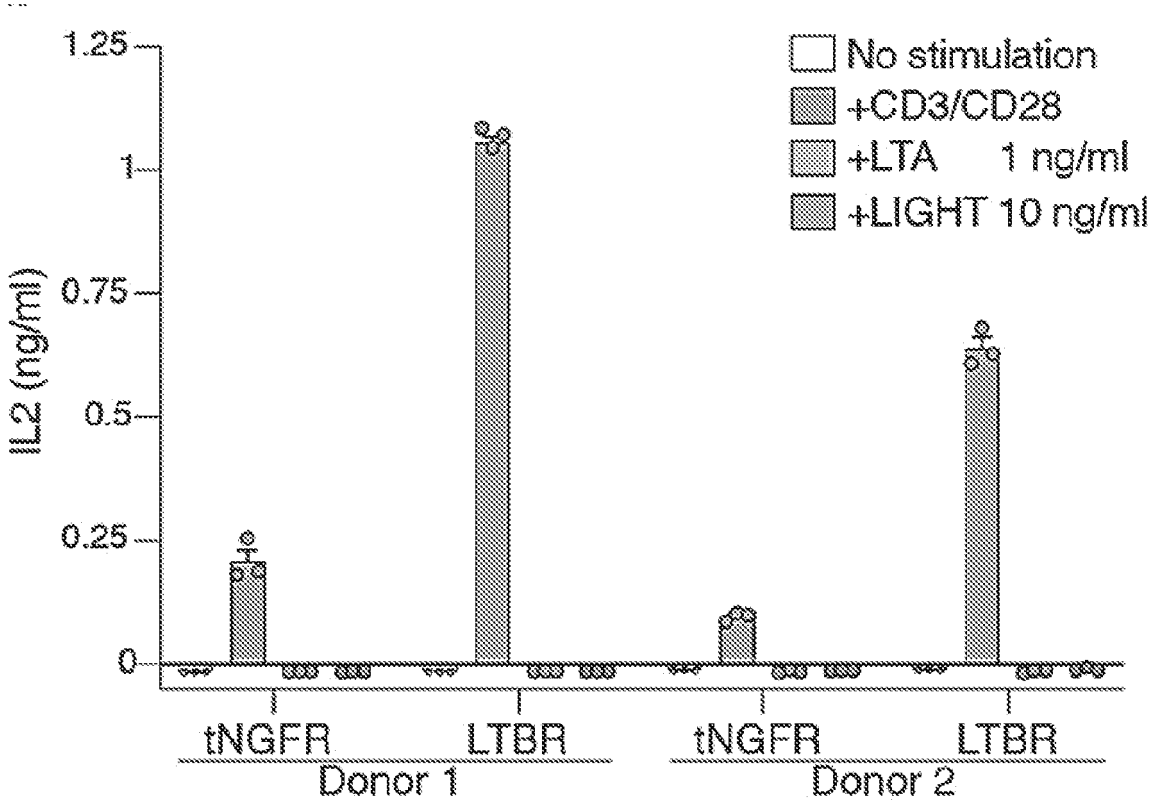


FIG. 11B



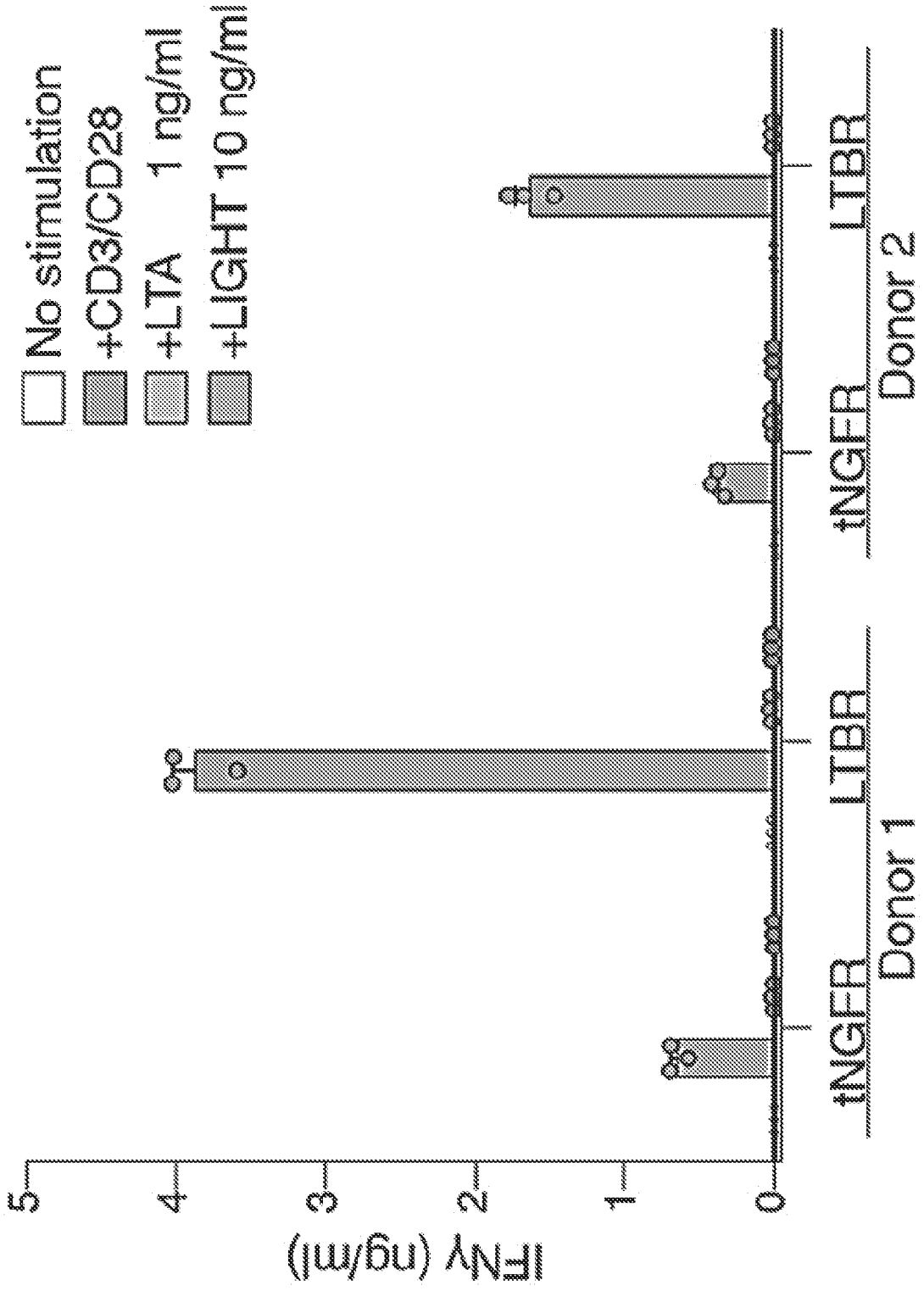

No stimulation
+CD3/CD28
+LTA 1 ng/ml
+LIGHT 10 ng/ml
IFNγ (ng/ml)
0
1
2
3
4
5
tNGFR
LTBR
tNGFR
LTBR
Donor 1
Donor 2

FIG. 11C

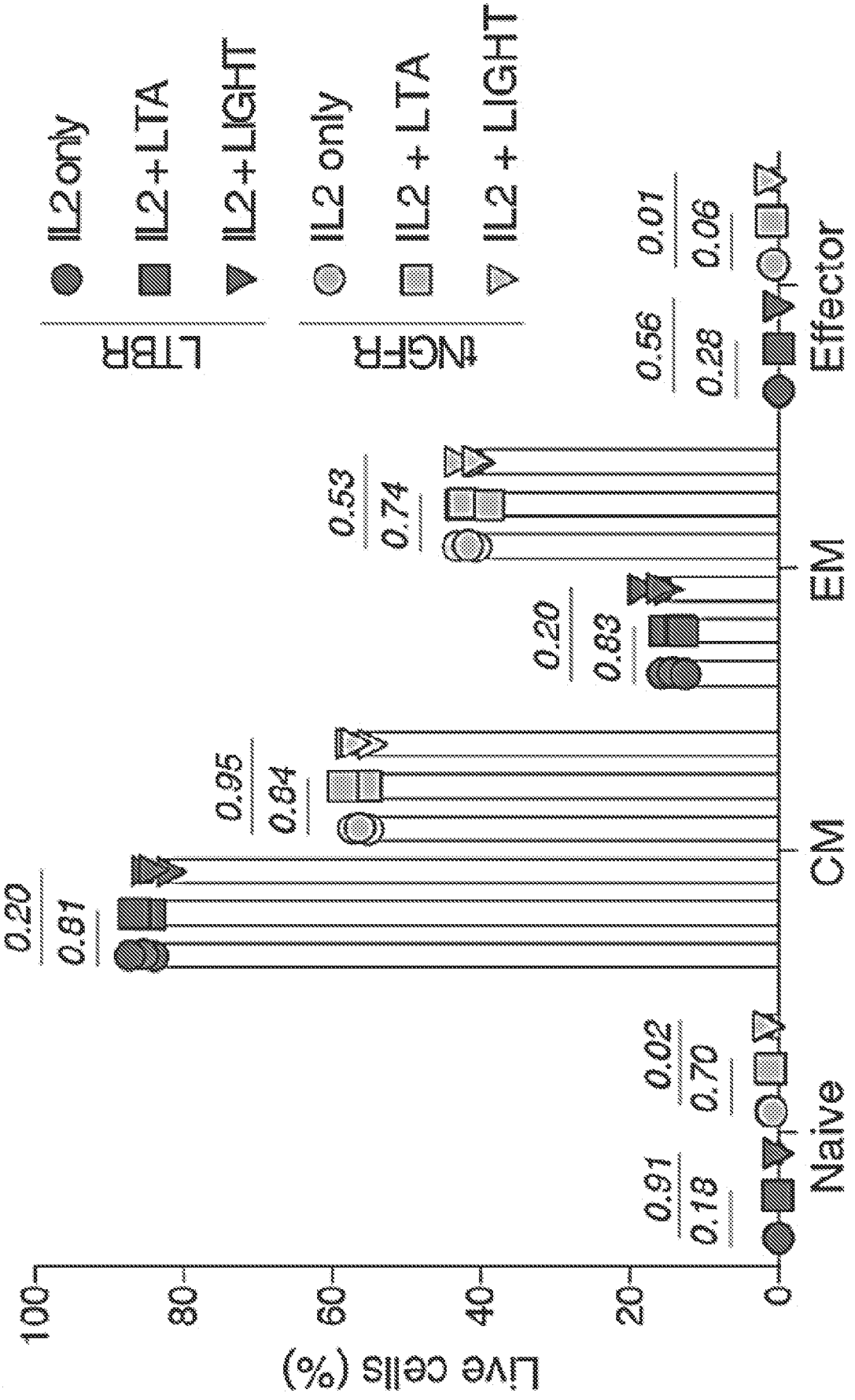

IL2only
IL2+LTA
IL2+LIGHT
LTBR
IL2 only
IL2 + LTA
IL2 + LIGHT
TNFR
Live cells (%)
100
80
60
40
20
0
0.91
0.18
0.02
0.70
0.20
0.81
0.95
0.84
0.20
0.83
0.53
0.74
0.56
0.28
0.01
0.06
Naive
CM
EM
Effector

FIG. 11D

FIG. 11E

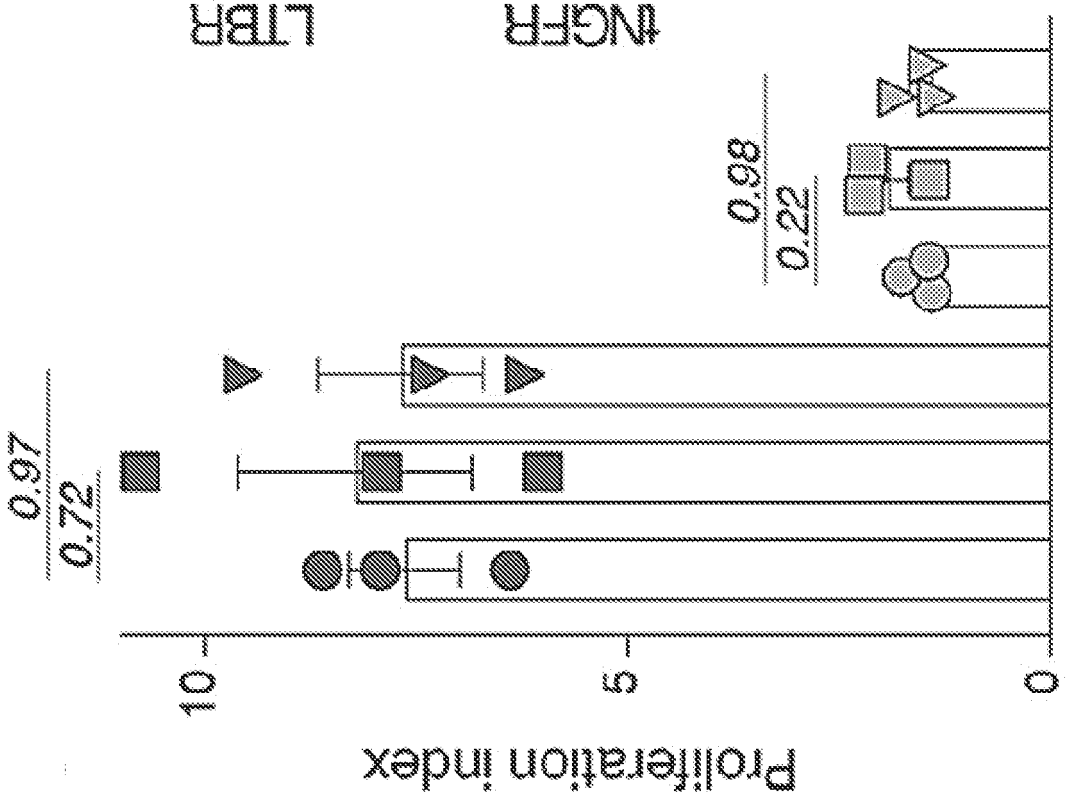


FIG. 11F

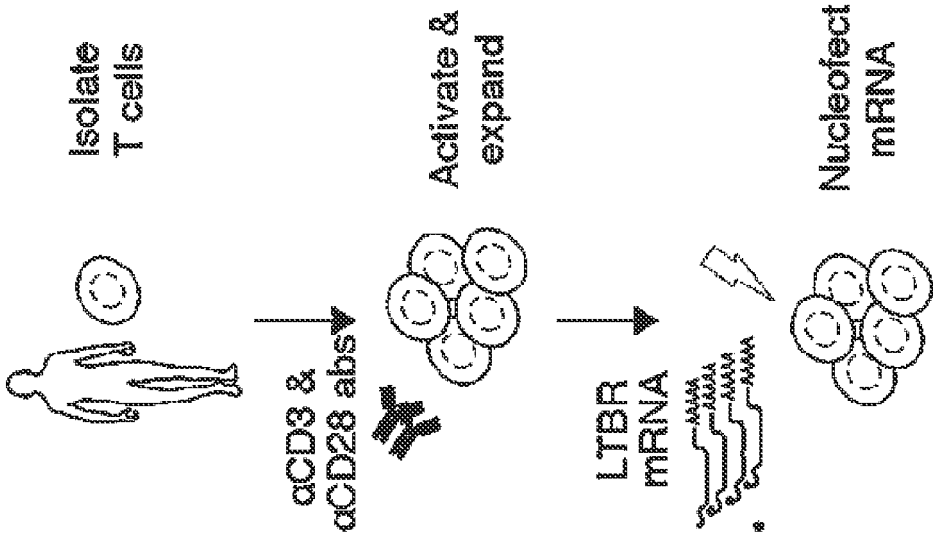


FIG. 11G

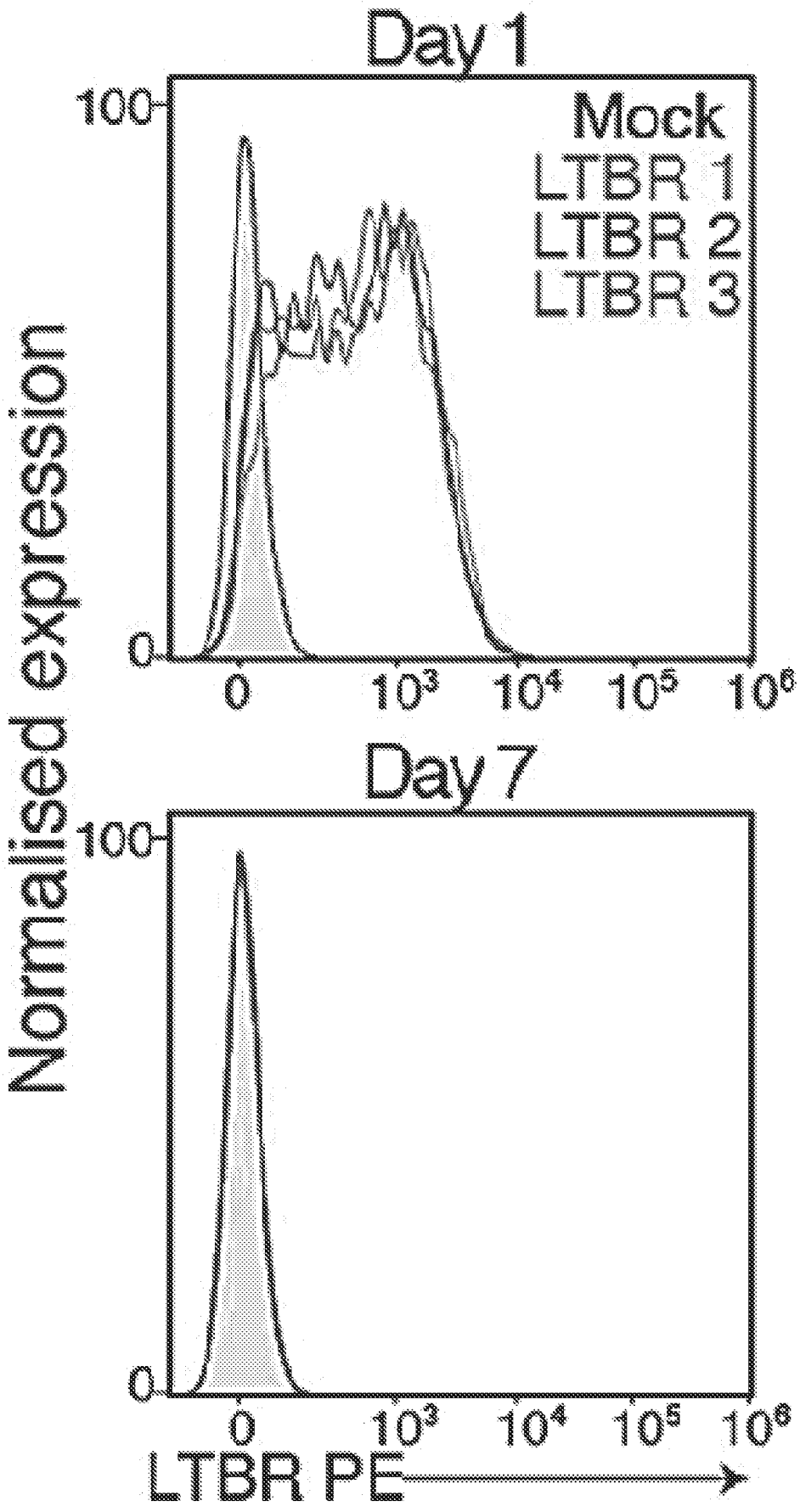

Day 1
100
0
Mock
LTBR 1
LTBR 2
LTBR 3
Normalised expression
0
10³
10⁴
10⁵
10⁶
Day 7
100
0
0
10³
10⁴
10⁵
10⁶
LTBR PE

FIG. 11H

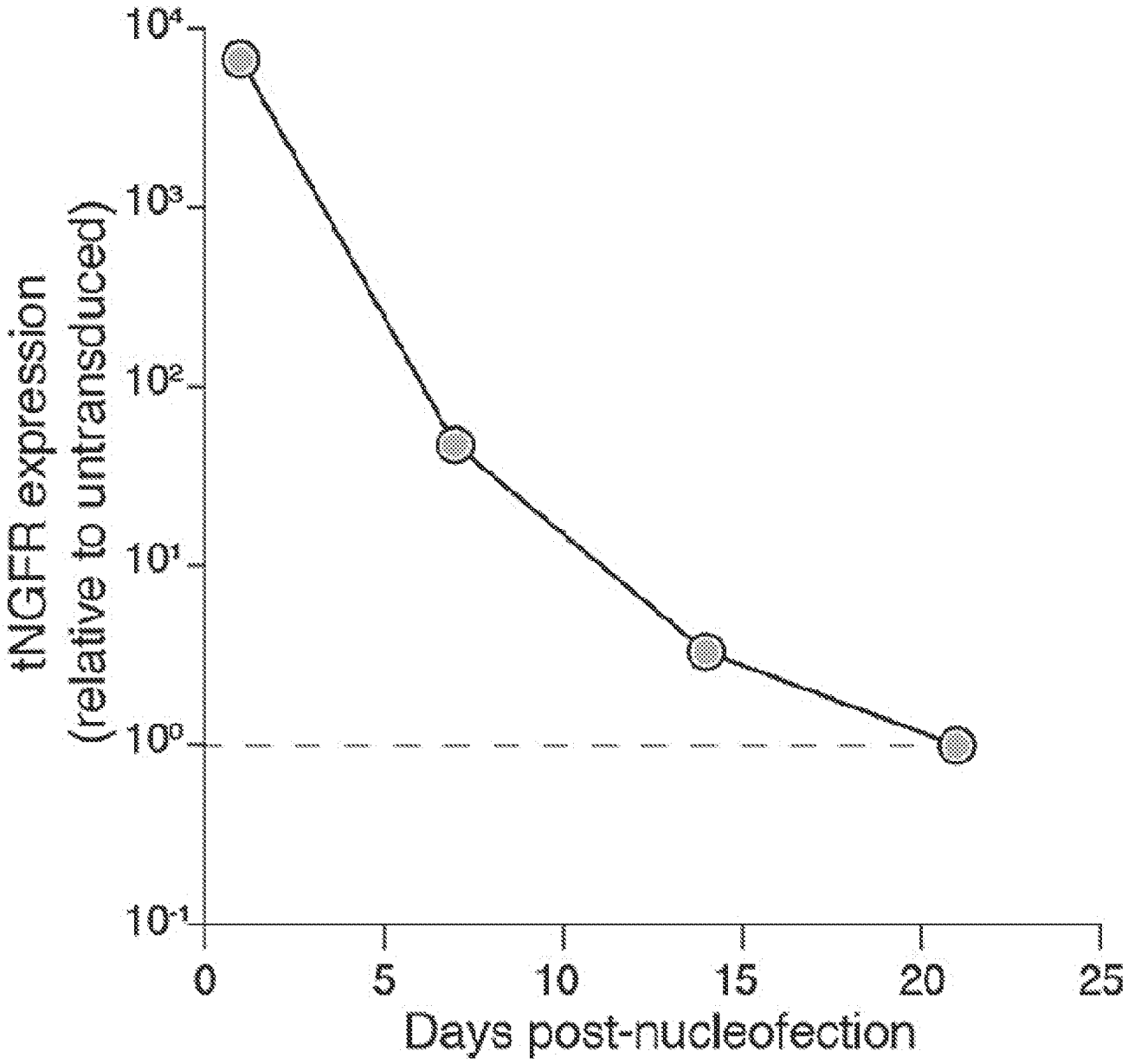

tNGFR expression
(relative to untransduced)
10⁴
10³
10²
10¹
10⁰
10⁻¹
0
5
10
15
20
25
Days post-nucleofection

FIG. 11I

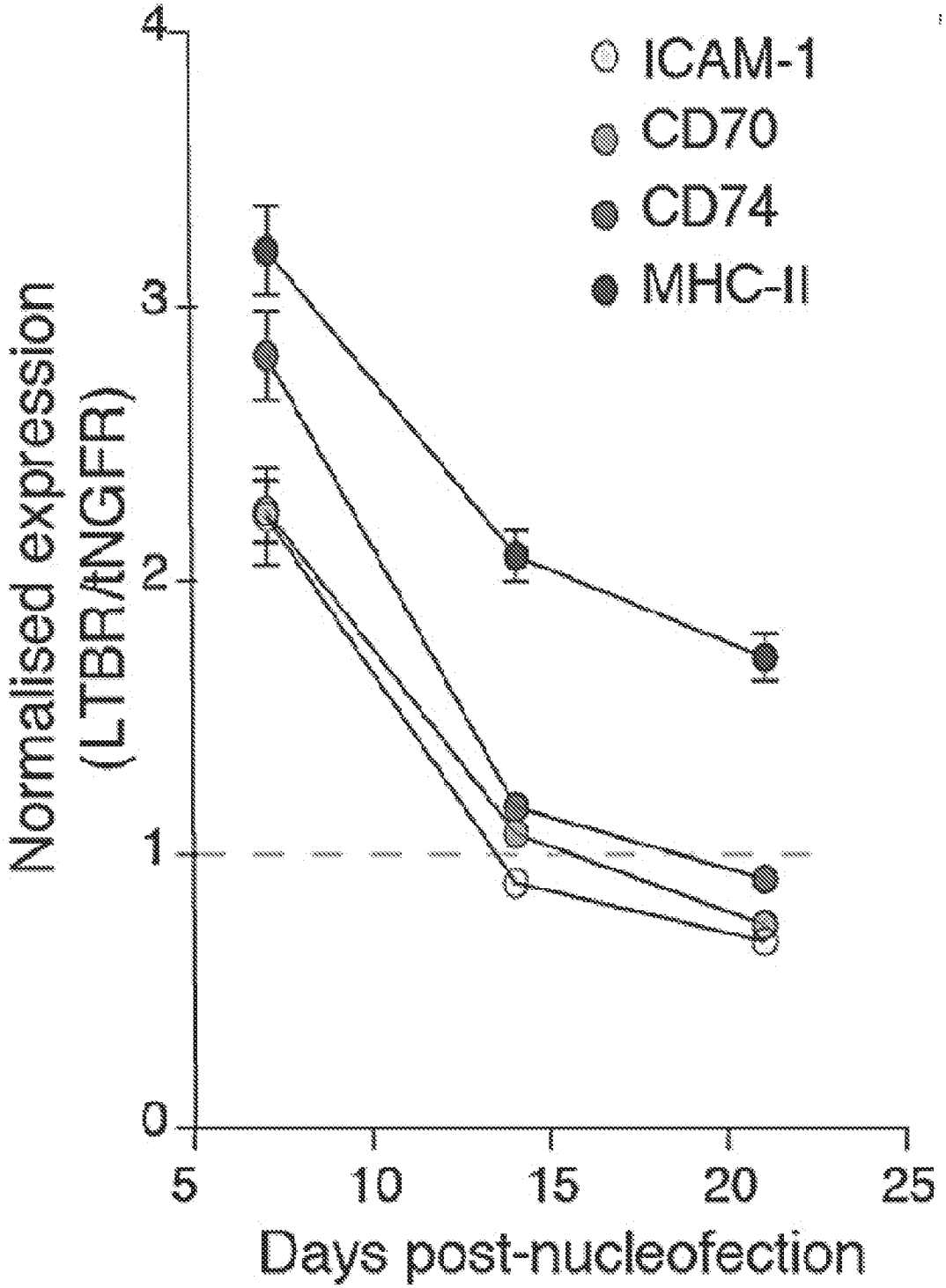

ICAM-1
CD70
CD74
MHC-II
Normalised expression
(LTBR/tNGFR)
0
1
2
3
4
5
10
15
20
25
Days post-nucleofection

FIG. 11J

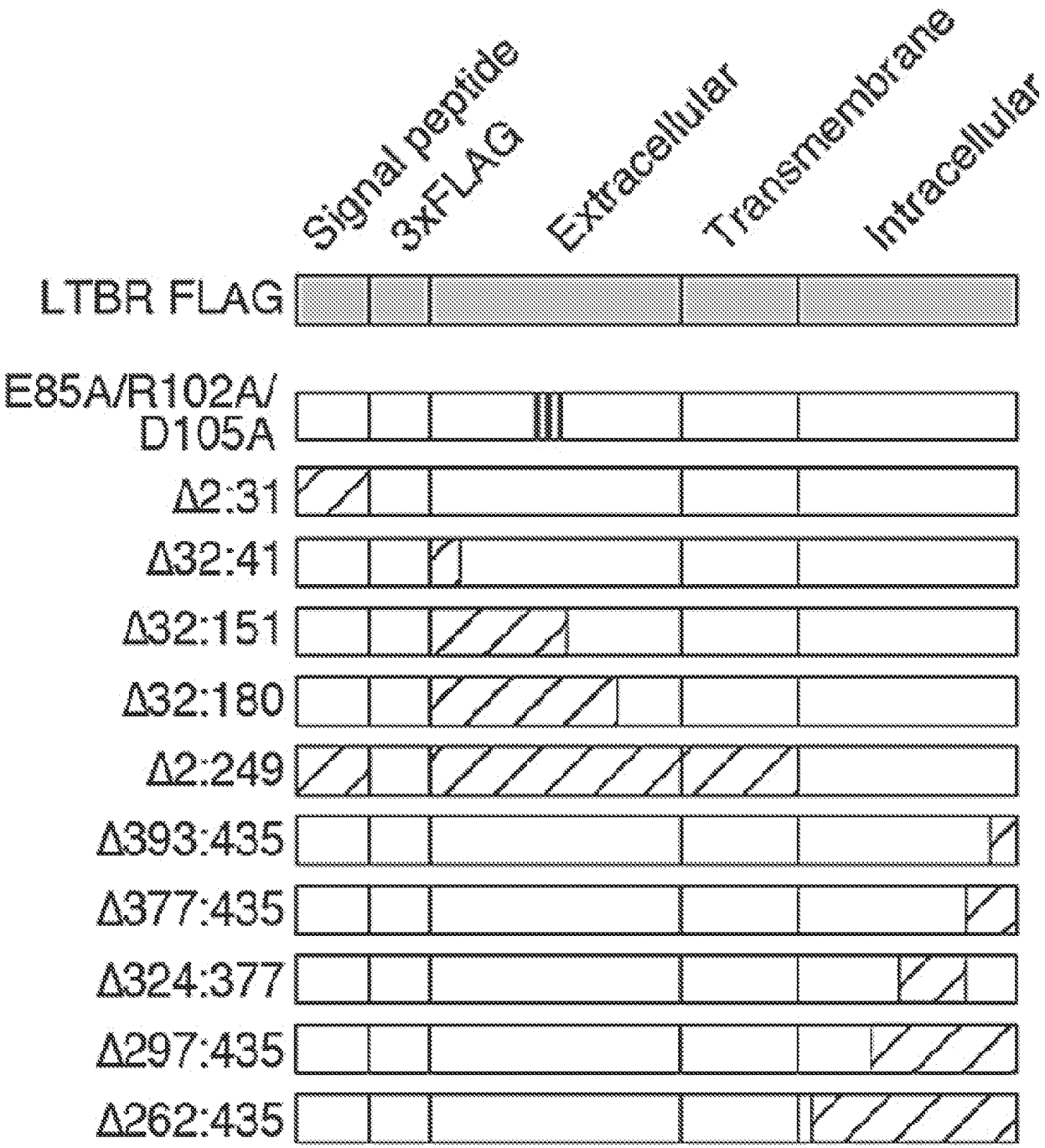
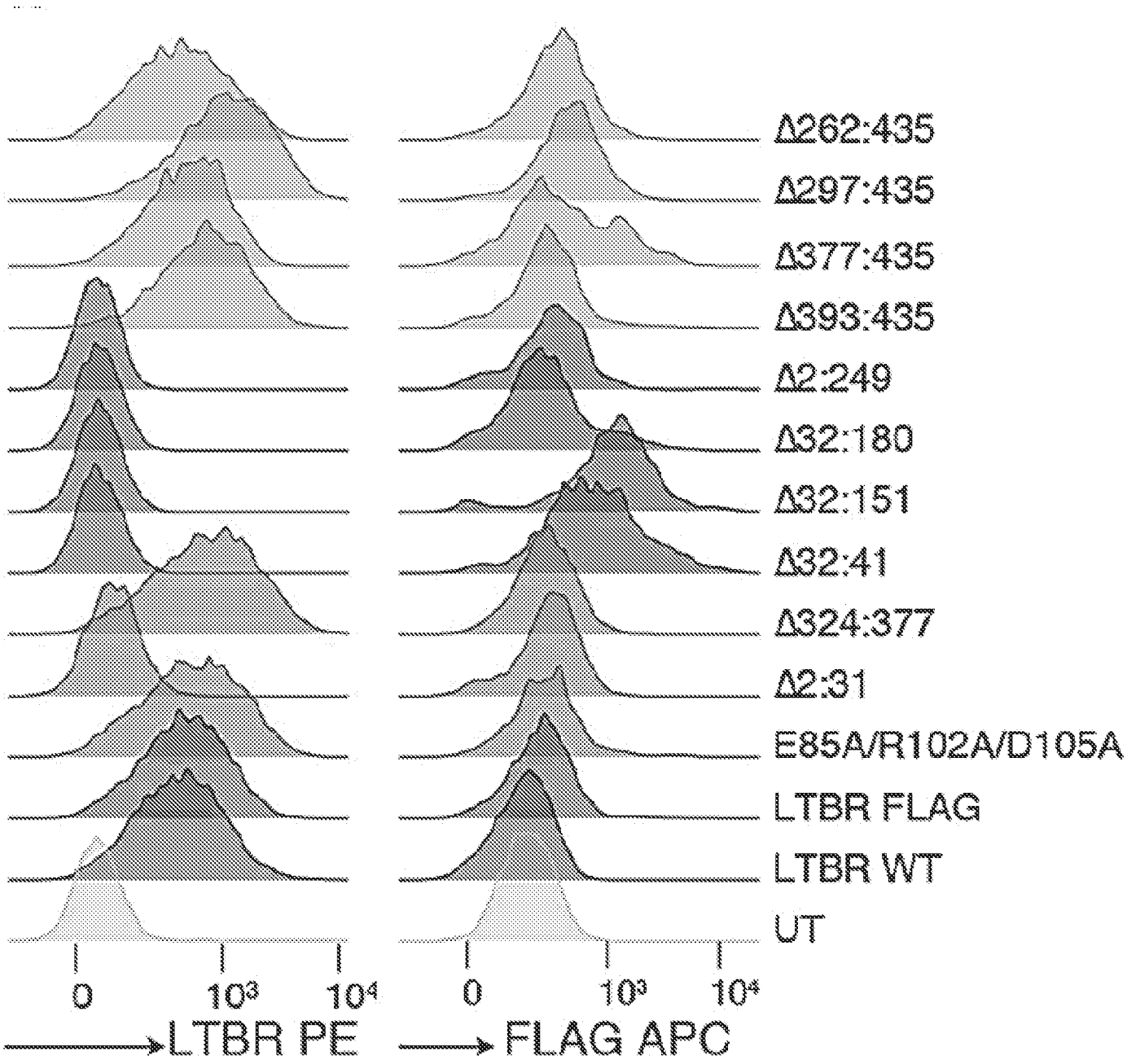

Signal peptide
3xFLAG
Extracellular
Transmembrane
Intracellular
LTBR FLAG
E85A/R102A/
D105A
Δ2:31
Δ32:41
Δ32:151
Δ32:180
Δ2:249
Δ393:435
Δ377:435
Δ324:377
Δ297:435
Δ262:435

FIG. 11K


Δ262:435
Δ297:435
Δ377:435
Δ393:435
Δ2:249
Δ32:180
Δ32:151
Δ32:41
Δ324:377
Δ2:31
E85A/R102A/D105A
LTBR FLAG
LTBR WT
UT
0
10³
10⁴
LTBR PE
0
10³
10⁴
FLAG APC

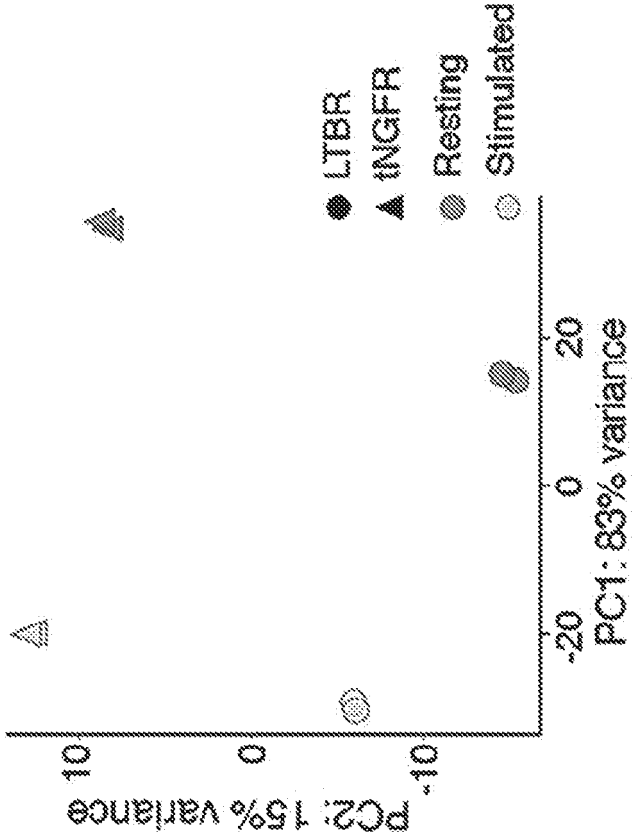


FIG. 12A

FIG. 12B

FIG. 12C

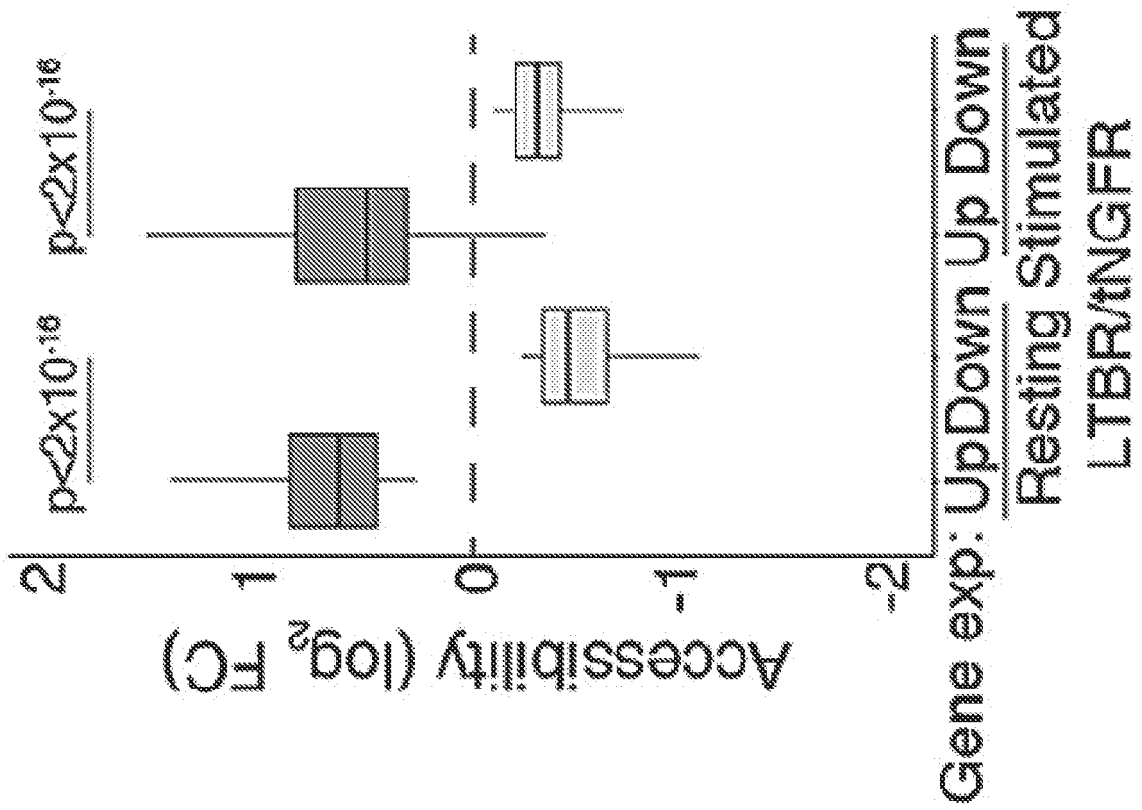


FIG. 12D

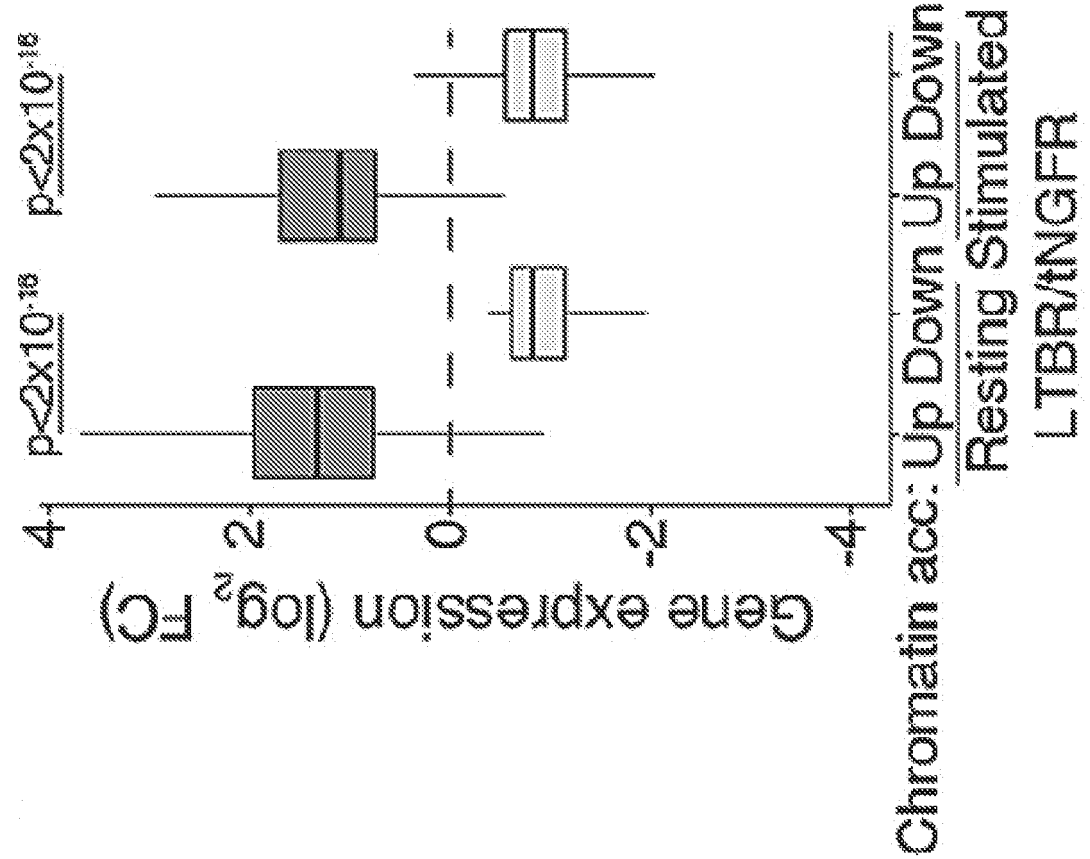


FIG. 12E

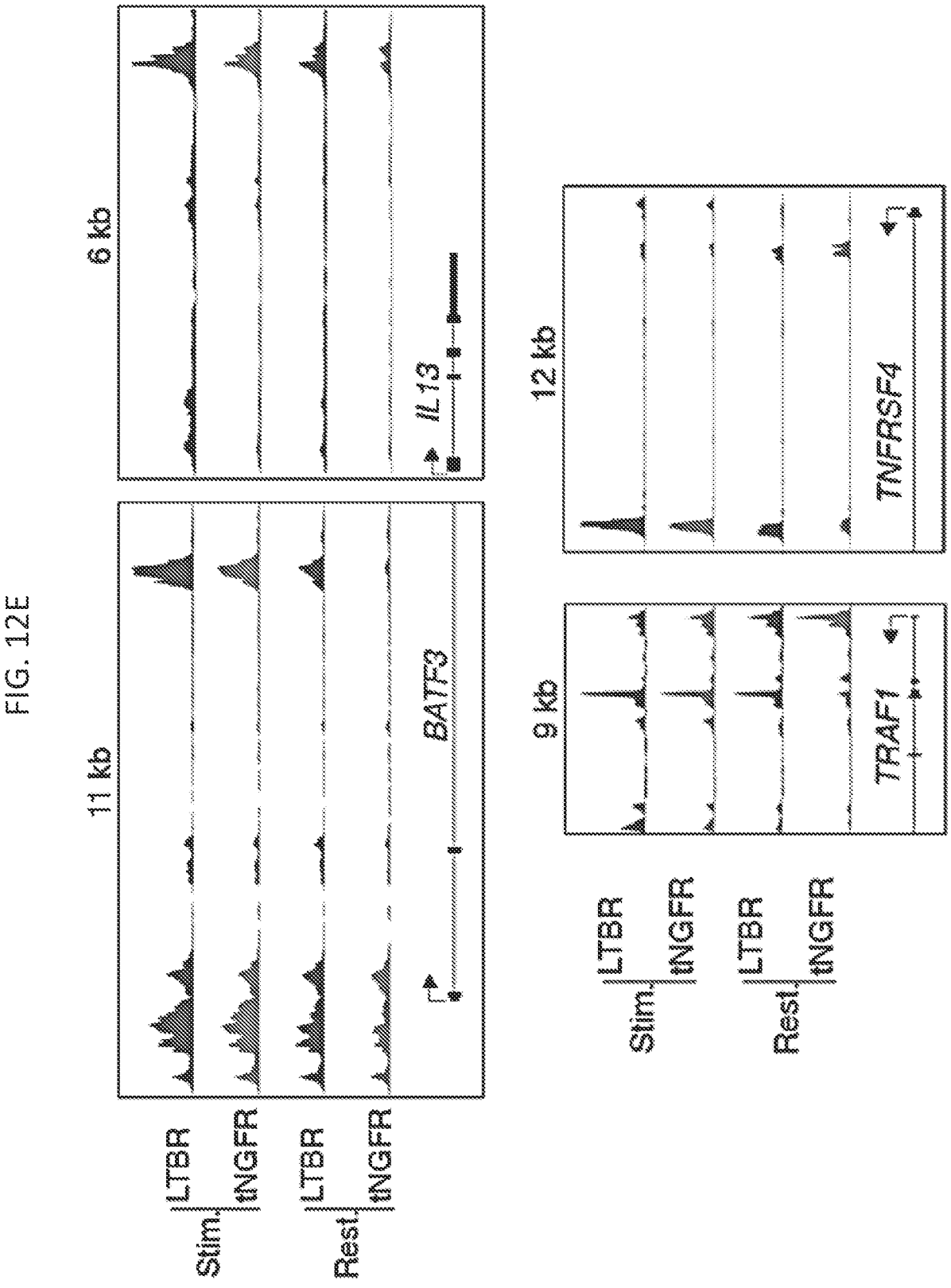

11 kb
BATF3
6 kb
IL13
9 kb
TRAF1
12 kb
TNFRSF4
Stim.
LTBR
tNGFR
Rest.
LTBR
tNGFR

FIG. 12F

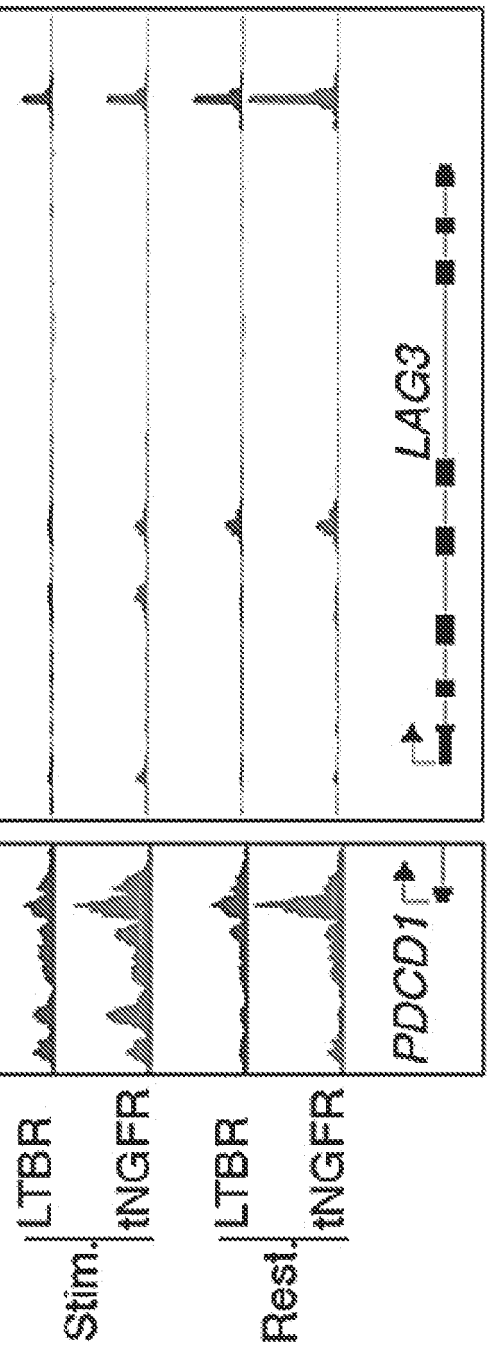


FIG. 12G

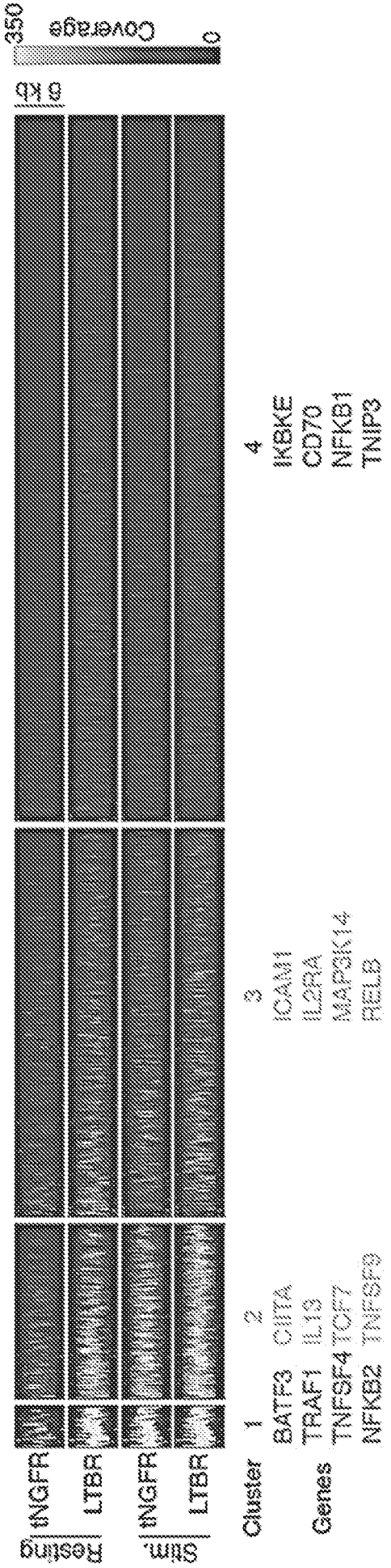


FIG. 12I

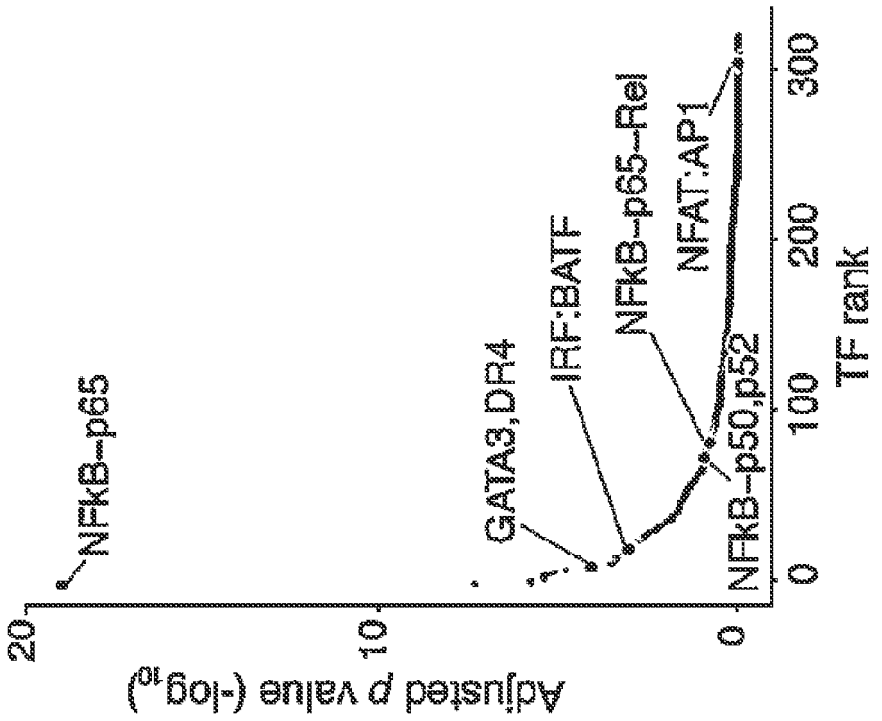


FIG. 12H

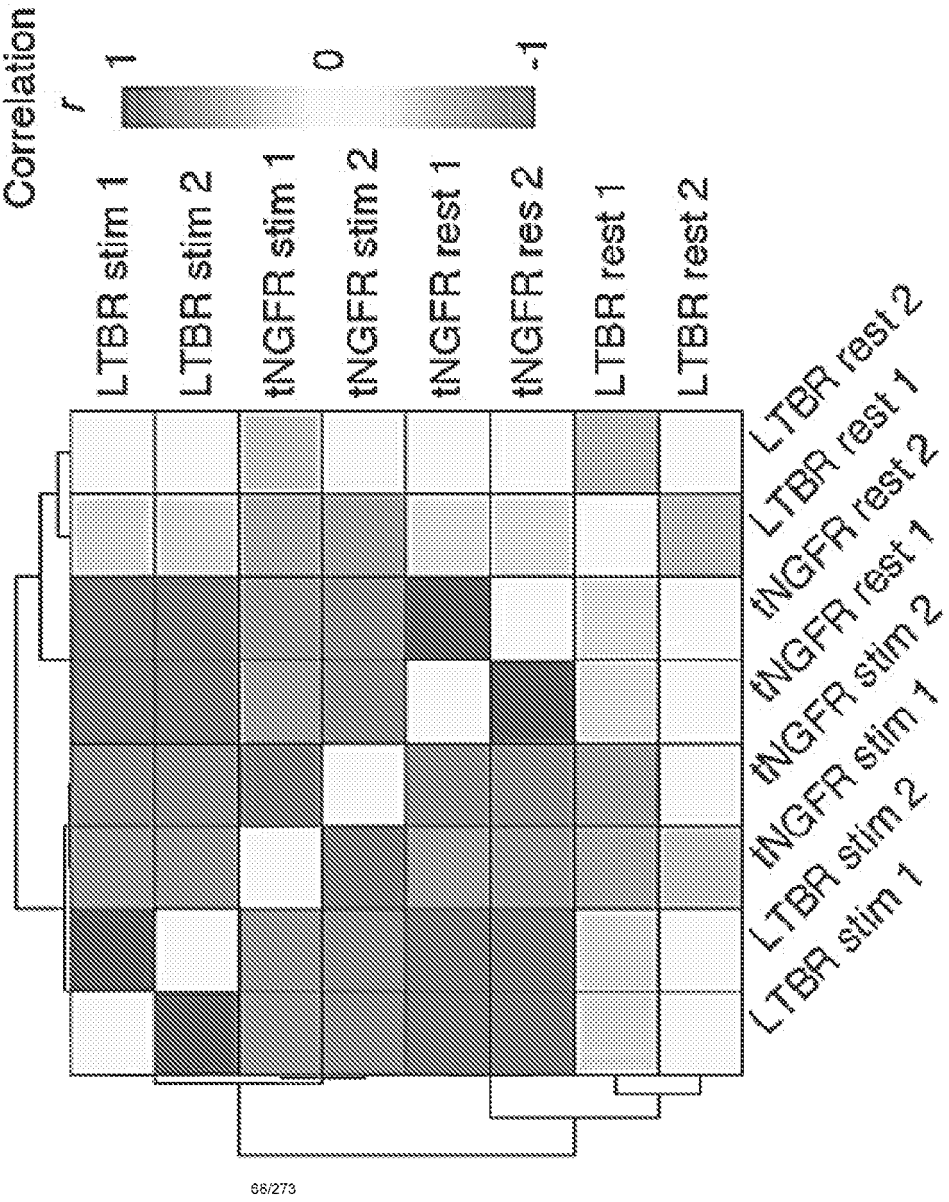


FIG. 13A

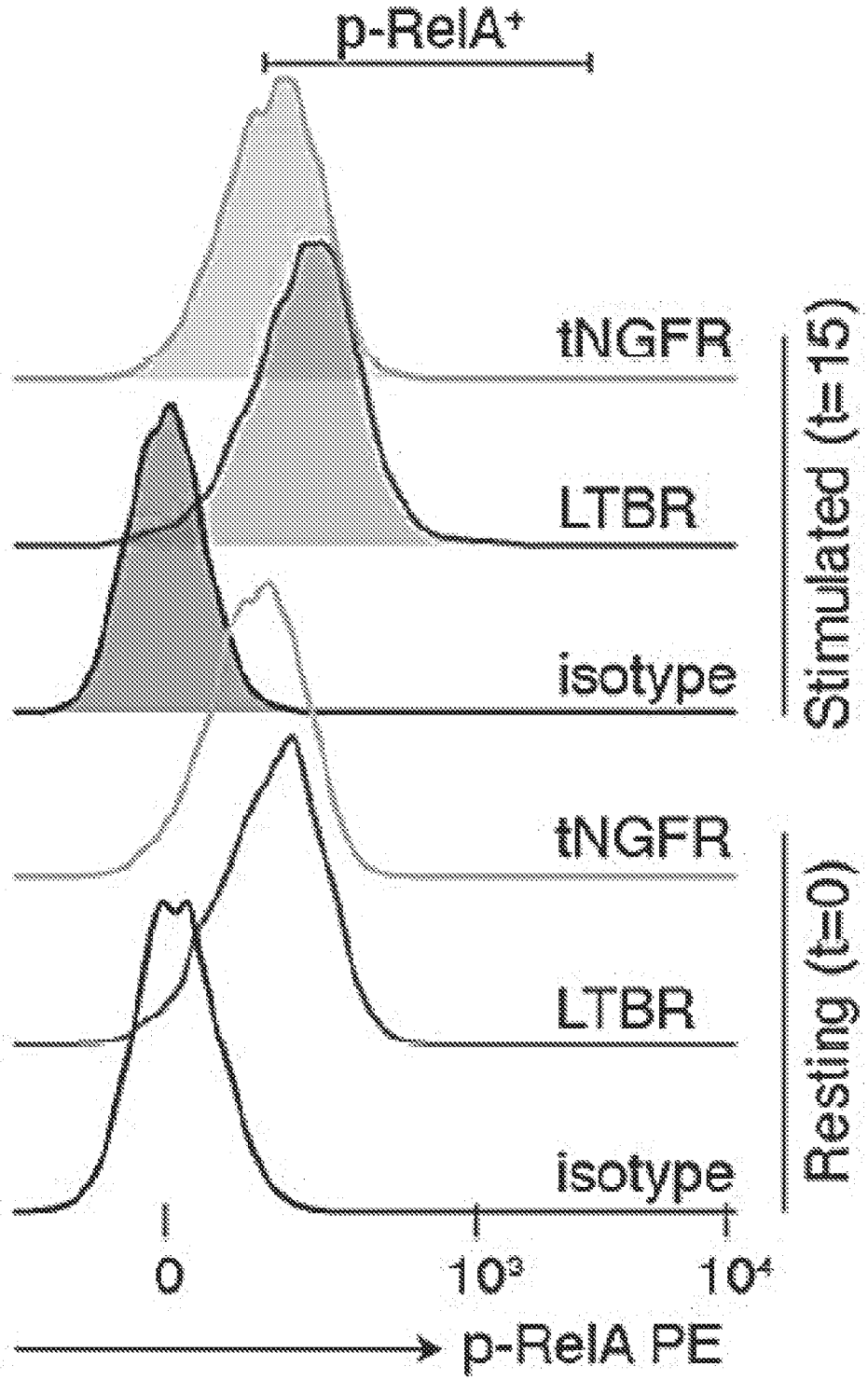

p-RelA+
tNGFR
LTBR
isotype
tNGFR
LTBR
isotype
Stimulated (t=15)
Resting (t=0)
0
10³
10⁴
p-RelA PE

FIG. 13B

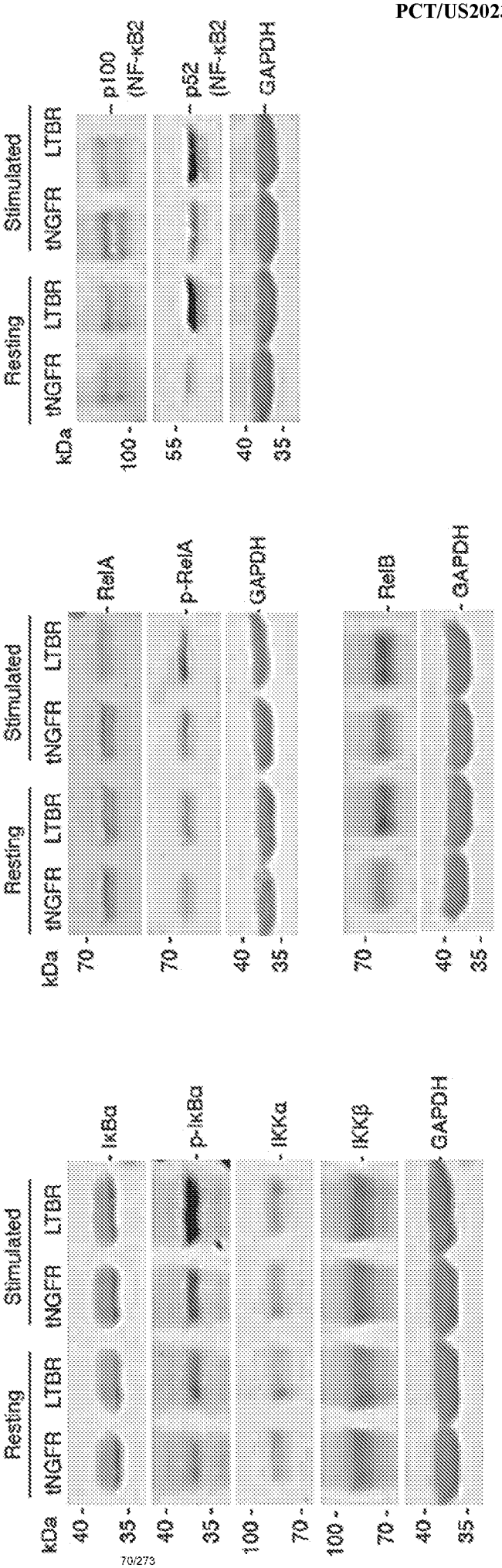
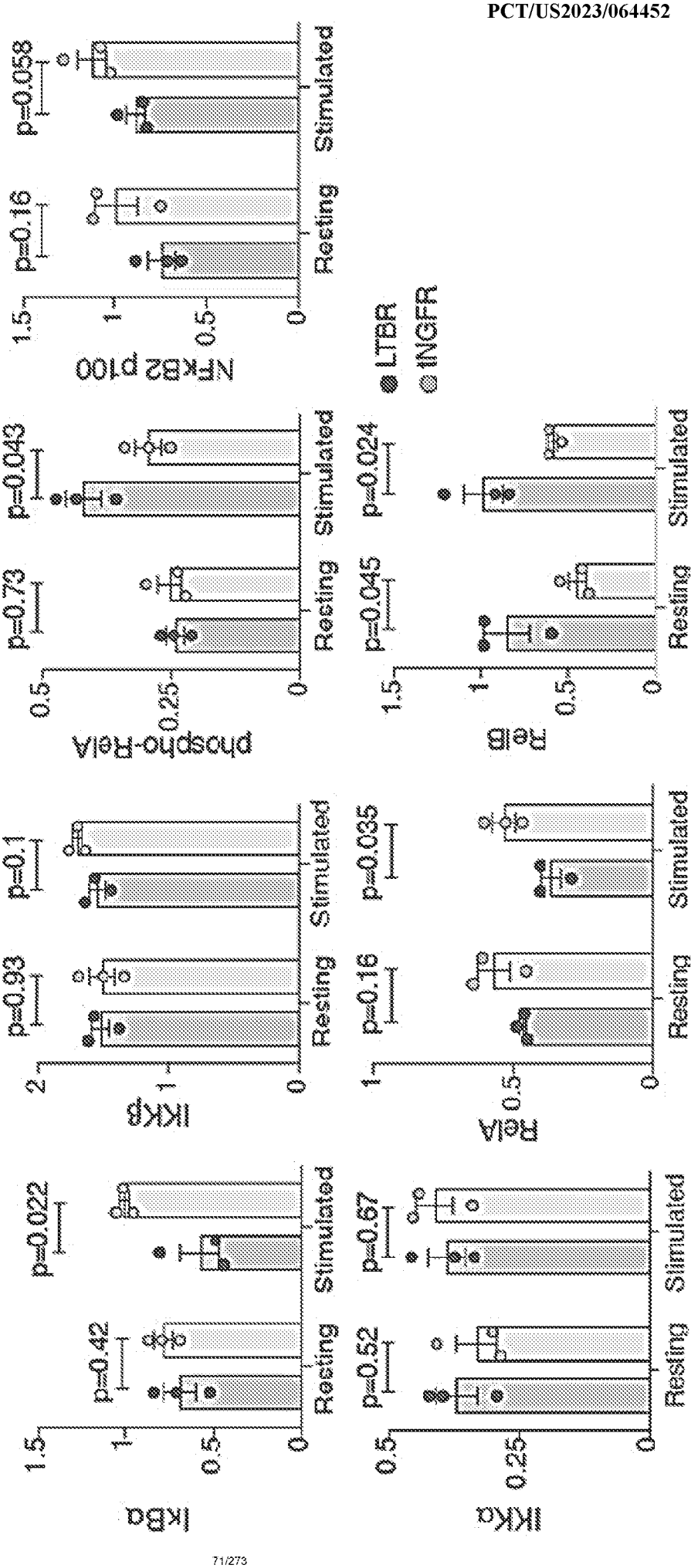

Resting
Stimulated
tNGFR
LTBR
kDa
IκBα
p-IκBα
IKKα
IKKβ
GAPDH
RelA
p-RelA
RelB
p100
(NF-κB2
p52
(NF-κB2

FIG. 13C


LTBR
INGFR
IκBα
IKKα
IKKβ
RelA
RelB
phospho-RelA
NFκB2 p100
Resting
Stimulated
p=0.022
p=0.42
p=0.52
p=0.67
p=0.1
p=0.93
p=0.035
p=0.16
p=0.024
p=0.045
p=0.043
p=0.73
p=0.058
p=0.16

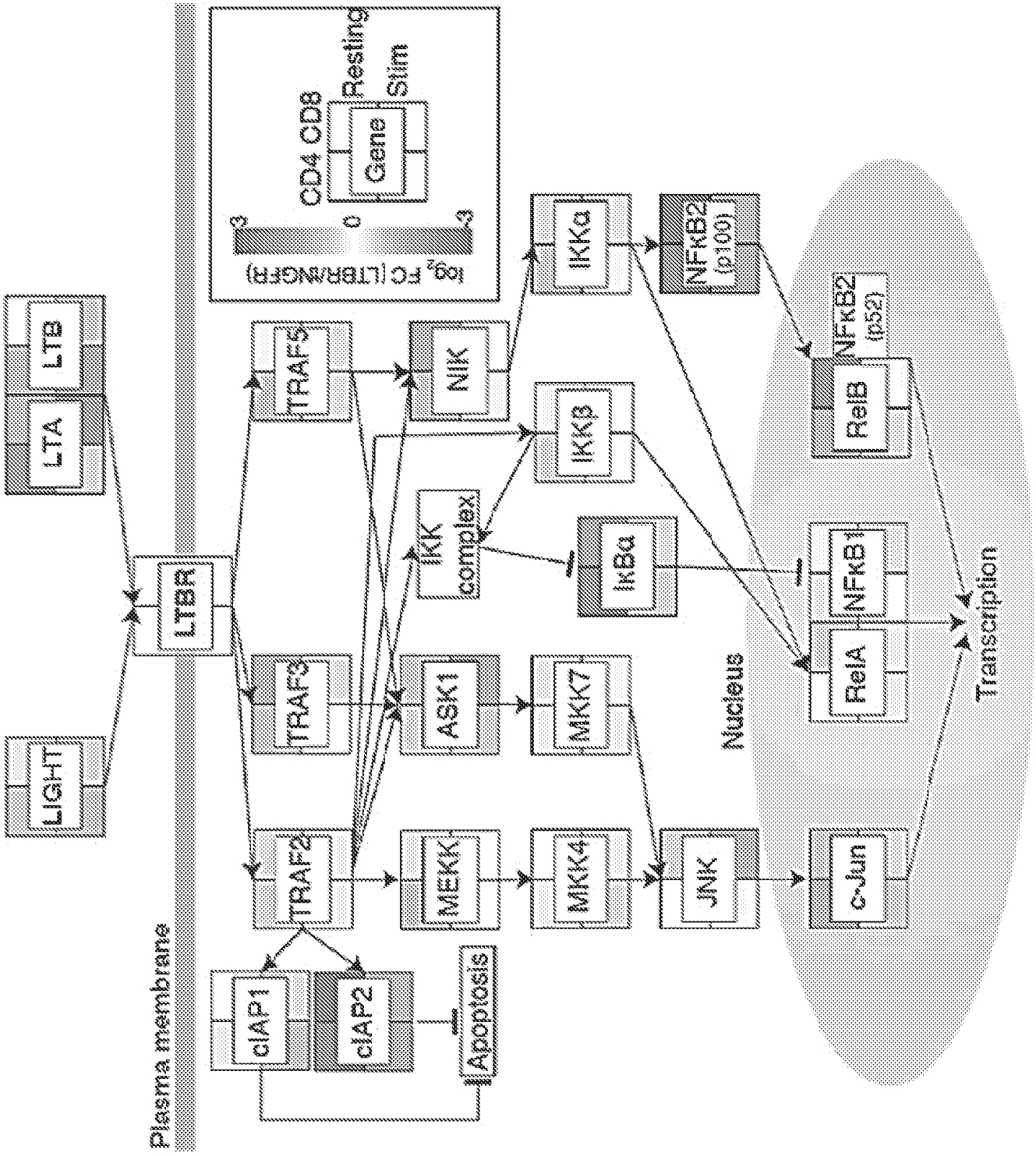

Resting
Stim
CD4 CD8
Gene
-3
0
3
log2 FC (LTBR/NGFR)
LTB
LTA
LIGHT
LTBR
TRAF5
TRAF3
TRAF2
NIK
IKK complex
IKKα
IKKβ
IκBα
ASK1
MEKK
MKK7
MKK4
JNK
NFκB2 (p100)
NFκB2 (p52)
RelB
NFκB1
RelA
c-Jun
Nucleus
Transcription
cIAP1
cIAP2
Apoptosis
Plasma membrane

FIG. 13D

FIG. 13E

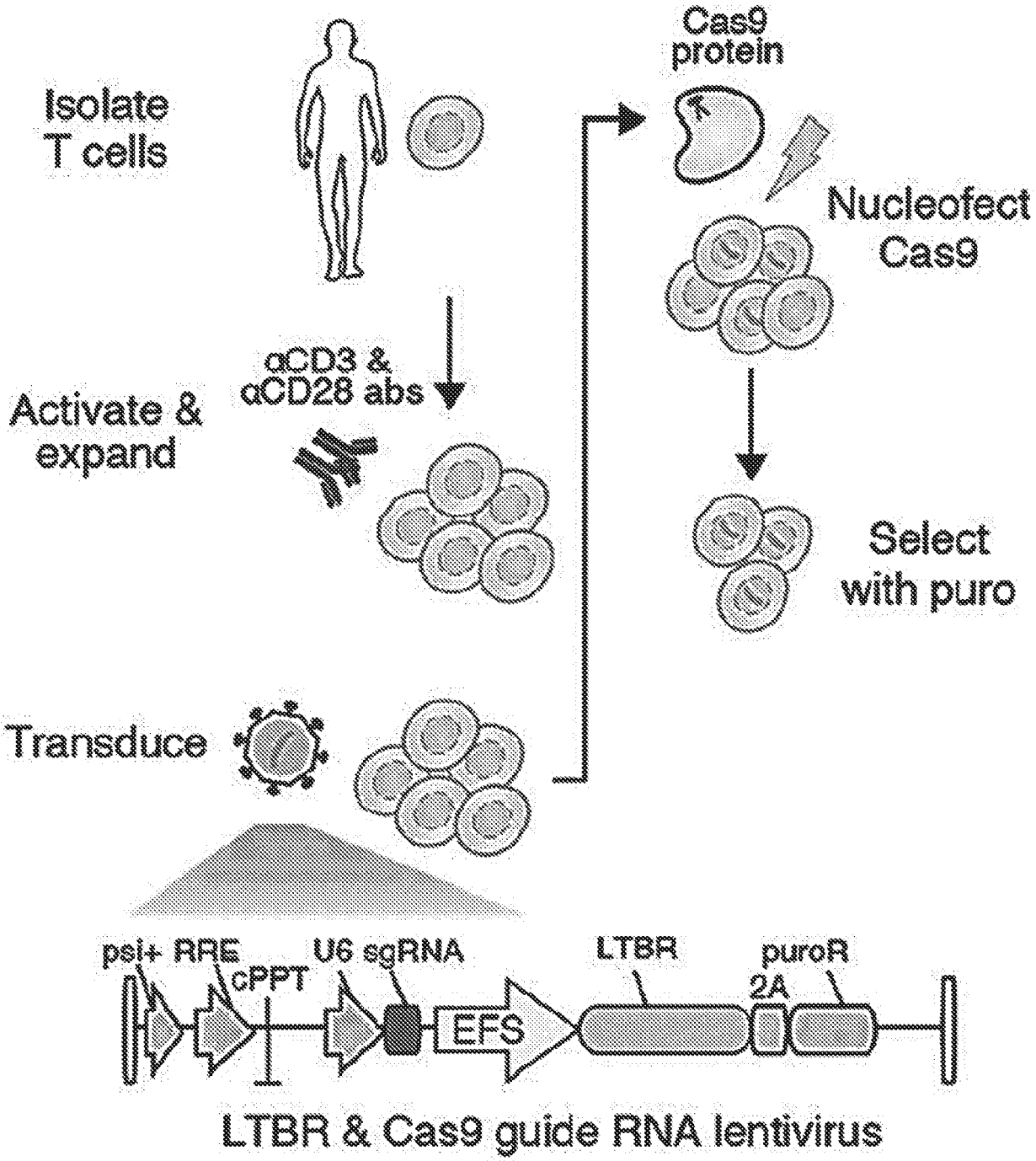

Isolate
T cells
Cas9
protein
Nucleofect
Cas9
αCD3 &
αCD28 abs
Activate &
expand
Select
with puro
Transduce
psi+
RRE
cPPT
U6 sgRNA
EFS
LTBR
puroR
2A
LTBR & Cas9 guide RNA lentivirus

FIG. 13F

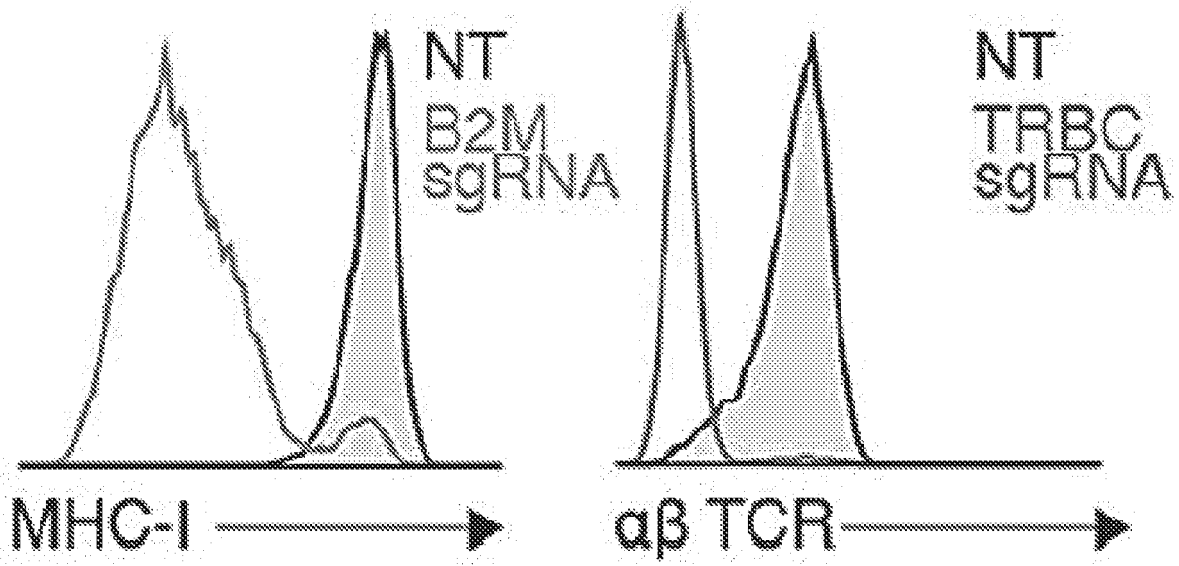


FIG. 13G

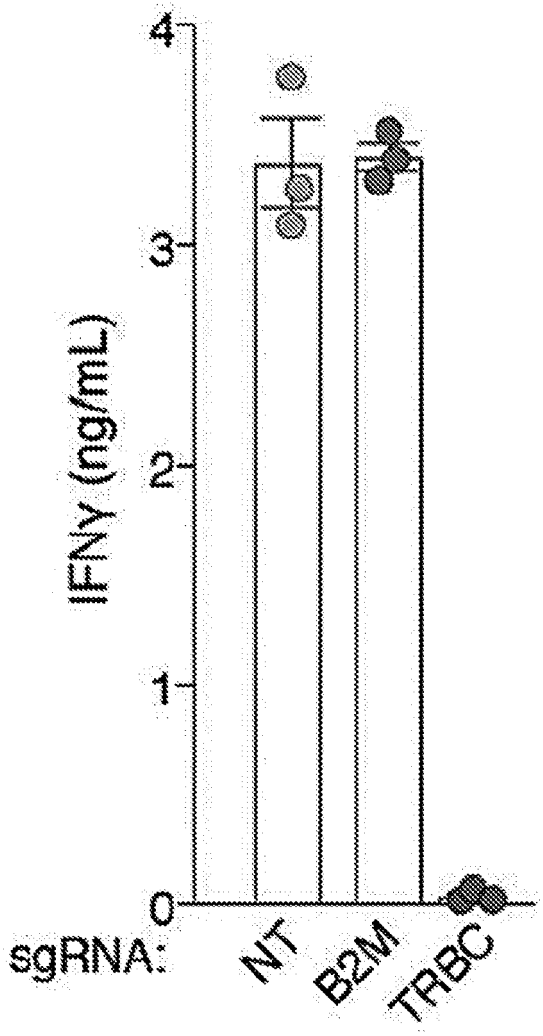


FIG. 13H

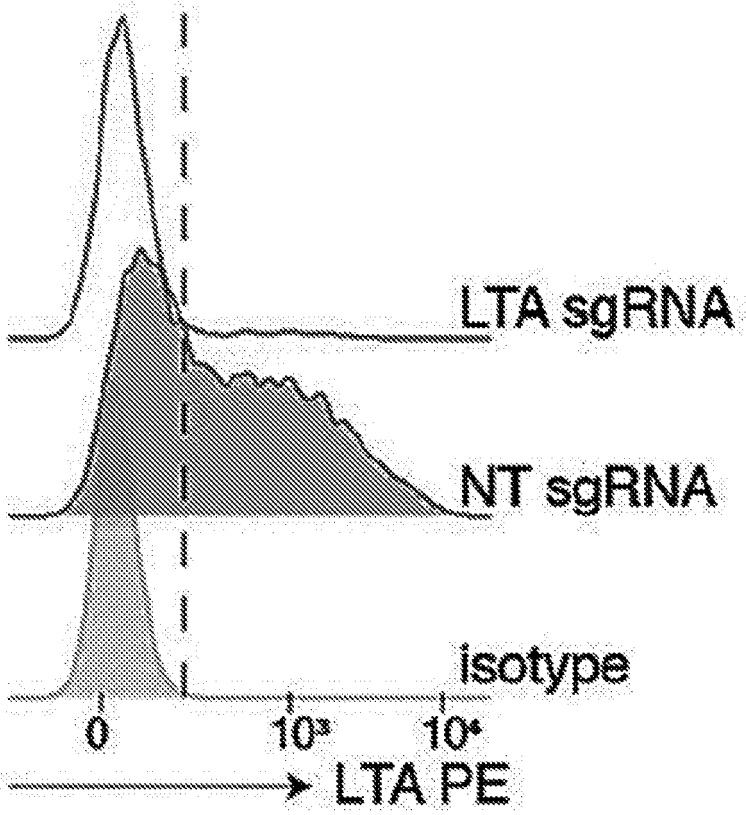


FIG. 13I

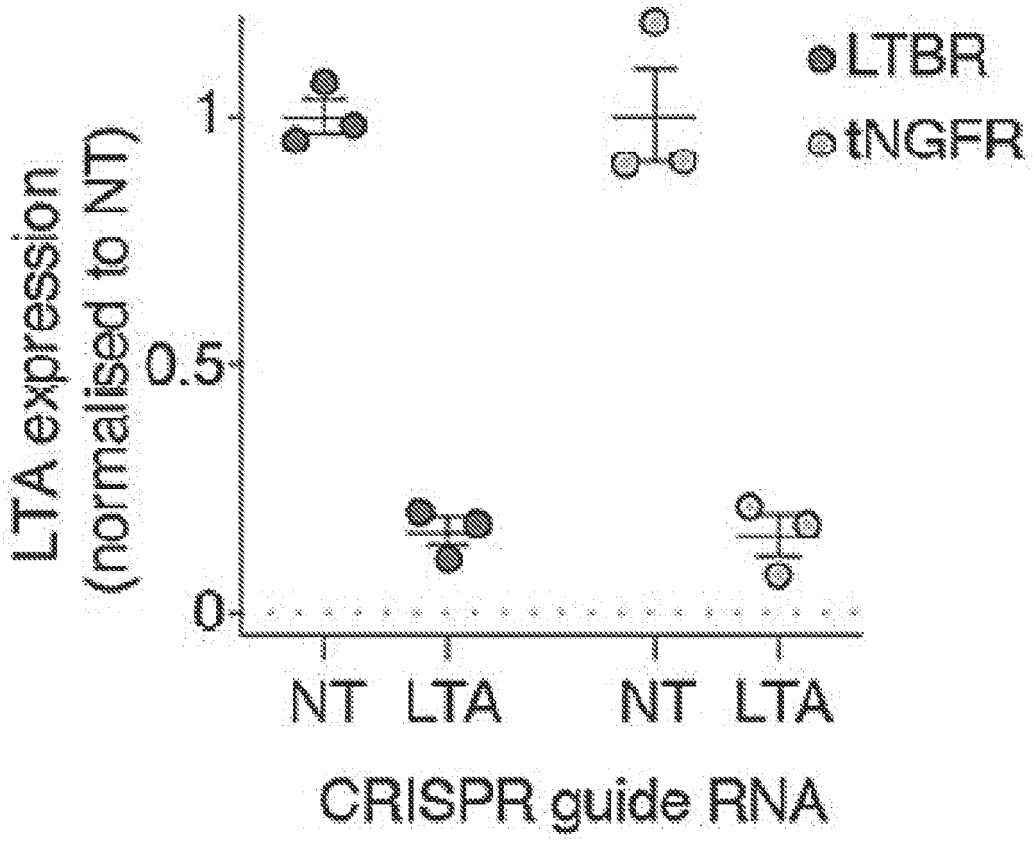


FIG. 13J

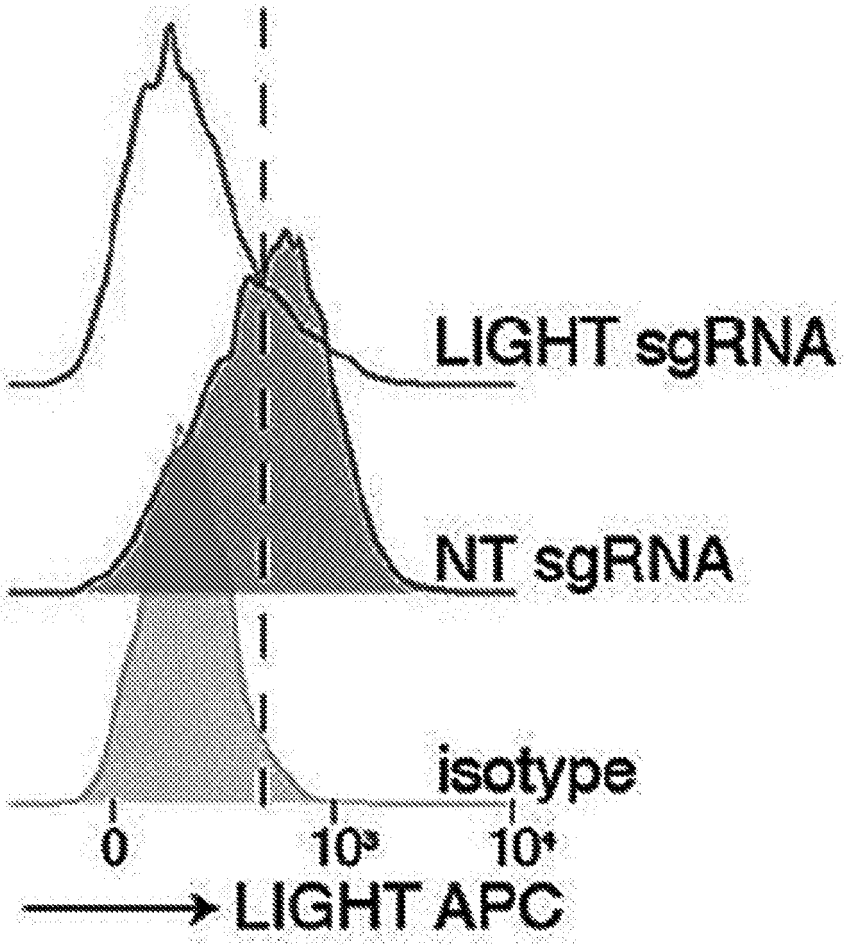


FIG. 13K

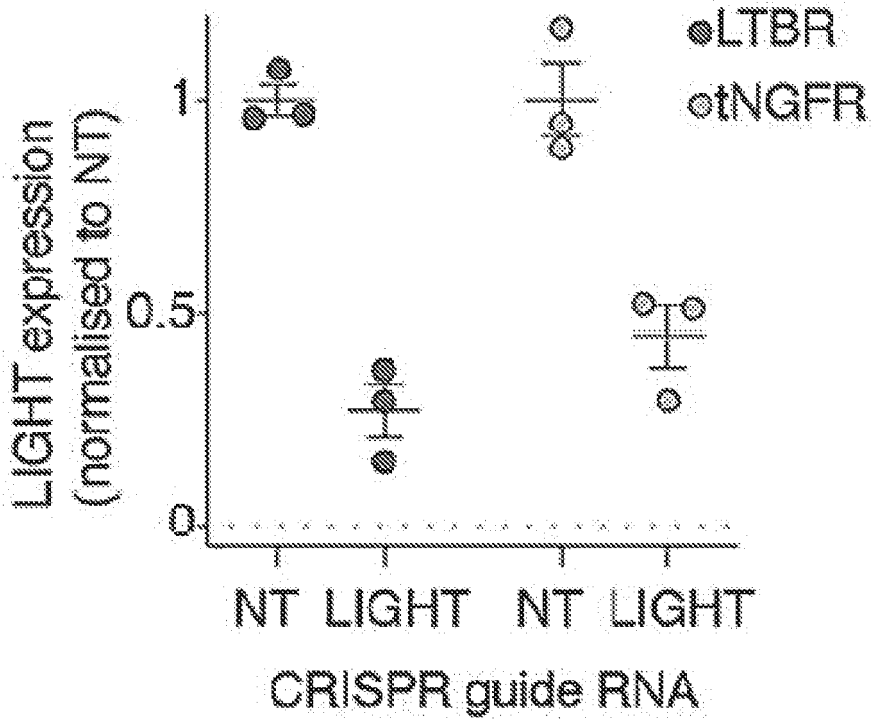


FIG. 13L

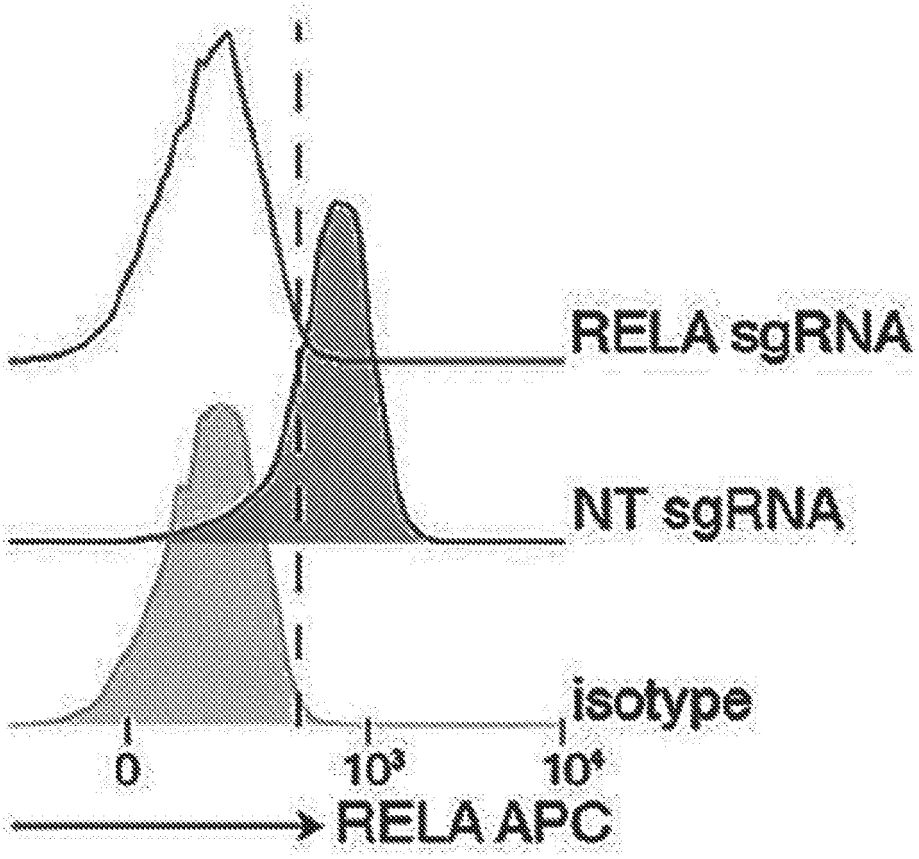


FIG. 13M

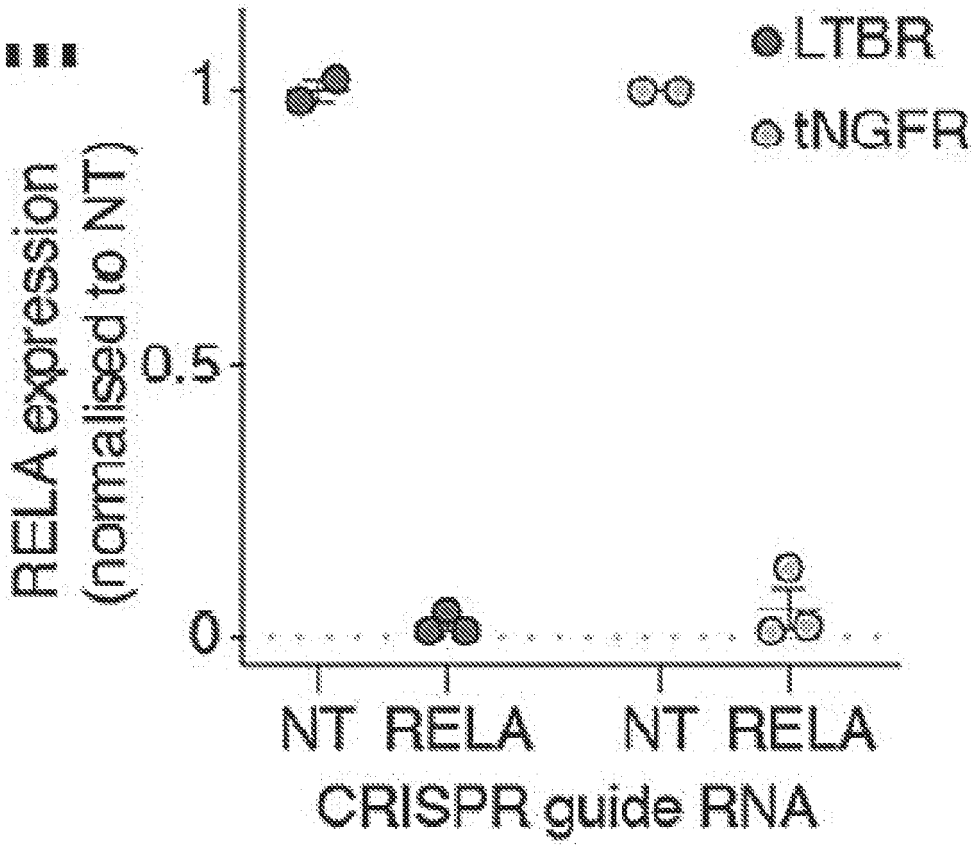


FIG. 13N

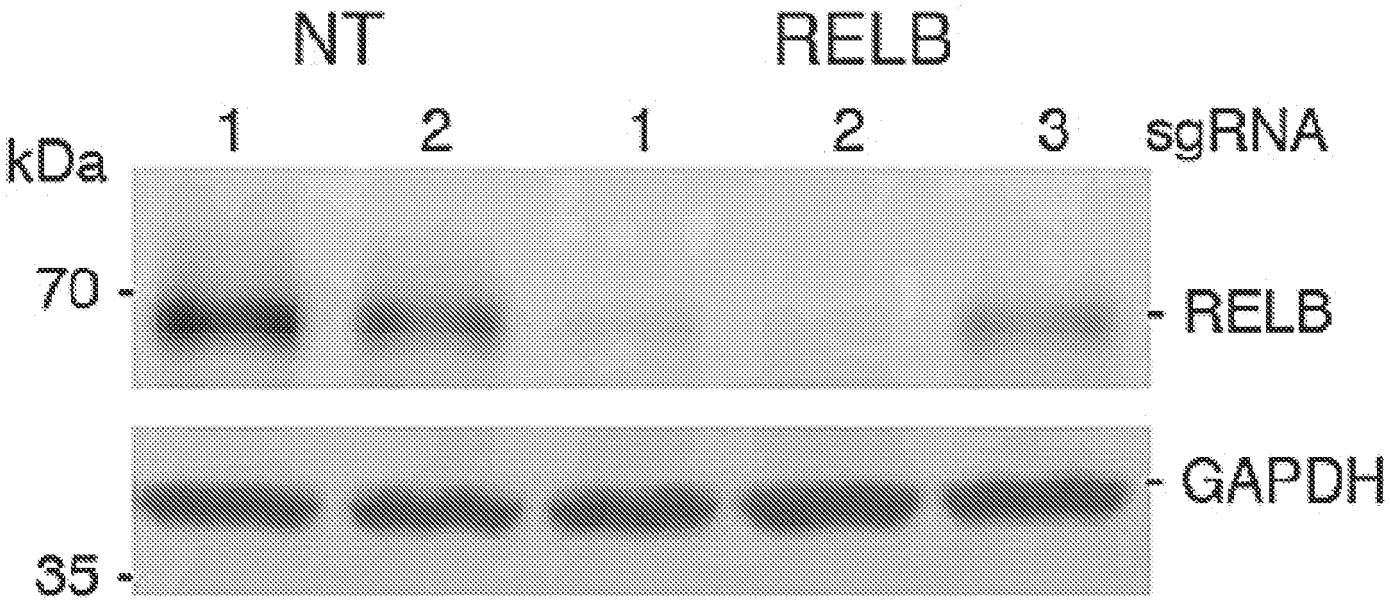


FIG. 13O

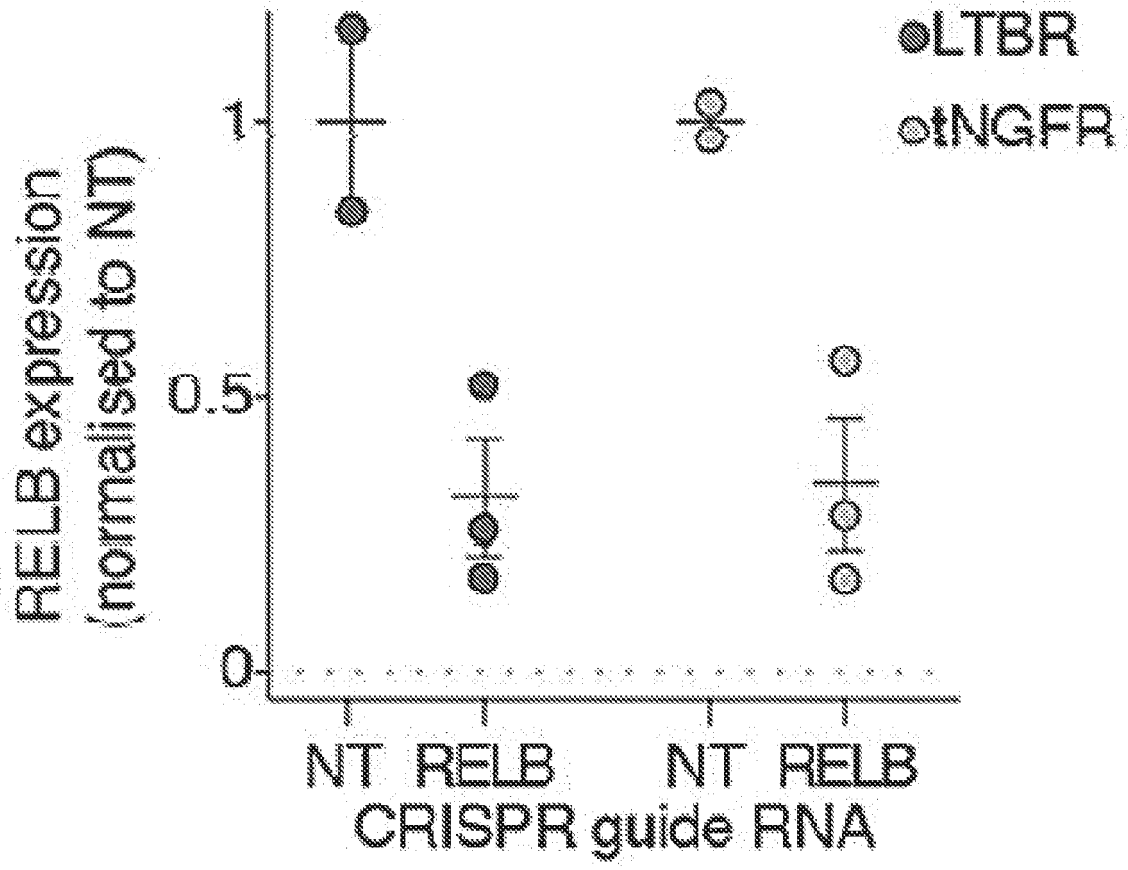


FIG. 13P

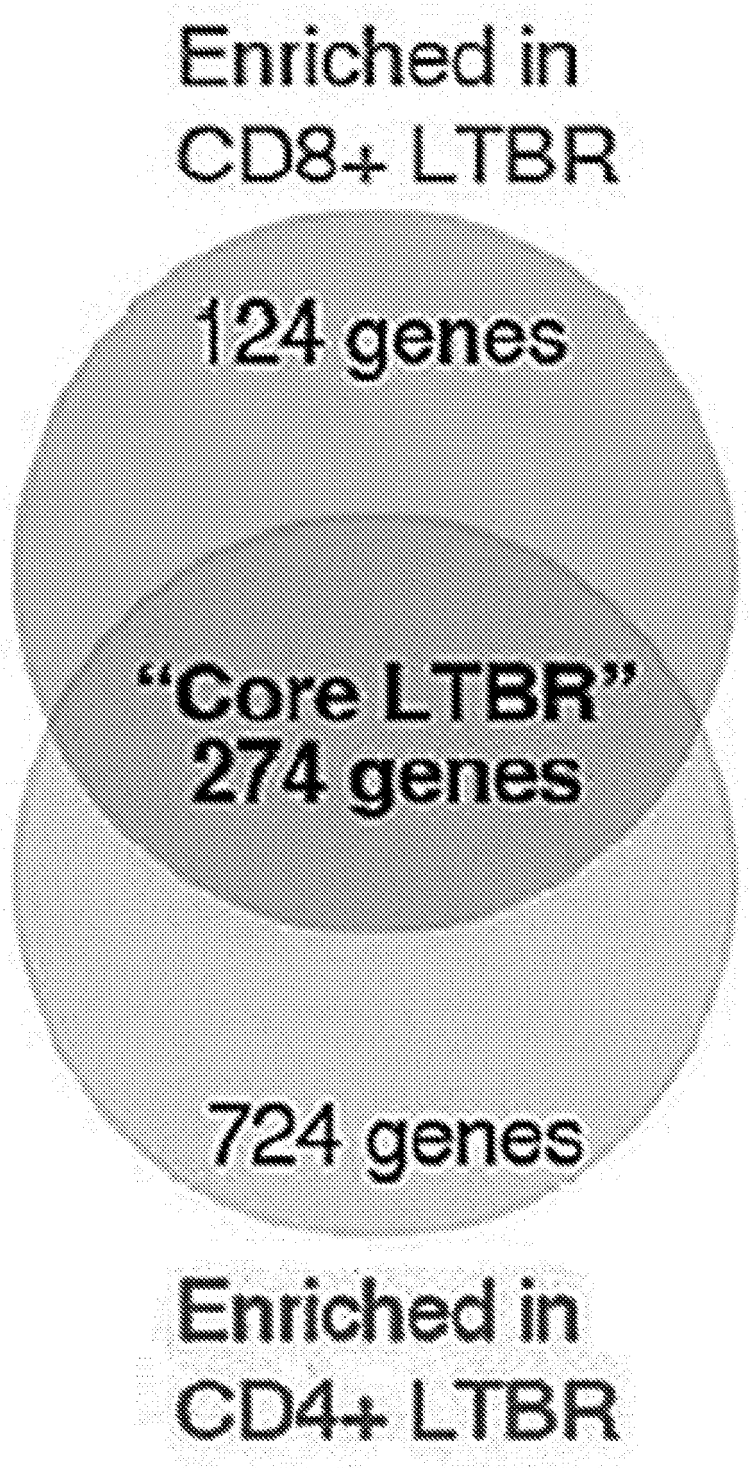

Enriched in
CD8+ LTBR
124 genes
"Core LTBR"
274 genes
724 genes
Enriched in
CD4+ LTBR

FIG. 14B

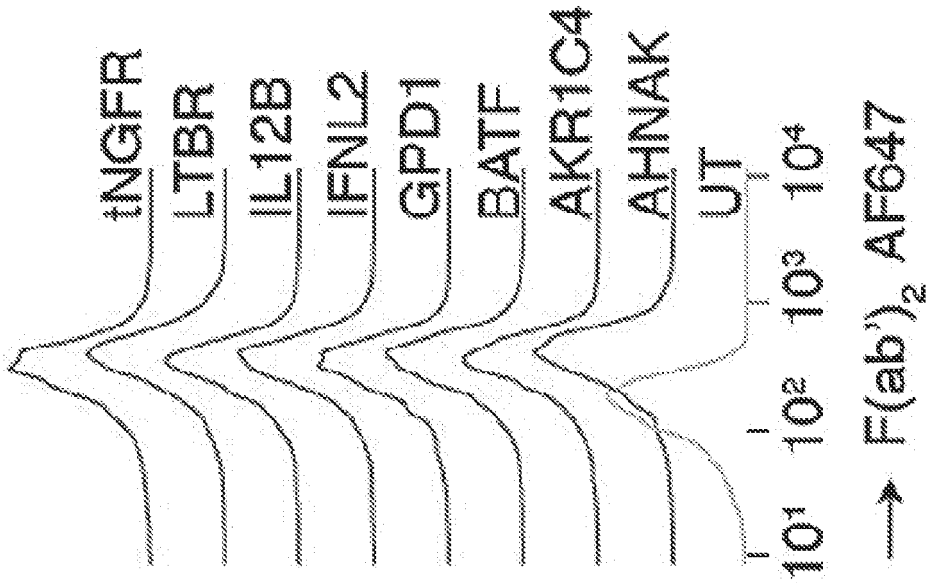


FIG. 14A

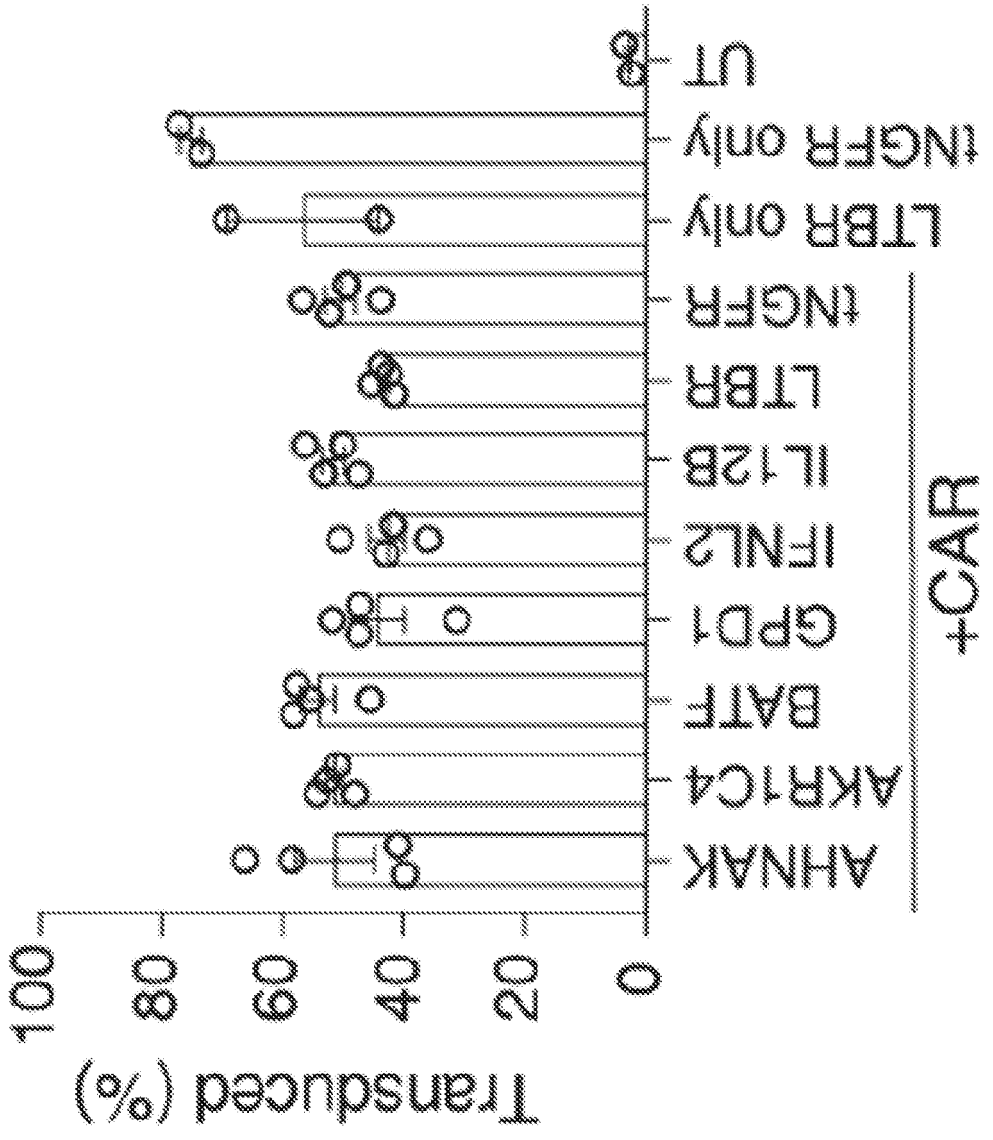


FIG. 14C

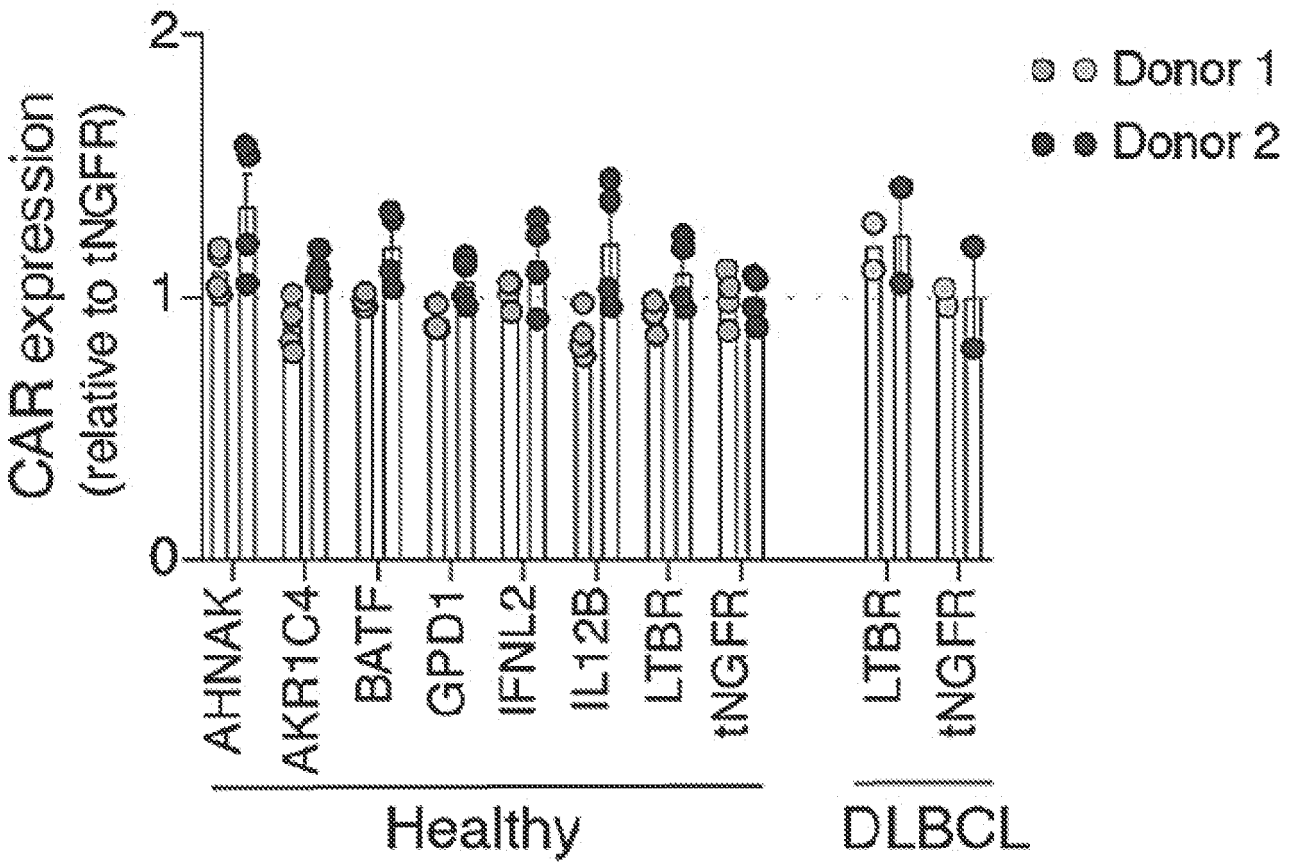


FIG. 14D

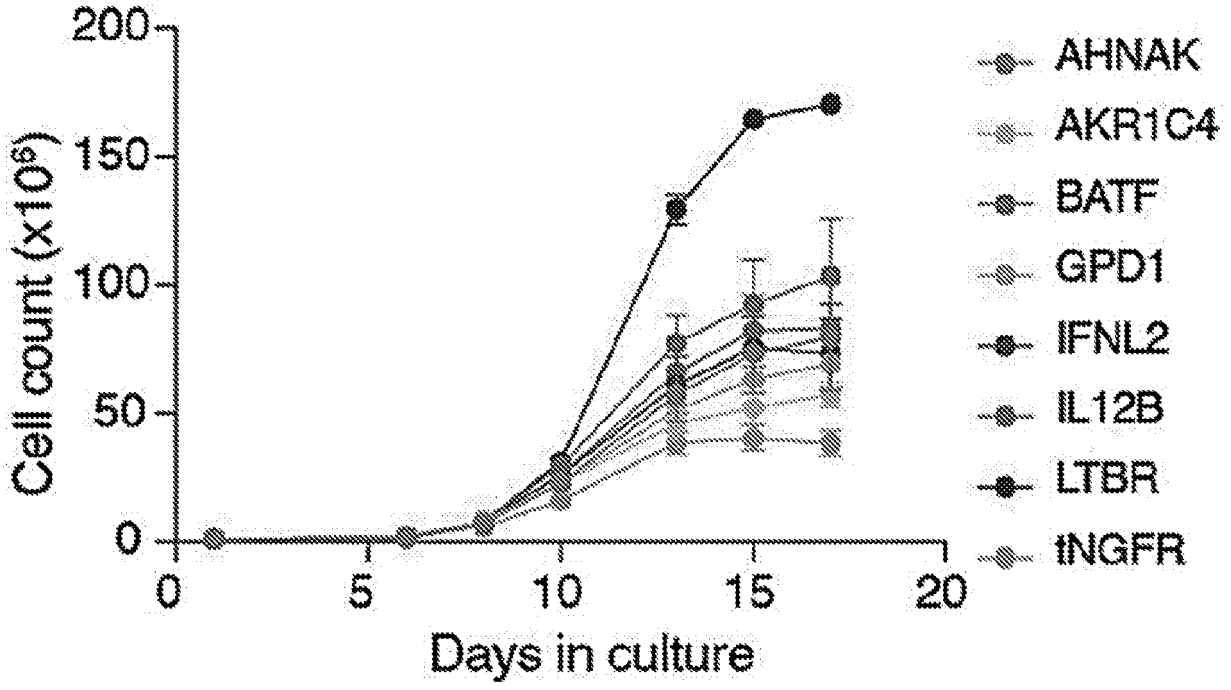


FIG. 14E

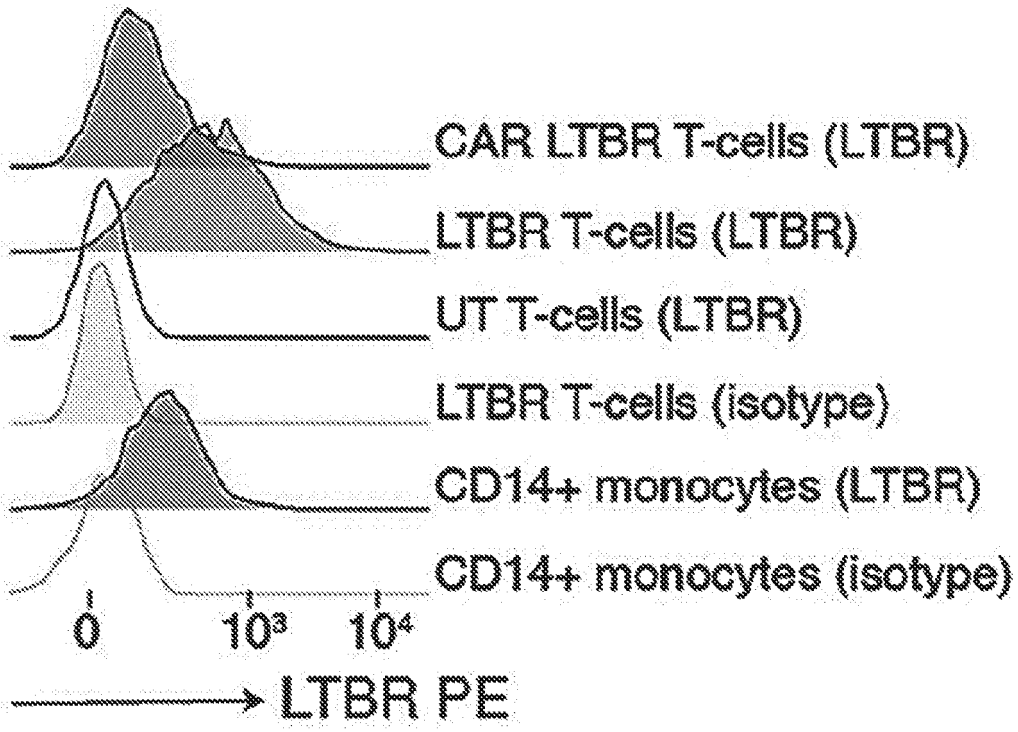


FIG. 14F

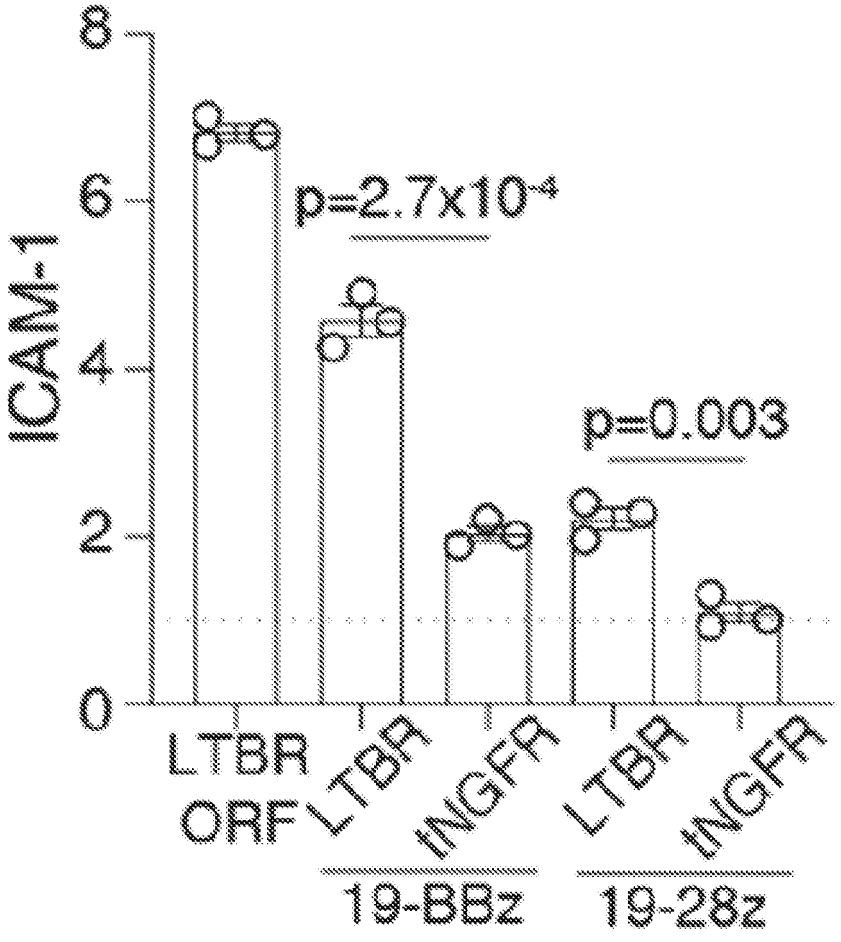


FIG. 14H

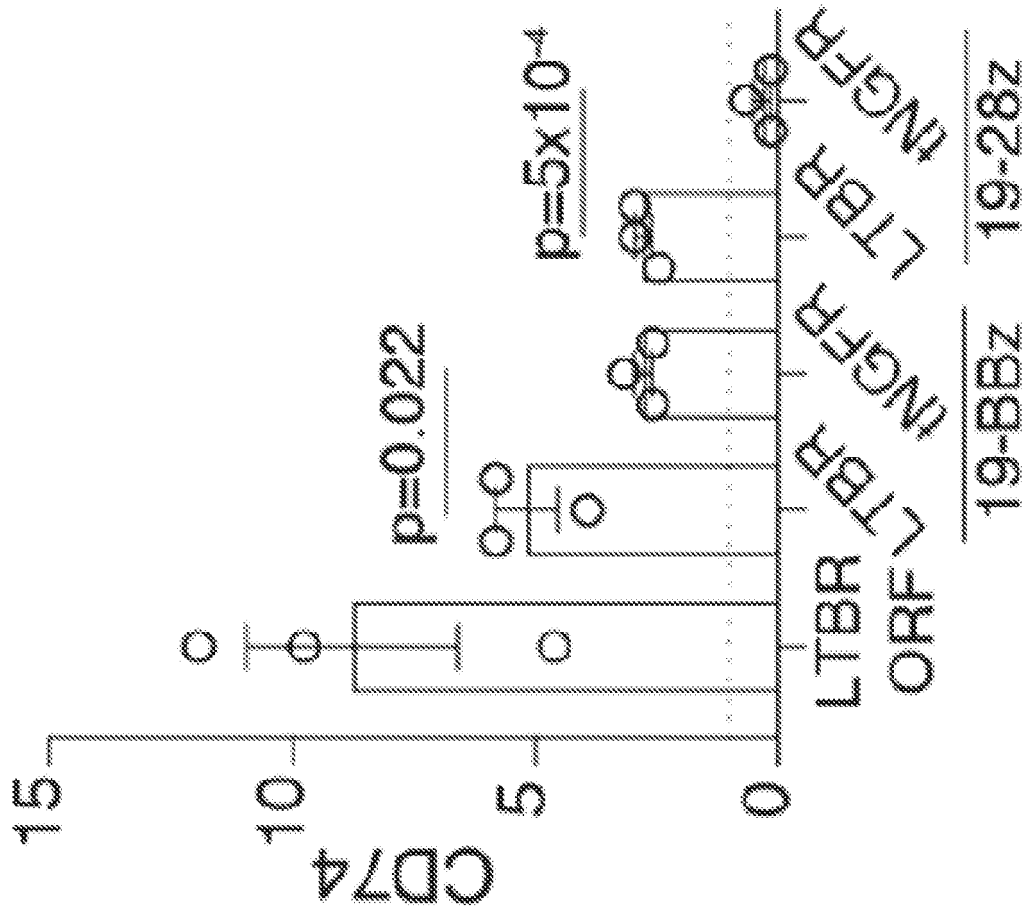


FIG. 14G

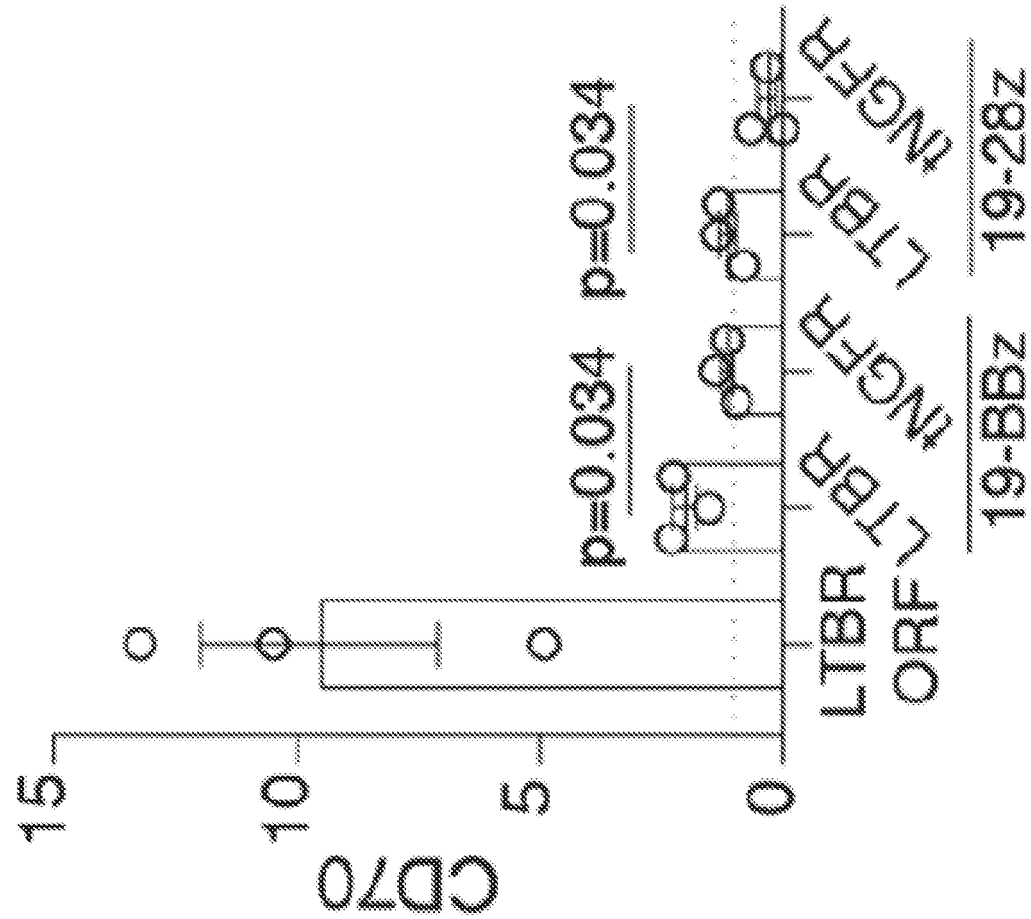


FIG. 14I

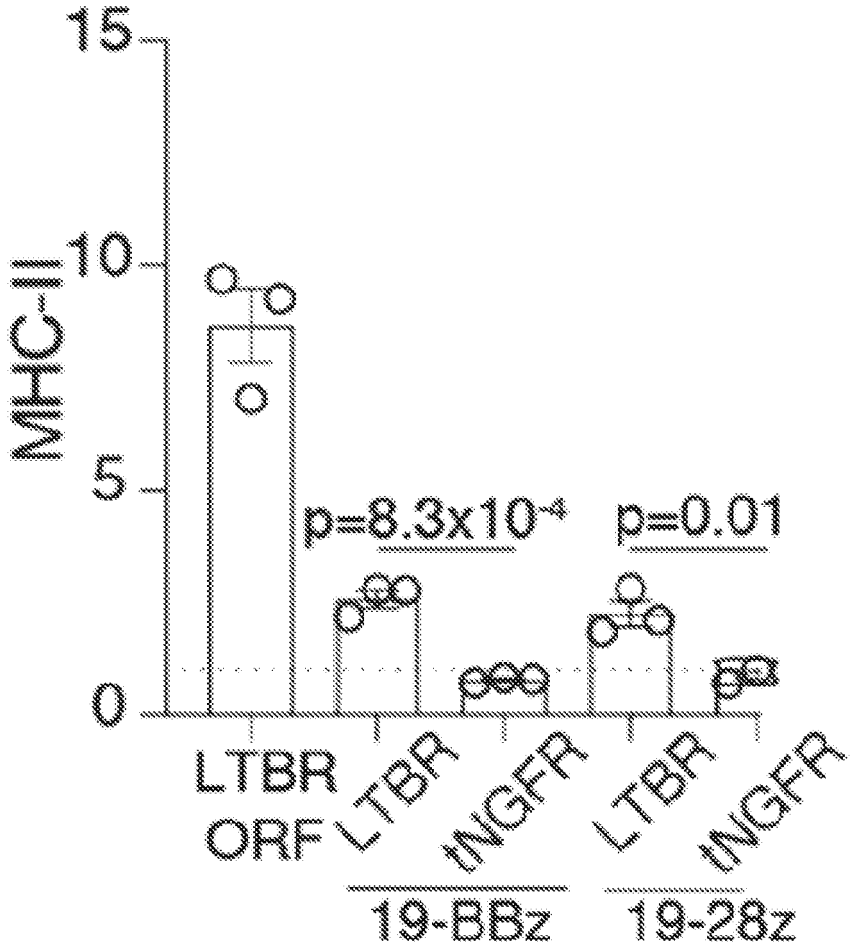


FIG. 14J

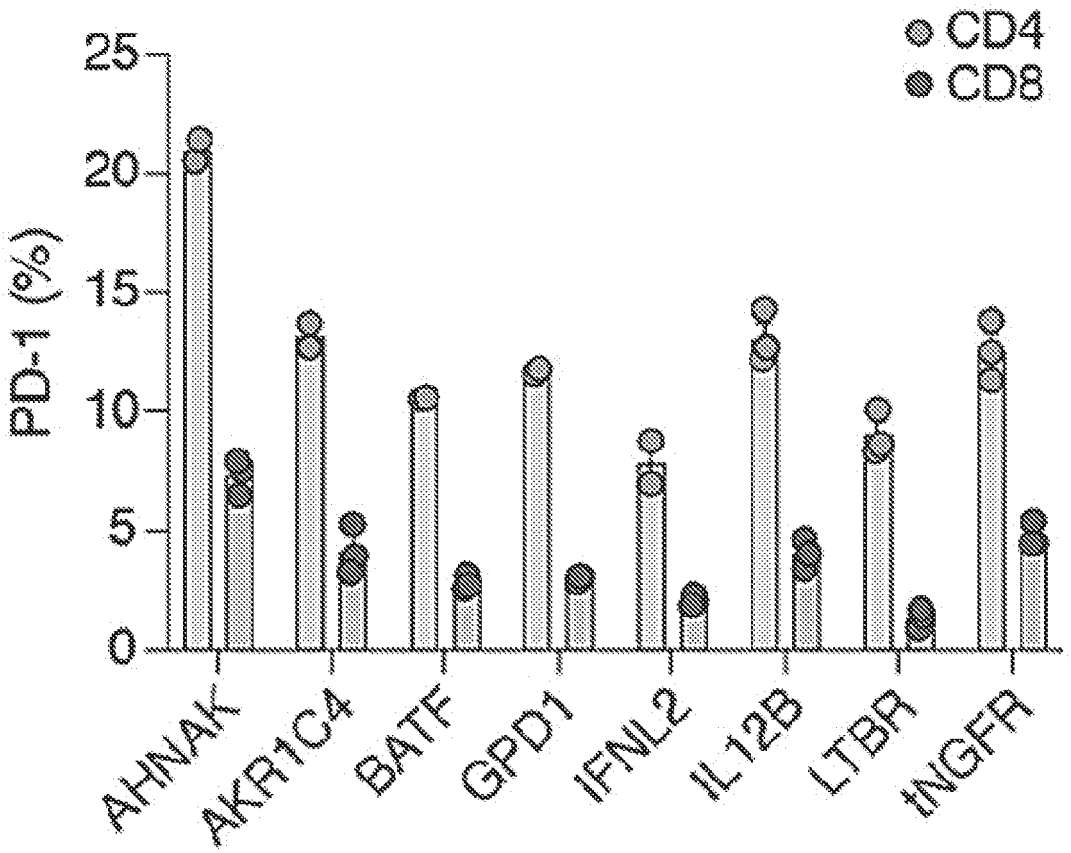


FIG. 14K

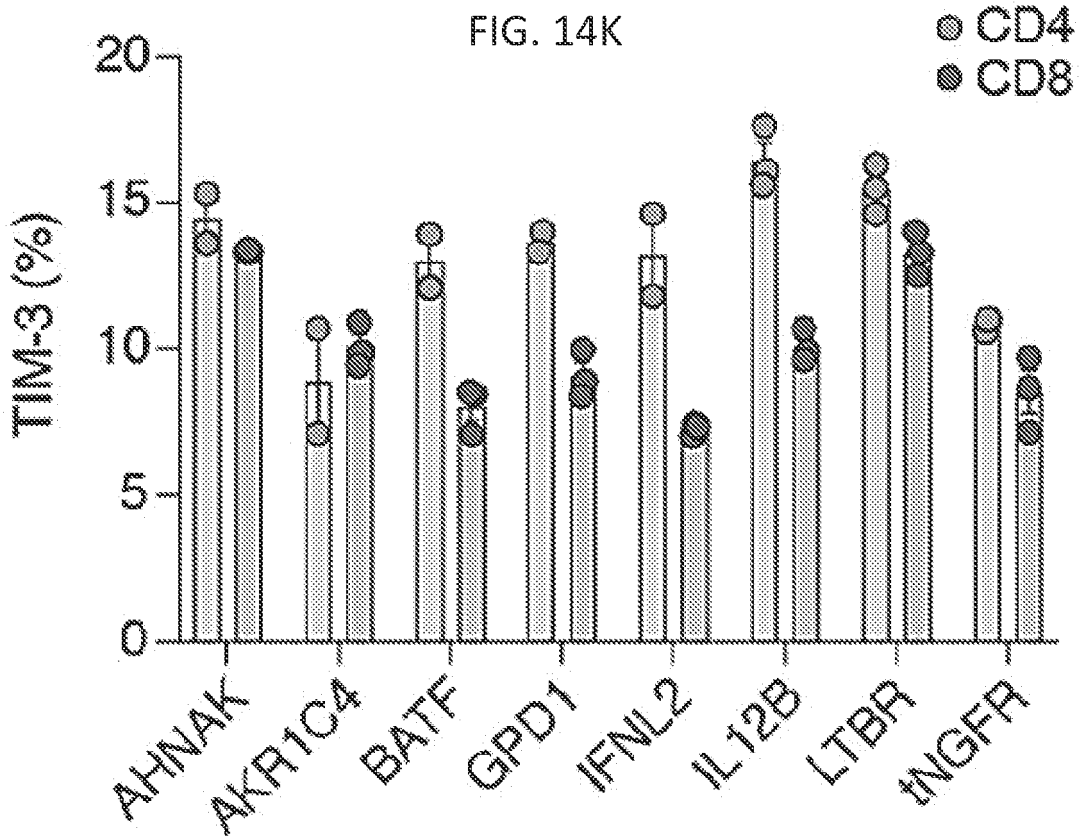


FIG. 14L

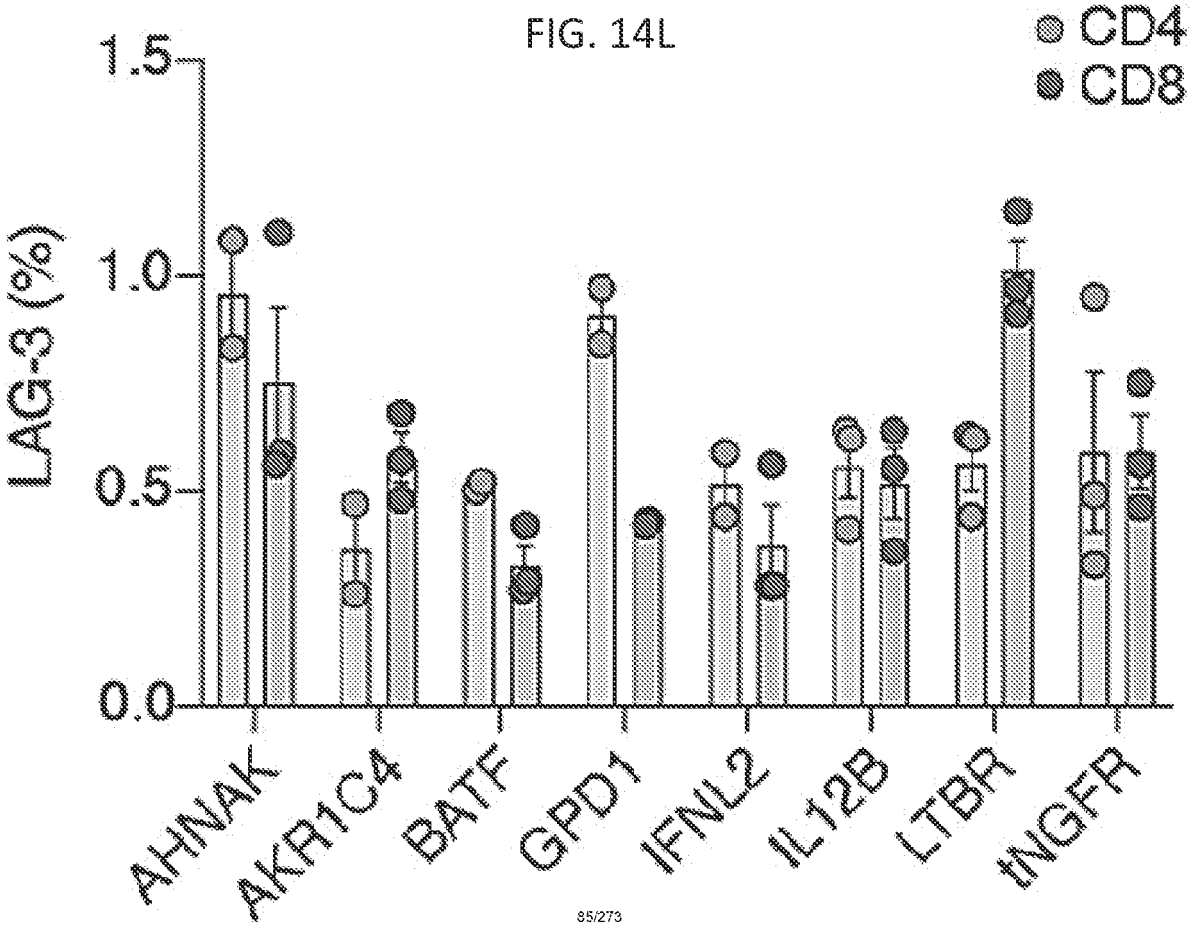


FIG. 14M

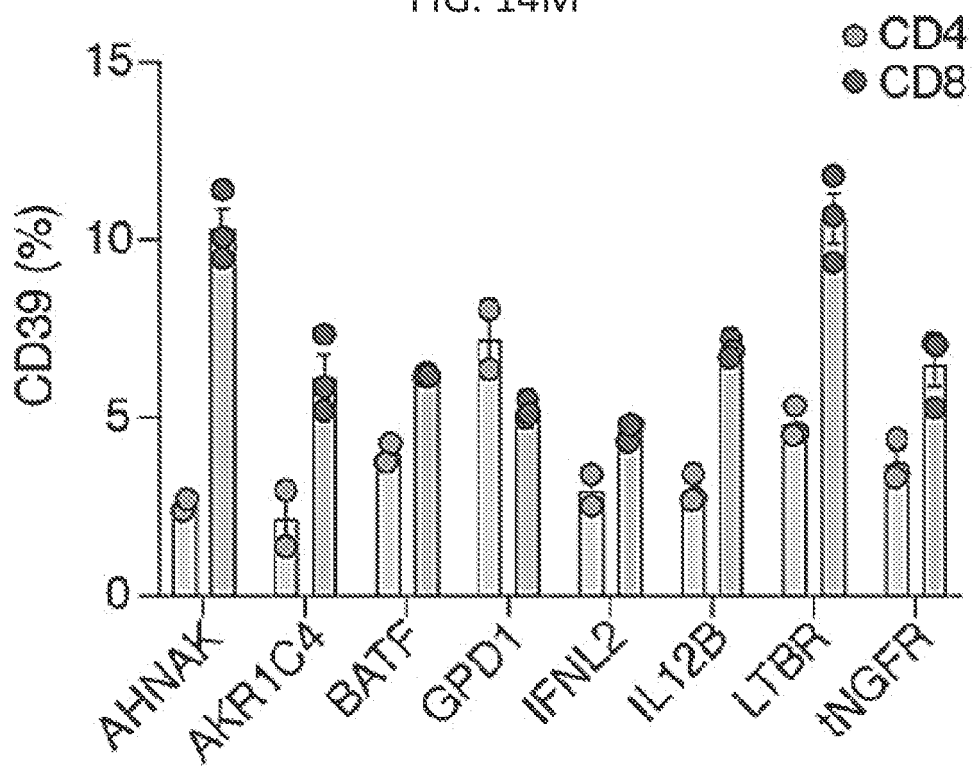


FIG. 14N

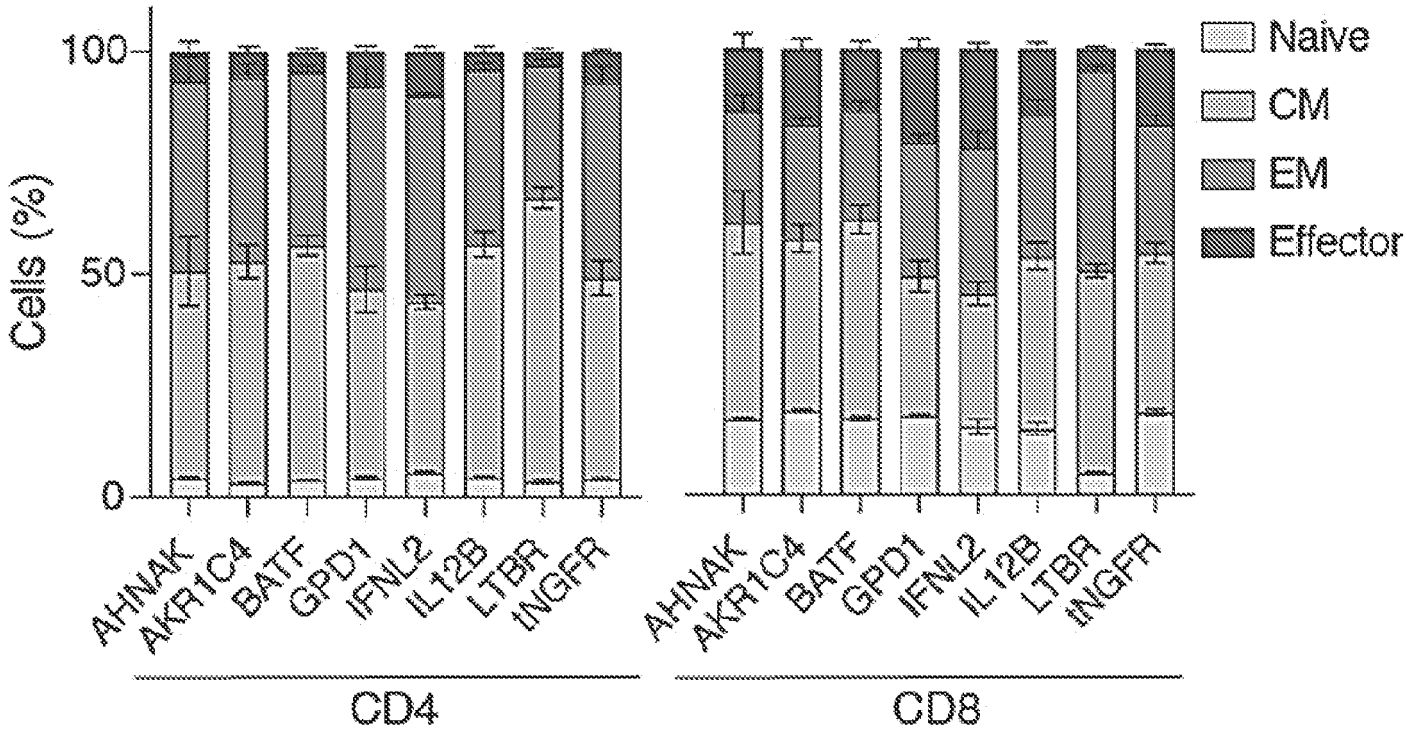


FIG. 14O

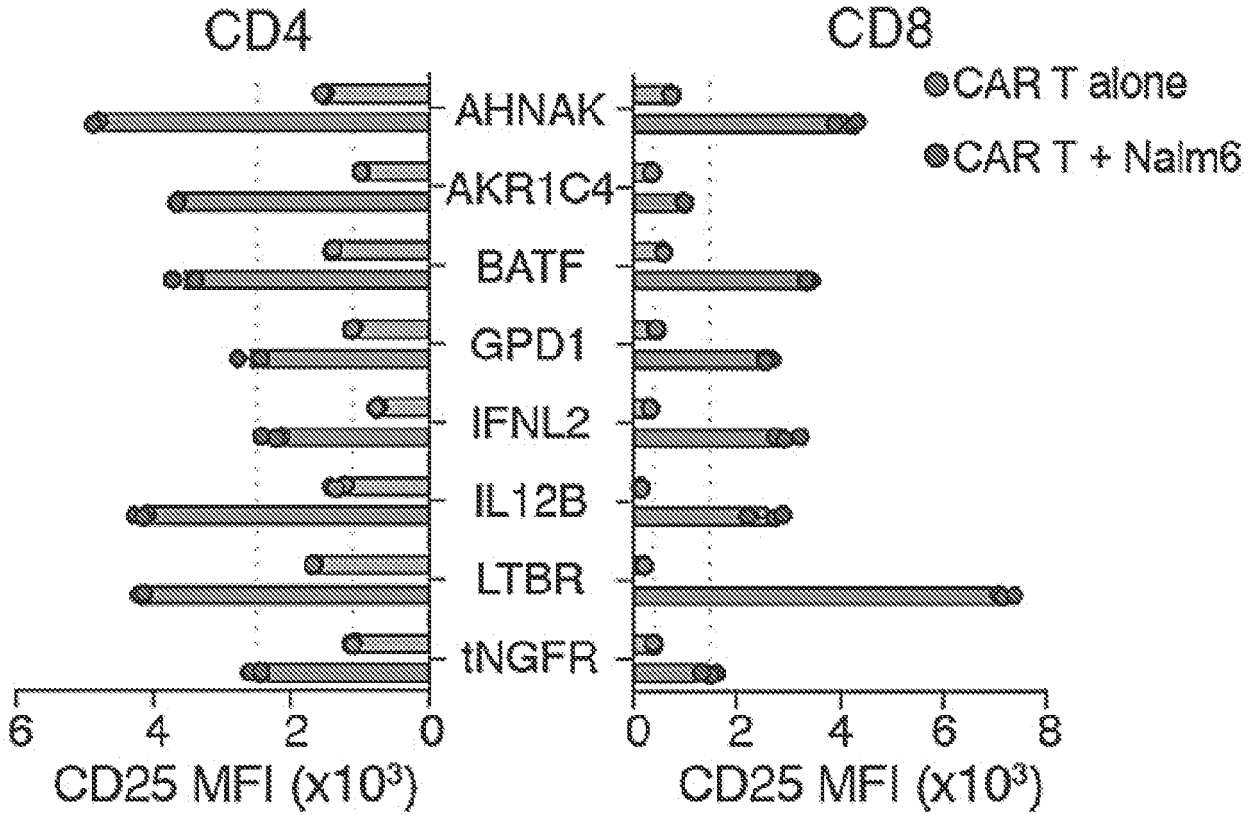


FIG. 14P

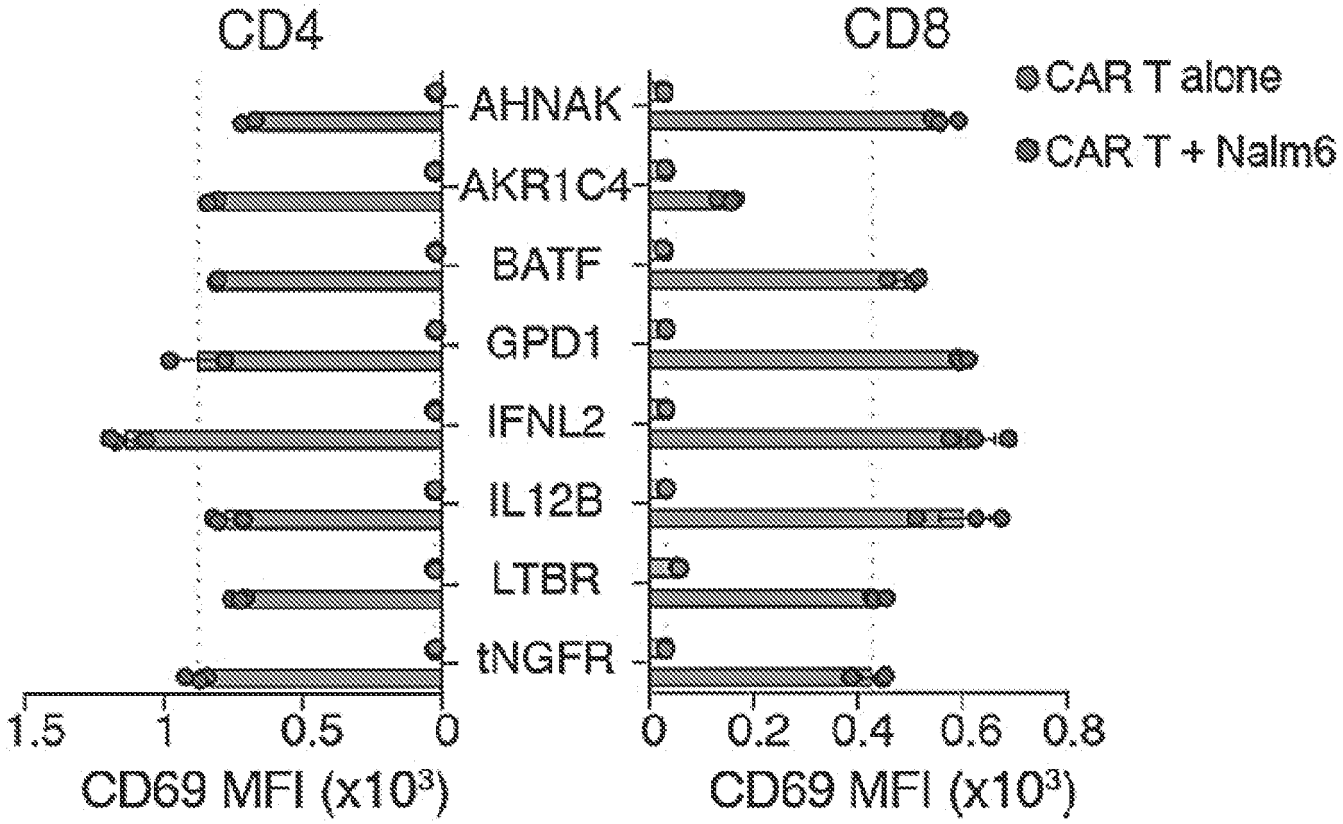


FIG. 15A

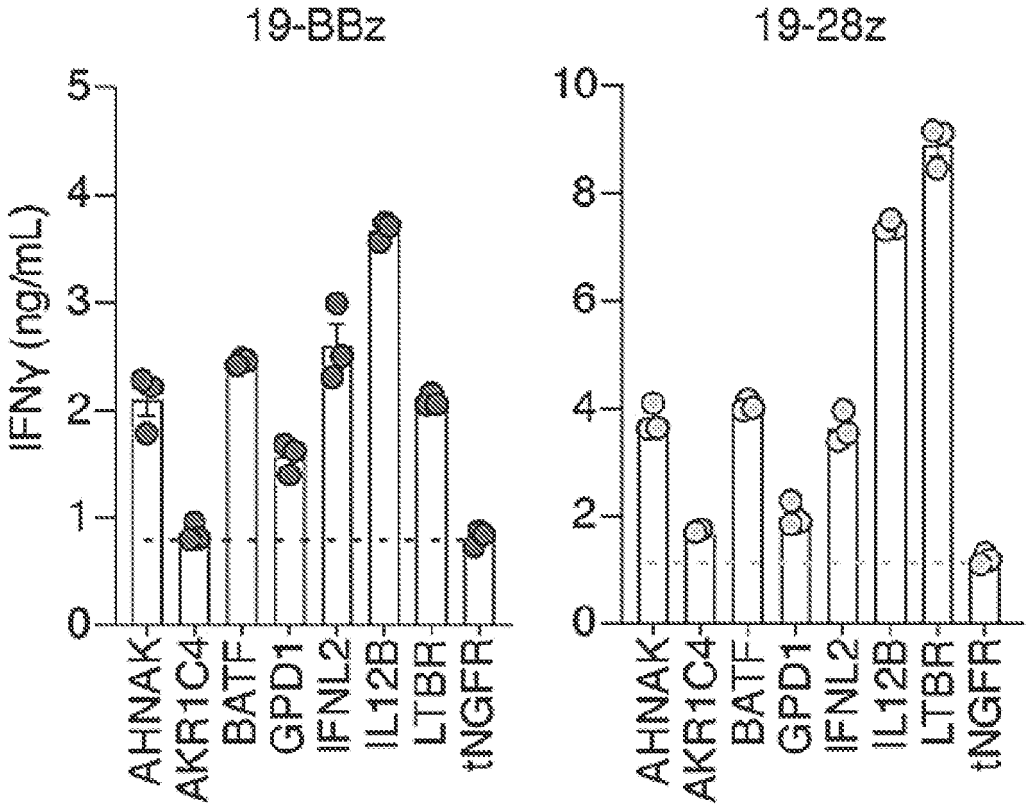


FIG. 15B

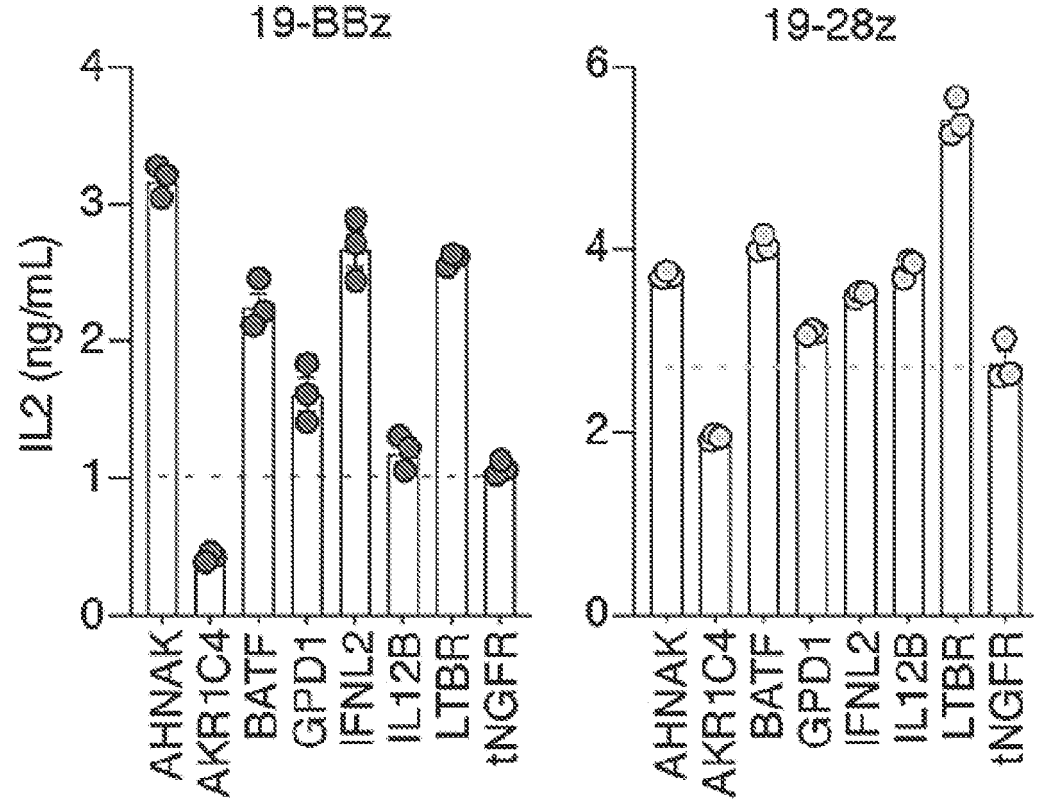


FIG. 15C

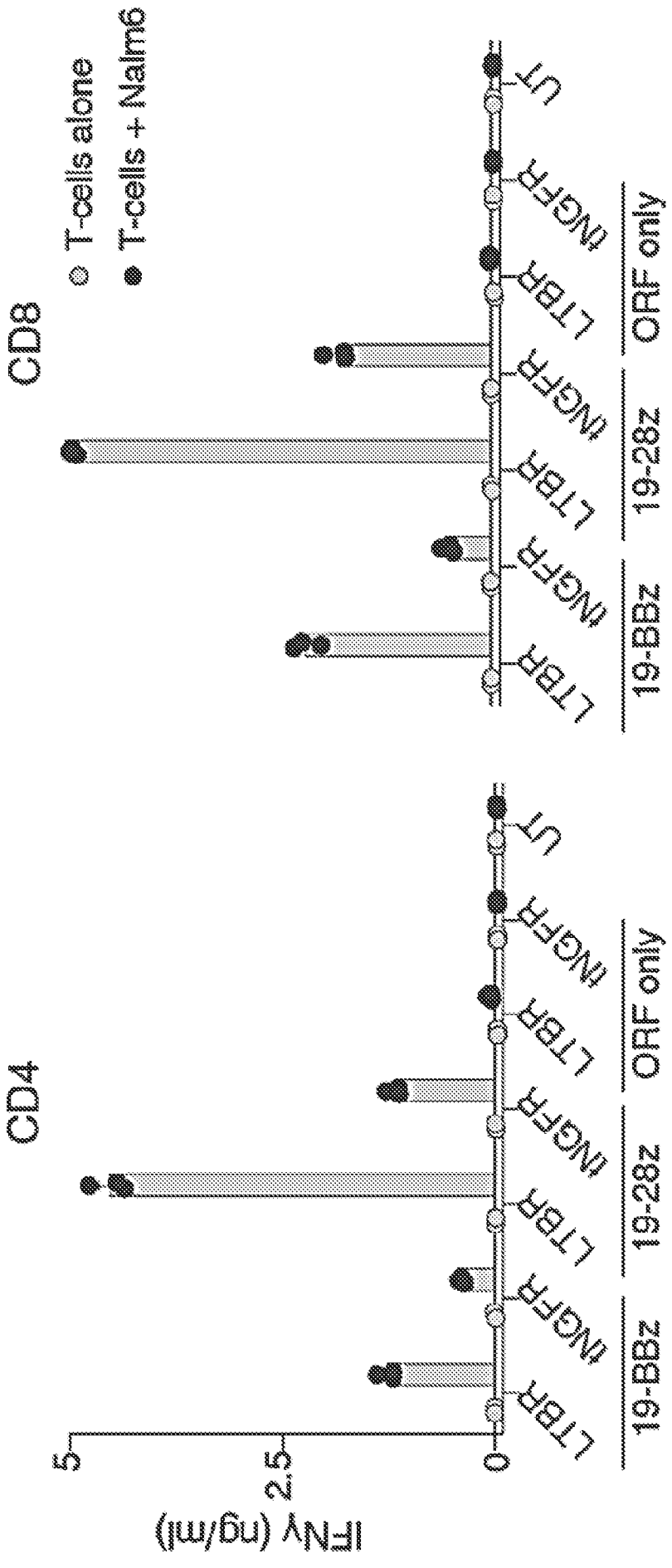

CD4
CD8
T-cells alone
T-cells + Nalm6
IFNγ (ng/ml)
0
2.5
5
UT
iNGFR
LTBR
19-BBz
19-28z
ORF only

FIG. 15D

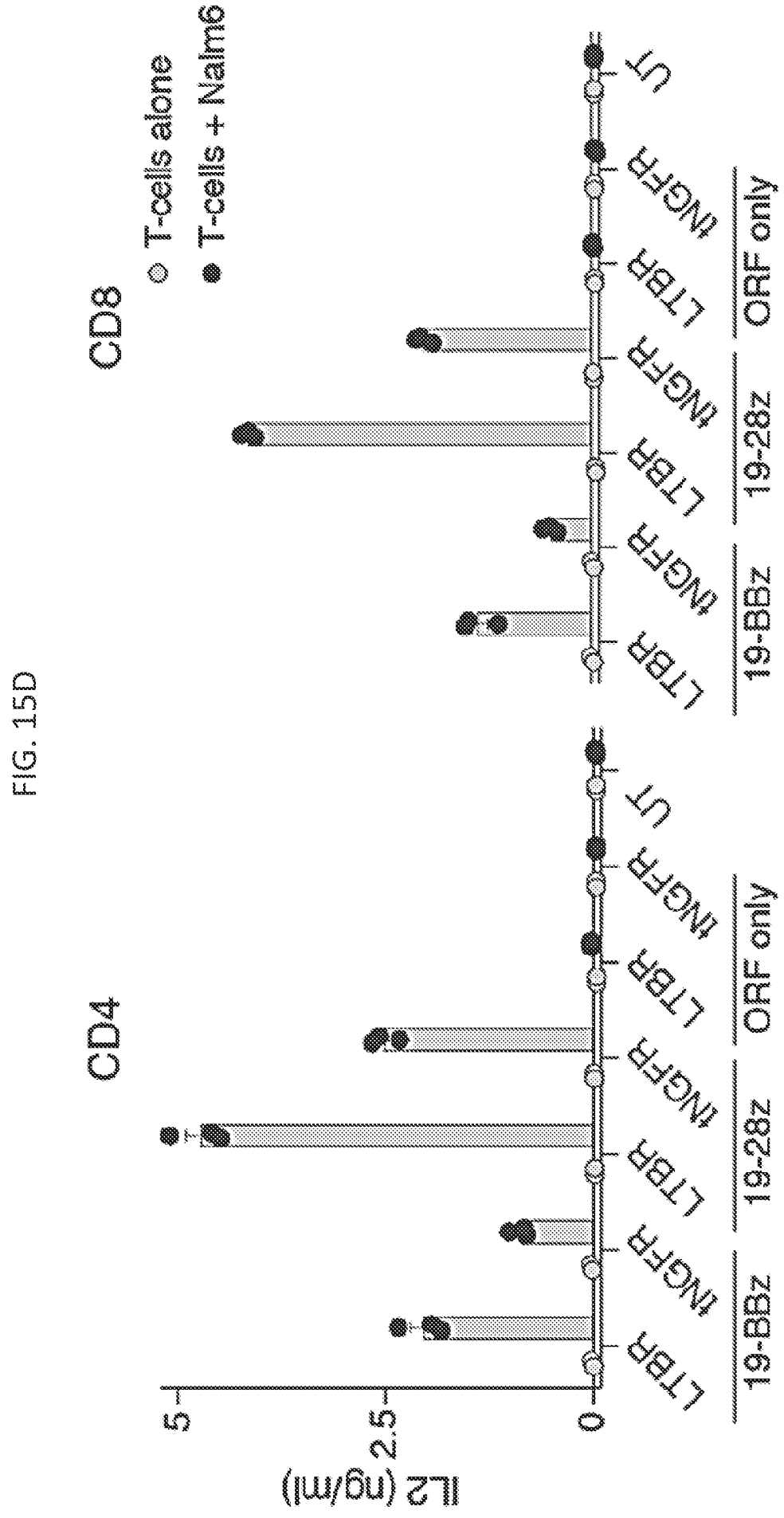

CD8
CD4
T-cells alone
T-cells + Nalm6
IL2 (ng/ml)
5
2.5
0
UT
iNGFR
LTBR
iNGFR
LTBR
iNGFR
LTBR
19-BBz
19-28z
ORF only

FIG. 15E

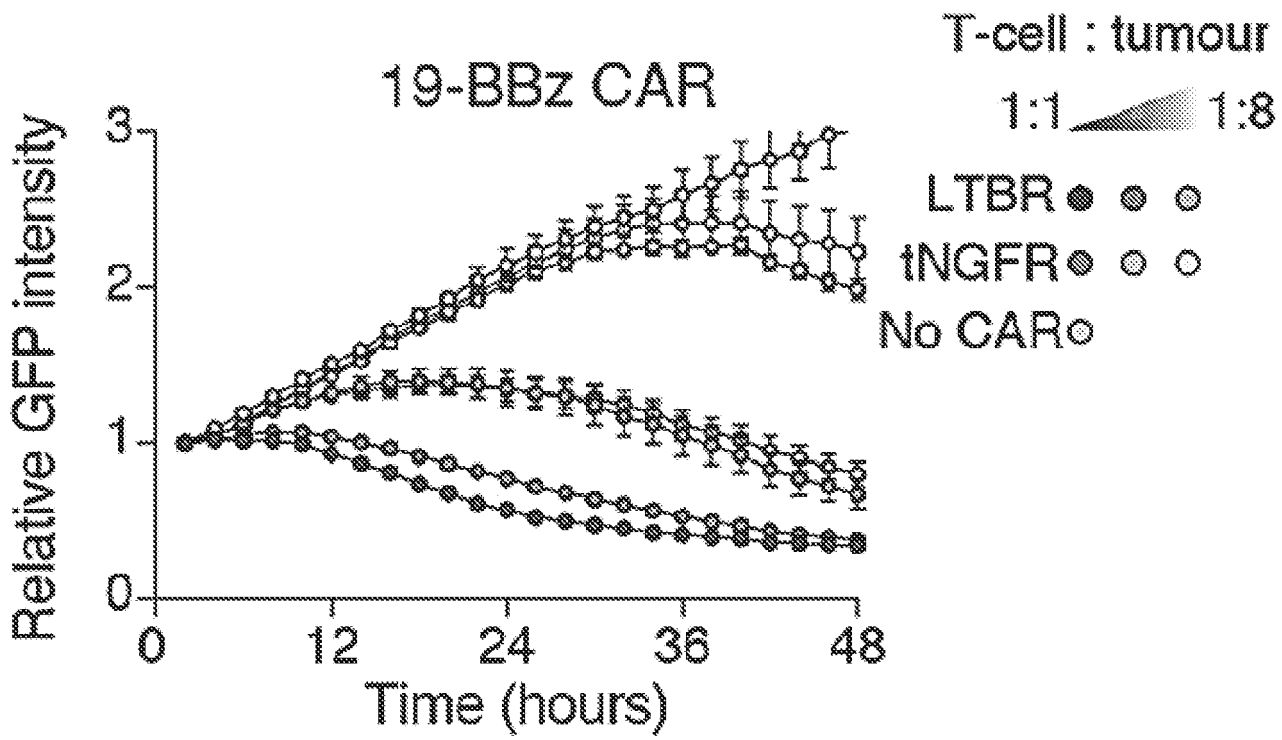


FIG. 15F

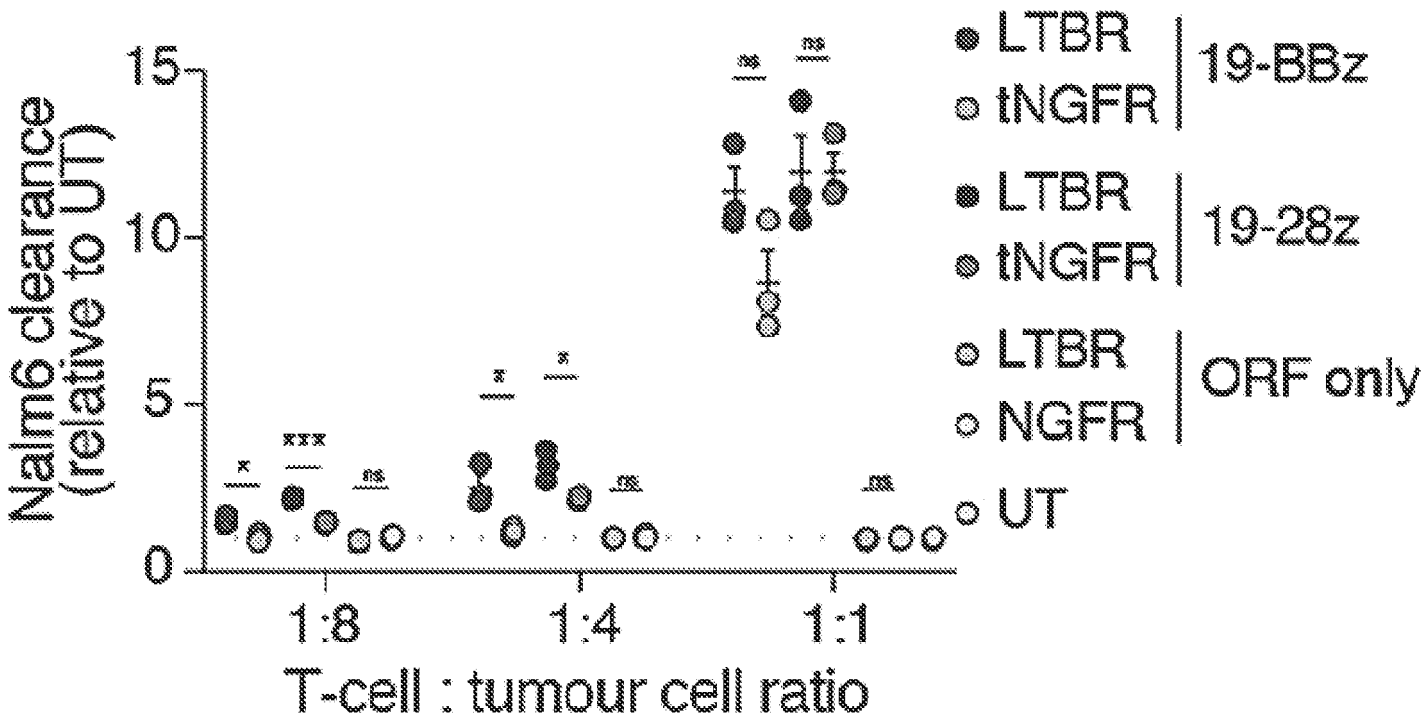


FIG. 15G

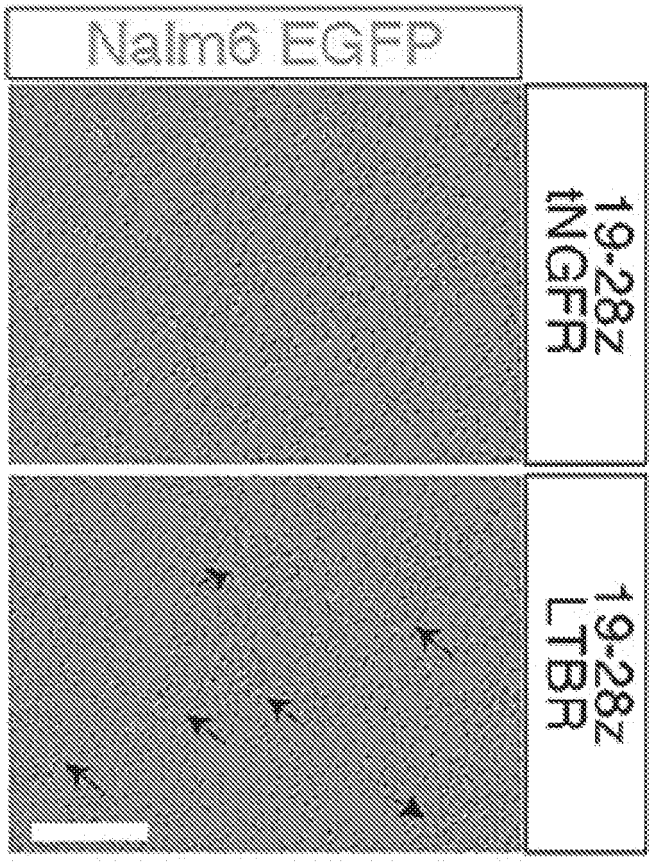


FIG. 15H

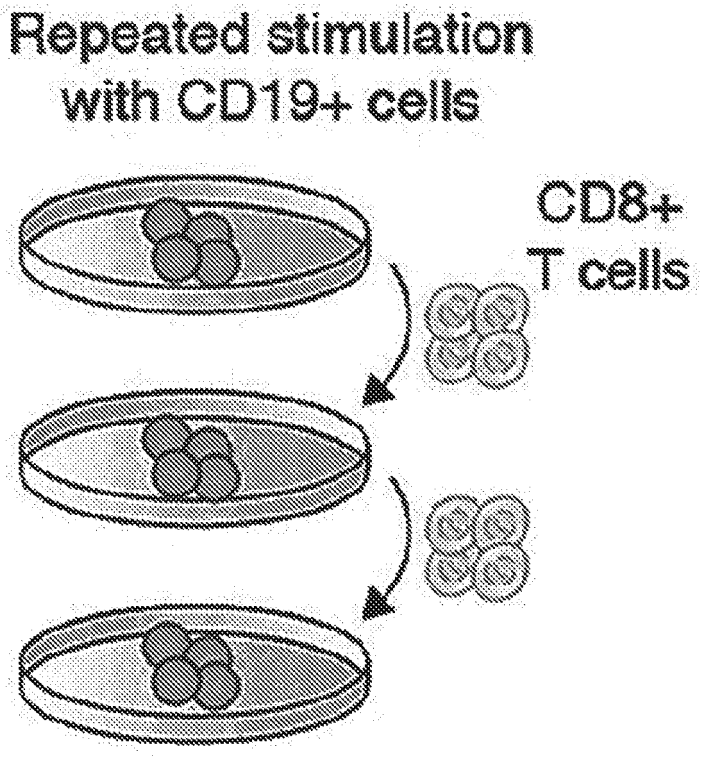


FIG. 15I

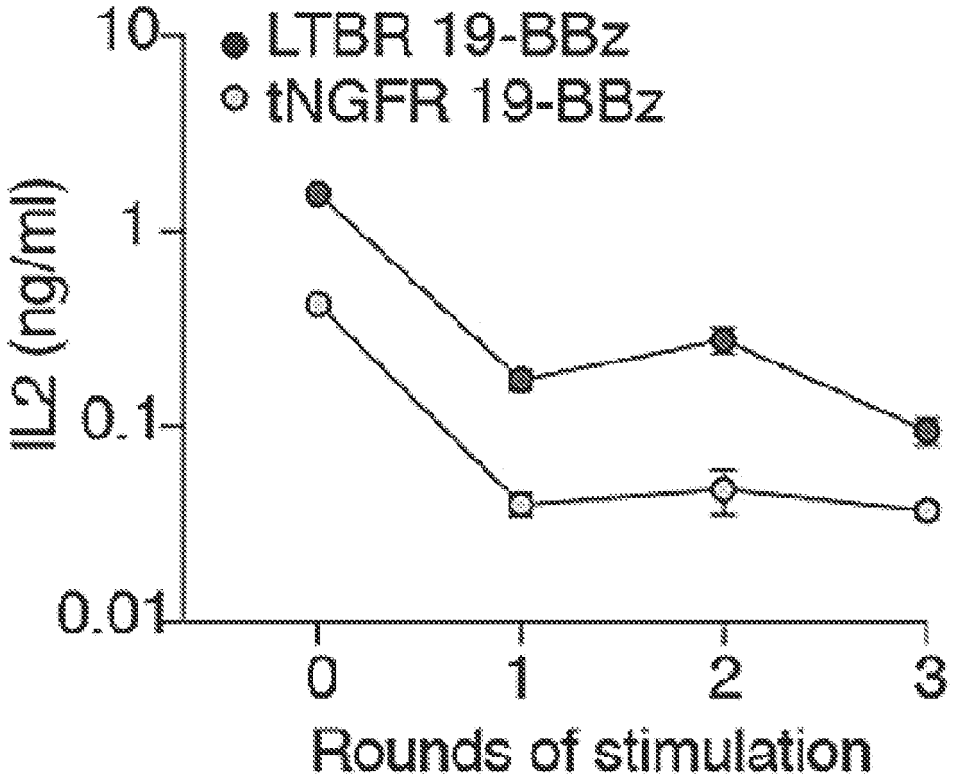


FIG. 15J

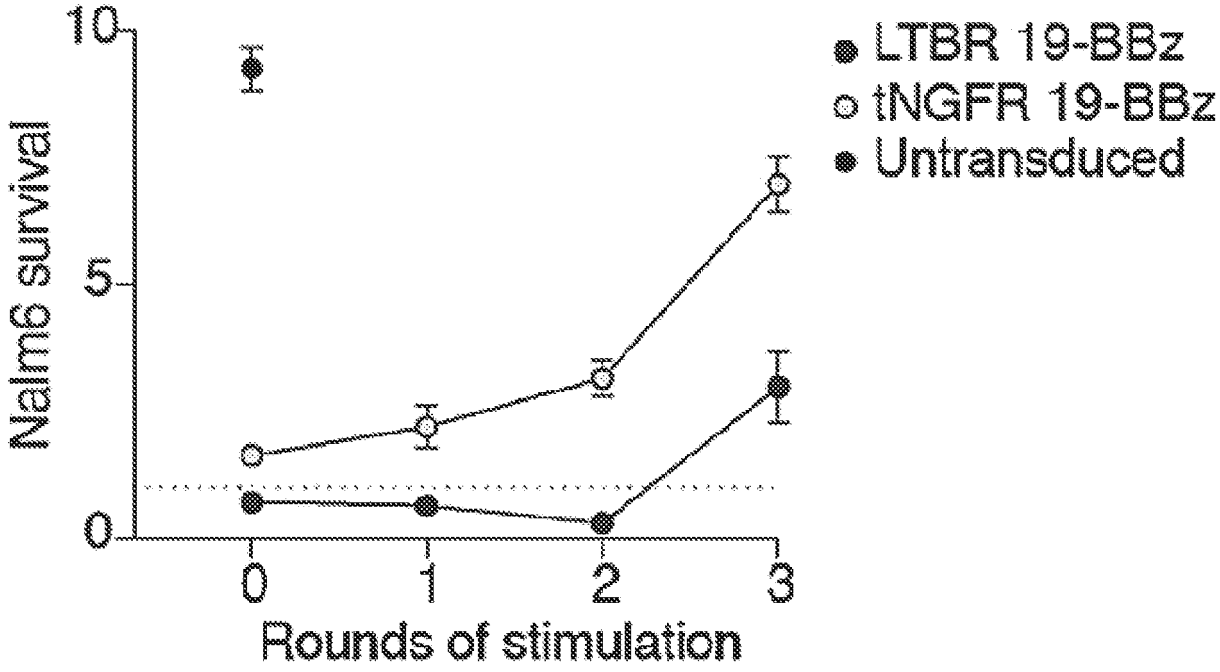


FIG. 15L

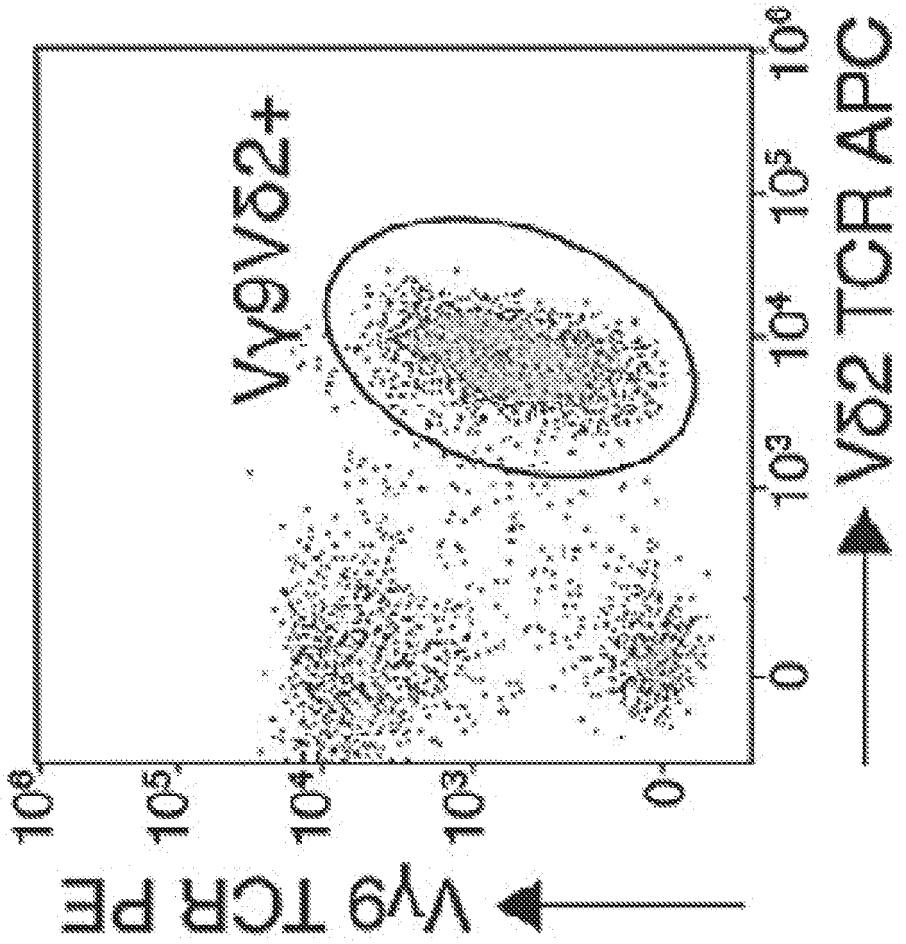
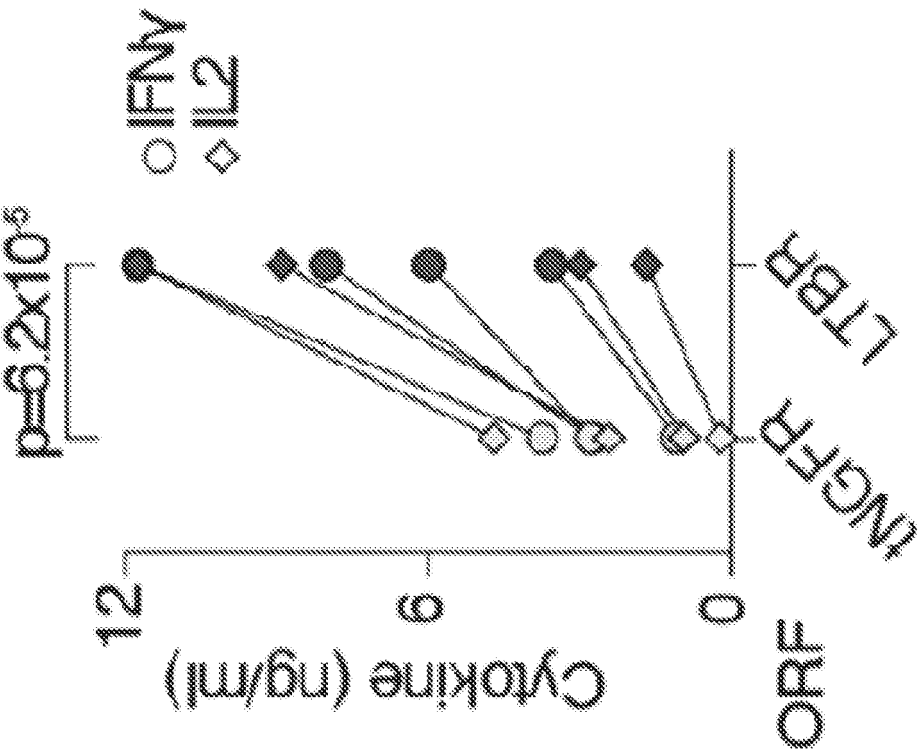


FIG. 15K



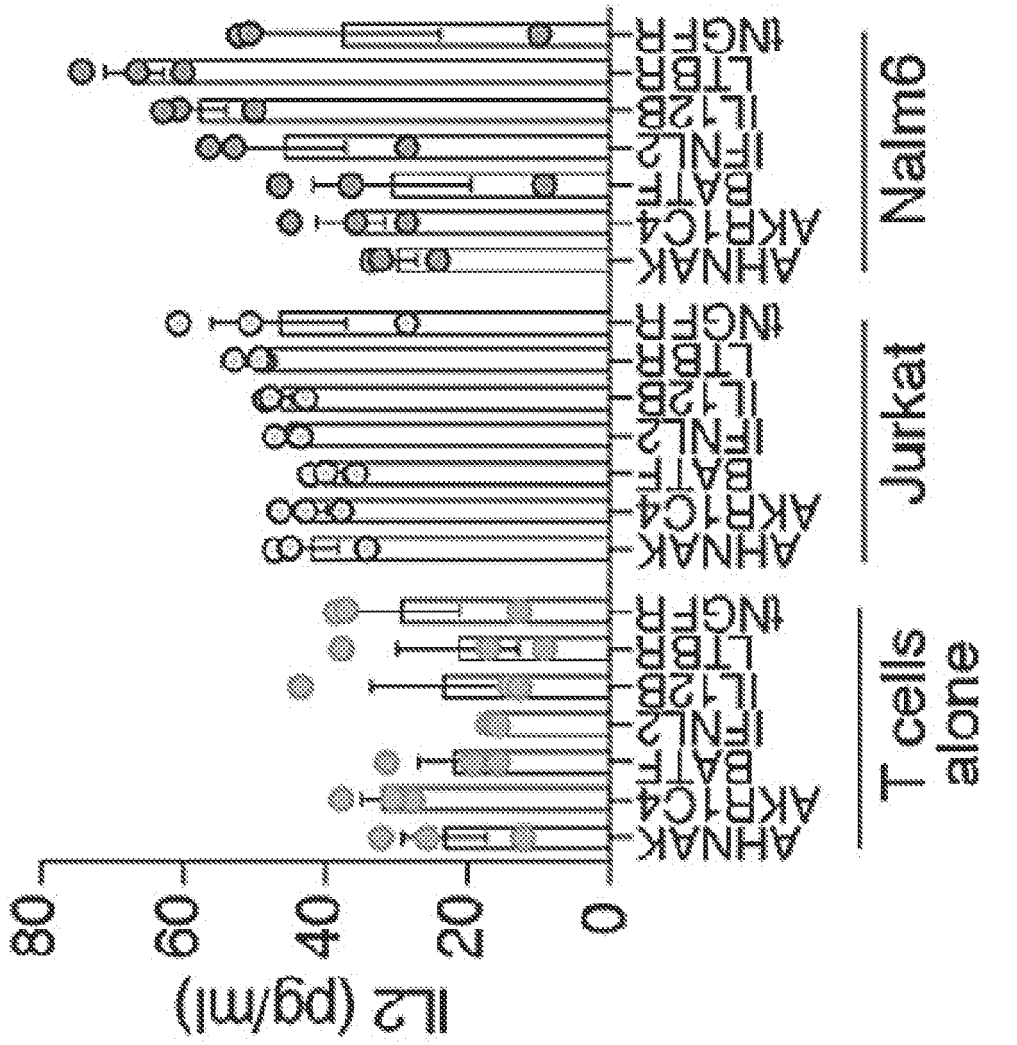


FIG. 15N

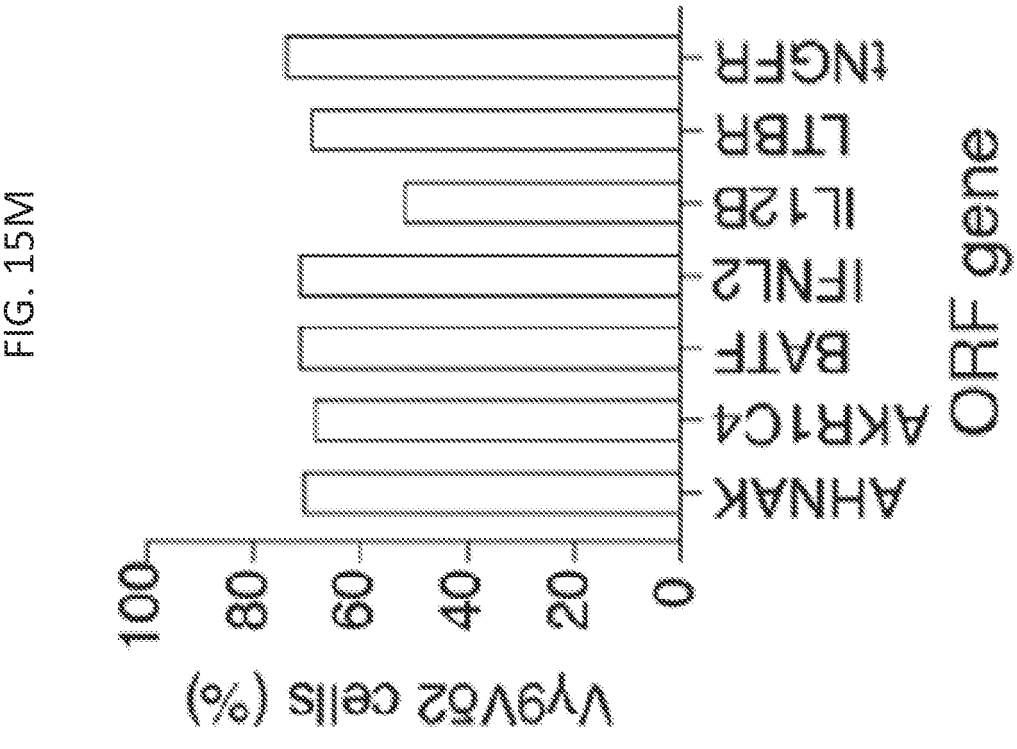


FIG. 15M

FIG. 15O

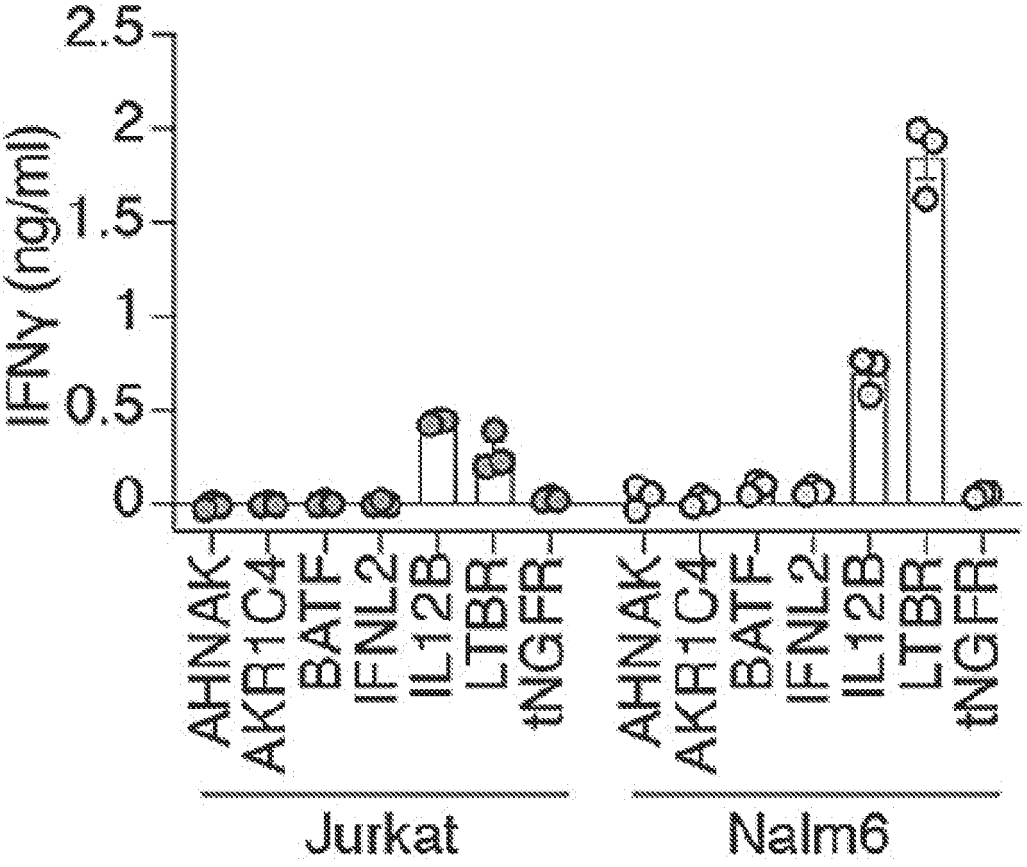


FIG. 15P

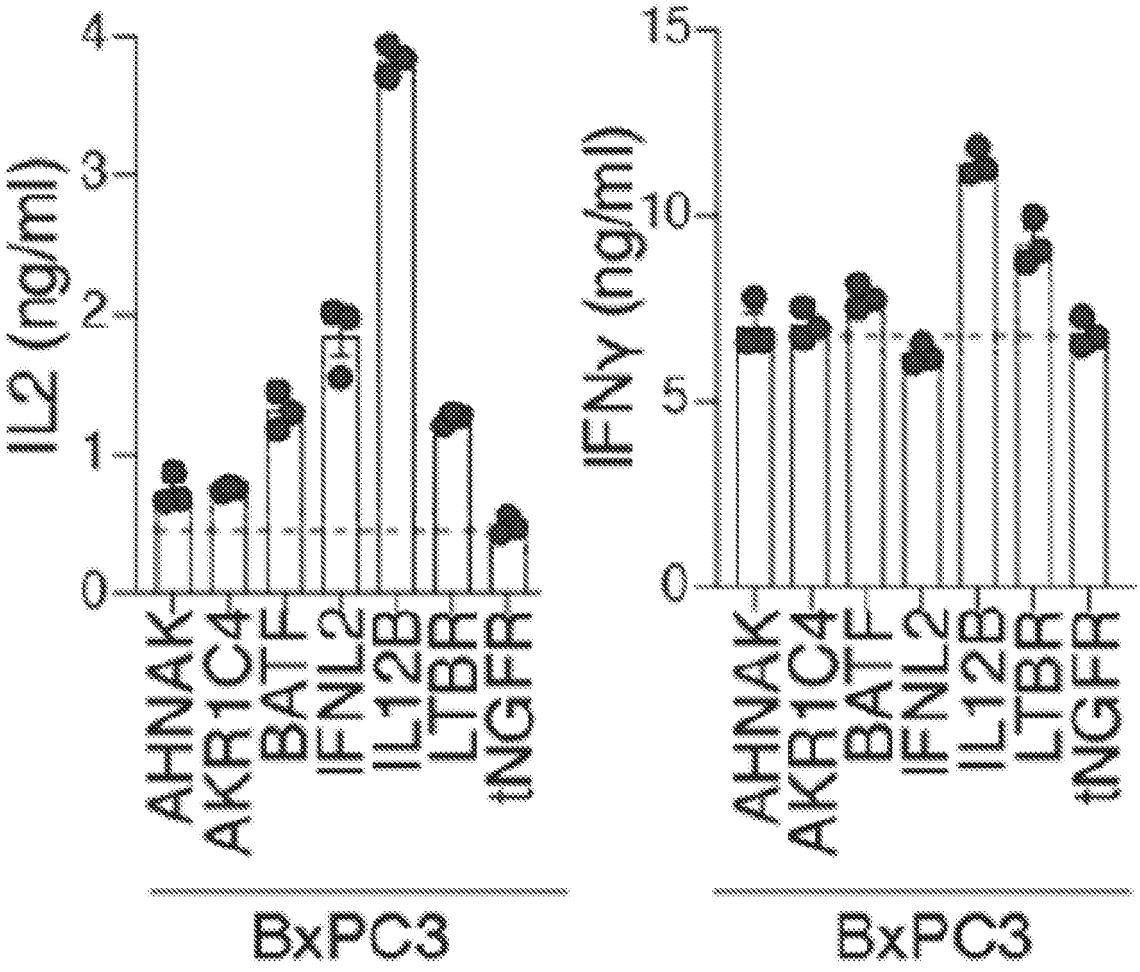
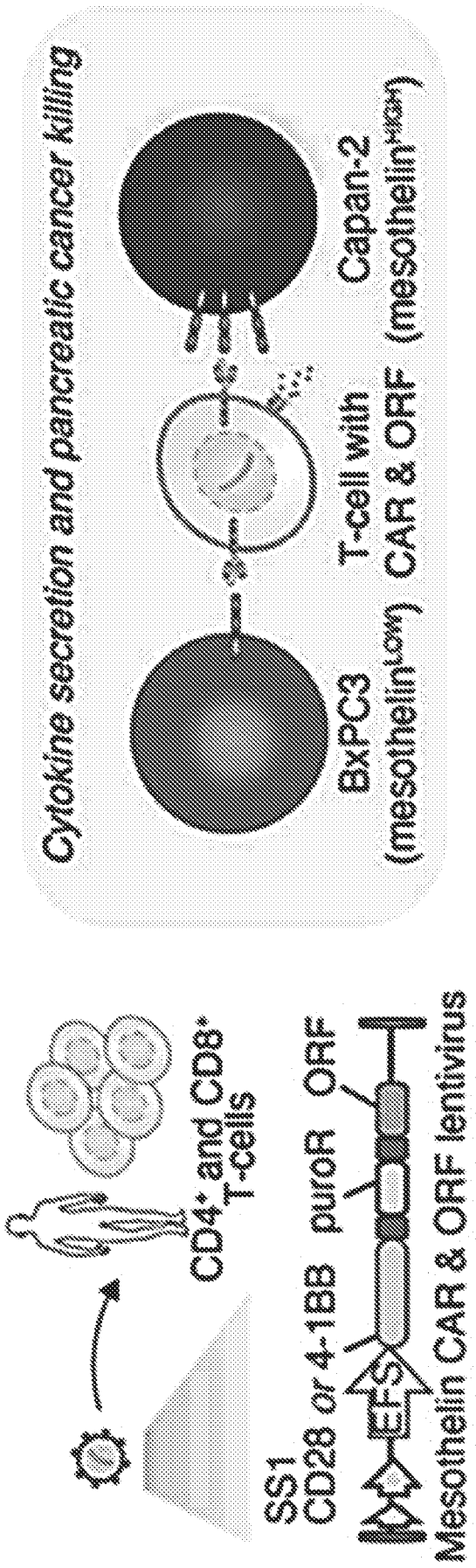


FIG. 16A


Cytokine secretion and pancreatic cancer killing
BxPC3
(mesothelin^Low)
T-cell with
CAR & ORF
Capan-2
(mesothelin^High)
CD4+ and CD8+
T-cells
SS1
CD28 or 4-1BB
puroR
ORF
EFS
Mesothelin CAR & ORF lentivirus

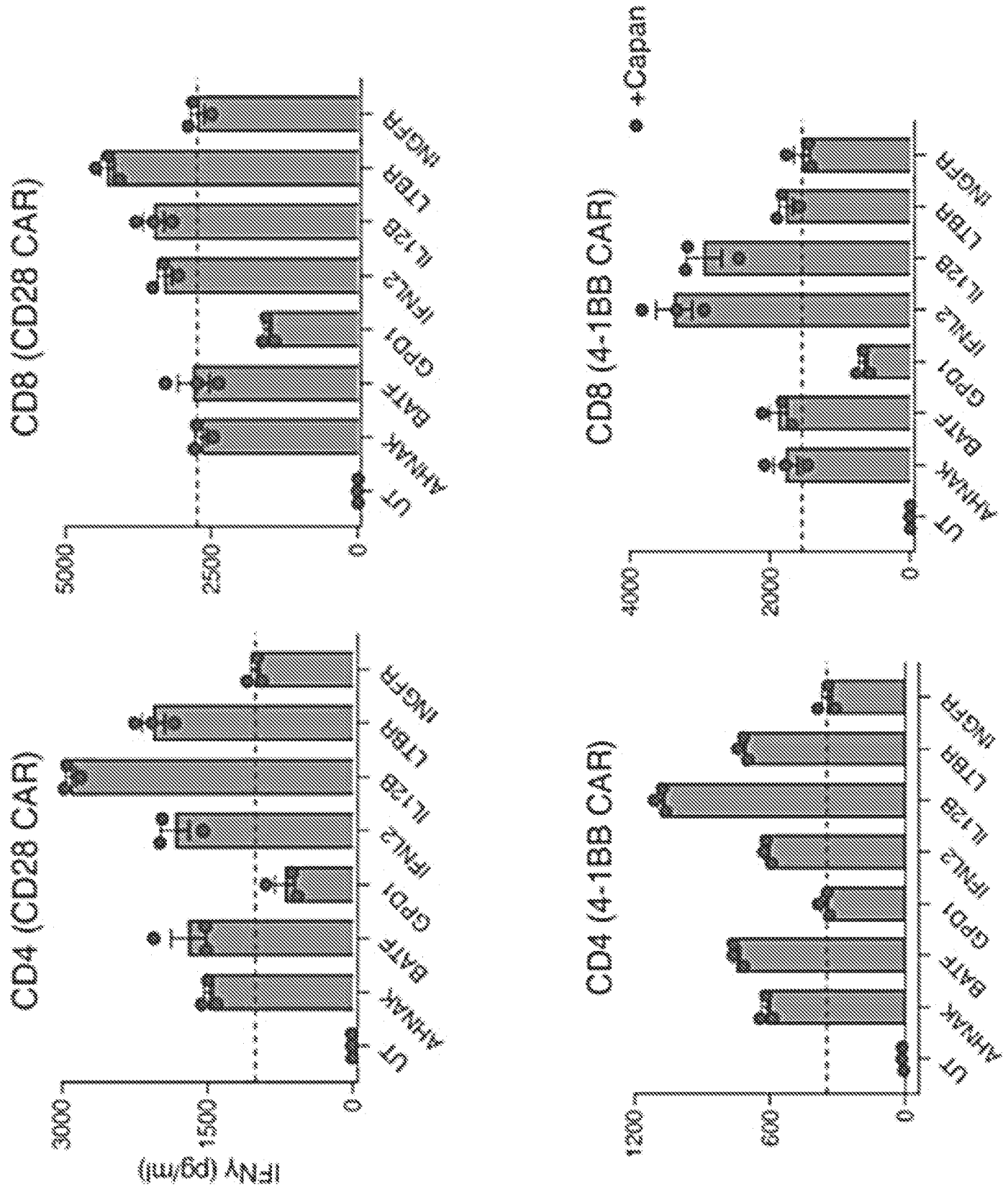

CD8 (CD28 CAR)
CD4 (CD28 CAR)
CD8 (4-1BB CAR)
CD4 (4-1BB CAR)
+Capan
IFNγ (pg/ml)
UT
AHNAK
BATF
GPD1
IFNL2
IL12B
LTBR
hNGFR

FIG. 16B

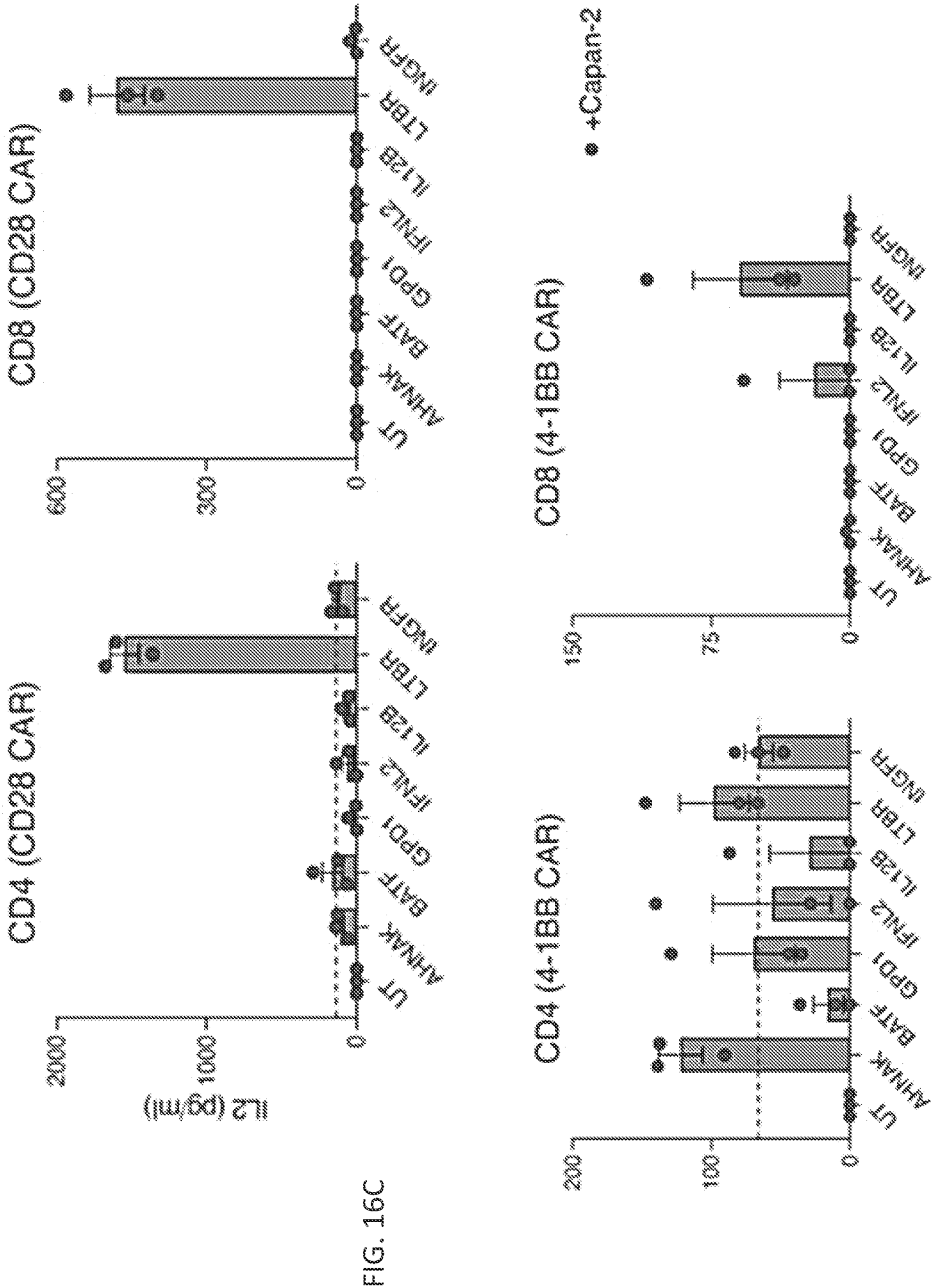
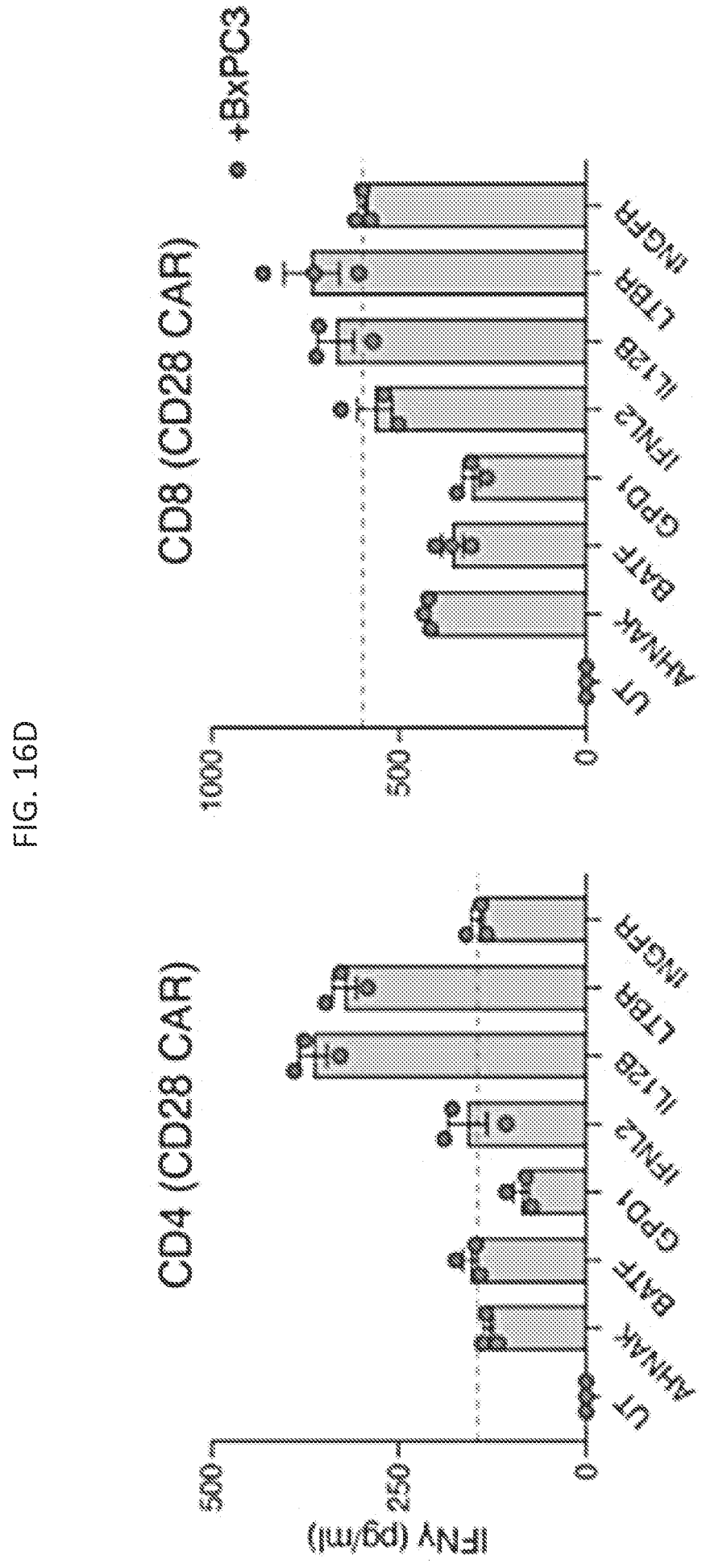

CD8 (CD28 CAR)
CD4 (CD28 CAR)
CD8 (4-1BB CAR)
CD4 (4-1BB CAR)
+Capan-2
IL2 (pg/ml)
UT
AHNAK
BATF
GPD1
IFNL2
IL12B
LTBR
NGFR

FIG. 16C

FIG. 16D


CD8 (CD28 CAR)
+BxPC3
1000
500
0
UT
AHNAK
BATF
GPD1
IFNL2
IL12B
LTBR
MGFR
CD4 (CD28 CAR)
500
250
0
IFNγ (pg/ml)

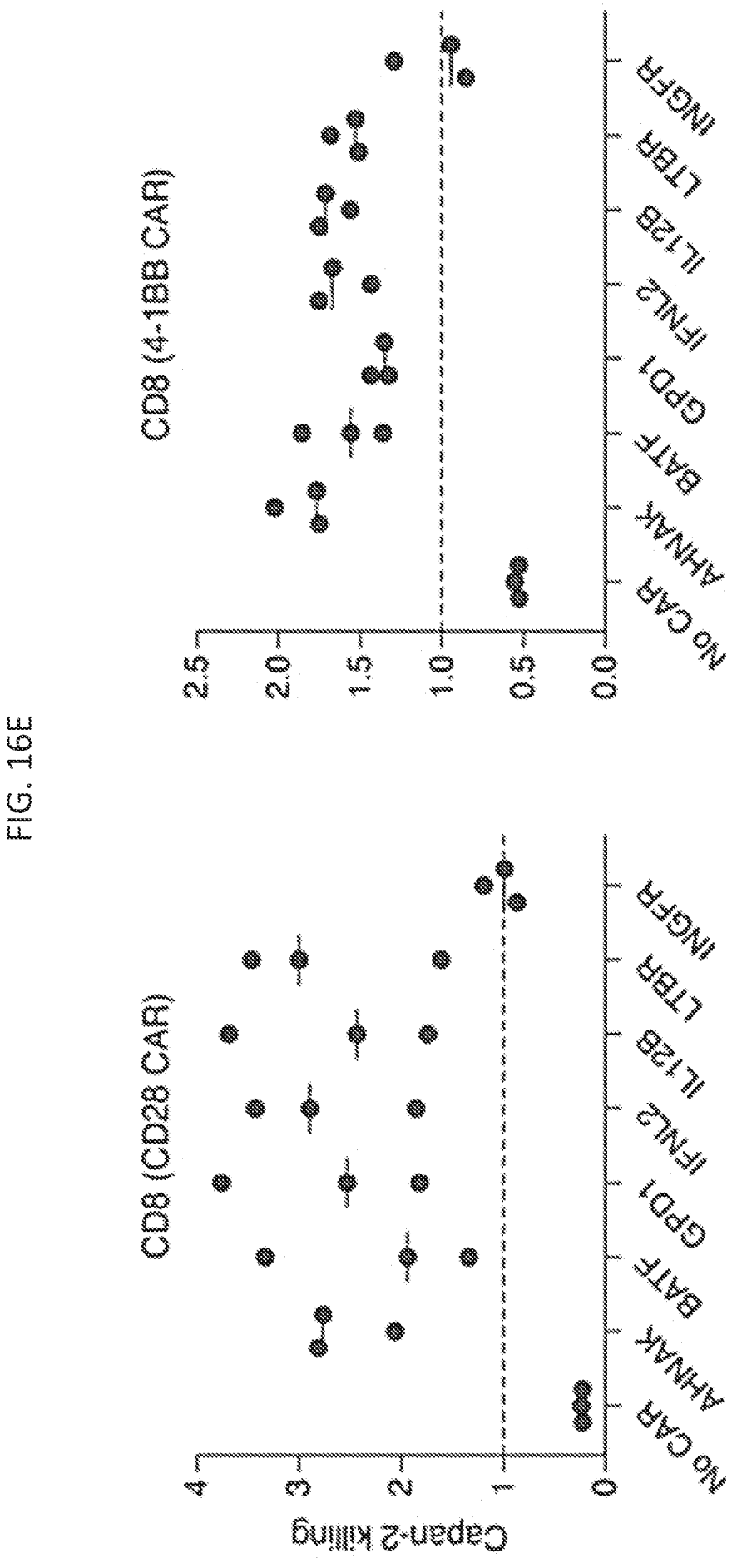

CD8 (CD28 CAR)
CD8 (4-1BB CAR)
Capan-2 killing
0
1
2
3
4
0.0
0.5
1.0
1.5
2.0
2.5
No CAR
AHNAK
BATF
GPD1
IFNL2
IL12B
LTBR
INGFR

FIG. 16E

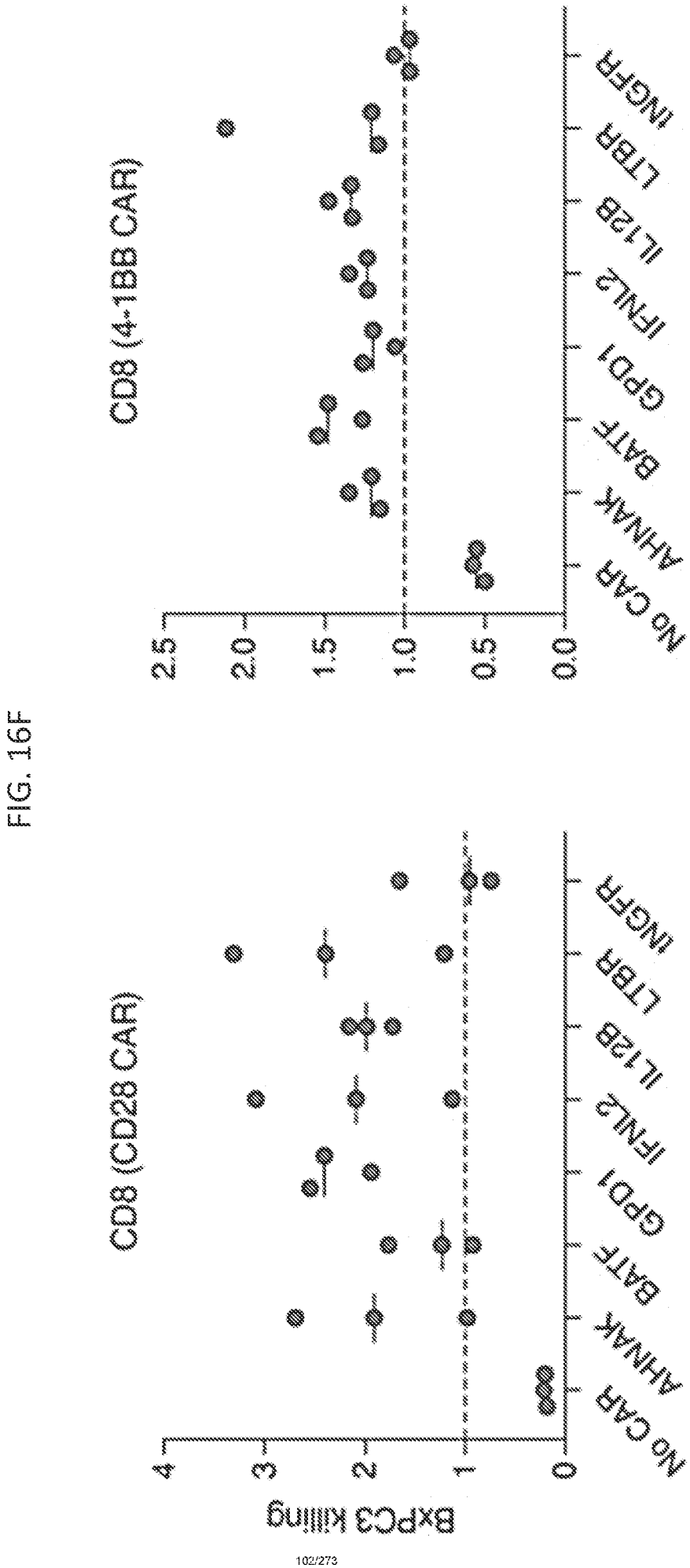

CD8 (CD28 CAR)
CD8 (4-1BB CAR)
BxPC3 killing
0
1
2
3
4
0.0
0.5
1.0
1.5
2.0
2.5
No CAR
AHNAK
BATF
GPD1
IFNL2
IL12B
LTBR
INGFR

FIG. 16F

FIG. 17A

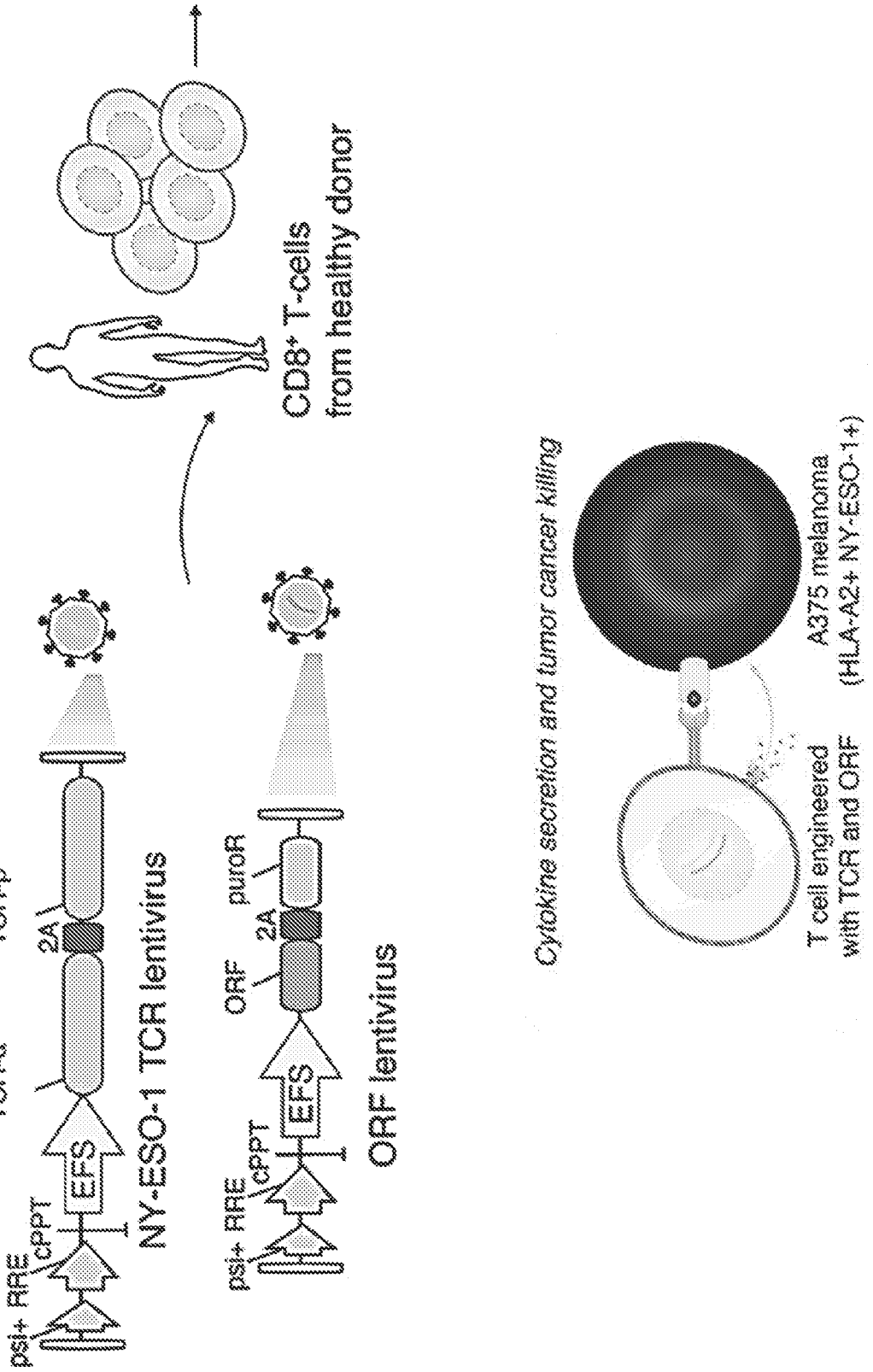

psi+ RRE
cPPT
EFS
TCR-α
2A
TCR-β
NY-ESO-1 TCR lentivirus
psi+ RRE
cPPT
EFS
ORF
2A
puroR
ORF lentivirus
CD8+ T-cells
from healthy donor
Cytokine secretion and tumor cancer killing
T cell engineered
with TCR and ORF
A375 melanoma
(HLA-A2+ NY-ESO-1+)

FIG. 17B

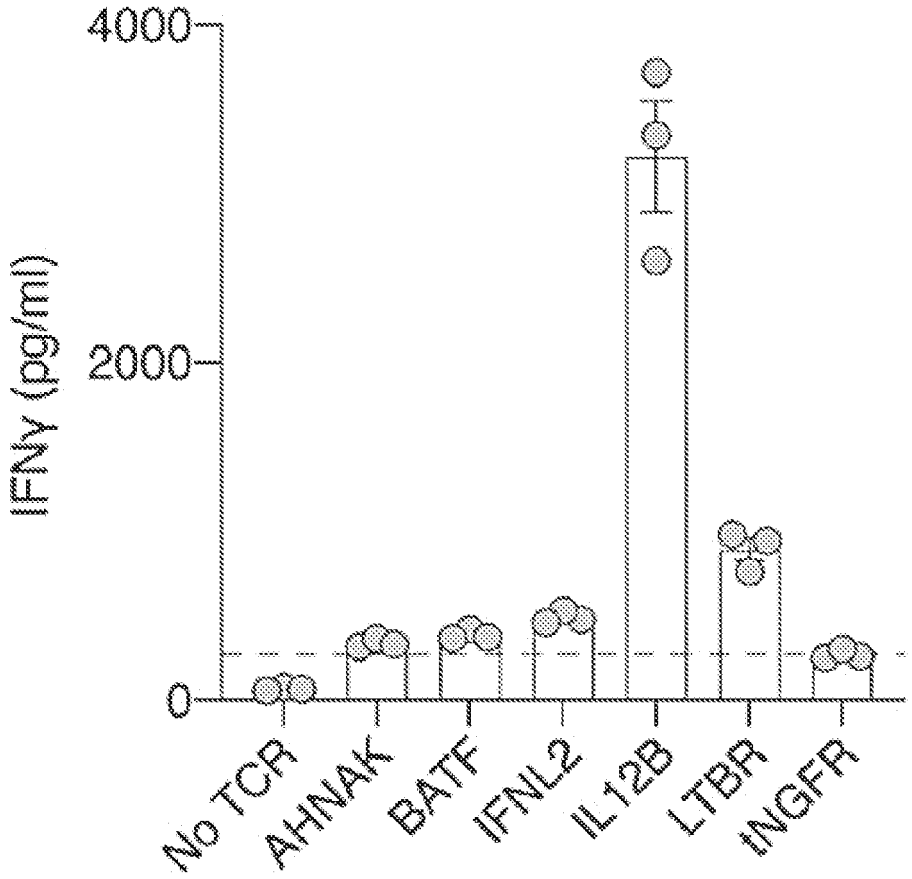


FIG. 17C

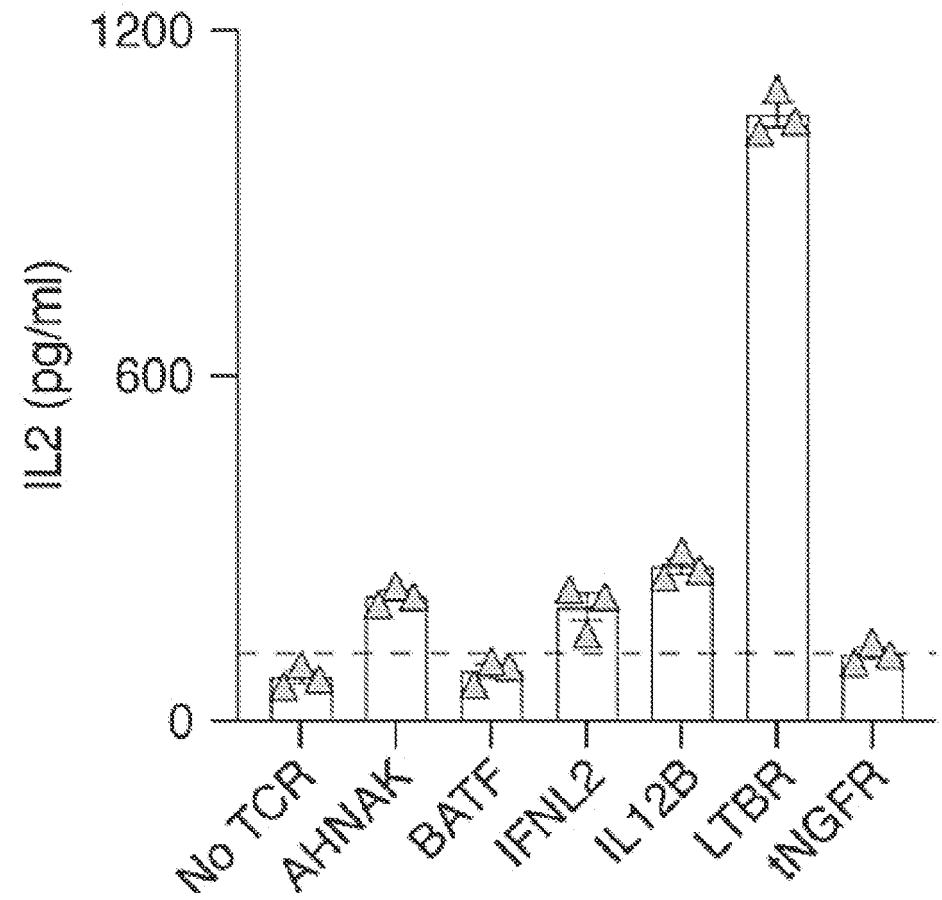


Fig. 17D

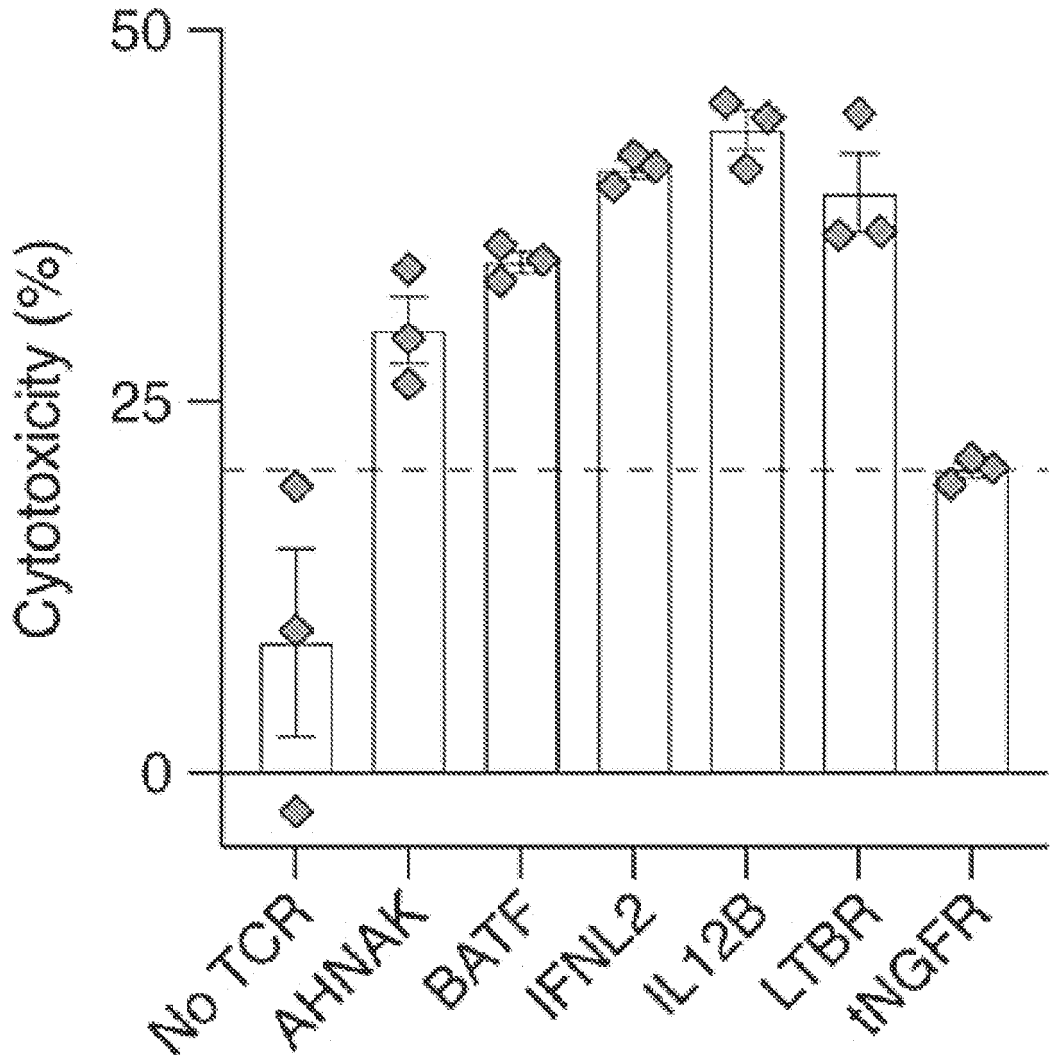

50
25
0
Cytotoxicity (%)
No TCR
AHNAK
BATF
IFNL2
IL12B
LTBR
tNGFR

FIG. 18A

ORF capture with OverCITE-seq

ORF capture is performed through 3 steps:

Steps:

1. Reverse transcription and template switching – capturing transcriptome and ORF on 10X bead *(combined)*
2. Transcriptome and ORF amplification *(combined)*
3. Amplification of transcriptome and ORF *(separate)*
    - Divide output of Step 2 into 2 aliquots and then use each one for transcriptome/ORF:
        - Aliquot 1 (*transcriptome cDNA*) processed directly for gene expression library (as per 10x protocol)
        - Aliquot 2 (*ORF*) undergoes 2 further PCRs to specifically amplify ORFs from the DNA pool (remember, most of the pool is transcriptome so the two-stage PCR is needed to specifically boost/amplify ORFs)

Different versions of OverCITE-seq were tried and had different yields. The optimized version ("Version 3") yielded the best data.

In addition to the schematics, we present a table that summarizes reagent differences between Versions 1 - 3 and another table detailing the specific changes to the primer sequences. We also provide the PCR protocols used in Step 3 ("Amplification of transcriptome and ORF") for all versions.

FIG. 18B

Overview and capture of ORF on 10x bead with OverCITE-seq – STEPS 1 and 2

1. Reverse transcription and template switching – capturing transcriptome and ORF on 10X bead

- The 5' ends of transcripts are captured on the 10X bead by template switching (10x Genomics 5' kit)
- **Key idea:** The lentiviral (ORF) transcript is very long so reverse transcription and bead capture is inefficient – hence a primer binding to a constant sequence downstream of the ORF is used
- To optimize ORF capture, we tested multiple ratios of puro RT to poly(dT) RT primer tested: 1:10 (version 1), 1:3 and 1:1 (version 2 & version 3)
  - In the initial (reverse-transcription, RT) step, we substitute the poly(dT) RT primer for a mix of a puro RT primer (captures the ORF) and the poly(dT) RT primer (captures the cellular transcriptome)

2. Transcriptome and ORF amplification *(combined)*

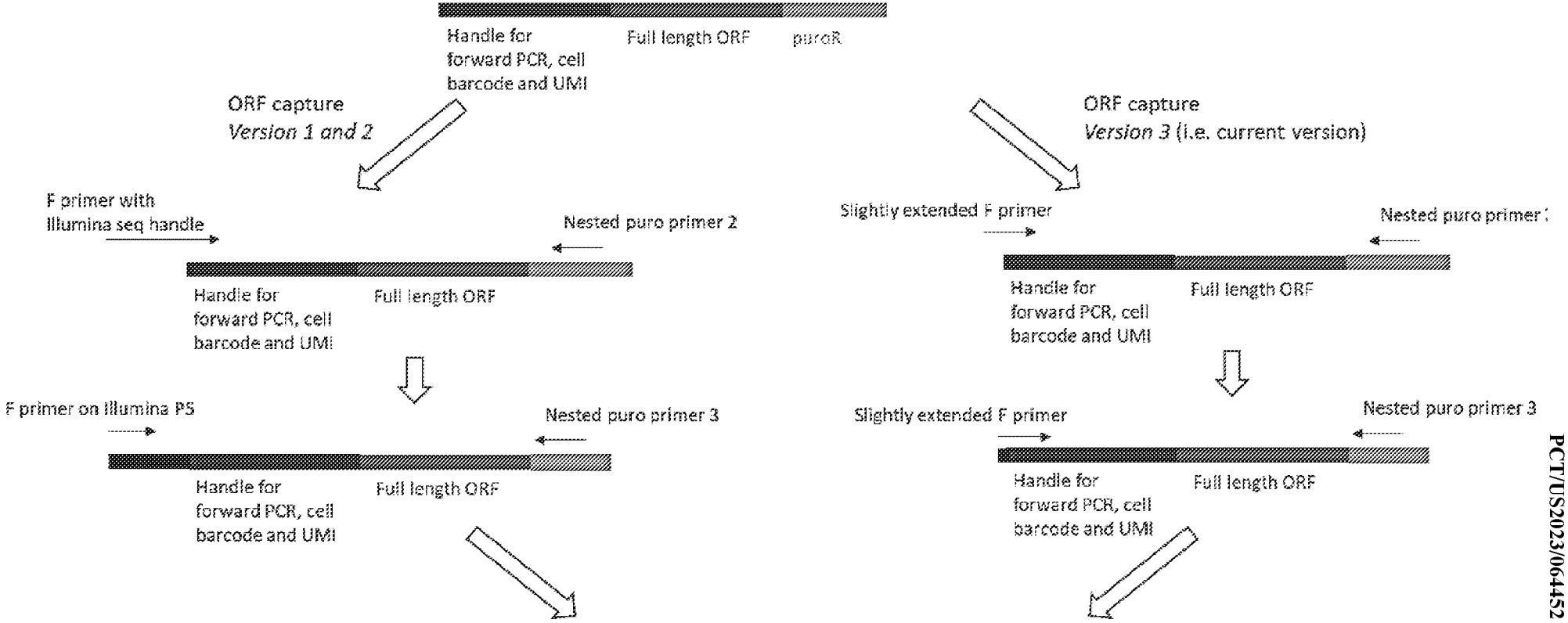
- cDNA captured on the 10X bead is amplified (to boost quantity) using a constant forward primer and reverse primers (one using a handle added to the end of the poly(dT) primer; the other nested within the puroR)

FIG. 18C

Overview and capture of ORF on 10x bead with OverCITE-seq – STEP 3

3. Amplification of transcriptome and ORF *(separate)*

Taking 2 aliquots from step 2: one processed directly for gene expression library (transcriptome), one subject to 2 further PCRs to specifically amplify ORFs from the DNA pool (most of the pool = transcriptome)



Fragmentation, adaptor ligation and indexing
PCR for Illumina sequencing

FIG. 18D

RT primer spike-in and PCR strategy

OverCITE-seq version number			
	Version 1	**Version 2**	**Version 3**
Puro RT to poly(dT)RT	1:10		1:1 or 1:3
Puro RT primer final conc.	0.18 uM		0.9 uM (1:1) or 0.5 uM (1:3)
Poly(dT) RT primer final conc.	1.8 uM		0.9 uM (1:1) or 1.4 uM (1:3)
Primers for ORF amplification **Step 3**	2 different forward primers for **Step 3** PCRs	2 different forward primers for **Step 3** PCRs	Different forward primer sequence than version 1 or version 2.... .... But the same forward primer is used in both **Step 3** PCRs

FIG. 18E

Primer Sequences for ORF RT and amplification

	Version 1	Version 2	Version 3
Step 1 - Puro RT		GCCTTCCATCTGTTGCTGC SEQ. ID No. 55	
Step 2 - Nested puro primer *cDNA amplification*		ACACCTTGCCGATGTCG*A*G SEQ. ID No. 56	
Step 3 *PCR1 - forward*	AATGATACGGCGACCACCGAGATCTACACTCTTTCCCTACACG ACGCTC SEQ. ID No. 57		GATCTACACTCTTTCCCTACAC GACGC SEQ. ID No. 58
Step 3 *PCR1 - reverse*		AGGAAGAGTTCTTGCAGCTCG SEQ. ID No. 59	
Step 3 *PCR2 - forward*		AATGATACGGCGACCACCGAGATCT SEQ. ID No. 60	GATCTACACTCTTTCCCTACAC GACGC SEQ. ID No. 61
Step 3 *PCR2 - reverse*		ACCGTGGGCTTGTACTC SEQ. ID No. 62	

Step 1 and 2 reactions are performed in the same manner as for transcriptome (10x 5' protocol) and the ORF library is not yet separated (everything in one tube — ORF and transcriptome).

FIG. 18F

PCR protocols for ORF amplification (Step 3) for each version

Step 3 separates ORF and transcriptome.

PCR protocol (same for V1, V2, V3 – the only differences are in primer sequences):

PCR1:

Composition: 50 ng cDNA (step 2), 20 ul 5X Q5 buffer, 2 ul 10 mM dNTP, 4 ul 10 uM forward primer (Step 3 – PCR1 forward), 4 ul 10 uM reverse primer (Step 3 – PCR1 reverse), 1 ul Q5 polymerase, ddH2O to 100 ul

Cycling: 98C for 45s, then 10 cycles of: 98C – 20s, 62C – 30s, 72C – 2 min; and final extension for 1 min at 72C

Purify the PCR reaction using 0.8X SPRI beads, elute in 35 ul water and proceed to PCR2.

PCR2:

Composition: 35 ul elution (step 3 PCR1), 20 ul 5X Q5 buffer, 2 ul 10 mM dNTP, 4 ul 10 uM forward primer (Step 3 – PCR2 forward), 4 ul 10 uM reverse primer (Step 3 – PCR2 reverse), 1 ul Q5 polymerase, ddH2O to 100 ul

Cycling: 98C for 45s, then 10 cycles of: 98C – 20s, 62C – 30s, 72C – 2 min; and final extension for 1 min at 72C

Purify the PCR reaction using 0.8X SPRI beads, elute in 35 ul water and proceed to library construction (same as 10X transcriptome library construction).

FIG. 18G

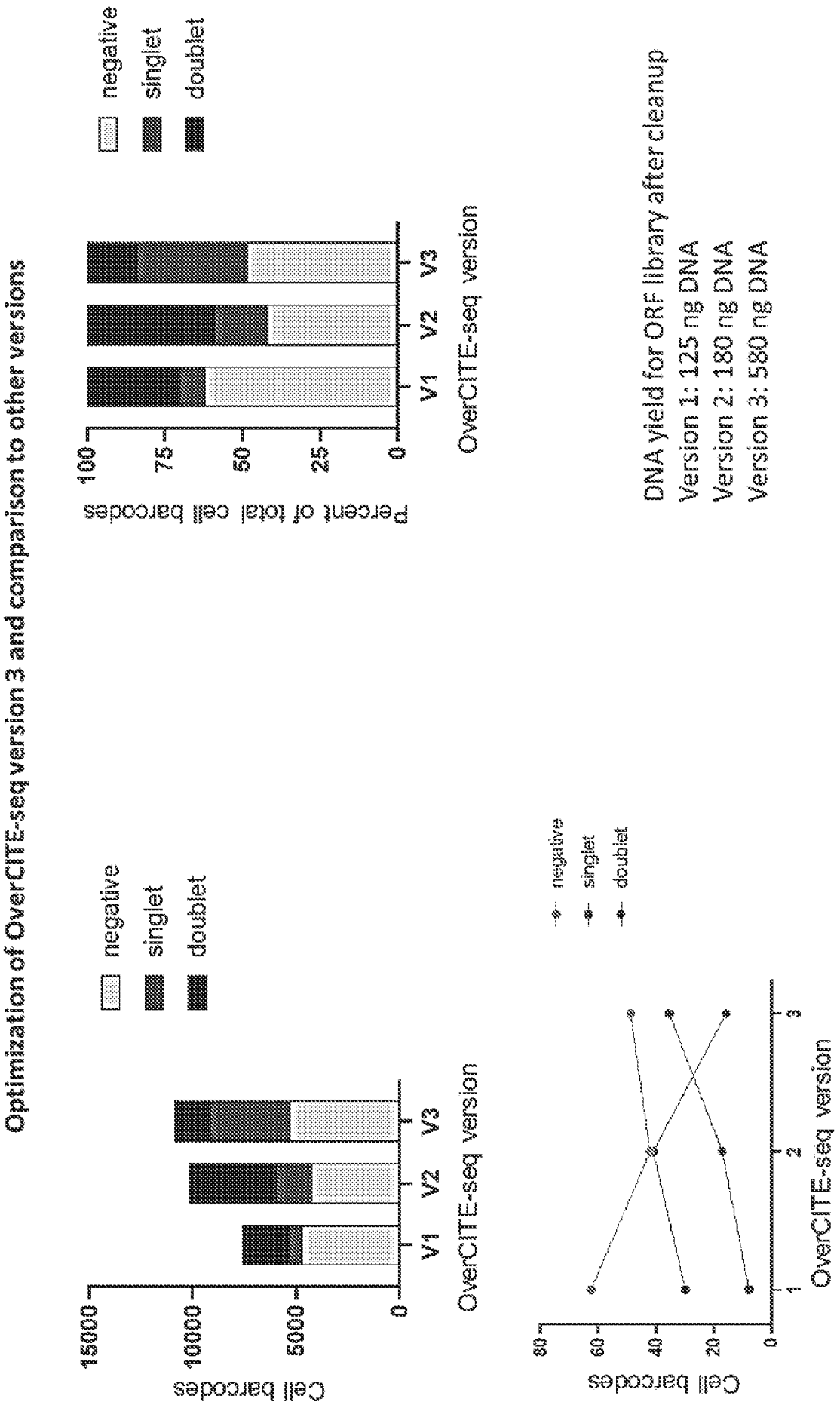

Optimization of OverCITE-seq version 3 and comparison to other versions
negative
singlet
doublet
Percent of total cell barcodes
100
75
50
25
0
V1
V2
V3
OverCITE-seq version
Cell barcodes
15000
10000
5000
0
DNA yield for ORF library after cleanup
Version 1: 125 ng DNA
Version 2: 180 ng DNA
Version 3: 580 ng DNA
80
60
40
20
1
2
3

FIG. 19-1

NCT Number	Title	Conditions	Interventions	URL
NCT03423992	Personalized Chimeric Antigen Receptor T Cell Immunotherapy for Patients With Recurrent Malignant Gliomas	Glioma|Malignant Glioma of Brain|Recurrence Tumor	Biological: chimeric antigen receptor T cells	https://ClinicalTrials.gov/show/NCT03423992
NCT04650724	Clinical Study of T Cell Infusion Targeting BCMA Chimeric Antigen Receptor	Multiple Myeloma	Drug: T cell infusion agent targeting BCMA chimeric antigen receptor	https://ClinicalTrials.gov/show/NCT04650724
NCT02644655	Immunotherapy Using Autologous T Cell-Engineered With CD19-specific Chimeric Antigen Receptor for the Treatment of Recurrent /Refractory B Cell Leukemia	Recurrent B-Cell Tumor|Refractory B-Cell Tumor	Biological: CD19-specific chimeric antigen receptor	https://ClinicalTrials.gov/show/NCT02644655
NCT04107142	Haplo / Allogeneic NKG2DL-targeting Chimeric Antigen Receptor-grafted γδ T Cells for Relapsed or Refractory Solid Tumour	Colorectal Cancer|Triple Negative Breast Cancer|Sarcoma|Nasopharyngeal Carcinoma|Prostate Cancer|Gastric Cancer	Biological: Adoptive Cell Transfer of NKG2DL-targetting Chimeric Antigen Receptor-grafted Gamma Delta T cell	https://ClinicalTrials.gov/show/NCT04107142
NCT03758417	A Study of LCAR-B38M CAR-T Cells, a Chimeric Antigen Receptor T-cell (CAR-T) Therapy Directed Against B-cell Maturation Antigen (BCMA) in Chinese Participants With Relapsed or Refractory Multiple Myeloma	Multiple Myeloma	Biological: LCAR-B38M CAR-T Cell	https://ClinicalTrials.gov/show/NCT03758417
NCT03874897	Chimeric Antigen Receptor T Cells Targeting claudin18.2 in Solid Tumors.	Advanced Solid Tumor	Drug: CAR-CLDN18.2 T-Cells	https://ClinicalTrials.gov/show/NCT03874897
NCT03938987	Anti-CD19, Dual Co-stimulatory (4-1BB, CD3ζ) Chimeric Antigen Receptor T-cells in Patients With Relapsed/Refractory Aggressive Lymphoma or Acute Lymphoblastic Leukemia (ALL)	Relapsed Non Hodgkin Lymphoma|Relapsed Adult ALL|Relapsed Pediatric ALL	Biological: autologous CD19-directed chimeric antigen receptor (CAR) T-cells	https://ClinicalTrials.gov/show/NCT03938987
NCT03241940	Phase I Dose Escalation Study of CD19/CD22 Chimeric Antigen Receptor (CAR) T Cells in Children and Young Adults With Recurrent or Refractory B Cell Malignancies	B Acute Lymphoblastic Leukemia|CD19 Positive|Minimal Residual Disease|Philadelphia Chromosome Positive|Recurrent Adult Acute Lymphoblastic Leukemia|Recurrent Childhood Acute Lymphoblastic Leukemia|Refractory Acute Lymphoblastic Leukemia	Biological: Chimeric Antigen Receptor T-Cell Therapy|Drug: Cyclophosphamide|Drug: Fludarabine Phosphate|Other: Laboratory Biomarker Analysis|Other: Questionnaire Administration	https://ClinicalTrials.gov/show/NCT03241940
NCT02659943	T Cells Expressing a Fully-human AntiCD19 Chimeric Antigen Receptor for Treating B-cell Malignancies	Lymphoma, B-Cell|Lymphoma, Non-hodgkins	Biological: Anti-cluster of differentiation 19 (CD19)-Chimeric Antigen Receptor (CAR) T cells|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT02659943
NCT03884751	Chimeric Antigen Receptor T Cells Targeting Glypican-3	Hepatocellular Carcinoma	Biological: CAR-GPC3 T Cells	https://ClinicalTrials.gov/show/NCT03884751

FIG. 19-2

NCT Number	Title	Conditions	Interventions	URL
NCT02442297	T Cells Expressing HER2-specific Chimeric Antigen Receptors(CAR) for Patients With HER2-Positive CNS Tumors	Brain Tumor, Recurrent|Brain Tumor, Refractory	Biological: HER2-specific T cells	https://ClinicalTrials.gov/show/NCT02442297
NCT03233854	CD19/CD22 Chimeric Antigen Receptor(CAR) T Cells in Adults With Recurrent/Refractory B Cell Malignancies	B Acute Lymphoblastic Leukemia|CD19 Positive|Diffuse Large B-Cell Lymphoma Associated With Chronic Inflammation|Diffuse Large B-Cell Lymphoma, Not Otherwise Specified|Epstein-Barr Virus Positive Diffuse Large B-Cell Lymphoma of the Elderly|Minimal Residual Disease|Philadelphia Chromosome Positive|Recurrent Diffuse Large B-Cell Lymphoma|Recurrent Mediastinal (Thymic) Large B-Cell Cell Lymphoma|Refractory Diffuse Large B-Cell Lymphoma|Refractory Mediastinal (Thymic) Large B-Cell Cell Lymphoma|T-Cell/Histiocyte-Rich Large B-Cell Lymphoma	Biological: Chimeric Antigen Receptor T-Cell Therapy|Drug: Cyclophosphamide|Drug: Fludarabine Phosphate|Other: Laboratory Biomarker Analysis|Other: Questionnaire Administration	https://ClinicalTrials.gov/show/NCT03233854
NCT03434769	AntiCD19 Chimeric Antigen Receptor T Cells for Relapsed or Refractory Non Hodgkin Lymphoma	Non-Hodgkin Lymphoma	Drug: Cyclophosphamide|Drug: Fludarabine|Biological: CAR-T Cells	https://ClinicalTrials.gov/show/NCT03434769
NCT04153799	Study of CXCR5 Modified EGFE Chimeric Antigen Receptor Autologous T Cells in EGFR- Positive Patients With Advanced Non-small Cell Lung Cancer	Non Small Cell Lung Cancer	Biological: CXCR5 modified EGFR Chimeric Antigen Receptor Autologous T cells	https://ClinicalTrials.gov/show/NCT04153799
NCT03118180	CD19 Targeted Chimeric Antigen Receptor T Cells for B Cell Lymphoma	Lymphoma	Biological: CD19 targeted chimeric antigen receptor T cells	https://ClinicalTrials.gov/show/NCT03118180
NCT04888338	Outcomes After Chimeric Antigen Receptor Therapy and Radiation Therapy for Hematologic Malignancies	Hematopoietic and Lymphoid Cell Neoplasm	Other: Data Capture|Other: Electronic Medical Record	https://ClinicalTrials.gov/show/NCT04888338
NCT02992834	Anti-CD19:TCR¶ Chimeric Antigen Receptor-T Cells in the Treatment for CD19+ B Cell Lymphoma	Lymphoma, B Cell	Biological: IL-2 pre-treated CD19 cells|Biological: IL-7/IL-15 pre-treated CD19 cells	https://ClinicalTrials.gov/show/NCT02992834
NCT04480788	CD7-CART in the Treatment of r / r CD7 Positive Hemolymph System Malignancies on Increasing Dose and Open Label Study	T Lymphoblastic Leukemia/Lymphoma|Extramedullary NK-T-cell Lymphoma, Nasal Type|Peripheral T-cell Lymphoma, Nonspecific|Angioimmunoblastic T-cell Lymphoma|Enteropathy-Associated T-Cell Lymphoma|Anaplastic Large Cell Lymphoma, ALK-negative|T-cell Lymphoblastic Leukemia	Biological: T cell injection targeting CD7 chimeric antigen receptor	https://ClinicalTrials.gov/show/NCT04480788
NCT02349698	A Clinical Research of CAR T Cells Targeting CD19 Positive Malignant B-cell Derived Leukemia and Lymphoma	Leukemia|Lymphoma	Biological: Chimeric Antigen Receptor Modified T cells Targeting CD19	https://ClinicalTrials.gov/show/NCT02349698

FIG. 19-3

NCT Number	Title	Conditions	Interventions	URL
NCT04205838	Anakinra in Preventing Severe Chimeric Antigen Receptor T-Cell Related Encephalopathy Syndrome in Patients With Recurrent or Refractory Large B-cell Lymphoma	Diffuse Large B-Cell Lymphoma, Not Otherwise Specified|High Grade B-Cell Lymphoma|Progressive Disease|Recurrent Diffuse Large B-Cell Lymphoma|Recurrent High Grade B-Cell Lymphoma|Recurrent Primary Mediastinal (Thymic) Large B-Cell Cell Lymphoma|Recurrent Transformed Follicular Lymphoma to Diffuse Large B-Cell Lymphoma|Refractory Diffuse Large B-Cell Lymphoma|Refractory High Grade B-Cell Lymphoma|Refractory Primary Mediastinal (Thymic) Large B-Cell Cell Lymphoma|Refractory Transformed Follicular Lymphoma to Diffuse Large B-Cell Lymphoma	Biological: Anakinra|Biological: Axicabtagene Ciloleucel|Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Fludarabine Phosphate	https://ClinicalTrials.gov/show/NCT04205838
NCT04340154	Study of Sequential CAR-T Cell Treating Leukemia Children	Acute Lymphoblastic Leukemia|Acute Lymphoblastic Leukemia, in Relapse|Refractory Acute Lymphoid Leukemia	Biological: chimeric antigen receptor T cell	https://ClinicalTrials.gov/show/NCT04340154
NCT03624686	Production of Clinical-grade Anti-CD19 Chimeric Antigen Receptor T Cells for Refractory B-cell Malignancies	Leukemia	Other: peripheral blood	https://ClinicalTrials.gov/show/NCT03624686
NCT04870853	Cardiovascular Events Among Adults Patients With Relapsed or Refractory Aggressive B-Cell Lymphoma Treated With Standard of Care Chimeric Antigen Receptor T Cell Therapy	Recurrent Aggressive B-Cell Non-Hodgkin Lymphoma|Recurrent Diffuse Large B-Cell Lymphoma|Recurrent High Grade B-Cell Lymphoma|Recurrent Primary Mediastinal (Thymic) Large B-Cell Lymphoma|Recurrent Transformed Follicular Lymphoma to Diffuse Large B-Cell Lymphoma|Refractory Aggressive B-Cell Non-Hodgkin Lymphoma|Refractory Diffuse Large B-Cell Lymphoma|Refractory High Grade B-Cell Lymphoma|Refractory Primary Mediastinal (Thymic) Large B-Cell Lymphoma|Refractory Transformed Follicular Lymphoma to Diffuse Large B-Cell Lymphoma	Other: Electronic Health Record Review	https://ClinicalTrials.gov/show/NCT04870853
NCT04864821	Clinical Study of CD276 Targeted Autologous Chimeric Antigen Receptor T Cell Infusion in Patients With CD276 Positive Advanced Solid Tumor	Osteosarcoma|Neuroblastoma|Gastric Cancer|Lung Cancer	Drug: Targeting CD276 CAR T cells	https://ClinicalTrials.gov/show/NCT04864821
NCT04279470	Chimeric Antigen Receptor T-cell and Cellular Therapies for the Treatment of cAncer or BLood Diseases: Evaluation of Reporting of Adverse Events	Adverse Drug Reactions|Cancer	Drug: CAR T-cell and Cellular Therapies	https://ClinicalTrials.gov/show/NCT04279470
NCT03291444	CAR-T Cells Combined With Peptide Specific Dendritic Cell in Relapsed/Refractory Leukemia/MDS	Leukemia, Acute Lymphocytic (ALL)|Leukemia, Acute Myelogenous (AML)|Myelodysplastic Syndromes	Biological: Chimeric antigen receptor T cells|Biological: peptide specific dendritic cell	https://ClinicalTrials.gov/show/NCT03291444
NCT04082910	Metoprolol for the Treatment of Cytokine Release Syndrome in Patients Treated With Chimeric Antigen Receptor T Cells	Solid Tumor|Hematological Malignancy	Drug: Metoprolol|Drug: anti-TNFÎ± antibody	https://ClinicalTrials.gov/show/NCT04082910

FIG. 19-4

NCT Number	Title	Conditions	Interventions	URL
NCT02959151	A Study of Chimeric Antigen Receptor T Cells Combined With Interventional Therapy in Advanced Liver Malignancy	Carcinoma, Hepatocellular|Pancreatic Cancer Metastatic|Colorectal Cancer Metastatic	Drug: CAR-T cell	https://ClinicalTrials.gov/show/NCT02959151
NCT04169022	AML Cell Immunotherapy Using Chimeric Antigen Receptor T-cells	Acute Myeloid Leukemia	Other: Sample collection	https://ClinicalTrials.gov/show/NCT04169022
NCT04049513	ENABLE (Engaging Toll-like Receptor Signalling for B-cell Lymphoma Chimeric Antigen Receptor Therapy)	Lymphomas Non-Hodgkin's B-Cell|Diffuse Large B-cell Lymphoma (DLBCL)|Primary Mediastinal B-cell Lymphoma (PMBCL)|Transformed Follicular Lymphoma (TFL)|Follicular Lymphoma (FL)|Mantle Cell Lymphoma (MCL)	Biological: WZTL002-1 (1928T2z CAR-T cells)|Drug: Cyclophosphamide and Fludarabine lymphodepleting chemotherapy	https://ClinicalTrials.gov/show/NCT04049513
NCT03086954	Study Evaluating the Efficacy and Safety With CAR-T Immunotherapy for CD19 Positive Lymphoma	Lymphoma	Biological: The Chimeric Antigen Receptor T Cell Immunotherapy (CAR-T)	https://ClinicalTrials.gov/show/NCT03086954
NCT03267173	Evaluate the Safety and Efficacy of CAR-T in the Treatment of Pancreatic Cancer.	Pancreatic Cancer|CAR	Drug: Chimeric antigen receptor T cell	https://ClinicalTrials.gov/show/NCT03267173
NCT01593696	Anti-CD19 White Blood Cells for Children and Young Adults With B Cell Leukemia or Lymphoma	ALL|B Cell Lymphoma|Leukemia|Large Cell Lymphoma|Non-Hodgkin Lymphoma	Biological: Anti-Cluster of Differentiation (CD)19-Chimeric antigen receptor (CAR)	https://ClinicalTrials.gov/show/NCT01593696
NCT04223765	Study of Kappa Chimeric Antigen Receptor (CAR) T Lymphocytes Co-Expressing the Kappa and CD28 CARs for Relapsed/Refractory Kappa+ Non-Hodgkin Lymphoma and Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma.	Mantle Cell Lymphoma|Follicular Lymphoma|Splenic Marginal Zone Lymphoma|Extranodal Marginal Zone Lymphoma of Mucosa-Associated Lymphoid Tissue|Nodal Marginal Zone Lymphoma|Indolent Non-hodgkin Lymphoma	Drug: CAR.k.28|Drug: Fludarabine|Drug: Cyclophosphamide|Drug: Bendamustine	https://ClinicalTrials.gov/show/NCT04223765
NCT02742727	CAR-pNK Cell Immunotherapy in CD7 Positive Leukemia and Lymphoma	Acute Myeloid Leukemia|Precursor T-Cell Lymphoblastic Leukemia-Lymphoma|T-cell Prolymphocytic Leukemia|T-cell Large Granular Lymphocytic Leukemia|Peripheral T-cell Lymphoma, NOS|Angioimmunoblastic T-cell Lymphoma|Extranodal NK/T-cell Lymphoma, Nasal Type|Enteropathy-type Intestinal T-cell Lymphoma|Hepatosplenic T-cell Lymphoma	Biological: anti-CD7 CAR-pNK cells	https://ClinicalTrials.gov/show/NCT02742727
NCT04219163	Chimeric Antigen Receptor T-cells for The Treatment of AML Expressing CLL-1 Antigen	Acute Myeloid Leukemia	Biological: CLL-1.CAR T cells	https://ClinicalTrials.gov/show/NCT04219163
NCT04214392	Chimeric Antigen Receptor (CAR) T Cells With a Chlorotoxin Tumor-Targeting Domain for the Treatment of MPP2+ Recurrent or Progressive Glioblastoma	Recurrent Glioblastoma|Recurrent Malignant Glioma|Recurrent WHO Grade II Glioma|Recurrent WHO Grade III Glioma	Biological: Chlorotoxin (EQ)-CD28-CD3zeta-CD19t-expressing CAR T-lymphocytes	https://ClinicalTrials.gov/show/NCT04214392
NCT04691349	CAR-T for r/r Malignant Tumors in Children	CAR-T|Child, Only|Malignant Tumor	Drug: CAR-T	https://ClinicalTrials.gov/show/NCT04691349

FIG. 19-5

NCT Number	Title	Conditions	Interventions	URL
NCT02439788	3RD GENERATION GD2 SPECIFIC CHIMERIC ANTIGEN RECEPTOR TRANSDUCED AUTOLOGOUS NATURAL KILLER T-CELLS FOR NEUROBLASTOMA	Neuroblastoma	Drug: cyclophosphamide|Drug: Fludarabine|Genetic: GINAKIT Cells	https://ClinicalTrials.gov/show/NCT02439788
NCT04029038	Modified Immune Cells (CD19-CD22 CAR T Cells) in Treating Patients With Recurrent or Refractory CD19 Positive, CD22 Positive Leukemia or Lymphoma	CD19 Positive|CD22 Positive|Minimal Residual Disease|Progressive Disease|Recurrent B Acute Lymphoblastic Leukemia|Recurrent Chronic Lymphocytic Leukemia|Recurrent Non-Hodgkin Lymphoma|Refractory B Acute Lymphoblastic Leukemia|Refractory Chronic Lymphocytic Leukemia|Refractory Non-Hodgkin Lymphoma	Biological: Autologous CD19/CD22 Chimeric Antigen Receptor T-cells|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT04029038
NCT03327285	C-CAR011 Treatment in Subjects With ALL After HSCT	Acute Lymphoblastic Leukemia(ALL)	Biological: C-CAR011	https://ClinicalTrials.gov/show/NCT03327285
NCT04796688	Universal Chimeric Antigen Receptor-modified AT19 Cells for CD19+ Relapsed/Refractory Hematological Malignancies	Acute Lymphoblastic Leukemia|Chronic Lymphoblastic Leukemia|B-cell Lymphoma	Drug: Fludarabine + Cyclophosphamide + CAR-NK-CD19 Cells	https://ClinicalTrials.gov/show/NCT04796688
NCT03980288	4th Generation Chimeric Antigen Receptor T Cells Targeting Glypican-3	Advanced Hepatocellular Carcinoma	Drug: CAR-GPC3 T Cells	https://ClinicalTrials.gov/show/NCT03980288
NCT04545762	Anti-CD19 Chimeric Antigen Receptor T Cells for Treatment of Relapsed or Refractory Non-Hodgkin Lymphoma	Refractory Non-Hodgkin Lymphoma|Burkitt Lymphoma|Mantle Cell Lymphoma|Follicular Lymphoma|Lymphoplasmacytic Lymphoma|Primary Mediastinal Large B Cell Lymphoma|Diffuse Large B Cell Lymphoma|Small Lymphocytic Lymphoma|Transformed Lymphoma	Drug: Fludarabine|Drug: Cyclophosphamide|Biological: anti-CD19 CAR-T cells	https://ClinicalTrials.gov/show/NCT04545762
NCT04231747	A Study of CC-97540, CD19-targeted NEX-T Chimeric Antigen Receptor (CAR) T Cells, in Subjects With Relapsed or Refractory B-cell Non-Hodgkin Lymphoma	Lymphoma Non-Hodgkin|Agressive Lymphoma|Diffuse-large B-cell Lymphoma (DLBCL)	Biological: CC-97540	https://ClinicalTrials.gov/show/NCT04231747
NCT04351022	CD38-targeted Chimeric Antigen Receptor T Cell (CART) in Relapesd or Refractory Acute Myeloid Leukemia	Acute Myeloid Leukemia	Biological: CART-38	https://ClinicalTrials.gov/show/NCT04351022
NCT04626908	Clinical Study of Targeting CD19 and CD22 Chimeric Antigen Receptor T Lymphocytes in the Treatment of Recurrent or Refractory B Cell Non-Hodgkin Lymphoma	Relapsed and Refractory|Lymphoid Hematological Malignancies	Drug: GC022F CAR-T cells	https://ClinicalTrials.gov/show/NCT04626908
NCT02813837	Chimeric Antigen Receptor T Cells (CART) Therapy in Refractory/Relapsed B Cell Hematologic Malignancies	Leukemia, B-Cell|Lymphoma, B-Cell	Biological: CD19CART	https://ClinicalTrials.gov/show/NCT02813837

FIG. 19-6

NCT Number	Title	Conditions	Interventions	URL
NCT04702841	CAR - [3] T Cells in the Treatment of Relapsed and Refractory CD7 Positive T Cell-derived Malignant Tumors	CAR | Malignant Tumors	Drug: Chimeric antigen receptor modified [3] T cells	https://ClinicalTrials.gov/show/NCT04702841
NCT04691713	CD276 CAR-T for Patients With Advanced CD276+ Solid Tumors	CAR | Solid Tumor	Drug: Targeting CD276 autologous chimeric antigen receptor T cells	https://ClinicalTrials.gov/show/NCT04691713
NCT04337606	Chidamide in Combination With Decitabine in Non-Hodgkin's Lymphoma Relapsed After Chimeric Antigen Receptor	Non Hodgkin Lymphoma	Drug: Chidamide | Drug: Decitabine | Drug: Camrelizumab	https://ClinicalTrials.gov/show/NCT04337606
NCT04692948	TAA6 Cell Injection In The Treatment of Patients With Relapsed / Refractory Acute Myeloid Leukemia	CAR | Acute Myeloid Leukemia	Other: Chimeric antigen receptor T cells (car-t)	https://ClinicalTrials.gov/show/NCT04692948
NCT02259556	CD30-directed Chimeric Antigen Receptor T (CART30) Therapy in Relapsed and Refractory CD30 Positive Lymphomas	Hodgkin's Lymphoma | Non-Hodgkin's Lymphoma	Biological: CART30	https://ClinicalTrials.gov/show/NCT02259556
NCT02107963	A Phase I Trial of T Cells Expressing an Anti-GD2 Chimeric Antigen Receptor in Children and Young Adults With GD2+ Solid Tumors	Sarcoma | Osteosarcoma | Neuroblastoma | Meianoma	Biological: Anti-GD2-CAR engineered T cells | Drug: AP1903 | Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT02107963
NCT04404595	Claudin18.2 CAR-T (CT041) in Patients With Gastric or Pancreatic Cancer	Gastric Cancer | Pancreatic Cancer	Biological: CT041	https://ClinicalTrials.gov/show/NCT04404595
NCT01087294	Administration of Anti-CD19-chimeric-antigen-receptor-transduced T Cells From the Original Transplant Donor to Patients With Recurrent or Persistent B-cell Malignancies After Allogeneic Stem Cell Transplantation	Leukemia, B-cell | Lymphoma, Hodgkins | Lymphoma, Non-hodgkins | Lymphoma, B-Cell	Procedure: Allogeneic stem cell transplant | Biological: Anti-CD19-chimeric- antigen-receptor- transduced T cells | Procedure: Leukapheresis	https://ClinicalTrials.gov/show/NCT01087294
NCT04209829	Response to Chimeric Antigen Receptor (CAR)-T Cells Therapy in Patients With Hematologic Malignancies Depending on Tumor Characteristics	Hematologic Diseases		https://ClinicalTrials.gov/show/NCT04209829
NCT03829540	CD4CAR for CD4+ Leukemia and Lymphoma	T-cell Lymphoma | T-cell Leukemia	Biological: CD4CAR	https://ClinicalTrials.gov/show/NCT03829540
NCT02209376	Autologous T Cells Redirected to EGFRVIII- With a Chimeric Antigen Receptor in Patients With EGFRVIII+ Glioblastoma	Patients With Residual or Reccurent EGFRvIII+ Glioma	Biological: CART-EGFRvIII T cells	https://ClinicalTrials.gov/show/NCT02209376

FIG. 19-7

NCT Number	Title	Conditions	Interventions	URL
NCT04394650	A Study of CC-98633, BCMA-targeted Chimeric Antigen Receptor (CAR) T Cells, in Subjects With Relapsed and/or Refractory Multiple Myeloma	Multiple Myeloma	Biological: CC-98633	https://ClinicalTrials.gov/show/NCT04394650
NCT03076437	Anti-CD19 Chimeric Antigen Receptor (CAR)-Transduced T Cell Therapy for Patients With B Cell Malignancies	Acute Lymphocytic Leukemia|Chronic Lymphocytic Leukemia|Lymphoma	Combination Product: Drugs and Anti-CD19-CAR transduced T cells	https://ClinicalTrials.gov/show/NCT03076437
NCT02203825	Safety Study of Chimeric Antigen Receptor Modified T-cells Targeting NKG2D-Ligands	Acute Myeloid Leukemia|Myelodysplastic Syndrome|Multiple Myeloma	Biological: CM-CS1 T-cell infusion	https://ClinicalTrials.gov/show/NCT02203825
NCT03971799	Study of Anti-CD33 Chimeric Antigen Receptor-Expressing T Cells (CD33CART) in Children and Young Adults With Relapsed/Refractory Acute Myeloid Leukemia	Acute Myelogenous Leukemia	Biological: CD33CART	https://ClinicalTrials.gov/show/NCT03971799
NCT02588456	Pilot Study of Autologous Anti-CD22 Chimeric Antigen Receptor Redirected T Cells in Patients With Chemotherapy Resistant Or Refractory Acute Lymphoblastic Leukemia	Relapsed or Refractory B-cell Acute Lymphoblastic Leukemia	Biological: CART22 cells	https://ClinicalTrials.gov/show/NCT02588456
NCT02186860	Chimeric Antigen Receptor (CAR)-Modified T Cell Therapy in Treating Patients With Acute Lymphoblastic Leukemia	Acute Lymphoblastic Leukemia	Biological: CAR-T cells	https://ClinicalTrials.gov/show/NCT02186860
NCT04785833	CD7 CAR-T in the Treatment of CD7 Positive Refractory Relapsed Acute Leukemia	T-ALL	Drug: T cell injection targeting CD7 chimeric antigen receptor	https://ClinicalTrials.gov/show/NCT04785833
NCT04555551	MCARH109 Chimeric Antigen Receptor (CAR) Modified T Cells for the Treatment of Multiple Myeloma	Multiple Myeloma	Biological: Infusion of MCARH109 T cells	https://ClinicalTrials.gov/show/NCT04555551
NCT02905188	Glypican 3-specific Chimeric Antigen Receptor Expressing T Cells for Hepatocellular Carcinoma (GLYCAR)	Hepatocellular Carcinoma	Genetic: GLYCAR T cells|Drug: Cytoxan|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT02905188
NCT02932956	Glypican 3-specific Chimeric Antigen Receptor Expressed in T Cells for Patients With Pediatric Solid Tumors (GAP)	Liver Cancer	Genetic: GAP T cells|Drug: Cytoxan|Drug: Fludara	https://ClinicalTrials.gov/show/NCT02932956
NCT04377932	Interleukin-15 Armored Glypican 3-specific Chimeric Antigen Receptor Expressed in T Cells for Pediatric Solid Tumors	Liver Cancer|Rhabdomyosarcoma|Malignant Rhabdoid Tumor|Liposarcoma|Wilms Tumor|Yolk Sac Tumor	Genetic: AGAR T cells|Drug: Cytoxan|Drug: Fludara	https://ClinicalTrials.gov/show/NCT04377932

FIG. 19-8

NCT Number	Title	Conditions	Interventions	URL
NCT02456350	Anti-CD19 Chimeric Antigen Receptor (CAR)-Transduced T Cell Therapy for Patients With B Cell Malignancies	Chronic Lymphocytic Leukemia|Acute Lymphocytic Leukemia|Lymphoma	Drug: Fludarabine|Drug: Cyclophosphamide|Biological: Anti-CD19-CAR transduced T cells	https://ClinicalTrials.gov/show/NCT02456350
NCT04715191	Interleukin-15 and -21 Armored Glypican-3-specific Chimeric Antigen Receptor Expressed in T Cells for Pediatric Solid Tumors	Liver Cancer|Rhabdomyosarcoma|Malignant Rhabdoid Tumor|Liposarcoma|Wilms Tumor|Yolk Sac Tumor	Genetic: CARE T cells|Drug: Cytoxan|Drug: Fludara	https://ClinicalTrials.gov/show/NCT04715191
NCT04325841	Phase II Study of Anti-CD19 CAR-T Cells Treating Leukemia Children	Acute Lymphoblastic Leukemia, Pediatric|Acute Lymphoblastic Leukemia, in Relapse|Refractory Acute Lymphoblastic Leukemia	Biological: Murine autologous anti-CD19 chimeric antigen receptor T cells	https://ClinicalTrials.gov/show/NCT04325841
NCT04093648	T Cells co- Expressing a Second Generation Glypican 3-specific Chimeric Antigen Receptor With Cytokines Interleukin-21 and 15 as Immunotherapy for Patients With Liver Cancer (TEGAR)	Hepatocellular Carcinoma|Hepatoblastoma	Genetic: TEGAR T cells|Drug: Cytoxan|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT04093648
NCT04340167	Study of Anti-CD22 CAR-T Cells Treating Leukemia Children	Acute Lymphoblastic Leukemia|Acute Lymphoblastic Leukemia, in Relapse|Refractory Acute Lymphoblastic Leukemia	Biological: Autologous humanized anti-CD22 chimeric antigen receptor T cells	https://ClinicalTrials.gov/show/NCT04340167
NCT04500431	Clinical Study to Evaluate the Safety and Feasibility of spCART-269 Injection in the Treatment of MM	Multiple Myeloma	Biological: Targeting CD269 chimeric antigen receptor engineered T cells	https://ClinicalTrials.gov/show/NCT04500431
NCT03548207	A Study of JNJ-68284528, a Chimeric Antigen Receptor T Cell (CAR-T) Therapy Directed Against B-Cell Maturation Antigen (BCMA) in Participants With Relapsed or Refractory Multiple Myeloma	Multiple Myeloma	Biological: JNJ-68284528	https://ClinicalTrials.gov/show/NCT03548207
NCT04452994	Individual Patient Investigational New Drug (IND) Expanded Access Program of JNJ-68284528, a Chimeric Antigen Receptor T Cell (CAR-T) Therapy for Participant With Multiple Myeloma	Multiple Myeloma	Drug: JNJ-68284528	https://ClinicalTrials.gov/show/NCT04452994
NCT04151186	A Clinical Study on the Safety and Efficacy of CAR-T Therapy for the TM4SF1- and EpCAM-positive Solid Tumors	Advanced Solid Tumor|Neoplasms	Biological: TM4SF1- and EpCAM-positive chimeric antigen receptor T-cell therapy	https://ClinicalTrials.gov/show/NCT04151186
NCT03302403	Clinical Study of Redirected Autologous T Cells With a Chimeric Antigen Receptor in Patients With Malignant Tumors	B Cell Lymphoma|B Cell Leukemia|Myeloma|Hepatocellular Carcinoma|Pancreatic Carcinoma|Adenocarcinoma of Esophagogastric Junction	Genetic: CAR-CD19 T cell|Genetic: CAR-BCMA T cell|Genetic: CAR-GPC3 T cell|Genetic: CAR-CLD18 T cell|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03302403

FIG. 19-9

NCT Number	Title	Conditions	Interventions	URL
NCT01822652	3rd Generation GD-2 Chimeric Antigen Receptor and iCaspase Suicide Safety Switch, Neuroblastoma, GRAIN	Neuroblastoma	Genetic: iC9-GD2 T Cells - frozen|Genetic: iC9-GD2 T Cells - fresh|Drug: Cytoxan|Drug: Fludara|Drug: Keytruda|Genetic: iC9-GD2 T cells	https://ClinicalTrials.gov/show/NCT01822652
NCT04778579	Study of the Infusion of ARI-0001 Cells in Patients With CD19 + Acute Lymphoid Leukemia Resistant or Refractory to Therapy	Acute Lymphoid Leukemia	Drug: ARI-0001 cells	https://ClinicalTrials.gov/show/NCT04778579
NCT04767308	Safety and Efficacy of CT125A Cells for Treatment of Relapsed/Refractory CD5+ Hematopoietic Malignancies	CD5+ Relapsed/Refractory Hematopoietic Malignancies|Chronic Lymphocytic Leukemia (CLL)|Mantle Cell Lymphoma (MCL)|Diffuse Large B-cell Lymphoma (DLBCL)|Follicular Lymphoma (FL)|Peripheral T-cell Lymphomas (PTCL)	Biological: CT125A cells|Drug: Cyclophosphamide, fludarabine	https://ClinicalTrials.gov/show/NCT04767308
NCT02723942	CAR-T Cell Immunotherapy for HCC Targeting GPC3	GPC3 Positive Hepatocellular Carcinoma|CAR-T Cell Immunotherapy	Biological: CAR-T cell immunotherapy	https://ClinicalTrials.gov/show/NCT02723942
NCT03500991	HER2-specific CAR T Cell Locoregional Immunotherapy for HER2-positive Recurrent/Refractory Pediatric CNS Tumors	Central Nervous System Tumor, Pediatric|Glioma|Ependymoma|Medulloblastoma|Germ Cell Tumor|Atypical Teratoid/Rhabdoid Tumor|Primitive Neuroectodermal Tumor|Choroid Plexus Carcinoma|Pineoblastoma	Biological: HER2-specific chimeric antigen receptor (CAR) T cell	https://ClinicalTrials.gov/show/NCT03500991
NCT00902044	Her2 Chimeric Antigen Receptor Expressing T Cells in Advanced Sarcoma	Sarcoma	Genetic: Autologous HER2-specific T cells|Drug: Fludarabine|Drug: Cyclophosphamide|Genetic: Autologous CAR Positive T cells	https://ClinicalTrials.gov/show/NCT00902044
NCT03696030	HER2-CAR T Cells in Treating Patients With Recurrent Brain or Leptomeningeal Metastases	Malignant Neoplasm|Metastatic Malignant Neoplasm in the Brain|Metastatic Malignant Neoplasm in the Leptomeninges|Breast Cancer|HER2-positive Breast Cancer	Biological: Chimeric Antigen Receptor T-Cell Therapy	https://ClinicalTrials.gov/show/NCT03696030
NCT03144583	Pilot Study on the Infusion of ARI-0001 Cells in Patients With CD19+ Leukemia or Lymphoma Refractory to Therapy	Leukemia|Lymphoma	Biological: Adult differentiated autologous T-cells	https://ClinicalTrials.gov/show/NCT03144583
NCT02839954	CAR-pNK Cell Immunotherapy in MUC1 Positive Relapsed or Refractory Solid Tumor	Hepatocellular Carcinoma|Non-small Cell Lung Cancer|Pancreatic Carcinoma|Triple-Negative Invasive Breast Carcinoma|Malignant Glioma of Brain|Colorectal Carcinoma|Gastric Carcinoma	Biological: anti-MUC1 CAR-pNK cells	https://ClinicalTrials.gov/show/NCT02839954
NCT04892277	CD19-Directed CAR-T Cell Therapy for the Treatment of Relapsed/Refractory B Cell Malignancies	Recurrent B-Cell Non-Hodgkin Lymphoma|Recurrent Chronic Lymphocytic Leukemia|Recurrent Small Lymphocytic Lymphoma|Refractory B-Cell Non-Hodgkin Lymphoma|Refractory Chronic Lymphocytic Leukemia|Refractory Small Lymphocytic Lymphoma|Richter Syndrome	Biological: Chimeric Antigen Receptor T-Cell Therapy|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT04892277
NCT03448978	Autologous CD8+ T-cells Expressing an Anti-BCMA CAR in Patients With Myeloma	Multiple Myeloma	Biological: Descartes-08|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03448978
NCT04817774	Safety & Tolerability Study of Chimeric Antigen Receptor T-Reg Cell Therapy in Living Donor Renal Transplant Recipients	Kidney Transplant Rejection|End Stage Renal Disease	Biological: TX200-TR101	https://ClinicalTrials.gov/show/NCT04817774

FIG. 19-10

NCT Number	Title	Conditions	Interventions	URL
NCT03277729	A Phase I/II Study to Evaluate the Safety of Cellular Immunotherapy Using Autologous T Cells Engineered to Express a CD20-Specific Chimeric Antigen Receptor for Patients With Relapsed or Refractory B Cell Non-Hodgkin Lymphomas	Recurrent B-Cell Non-Hodgkin Lymphoma | Recurrent Chronic Lymphocytic Leukemia | Recurrent Diffuse Large B-Cell Lymphoma | Recurrent Follicular Lymphoma | Recurrent Lymphoplasmacytic Lymphoma | Recurrent Mantle Cell Lymphoma | Recurrent Marginal Zone Lymphoma | Refractory B-Cell Non-Hodgkin Lymphoma | Refractory Diffuse Large B-Cell Lymphoma | Refractory Follicular Lymphoma | Refractory Lymphoplasmacytic Lymphoma | Refractory Mantle Cell Lymphoma | Refractory Transformed Non-Hodgkin Lymphoma | Recurrent Transformed B-Cell Non-Hodgkin Lymphoma | Recurrent Transformed Chronic Lymphocytic Leukemia | Refractory Marginal Zone Lymphoma | Refractory Transformed B-Cell Non-Hodgkin Lymphoma | Refractory Transformed Chronic Lymphocytic Leukemia | Recurrent Small Lymphocytic Lymphoma | Refractory Chronic Lymphocytic Leukemia | Refractory Small Lymphocytic Lymphoma	Biological: Chimeric Antigen Receptor T-Cell Therapy | Drug: Cyclophosphamide | Other: Laboratory Biomarker Analysis | Procedure: Leukapheresis | Drug: Fludarabine Phosphate	https://ClinicalTrials.gov/show/NCT03277729
NCT03294954	GD2 Specific CAR and Interleukin-15 Expressing Autologous NKT Cells to Treat Children With Neuroblastoma	Neuroblastoma	Genetic: GINAKIT Cells | Drug: Cyclophosphamide | Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03294954
NCT04025216	A Study of CART-TnMUC1 in Patients With TnMUC1-Positive Advanced Cancers	Non-Small Cell Lung Cancer | Ovarian Cancer | Fallopian Tube Cancer | Triple Negative Breast Cancer | Multiple Myeloma | Pancreatic Ductal Adenocarcinoma	Biological: CART-TnMUC1 | Drug: Cyclophosphamide | Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT04025216
NCT02547961	Chimeric Antigen Receptor-Modified T Cells for Breast Cancer	Breast Cancer	Biological: HER-2-targeting CAR T Cells infusion	https://ClinicalTrials.gov/show/NCT02547961
NCT04240808	Study of Feasibility and Safety of UCD19 Chimeric Antigen Receptor (CAR) T Cells in Adult Subjects With Relapsed/Refractory (R/R) B-Cell Non-Hodgkin's Lymphoma (B-NHL)	Non Hodgkin Lymphoma	Biological: UCD19 CAR T Cells	https://ClinicalTrials.gov/show/NCT04240808
NCT03614858	CD19/CD22-targeted Chimeric Antigen Receptor Engineered T Cell (CART) in B-Cell Acute Lymphoblastic Leukemia.	Leukemia, B-cell	Biological: CART-19/22	https://ClinicalTrials.gov/show/NCT03614858
NCT04089215	CD19-targeted CAR T Cells for Relapsed and Refractory (R/R) Non-Hodgkins Lymphoma	Lymphoma, Non-Hodgkin | Diffuse Large B Cell Lymphoma | Follicular Lymphoma	Biological: CD19-targeted Chimeric Antigen Receptor (CAR) T Cells	https://ClinicalTrials.gov/show/NCT04089215
NCT04923919	Clinical Study of Chimeric Antigen Receptor T Lymphocytes (CAR-T) in the Treatment of Myeloid Leukemia	Acute Myeloid Leukemia	Drug: Anti-CLL1 CART cells	https://ClinicalTrials.gov/show/NCT04923919
NCT04718883	CD19-targeted CAR T Cells for Relapsed and Refractory (R/R) Mantle Cell Lymphoma	Mantle Cell Lymphoma	Biological: CD19-targeted Chimeric Antigen Receptor (CAR) T Cells	https://ClinicalTrials.gov/show/NCT04718883

FIG. 19-11

NCT Number	Title	Conditions	Interventions	URL
NCT03999697	A Clinical Research of CD22-Targeted CAR-T in B Cell Malignancies	Diffuse Large B Cell Lymphoma|Follicular Lymphoma|Primary Cutaneous Follicle Centre Lymphoma|Extranodal Marginal Zone Lymphoma of Mucosa-Associated Lymphoid Tissue|Mantle Cell Lymphoma|Plasma Cell Neoplasm|B Cell Lymphoma	Drug: Autologous chimeric antigen receptor T cell transfusing agent targeting CD22	https://ClinicalTrials.gov/show/NCT03999697
NCT04007029	Modified Immune Cells (CD19/CD20 CAR-T Cells) in Treating Patients With Recurrent or Refractory B-Cell Lymphoma or Chronic Lymphocytic Leukemia	CD19 Positive|CD20 Positive|Recurrent Chronic Lymphocytic Leukemia|Recurrent Diffuse Large B-Cell Lymphoma|Recurrent Follicular Lymphoma|Recurrent Mantle Cell Lymphoma|Recurrent Primary Mediastinal (Thymic) Large B-Cell Cell Lymphoma|Recurrent Small Lymphocytic Lymphoma|Refractory Chronic Lymphocytic Leukemia|Refractory Diffuse Large B-Cell Lymphoma|Refractory Follicular Lymphoma|Refractory Mantle Cell Lymphoma|Refractory Primary Mediastinal (Thymic) Large B-Cell Cell Lymphoma|Refractory Small Lymphocytic Lymphoma	Biological: Chimeric Antigen Receptor T-Cell Therapy|Drug: Cyclophosphamide|Drug: Fludarabine Phosphate|Biological: Tocilizumab	https://ClinicalTrials.gov/show/NCT04007029
NCT04409314	Hypoxia-Specific Imaging to Predict Outcomes of Chimeric Antigen Receptor T-cell Therapy	Recurrent Aggressive Non-Hodgkin Lymphoma|Recurrent Diffuse Large B-Cell Lymphoma|Recurrent High Grade B-Cell Lymphoma|Recurrent Malignant Neoplasm|Recurrent Plasma Cell Myeloma|Recurrent Primary Mediastinal (Thymic) Large B-Cell Cell Lymphoma|Refractory Aggressive Non-Hodgkin Lymphoma|Refractory Diffuse Large B-Cell Lymphoma|Refractory High Grade B-Cell Lymphoma|Refractory Malignant Neoplasm|Refractory Plasma Cell Myeloma|Refractory Primary Mediastinal (Thymic) Large B-Cell Cell Lymphoma	Drug: Fluorine F 18-fluoroazomycin Arabinoside|Procedure: Positron Emission Tomography	https://ClinicalTrials.gov/show/NCT04409314
NCT04214886	CD19 Chimeric Antigen Receptor (CAR) T Cells for Adults With Recurrent or Refractory B Cell Malignancies	B-Cell Acute Lymphoblastic Leukemia, Adult|B-cell Lymphoma Refractory|B-cell Lymphoma Recurrent	Drug: Fludarabine|Drug: Cyclophosphamide|Biological: CD19-CD34 CAR transduced T cells	https://ClinicalTrials.gov/show/NCT04214886
NCT04003649	IL13Ralpha2-Targeted Chimeric Antigen Receptor (CAR) T Cells With or Without Nivolumab and Ipilimumab in Treating Patients With Recurrent or Refractory Glioblastoma	Recurrent Glioblastoma|Refractory Glioblastoma	Biological: IL13Ralpha2-specific Hinge-optimized 4-1BB-co-stimulatory CAR/Truncated CD19-expressing Autologous TN/MEM Cells|Biological: Ipilimumab|Biological: Nivolumab|Other: Quality-of-Life Assessment|Other: Questionnaire Administration	https://ClinicalTrials.gov/show/NCT04003649
NCT04897321	B7-H3-Specific Chimeric Antigen Receptor Autologous T-Cell Therapy for Pediatric Patients With Solid Tumors (3CAR)	Pediatric Solid Tumor|Osteosarcoma|Rhabdomyosarcoma|Neuroblastoma|Ewing Sarcoma|Wilms Tumor|Adrenocortical Cancer|Desmoplastic Small Round Cell Tumor|Germ Cell Cancer|Rhabdoid Tumor|Clear Cell Sarcoma|Hepatoblastoma|Melanoma|Carcinoma|Malignant Peripheral Nerve Sheath Tumors|Soft Tissue Sarcoma	Drug: Fludarabine|Drug: Cyclophosphamide|Drug: MESNA|Drug: B7-H3 CAR T cells	https://ClinicalTrials.gov/show/NCT04897321

FIG. 19-12

NCT Number	Title	Conditions	Interventions	URL
NCT02765243	Anti-GD2 4th Generation CART Cells Targeting Refractory and/or Recurrent Neuroblastoma	Neuroblastoma|Effects of Immunotherapy	Biological: Anti-GD2 CART	https://ClinicalTrials.gov/show/NCT02765243
NCT04008251	Humanized CD19 Chimeric Antigen Receptor (CAR)-Modified T Cell Therapy in Treating Patients With B-cell Malignancies	Acute Lymphoblastic Leukemia|B Cell Lymphoma	Genetic: Second generation humanized CAR-T cells	https://ClinicalTrials.gov/show/NCT04008251
NCT02965092	CD19 Chimeric Antigen Receptor (CAR)-Modified T Cell Therapy in Treating Patients With B-cell Malignancies	Acute Lymphoblastic Leukemia|B Cell Lymphoma	Genetic: Second generation CAR-T cells	https://ClinicalTrials.gov/show/NCT02965092
NCT04464200	19(T2)28z1xx Chimeric Antigen Receptor (CAR) T Cells in People With B-Cell Cancers	Diffuse Large B Cell Lymphoma|Primary Mediastinal Large B Cell Lymphoma|Transformed Follicular Lymphoma to Diffuse Large B Cell Lymphoma|Chronic Lymphocytic Leukemia|Indolent Non-Hodgkin Lymphoma|Marginal Zone Lymphoma|Waldenstrom Macroglobulinemia|Burkitt's Lymphoma|Primary CNS Lymphoma	Drug: 19(T2)28z1xx CAR T cells	https://ClinicalTrials.gov/show/NCT04464200
NCT03203369	Study to Evaluate the Safety and Clinical Activity of UCART123 in Patients With BPDCN	Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)	Biological: UCART123	https://ClinicalTrials.gov/show/NCT03203369
NCT04732845	Human AntiCD19 Chimeric Antigen Receptor T Cells for Relapsed or Refractory Lymphoid Malignancies	Non Hodgkin Lymphoma|Acute Lymphoblastic Leukemia|Chronic Lymphocytic Leukemia	Biological: Fully human anti CD19 CAR-T Cell Dose|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04732845
NCT04184414	The Clinical Application of Chimeric Antigen Receptor T Cells in the Treatment of CD19 Positive Recurrent Refractory B Cell-derived Hematological Malignancies	B Acute Lymphoblastic Leukemia|Mantle Cell Lymphoma|Follicular Lymphoma	Drug: CD19-CART	https://ClinicalTrials.gov/show/NCT04184414
NCT04614987	Serum Neurofilament Light (NfL) as a Marker for Brain Injury in Individuals Undergoing Chimeric Antigen Receptor-modified T Therapy	Neurotoxicity		https://ClinicalTrials.gov/show/NCT04614987
NCT04712864	Study of CD4-Targeted Chimeric Antigen Receptor T-Cells (CD4-CAR-T) in Subjects With Relapsed or Refractory T-Cell Lymphoma	T-Cell Lymphoma|Peripheral T-Cell Lymphoma Refractory|Cutaneous T-Cell Lymphoma Refractory|Cutaneous T-Cell Lymphoma Recurrent|Peripheral T-Cell Lymphoma Recurrent	Biological: LB1901	https://ClinicalTrials.gov/show/NCT04712864
NCT02349724	A Clinical Research of CAR T Cells Targeting CEA Positive Cancer	Lung Cancer|Colorectal Cancer|Gastric Cancer|Breast Cancer|Pancreatic Cancer	Biological: Anti-CEA-CAR T	https://ClinicalTrials.gov/show/NCT02349724
NCT04160195	T Cells Expressing Fully-human Anti-CD19 and Anti-CD20 Chimeric Antigen Receptors for Treating B-cell Malignancies and Hodgkin Lymphoma	Lymphoma, B-Cell|Lymphoma, Non-hodgkins|Chronic Lymphocytic Leukemia|B-Cell Chronic Lymphocytic Leukemia	Biological: Anti-CD19-CAR and Anti-CD20-CAR T cells|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT04160195

FIG. 19-13

NCT Number	Title	Conditions	Interventions	URL
NCT04205409	Nivolumab for Relapsed, Refractory, or Detectable Disease Post Chimeric Antigen Receptor T-cell Treatment in Patients With Hematologic Malignancies	Recurrent Chronic Lymphocytic Leukemia|Recurrent Diffuse Large B-Cell Lymphoma|Recurrent Follicular Lymphoma|Recurrent Grade 1 Follicular Lymphoma|Recurrent Grade 2 Follicular Lymphoma|Recurrent Grade 3 Follicular Lymphoma|Recurrent Grade 3a Follicular Lymphoma|Recurrent Marginal Zone Lymphoma|Recurrent Non-Hodgkin Lymphoma|Recurrent Plasma Cell Myeloma|Refractory Chronic Lymphocytic Leukemia|Refractory Diffuse Large B-Cell Lymphoma|Refractory Follicular Lymphoma|Refractory Marginal Zone Lymphoma|Refractory Non-Hodgkin Lymphoma|Refractory Plasma Cell Myeloma|Recurrent Mantle Cell Lymphoma|Refractory Mantle Cell Lymphoma	Biological: Nivolumab	https://ClinicalTrials.gov/show/NCT04205409
NCT03851146	A Study of Anti-Lewis Y Chimeric Antigen Receptor-T Cells (LeY-CAR-T) in Patients With Solid Tumours	Advanced Cancer	Biological: LeY CAR T cells	https://ClinicalTrials.gov/show/NCT03851146
NCT04133636	A Study of JNJ-68284528, a Chimeric Antigen Receptor T Cell (CAR-T) Therapy Directed Against B-cell Maturation Antigen (BCMA) in Participants With Multiple Myeloma	Multiple Myeloma	Drug: JNJ-68284528|Drug: Lenalidomide|Drug: Daratumumab|Drug: Bortezomib|Drug: Dexamethasone	https://ClinicalTrials.gov/show/NCT04133636
NCT03448393	CD19/CD22 Chimeric Antigen Receptor (CAR) T Cells in Children and Young Adults With Recurrent or Refractory CD19/CD22-expressing B Cell Malignancies	Acute Lymphoid Leukemia|B-Cell Leukemia|Leukemia, Lymphocytic, B Cell|B-Cell Lymphoma|Lymphoma, Non-Hodgkin	Biological: CD19/CD22 CAR T-Cells|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03448393
NCT02772198	T-cells Expressing Anti-CD19 CAR in Pediatric and Young Adults With B-cell Malignancies	Acute Lymphoblastic Leukemia, B-precursor|Non-Hodgkin Lymphoma, B-cell	Biological: CD19 CAR T cells	https://ClinicalTrials.gov/show/NCT02772198
NCT02830724	Administering Peripheral Blood Lymphocytes Transduced With a CD70-Binding Chimeric Antigen Receptor to People With CD70 Expressing Cancers	Pancreatic Cancer|Renal Cell Cancer|Breast Cancer|Melanoma|Ovarian Cancer	Drug: Cyclophospharnide|Drug: Fludarabine|Drug: Aldesleukin|Biological: Anti-hCD70 CAR transduced PBL	https://ClinicalTrials.gov/show/NCT02830724
NCT03954106	A Safety and Efficacy Study of Defibrotide in the Prevention of Chimeric Antigen Receptor-T-cell-associated Neurotoxicity	DLBCL|Neurotoxicity Syndromes	Drug: Defibrotide	https://ClinicalTrials.gov/show/NCT03954106
NCT04121273	GPC3-targeted CAR-T Cell for Treating GPC3 Positive Advanced HCC	Hepatocellular Carcinoma	Biological: CAR-T cell immunotherapy	https://ClinicalTrials.gov/show/NCT04121273
NCT03638167	EGFR806-specific CAR T Cell Locoregional Immunotherapy for EGFR-positive Recurrent or Refractory Pediatric CNS Tumors	Central Nervous System Tumor, Pediatric|Glioma|Ependymoma|Medulloblastoma|Germ Cell Tumor|Atypical Teratoid/Rhabdoid Tumor|Primitive Neuroectodermal Tumor|Choroid Plexus Carcinoma|Pineoblastoma	Biological: EGFR806-specific chimeric antigen receptor (CAR) T cell	https://ClinicalTrials.gov/show/NCT03638167

FIG. 19-14

NCT Number	Title	Conditions	Interventions	URL
NCT03497819	Autologous CARTmeso/19 Against Pancreatic Cancer	Pancreatic Cancer	Biological: CARTmeso CART19	https://ClinicalTrials.gov/show/NCT03497819
NCT01454596	CAR T Cell Receptor Immunotherapy Targeting EGFRvIII for Patients With Malignant Gliomas Expressing EGFRvIII	Malignant Glioma|Glioblastoma|Brain Cancer|Gliosarcoma	Biological: Epidermal growth factor receptor(EGFRv)III Chimeric antigen receptor (CAR) transduced PBL|Drug: Aldesleukin|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT01454596
NCT03252171	CAR-T Cell Immunotherapy for GD2 Positive Glioma Patients	GD2 Positive Glioma|CAR-T Cell Immunotherapy	Biological: CAR-T cell immunotherapy	https://ClinicalTrials.gov/show/NCT03252171
NCT03126864	Study of Adoptive Cellular Therapy Using Autologous T Cells Transduced With Lentivirus to Express a CD33 Specific Chimeric Antigen Receptor in Patients With Relapsed or Refractory CD33-Positive Acute Myeloid Leukemia	Hematopoietic/Lymphoid Cancer|Acute Myeloid Leukemia	Procedure: Leukapheresis|Drug: Fludarabine|Drug: Cyclophosphamide|Biological: CD33-CAR-T Cell Infusion	https://ClinicalTrials.gov/show/NCT03126864
NCT03502577	BCMA-Specific CAR T-Cells Combined With a Gamma Secretase Inhibitor (JSMD194) to Treat Relapsed or Persistent Multiple Myeloma	Recurrent Plasma Cell Myeloma|Refractory Plasma Cell Myeloma	Biological: BCMA-specific CAR-expressing T Lymphocytes|Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Gamma-Secretase Inhibitor LY3039478|Other: Laboratory Biomarker Analysis|Other: Pharmacokinetic Study	https://ClinicalTrials.gov/show/NCT03502577
NCT02640209	Pilot Trial Of Autologous T Cells Engineered To Express Anti-CD19 Chimeric Antigen Receptor (CART19)In Combination With Ibrutinib In Patients With Relapsed Or Refractory CD19+ Chronic Lymphocytic Leukemia (CLL)Or Small Lymphocytic Lymphoma (SLL)	LYMPHOCYTIC LEUKEMIA (CLL) OR SMALL LYMPHOCYTIC LYMPHOMA (SLL)	Biological: CART 19	https://ClinicalTrials.gov/show/NCT02640209
NCT03018093	A Phase I Study Evaluating Safety and Efficacy of C-CAR011 Treatment in Adult Subjects With r/r CD19+B-ALL	Relapsed or Refractory Acute Lymphoblastic Leukemia	Biological: C-CAR-011	https://ClinicalTrials.gov/show/NCT03018093

FIG. 19-15

NCT Number	Title	Conditions	Interventions	URL
NCT04185038	Study of B7-H3-Specific CAR T Cell Locoregional Immunotherapy for Diffuse Intrinsic Pontine Glioma/Diffuse Midline Glioma and Recurrent or Refractory Pediatric Central Nervous System Tumors	Central Nervous System Tumor|Diffuse Intrinsic Pontine Glioma|Diffuse Midline Glioma|Ependymoma|Medulloblastoma, Childhood|Germ Cell Tumor|Atypical Teratoid/Rhabdoid Tumor|Primitive Neuroectodermal Tumor|Choroid Plexus Carcinoma|Pineoblastoma, Childhood|Glioma	Biological: SCRI-CARB7H3(s); B7H3-specific chimeric antigen receptor (CAR) T cel	https://ClinicalTrials.gov/show/NCT04185038
NCT02575261	CAR-T Cell Immunotherapy for EphA2 Positive Malignant Glioma Patients	EphA2 Positive Malignant Glioma|CAR-T Cell Immunotherapy	Biological: CAR-T cell immunotherapy	https://ClinicalTrials.gov/show/NCT02575261
NCT02919046	Study Evaluating the Efficacy and Safety With CAR-T for Relapsed or Refractory Neuroblastoma in Children	Relapsed or Refractory Neuroblastoma	Biological: GD2-targeted CAR-T cells	https://ClinicalTrials.gov/show/NCT02919046
NCT02529813	CD19-Specific T-cells in Treating Patients With Advanced Lymphoid Malignancies	Acute Biphenotypic Leukemia|Acute Lymphoblastic Leukemia|Blasts 5 Percent or More of Bone Marrow Nucleated Cells|CD19 Positive|Minimal Residual Disease|Non-Hodgkin Lymphoma|Small Lymphocytic Lymphoma|Stage III Chronic Lymphocytic Leukemia|Stage IV Chronic Lymphocytic Leukemia	Drug: Cyclophosphamide|Drug: Fludarabine Phosphate|Other: Laboratory Biomarker Analysis|Biological: Tisagenlecleucel	https://ClinicalTrials.gov/show/NCT02529813
NCT03355859	Study Evaluating the Safety and Efficacy of JWCAR029 in Adult Subjects With Relapsed and Refractory B-cell Non-Hodgkin Lymphoma	Non Hodgkin Lymphoma	Biological: JWCAR029	https://ClinicalTrials.gov/show/NCT03355859
NCT03344367	Study Evaluating the Safety and Efficacy of JWCAR029 in Adult Subjects With Relapsed and Refractory B-cell Non-Hodgkin Lymphoma	Non Hodgkin Lymphoma	Biological: JWCAR029	https://ClinicalTrials.gov/show/NCT03344367
NCT01840566	High Dose Therapy and Autologous Stem Cell Transplantation Followed by Infusion of Chimeric Antigen Receptor (CAR) Modified T-Cells Directed Against CD19+ B-Cells for Relapsed and Refractory Aggressive B Cell Non-Hodgkin Lymphoma	Non-Hodgkin's Lymphoma	Drug: Carmustine|Drug: Etoposide|Drug: Cytarabine|Drug: Melphalan|Biological: Pegfilgrastim|Biological: 19-28z T CELLS|Procedure: Autologous Stem Cell Transplantation	https://ClinicalTrials.gov/show/NCT01840566
NCT01747486	Dose Optimization Trial of CD19 Redirected Autologous T Cells	Adult Patients Who Have Relapsed or Refractory CLL (3rd Line) or SLL	Biological: CART-19	https://ClinicalTrials.gov/show/NCT01747486
NCT04787263	CD19-CAR_Lenti T Cells in Pediatric Patients Affected by Relapsed/Refractory CD19+ ALL and DLBCL or PML	Acute Lymphoblastic Leukemia|Diffuse Large B Cell Lymphoma|Primary Mediastinal Lymphoma	Biological: CD19-CAR_Lenti T cell	https://ClinicalTrials.gov/show/NCT04787263

FIG. 19-16

NCT Number	Title	Conditions	Interventions	URL
NCT04186052	Clinical Trial of BCMA CAR T Cell Infusion in Patients With BCMA-positive r/r Multiple Myeloma	Multiple Myeloma	Biological: BCMA-CART cells	https://ClinicalTrials.gov/show/NCT04186052
NCT03919240	CAR-T Cell Therapy Targeting to CD19 for R/R ALL	Acute Lymphoblastic Leukemia With Failed Remission	Biological: CAR T-cell therapy	https://ClinicalTrials.gov/show/NCT03919240
NCT03154775	Study of Safety and Efficacy of C-CAR011 in B-NHL Patients	Refractory or Relapsed Non-Hodgkin Lymphoma	Biological: C-CAR011	https://ClinicalTrials.gov/show/NCT03154775
NCT02944162	CAR-pNK Cell Immunotherapy for Relapsed/Refractory CD33+ AML	Acute Myelogenous Leukemia|Acute Myeloid Leukemia|Acute Myeloid Leukemia With Maturation|Acute Myeloid Leukemia Without Maturation|ANLL	Biological: anti-CD33 CAR-NK cells	https://ClinicalTrials.gov/show/NCT02944162
NCT04768608	PD1 Integrated Anti-PSMA CART in Treating Patients With Castrate-Resistant Prostate Cancer	Castrate-Resistant Prostate Cancer	Drug: PD1-PSMA-CART cells	https://ClinicalTrials.gov/show/NCT04768608
NCT03483688	A Phaseâ... b Study Evaluating Safety and Efficacy of C-CAR011 Treatment in B- NHL Subjects	B-cell Non-Hodgkin Lymphoma	Biological: CD19-directed CAR-T cells	https://ClinicalTrials.gov/show/NCT03483688
NCT02915445	EpCAM CAR-T for Treatment of Nasopharyngeal Carcinoma and Breast Cancer	Malignant Neoplasm of Nasopharynx TNM Staging Distant Metastasis (M)|Breast Cancer Recurrent	Biological: CAR-T cells recognizing EpCAM	https://ClinicalTrials.gov/show/NCT02915445
NCT04288726	Allogeneic CD30.CAR-EBVSTs in Patients With Relapsed or Refractory CD30-Positive Lymphomas	Extranodal Natural Killer/T-Cell Lymphoma, Nasal Type|Classical Hodgkin Lymphoma	Biological: CD30.CAR-EBVST cells	https://ClinicalTrials.gov/show/NCT04288726
NCT03373097	Anti-GD2 CAR T Cells in Pediatric Patients Affected by High Risk and/or Relapsed/Refractory Neuroblastoma or Other GD2-positive Solid Tumors	Neuroblastoma|Neuroblastoma Recurrent|GD2-positive Solid Tumors	Biological: GD2-CART01	https://ClinicalTrials.gov/show/NCT03373097
NCT02892695	PCAR-119 Bridge Immunotherapy Prior to Stem Cell Transplant in Treating Patients With CD19 Positive Leukemia and Lymphoma	Acute Lymphocytic Leukemia|Chronic Lymphocytic Leukemia|Follicular Lymphoma|Mantle Cell Lymphoma|B-cell Prolymphocytic Leukemia|Diffuse Large Cell Lymphoma	Biological: anti-CD19 CAR-NK cells	https://ClinicalTrials.gov/show/NCT02892695
NCT04227275	A Study of CART-PSMA-TGFÎ²RDN in Patients With Metastatic Castration Resistant Prostate Cancer	Metastatic Castration-resistant Prostate Cancer	Biological: CART-PSMA-TGFÎ²RDN|Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Anakinra	https://ClinicalTrials.gov/show/NCT04227275
NCT02664363	EGFRvIII CAR T Cells for Newly-Diagnosed WHO Grade IV Malignant Glioma	Glioblastoma|Gliosarcoma	Biological: EGFRvIII CAR T cells	https://ClinicalTrials.gov/show/NCT02664363
NCT03373071	Anti-CD19 CAR T Cells in Pediatric Patients Affected by Relapsed/Refractory CD19+ ALL and NHL	CD19-ALL|CD19-LNH	Biological: CD19-CAR T cell	https://ClinicalTrials.gov/show/NCT03373071

FIG. 19-17

NCT Number	Title	Conditions	Interventions	URL
NCT04309981	Clinical Trial Using Humanized CART Directed Against BCMA (ARI0002h) in Patients With Relapsed/Refractory Multiple Myeloma to Proteasome Inhibitors, Immunomodulators and Anti-CD38 Antibody.	Relapsed/Refractory Multiple Myeloma	Biological: Adult differentiated autologous T-cells with anti-BCMA specificity	https://ClinicalTrials.gov/show/NCT04309981
NCT03344705	Safety and Efficacy Evaluation of IM19 Cells	Hematological Malignancies	Biological: IM19 CAR-T | Drug: Fludarabine | Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03344705
NCT04206943	Study of CD19 Specific Chimeric Antigen Receptor Positive T Cells (CAR-T) in ALL and NHL	Acute Lymphoblastic Leukemia | Non Hodgkin Lymphoma	Biological: Car-T Cell Therapy	https://ClinicalTrials.gov/show/NCT04206943
NCT03873805	PSCA-CAR T Cells in Treating Patients With PSCA+ Metastatic Castration Resistant Prostate Cancer	Castration-Resistant Prostate Carcinoma | Metastatic Prostate Carcinoma | Stage IV Prostate Cancer AJCC v8 | Stage IVA Prostate Cancer AJCC v8 | Stage IVB Prostate Cancer AJCC v8	Biological: Autologous Anti-PSCA-CAR-4-1BB/TCRzeta-CD19t-expressing T-lymphocytes | Drug: Cyclophosphamide | Drug: Fludarabine | Drug: Fludarabine Phosphate	https://ClinicalTrials.gov/show/NCT03873805
NCT04792489	DALY 2.0 USA/ MB-CART2019.1 for DLBCL	DLBCL	Biological: MB-CART2019.1	https://ClinicalTrials.gov/show/NCT04792489
NCT04835519	Open-Label, Nonramdominzed, Single-Arm Phase 1 Study to Evaluate the Safety and Tolerability of Functionally Enhanced CD33 CAR T Cells in Subjects With Relapsed or Refractory Acute Myeloid Leukemia	Acute Myeloid Leukemia | Relapse Leukemia | Refractory Acute Myeloid Leukemia	Biological: chimeric antigen receptor T cell	https://ClinicalTrials.gov/show/NCT04835519
NCT02706392	Genetically Modified T-Cell Therapy in Treating Patients With Advanced ROR1+ Malignancies	Hematopoietic and Lymphoid Cell Neoplasm | Malignant Solid Neoplasm | Metastatic Lung Non-Small Cell Carcinoma | Metastatic Triple-Negative Breast Carcinoma | Recurrent Acute Lymphoblastic Leukemia | Recurrent Mantle Cell Lymphoma | Refractory Chronic Lymphocytic Leukemia | Stage III Lung Non-Small Cell Cancer AJCC v7 | Stage IIIA Lung Non-Small Cell Cancer AJCC v7 | Stage IIIB Lung Non-Small Cell Cancer AJCC v7 | Stage IV Breast Cancer AJCC v6 and v7 | Stage IV Lung Non-Small Cell Cancer AJCC v7 | Unresectable Lung Non-Small Cell Carcinoma	Other: Laboratory Biomarker Analysis | Biological: ROR1 CAR-specific Autologous T-Lymphocytes	https://ClinicalTrials.gov/show/NCT02706392
NCT03599375	Immunotherapy With CD19 CART-cells for B Cell Acute Lymphoblastic Leukemia	Leukemia, B-Cell	Biological: CD19-targeted CART cells	https://ClinicalTrials.gov/show/NCT03599375
NCT04840875	Phase I Clinical Trial of Autologous CD7-CAR T Cells in the Treatment of High-risk Acute T-cell Leukemia / Lymphoma	T Cell Lymphoma | T-cell Leukemia	Biological: chimeric antigen receptor T cell treatment	https://ClinicalTrials.gov/show/NCT04840875

FIG. 19-18

NCT Number	Title	Conditions	Interventions	URL
NCT04689659	Multi-centers, Open-Label, Phase 2 Study to Evaluate the Efficacy and Safety of Donor-Derived CD7 CAR T Cells in Subjects With Relapsed or Refractory T-cell Malignancies	T-cell Leukemia|Refractory Leukemia|Relapse Leukemia	Biological: chimeric antigen receptor T cell treatment	https://ClinicalTrials.gov/show/NCT04689659
NCT04142619	Study Evaluating Safety and Efficacy of UCART Targeting CS1 in Patients With Relapsed/Refractory Multiple Myeloma (MELANI-01)	Relapsed/Refractory Multiple Myeloma	Biological: UCARTCS1A	https://ClinicalTrials.gov/show/NCT04142619
NCT01683279	A Pediatric Trial of Genetically Modified Autologous T Cells Directed Against CD19 for Relapsed CD19+ Acute Lymphoblastic Leukemia	B Cell Leukemia	Biological: Autologous CD19 CAR+ EGFTt + T cells	https://ClinicalTrials.gov/show/NCT01683279
NCT04237428	CD19-CART in the Treatment of R/R CD19 Positive Non-Hodgkin's Lymphoma	Non Hodgkin Lymphoma	Biological: CD19 CAR-T cells infusion	https://ClinicalTrials.gov/show/NCT04237428
NCT04556266	A Phase I Trial of Donor-Derived 19-28z CAR T Cells Following Allogeneic Transplant for the Treatment of CD19 Malignancies	Leukemia|Lymphoma|Lymphoma, B-Cell	Biological: CAR T-Cell Infusion	https://ClinicalTrials.gov/show/NCT04556266
NCT03840317	SenI_1904A and SenI_1904B Chimeric Antigen Receptor ï¼ˆCARï¼‰ T-Cell in the Treatment of r/r Acute B Lymphocytic Leukemia	Acute Lymphocytic Leukemia	Biological: Autologous CD19-targeting CAR T cells	https://ClinicalTrials.gov/show/NCT03840317
NCT04780529	CART Therapy in Digestive System Tumors	Malignant Neoplasms of Digestive Organs	Biological: gucy2c cart cells	https://ClinicalTrials.gov/show/NCT04780529
NCT04605666	CD19-CAR-T2 Cells for CD19 Positive Acute Lymphoblastic Leukemia	Acute Lymphoblastic Leukemia, in Relapse|Acute Lymphoblastic Leukemia Not Having Achieved Remission|Acute Lymphoblastic Leukemia, Adult	Biological: CD19-CAR-T2 Cells	https://ClinicalTrials.gov/show/NCT04605666
NCT04762485	Humanized CD7 CAR T-cell Therapy for r/r CD7+ Acute Leukemia	T Lymphoblastic Leukemia/Lymphoma|Mixed Phenotype Acute Leukemia|Acute Myeloid Leukemia	Biological: Humanized CD7 CAR-T cells	https://ClinicalTrials.gov/show/NCT04762485
NCT04385173	Pilot Study of B7-H3 CAR-T in Treating Patients With Recurrent and Refractory Glioblastoma	Recurrent Glioblastoma|Refractory Glioblastoma	Drug: B7-H3 CAR-T|Drug: Temozolomide	https://ClinicalTrials.gov/show/NCT04385173
NCT03114670	Donor-derived Anti-CD123-CART Cells for Recurred AML After Allo-HSCT	Adult Acute Myeloid Leukemia	Biological: CD123CAR-41BB-CD3zeta-EGFRt-expressing T cells	https://ClinicalTrials.gov/show/NCT03114670
NCT03240328	The Effect of Chimeric Antigen Receptor (CAR)-T Cell Therapy on the Reconstitution of HIV-specific Immune Function	HIV/AIDS	Biological: CAR-T cells	https://ClinicalTrials.gov/show/NCT03240328

FIG. 19-19

NCT Number	Title	Conditions	Interventions	URL
NCT04150497	Phase 1 Study of UCART22 in Patients With Relapsed or Refractory CD22+ B-cell Acute Lymphoblastic Leukemia (BALLI-01)	B-cell Acute Lymphoblastic Leukemia	Biological: UCART22	https://ClinicalTrials.gov/show/NCT04150497
NCT03190278	Study Evaluating Safety and Efficacy of UCART123 in Patients With Relapsed/ Refractory Acute Myeloid Leukemia	Relapsed/Refractory Acute Myeloid Leukemia	Biological: UCART123v1.2	https://ClinicalTrials.gov/show/NCT03190278
NCT04203459	The Mechanism of Enhancing the Anti-tumor Effects of CAR-T on PC by Gut Microbiota Regulation	Pancreatic Cancer|Gut Microbiota|CAR-T		https://ClinicalTrials.gov/show/NCT04203459
NCT03262298	Anti-CD22 CAR-T Cell Therapy Targeting B Cell Malignancies	Leukemia|Lymphoma	Biological: Anti-CD22-CAR-transduced T cells	https://ClinicalTrials.gov/show/NCT03262298

FIG. 19-20

NCT Number	Title	Conditions	Interventions	URL
NCT02761915	A Cancer Research UK Trial of Anti-GD2 T-cells (1RG-CART)	Relapsed or Refractory Neuroblastoma	Genetic: 1RG-CART/m^2 (Dose Level 1)|Genetic: 1RG-CART/m^2 (Dose Level 2)|Genetic: 1RG-CART/m^2 (Dose Level 3)|Genetic: 1RG-CART/m^2 (Dose Level 4)|Drug: Cyclophosphamide|Drug: Fludarabine|Genetic: 1RG-CART/m^2 (Dose Level 5)	https://ClinicalTrials.gov/show/NCT02761915
NCT03275493	Humanized CD19 CAR-T Cells With CRS Suppression Technology for r/r CD19+ Acute Lymphoblastic Leukemia	Acute Lymphoblastic Leukemia|CD19 Positive|Relapse|Refractory	Biological: Humanized CD19 CAR-T cells|Biological: Humanized CD19 CAR-T cells with CRS suppression technology	https://ClinicalTrials.gov/show/NCT03275493
NCT03298828	CD19 CAR and PD-1 Knockout Engineered T Cells for CD19 Positive Malignant B-cell Derived Leukemia and Lymphoma	Acute Lymphoblastic Leukemia|Burkitt Lymphoma	Biological: CD19 CAR and PD-1 knock out engineered T-cells|Biological: CD19 CAR T-cells	https://ClinicalTrials.gov/show/NCT03298828
NCT02844062	Pilot Study of Autologous Anti-EGFRvIII CAR T Cells in Recurrent Glioblastoma Multiforme	Glioblastoma Multiforme	Biological: anti-EGFRvIII CAR T cells|Drug: cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT02844062
NCT03706547	Anti-CD19/BCMA Bispecific CAR-T Cell Therapy for R/R MM	Multiple Myeloma in Relapse|Multiple Myeloma Progression	Biological: anti-CD19/BCMA CAR-T cells|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03706547
NCT03030001	PD-1 Antibody Expressing CAR T Cells for Mesothelin Positive Advanced Malignancies	Solid Tumor, Adult|Advanced Cancer	Biological: PD-1 antibody expressing mesothelin specific CAR-T cells	https://ClinicalTrials.gov/show/NCT03030001
NCT04884984	Anti-CLL1 CAR T-cell Therapy in CLL1 Positive Relapsed/Refractory Acute Myeloid Leukemia (AML)	Acute Myeloid Leukemia	Biological: anti-CLL1 CART	https://ClinicalTrials.gov/show/NCT04884984
NCT02799680	Allogeneic CART-33 for Relapsed/Refractory CD33+ AML	Relapsed and/or Refractory CD33+ AML	Biological: allogeneic CART-33	https://ClinicalTrials.gov/show/NCT02799680
NCT02799550	Allogeneic CART-19 for Elderly Relapsed/Refractory CD19+ ALL	Leukemia	Biological: allogeneic CART-19	https://ClinicalTrials.gov/show/NCT02799550
NCT04106076	Phase I Study of UCART123 in Patient With Adverse Genetic Risk Acute Myeloid Leukemia	Acute Myeloid Leukaemia	Biological: UCART123	https://ClinicalTrials.gov/show/NCT04106076
NCT04020575	Autologous huMNC2-CAR44 T Cells for Breast Cancer Targeting Cleaved Form of MUC1 (MUC1*)	Metastatic Breast Cancer	Biological: huMNC2-CAR44 CAR T cells|Biological: huMNC2-CAR44 CAR T cells @ RP2D	https://ClinicalTrials.gov/show/NCT04020575

FIG. 19-21

NCT Number	Title	Conditions	Interventions	URL
NCT03710421	CS1-CAR T Therapy Following Chemotherapy in Treating Patients With Relapsed or Refractory CS1 Positive Multiple Myeloma	Recurrent Plasma Cell Myeloma|Refractory Plasma Cell Myeloma	Procedure: CS1-CAR T Therapy|Drug: Cyclophosphamide|Drug: Fludarabine|Procedure: Leukapheresis	https://ClinicalTrials.gov/show/NCT03710421
NCT03896854	CART-19 T Cell in CD19 Positive Relapsed or Refractory Acute Myeloid Leukemia (AML)	Acute Myeloid Leukemia	Biological: CART-19	https://ClinicalTrials.gov/show/NCT03896854
NCT04094766	Safety and Efficacy of Dual Specificity CD19 and CD22 CAR-T Cell Immunotherapy in R/R Acute B Lymphoblastic Leukemia	Refractory B Acute Lymphoblastic Leukemia|Relapse B Acute Lymphoblastic Leukemia	Drug: Dual Specificity CD19 and CD22 CAR-T Cell Immunotherapy	https://ClinicalTrials.gov/show/NCT04094766
NCT03049449	T Cells Expressing a Fully-Human Anti-CD30 Chimeric Antigen Receptor for Treating CD30-Expressing Lymphomas	Lymphoma, Large-Cell, Anaplasitc|Enteropathy-Associated T-Cell Lymphoma|Lymphoma, Large B-Cell, Diffuse|Lymphoma, Extranodal NK-T-Cell|Lymphoma, T-Cell, Peripheral	Biological: Anti-CD30-CAR T cells|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03049449
NCT04923789	A Study of ASCT Bridging CART Cell Therapy in Relapsed/Refractory B-cell Lymphoma	Relapsed Non Hodgkin Lymphoma|Refractory Non-Hodgkin Lymphoma		https://ClinicalTrials.gov/show/NCT04923789
NCT04099797	C7R-GD2.CAR T Cells for Patients With GD2-expressing Brain Tumors (GAIL-B)	Diffuse Intrinsic Pontine Glioma|High Grade Glioma|Embryonal Tumor|Ependymal Tumor	Genetic: (C7R)-GD2.CART cells|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT04099797
NCT03545815	Study of CRISPR-Cas9 Mediated PD-1 and TCR Gene-knocked Out Mesothelin-directed CAR-T Cells in Patients With Mesothelin Positive Multiple Solid Tumors.	Solid Tumor, Adult	Biological: anti-mesothelin CAR-T cells	https://ClinicalTrials.gov/show/NCT03545815
NCT04173988	Study of alloCART-19 Cell Therapy in Pediatric Patients With Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia	ALL, Childhood B-Cell	Genetic: alloCART-19|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT04173988
NCT02706405	JCAR014 and Durvalumab in Treating Patients With Relapsed or Refractory B-cell Non-Hodgkin Lymphoma	Diffuse Large B-Cell Lymphoma, Not Otherwise Specified|Recurrent Diffuse Large B-Cell Lymphoma|Recurrent Primary Mediastinal (Thymic) Large B-Cell Lymphoma|Refractory Diffuse Large B-Cell Lymphoma|Refractory High Grade B-Cell Lymphoma With MYC, BCL2, and BCL6 Rearrangements|Refractory Primary Mediastinal (Thymic) Large B-Cell Lymphoma	Biological: Autologous Anti-CD19CAR-4-1BB-CD3zeta-EGFRt-expressing CD4+/CD8+ Central Memory T-lymphocytes JCAR014|Drug: Cyclophosphamide|Biological: Durvalumab|Drug: Fludarabine Phosphate|Other: Laboratory Biomarker Analysis|Other: Pharmacological Study	https://ClinicalTrials.gov/show/NCT02706405
NCT03854994	CD19 CAR-T Cell Therapy for Relapsed/Refractory B-cell Lymphoma and B-cell Acute Lymphoblastic Leukemia	B Cell Lymphoma|B-cell Acute Lymphoblastic Leukemia	Biological: Anti-CD19 CAR-T Cells Injection	https://ClinicalTrials.gov/show/NCT03854994

FIG. 19-22

NCT Number	Title	Conditions	Interventions	URL
NCT02842138	Autologous CD19 CAR T Cells in Relapsed or Refractory B-cell Lymphoma	B-cell Lymphoma	Biological: autologous anti-CD19 CAR T cells	https://ClinicalTrials.gov/show/NCT02842138
NCT03473496	CAR-T Cells Therapy in Relapsed/Refractory Multiple Myeloma	Relapsed/Refractory Multiple Myeloma(MM)	Biological: CART therapy in Relapsed/Refractory multiple myeloma	https://ClinicalTrials.gov/show/NCT03473496
NCT02930993	Anti-mesothelin CAR T Cells for Patients With Recurrent or Metastatic Malignant Tumors	Mesothelin Positive Tumors	Biological: anti-mesothelin CAR T cells	https://ClinicalTrials.gov/show/NCT02930993
NCT03283631	Intracerebral EGFR-vIII CAR-T Cells for Recurrent GBM	Recurrent Glioblastoma|Recurrent Gliosarcoma	Biological: EGFRvIII-CARs	https://ClinicalTrials.gov/show/NCT03283631
NCT04134325	Study of PD-1 Inhibitors After CD30.CAR T Cell Therapy in Relapsed/Refractory Hodgkin Lymphoma	Relapsed Hodgkin Lymphoma|Refractory Hodgkin Lymphoma	Biological: Nivolumab|Biological: Pembrolizumab	https://ClinicalTrials.gov/show/NCT04134325
NCT02431988	Evaluation of CAR19 T-cells as an Optimal Bridge to Allogeneic Transplantation	Diffuse Large B-Cell Lymphoma	Procedure: Leukapheresis|Drug: Cyclophosphamide|Drug: Fludarabine|Biological: CAR19 T-Cells	https://ClinicalTrials.gov/show/NCT02431988
NCT02134262	Gene Therapy for B-Cell Non-Hodgkin Lymphoma Using CD19 CAR Gene Transduced T Lymphocytes	Relapsed or Refractory B-Cell Non-Hodgkin Lymphoma	Drug: Cyclophosphamide or Bendamustine|Genetic: Dose Level -1|Genetic: Dose Level 1|Genetic: Dose Level 2|Genetic: Dose Level 3	https://ClinicalTrials.gov/show/NCT02134262
NCT03635632	C7R-GD2.CART Cells for Patients With Relapsed or Refractory Neuroblastoma and Other GD2 Positive Cancers (GAIL-N)	Relapsed Neuroblastoma|Refractory Neuroblastoma|Relapsed Osteosarcoma|Relapsed Ewing Sarcoma|Relapsed Rhabdomyosarcoma|Uveal Melanoma|Phyllodes Breast Tumor	Genetic: C7R-GD2.CART cells|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03635632
NCT02935543	CART19 in Adult Patients With Minimal Residual Disease During Upfront Treatment for ALL	Leukemia, Acute Lymphoblastic	Biological: CART 19	https://ClinicalTrials.gov/show/NCT02935543
NCT04626739	CAR-T Cells in Treating Patients With Relapsed or Refractory NHL	Refractory Indolent Adult Non-Hodgkin Lymphoma	Drug: CD19 CAR-T|Drug: CD22 CAR-T|Drug: CD19+CD22 CAR-T|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04626739
NCT02650414	CD22 Redirected Autologous T Cells for ALL	B Cell Leukemias|B Cell Lymphomas	Biological: CART22 cells transduced with a lentiviral vector to express anti-CD22 scFv TCRz:41BB	https://ClinicalTrials.gov/show/NCT02650414
NCT03721068	Study of CAR T-Cells Targeting the GD2 With IL-15+iCaspase9 for Relapsed/Refractory Neuroblastoma or Relapsed/Refractory Osteosarcoma	Neuroblastoma|Osteosarcoma	Biological: iC9.GD2.CAR.IL-15 T-cells|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03721068

FIG. 19-23

NCT Number	Title	Conditions	Interventions	URL
NCT04067414	Exploratory Study of CD19-targeted Chimeric Antigen Receptor T Cells(BZ019) for Relapsed and Refractory B-cell Lymphoma	Diffuse Large B Cell Lymphoma|High-grade B-cell Lymphoma|Transformed Lymphoma|Primary Mediastinal Large B Cell Lymphoma	Biological: BZ019	https://ClinicalTrials.gov/show/NCT04067414
NCT02537977	CD19-directed CAR T Cells Therapy in Relapsed/Refractory B Cell Malignancy	Leukemia|Lymphoma	Biological: CD19-directed CAR-T cells	https://ClinicalTrials.gov/show/NCT02537977
NCT03602157	Study of CAR-T Cells Expressing CD30 and CCR4 for r/r CD30+ HL and CTCL	Lymphoma|Immune System Diseases|Immunoproliferative Disorders|Lymphatic Diseases|Lymphoproliferative Disorders|Neoplasms|Cutaneous Lymphoma|Cutaneous Anaplastic Large Cell Lymphoma|Mycosis Fungoides|Sezary Syndrome|Lymphomatoid Papulosis|Cutaneous T Cell Lymphoma|Gray Zone Lymphoma	Biological: ATLCAR.CD30.CCR4 cells|Biological: ALTCAR.CD30 cells|Drug: Bendamustine|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03602157
NCT04289220	Anti-CD19 CAR in PiggyBac Transposon-Engineered T Cells for Relapsed/Refractory B-cell Lymphoma or B-cell Acute Lymphoblastic Leukemia	B Cell Lymphoma|B-cell Acute Lymphoblastic Leukemia	Biological: Anti-CD19 CAR-T Cells Injection	https://ClinicalTrials.gov/show/NCT04289220
NCT04700319	CAR-T CD19/CD20 for Patients With Advanced CD19/CD20+ B Cell Line Recurrent or Refractory Hematological Malignancies	CAR	Drug: CD19/CD20 CAR-T cell infusion	https://ClinicalTrials.gov/show/NCT04700319
NCT04275154	Evaluating Immunological Parameters, Neurocognitive Changes, Activity Levels, and Driving Fitness in Patients Undergoing CAR-T Cell Therapy	Hematologic Neoplasms		https://ClinicalTrials.gov/show/NCT04275154
NCT04484012	Modified Immune Cells (CD19 CAR T Cells) and Acalabrutinib for the Treatment of Relapsed or Refractory Mantle Cell Lymphoma	Recurrent Mantle Cell Lymphoma|Refractory Mantle Cell Lymphoma	Drug: Acalabrutinib|Biological: CD19CAR-CD28-CD3zeta-EGFRt-expressing Tn/mem-enriched T-lymphocytes	https://ClinicalTrials.gov/show/NCT04484012
NCT02976857	A Phase 1 Study Evaluating Safety and Efficacy of C-CAR011 Treatment in DLBCL Subjects	Refractory Diffuse Large B-Cell Lymphoma	Biological: C-CAR-011	https://ClinicalTrials.gov/show/NCT02976857
NCT02617134	CAR-T Cell Immunotherapy in MUC1 Positive Solid Tumor	Malignant Glioma of Brain|Colorectal Carcinoma|Gastric Carcinoma	Biological: anti-MUC1 CAR-T cells	https://ClinicalTrials.gov/show/NCT02617134
NCT03473457	CAR-T Cells Therapy in Relapsed/Refractory Acute Myeloid Leukemia	Relapsed/Refractory Acute Myeloid Leukemia(AML)	Biological: CART therapy in Acute myeloid leukemia(AML)	https://ClinicalTrials.gov/show/NCT03473457
NCT04146051	Descartes-08 CAR-T Cells in Generalized Myasthenia Gravis (MG)	Myasthenia Gravis, Generalized	Drug: Descartes-08	https://ClinicalTrials.gov/show/NCT04146051

FIG. 19-24

NCT Number	Title	Conditions	Interventions	URL
NCT02851589	Study Evaluating the Efficacy and Safety of PCAR-019 in CD19 Positive Relapsed or Refractory Leukemia and Lymphoma	Acute Lymphocytic Leukemia|Chronic Lymphocytic Leukemia|Follicular Lymphoma|Mantle Cell Lymphoma|B-cell Prolymphocytic Leukemia|Diffuse Large Cell Lymphoma	Biological: PCAR-019 (anti-CD19 CAR-T cells)	https://ClinicalTrials.gov/show/NCT02851589
NCT02819583	CAR-T Cell Immunotherapy in CD19 Positive Relapsed or Refractory Leukemia and Lymphoma	Acute Lymphocytic Leukemia|Chronic Lymphocytic Leukemia|Follicular Lymphoma|Mantle Cell Lymphoma|B-cell Prolymphocytic Leukemia|Diffuse Large Cell Lymphoma	Biological: PCAR-019 (anti-CD19 CAR-T cells)	https://ClinicalTrials.gov/show/NCT02819583
NCT03904069	Study Evaluating the Safety, Tolerability, and Efficacy of FLT3 CAR-T AMG 553 in FLT3-positive Relapsed/Refractory AML	Relapsed/Refractory Acute Myeloid Leukemia	Drug: AMG 553	https://ClinicalTrials.gov/show/NCT03904069
NCT02311621	Engineered Neuroblastoma Cellular Immunotherapy (ENCIT)-01	Neuroblastoma|Ganglioneuroblastoma	Biological: Patient Derived CD171 specific CAR T cells expressing EGFRt (2nd generation T cells)|Biological: Patient Derived CD171 specific CAR T cells expressing EGFRt (3rd generation T cells)|Biological: Patient Derived CD171 specific CAR T cells expressing EGFRt (long spacer 2nd generation T cells)	https://ClinicalTrials.gov/show/NCT02311621
NCT03617198	CD4 CAR+ ZFN-modified T Cells in HIV Therapy	Hiv	Biological: CD4 CAR+CCR5 ZFN T-cells	https://ClinicalTrials.gov/show/NCT03617198
NCT04846439	Sequential Infusion of CD19 and BCMA CAR-T Cells to Improve PTR in Patients With AL	Platelet Transfusion Refractoriness|Acute Leukemia in Remission	Biological: CAR-T infusion	https://ClinicalTrials.gov/show/NCT04846439
NCT03030976	A Study of CD19 Redirected Autologous T Cells for CD19 Positive Systemic Lupus Erythematosus (SLE)	Systemic Lupus Erythematosus (SLE)	Drug: cyclophosphamide|Drug: anti-CD19-CAR-T cells	https://ClinicalTrials.gov/show/NCT03030976
NCT02672501	A Study to Assess CD19-targeted Immunotherapy T Cells in Patients With Relapsed or Refractory CD19+ B Cell Leukemia	Leukemia, B-Cell	Drug: anti-CD19-CAR-T cells	https://ClinicalTrials.gov/show/NCT02672501
NCT02690545	Study of CD30 CAR for Relapsed/Refractory CD30+ HL and CD30+ NHL	Lymphoma|Lymphoma, Non-Hodgkin|Immune System Diseases|Immunoproliferative Disorders|Lymphatic Diseases|Lymphoproliferative Disorders|Neoplasms|Neoplasms by Histologic Type	Biological: ATLCAR.CD30 cells	https://ClinicalTrials.gov/show/NCT02690545
NCT04633148	Dose-escalating Trial With UniCAR02-T Cells and PSMA Target Module (TMpPSMA) in Patients With Progressive Disease After Standard Systemic Therapy in Cancers With Positive PSMA Marker	Renal Cancer|Transitional Cell Cancer of the Renal Pelvis and Ureter|Prostate Cancer|Non-small Cell Lung Cancer|Breast Cancer|Colorectal Cancer	Drug: Cyclophosphamide (Non-IMP)|Drug: Fludarabine (Non-IMP)|Drug: UniCAR02-T-pPSMA|Drug: UniCAR02-T (IMP)	https://ClinicalTrials.gov/show/NCT04633148

FIG. 19-25

NCT Number	Title	Conditions	Interventions	URL
NCT04230265	Dose-escalating Trial With UniCAR02-T Cells and CD123 Target Module (TM123) in Patients With Hematologic and Lymphatic Malignancies	Acute Myeloid Leukemia (AML)|B-cell Acute Lymphoblastic Leukemia (b-ALL)|Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)	Drug: Cyclophosphamide (Non-IMP)|Drug: Fludarabine (Non-IMP)|Drug: TM123 (IMP)|Drug: UniCAR02-T (IMP)	https://ClinicalTrials.gov/show/NCT04230265
NCT02933775	CD19-redirected Autologous Cells (CAR-CD19 T Cells)	CD19 Positive Malignant B-cell Leukemia and Lymphoma	Genetic: CAR-CD19 T cells|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT02933775
NCT01953900	iC9-GD2-CAR-VZV-CTLs/Refractory or Metastatic GD2-positive Sarcoma and Neuroblastoma	Osteosarcoma|Neuroblastoma	Genetic: GD2 T cells|Biological: VZV vaccine|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT01953900
NCT02663297	Administration of T Lymphocytes for Prevention of Relapse of Lymphomas	Hodgkin Disease|Lymphoma|Lymphoma, Non-Hodgkin|Immune System Diseases|Immunoproliferative Disorders|Lymphatic Diseases|Lymphoproliferative Disorders|Neoplasms|Neoplasms by Histologic Type	Drug: ATLCAR.CD30 cells	https://ClinicalTrials.gov/show/NCT02663297
NCT04539444	A Study of CD19/22 CART Cells Combined With PD-1 Inhibitor in Relapsed/Refractory B-cell Lymphoma	Relapsed Non Hodgkin Lymphoma|Refractory Non-Hodgkin Lymphoma	Biological: CD19/22 CART|Drug: Tislelizumab	https://ClinicalTrials.gov/show/NCT04539444
NCT04844086	RPM CD19-mbIL15-CAR-T Cells in Patient With Advanced Lymphoid Malignancies	B-cell Acute Lymphoblastic Leukemia|Non-Hodgkin's Lymphoma, Relapsed|Non-Hodgkin's Lymphoma Refractory|Primary Mediastinal Large B Cell Lymphoma|Diffuse Large B Cell Lymphoma|Follicular Lymphoma|Mantle Cell Lymphoma|High-grade B-cell Lymphoma	Biological: RPM CD19-mbIL15-CAR-T cells	https://ClinicalTrials.gov/show/NCT04844086
NCT03146234	CAR-GPC3 T Cells in Patients With Refractory Hepatocellular Carcinoma	Hepatocellular Carcinoma	Genetic: CAR-GPC3 T cells	https://ClinicalTrials.gov/show/NCT03146234
NCT03281551	Efficacy and Safety of PZ01 Treatment in Patients With r/r CD19+ B-cell Acute Lymphoblastic Leukemia/B Cell Lymphoma	B-cell Acute Lymphoblastic Leukemia|B-cell Lymphoma	Drug: PZ01 CAR-T cells	https://ClinicalTrials.gov/show/NCT03281551
NCT03159819	Clinical Study of CAR-CLD18 T Cells in Patients With Advanced Gastric Adenocarcinoma and Pancreatic Adenocarcinoma	Advanced Gastric Adenocarcinoma|Pancreatic Adenocarcinoma	Genetic: CAR-CLD18 T Cells	https://ClinicalTrials.gov/show/NCT03159819
NCT03692429	alloSHRINK - Standard cHemotherapy Regimen and Immunotherapy With Allogeneic NKG2D-based CYAD-101 Chimeric Antigen Receptor T-cells	Unresectable Metastatic Colorectal Cancer	Drug: CYAD-101|Drug: FOLFOX|Drug: FOLFIRI	https://ClinicalTrials.gov/show/NCT03692429
NCT03716856	Clinical Study of CAR-BCMA T in Patients With Refractory or Relapsed Multiple Myeloma	Refractory or Relapsed Multiple Myeloma	Genetic: CAR-BCMA T cells|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03716856

FIG. 19-26

NCT Number	Title	Conditions	Interventions	URL
NCT02050347	Activated T Lymphocytes Expressing CARs, Relapsed CD19+ Malignancies Post-Allo HSCT(CARPASCIO)	Non-Hodgkin's Lymphoma|B-Cell ALL|B-Cell CLL	Genetic: CD19.CAR-CD28Z T Cells - dose escalation 2|Genetic: CD19.CAR-CD28Z T Cells - dose escalation 1	https://ClinicalTrials.gov/show/NCT02050347
NCT03380039	Clinical Study of CAR-BCMA T Cells in Patients With Refractory or Relapsed Multiple Myeloma	Refractory or Relapsed Multiple Myeloma	Genetic: CAR-BCMA T cells|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03380039
NCT03685786	CART19 Cells Treatment of MRD of B Cell Malignancies and Then Auto-HSCT	Leukemia, Lymphocytic, Acute, B-Cell|Leukemia, Lymphocytic, Chronic, B-Cell|Lymphoma, B-Cell	Biological: CART19 cell and auto-HSCT	https://ClinicalTrials.gov/show/NCT03685786
NCT01109095	CMV-specific Cytotoxic T Lymphocytes Expressing CAR Targeting HER2 in Patients With GBM	Glioblastoma Multiforme (GBM)	Biological: HER.CAR CMV-specific CTLs	https://ClinicalTrials.gov/show/NCT01109095
NCT03642626	MT2017-45: CAR-T Cell Therapy for Heme Malignancies	Acute Lymphoblastic Leukemia|Large B-cell Lymphoma	Drug: KYMRIAH|Drug: YESCARTA|Drug: Fludarabine 30mg/m2 4 doses|Drug: Cyclophosphamide 500 mg/m2; 2 doses|Drug: Fludarabine 30mg/m2 3 doses|Drug: Cyclophosphamide 500 mg/m2; 3 doses|Drug: Fludarabine 25mg/m2 3 days|Drug: Cyclophosphamide 250 mg/m2; 3 days|Drug: Tecartus	https://ClinicalTrials.gov/show/NCT03642626
NCT01316146	Administration of T Lymphocytes for Hodgkin's Lymphoma and Non-Hodgkin's Lymphoma (CART CD30)	Non-Hodgkin's Lymphoma|Hodgkin's Lymphoma	Drug: CAR.CD30 T cells	https://ClinicalTrials.gov/show/NCT01316146
NCT02081937	CART-19 Immunotherapy in Mantle Cell Lymphoma	Hematopoietic/Lymphoid Cancer|Non-hodgkin Lymphoma,B Cell|Mantle Cell Lymphoma	Biological: anti-CD19-CAR vector-transduced T cells	https://ClinicalTrials.gov/show/NCT02081937
NCT04923893	A Study of Bortezomib, Lenalidomide and Dexamethasone (VRd) Followed by Cilta-cel, a CAR-T Therapy Directed Against BCMA Versus VRd Followed by Lenalidomide and Dexamethasone (Rd) Therapy in Participants With Newly Diagnosed Multiple Myeloma for Whom ASCT is Not Planned as Initial Therapy	Multiple Myeloma	Drug: Bortezomib|Drug: Dexamethasone|Drug: Lenalidomide|Drug: Cilta-cel|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT04923893
NCT04257175	CAR-T CD19 for Acute Myelogenous Leukemia With t 8:21 and CD19 Expression	Acute Myeloid Leukemia	Biological: CAR-T CD19	https://ClinicalTrials.gov/show/NCT04257175

FIG. 19-27

NCT Number	Title	Conditions	Interventions	URL
NCT04181827	A Study Comparing JNJ-68284528, a CAR-T Therapy Directed Against B-cell Maturation Antigen (BCMA), Versus Pomalidomide, Bortezomib and Dexamethasone (PVd) or Daratumumab, Pomalidomide and Dexamethasone (DPd) in Participants With Relapsed and Lenalidomide-Refractory Multiple Myeloma	Multiple Myeloma	Drug: JNJ-68284528|Drug: Pomalidomide|Drug: Bortezomib|Drug: Dexamethasone|Drug: Daratumumab	https://ClinicalTrials.gov/show/NCT04181827
NCT04318327	BCMA-directed CAR-T Cell Therapy in Adult Patients With Relapsed and/or Refractory Multiple Myeloma	Multiple Myeloma	Biological: PHE885	https://ClinicalTrials.gov/show/NCT04318327
NCT04088890	Autologous CD22 CAR T Cells in Adults w/ Recurrent or Refractory B Cell Malignancies	B-ALL|B-cell Non Hodgkin Lymphoma|DLBCL	Drug: Fludarabine|Drug: Cyclophosphamide|Drug: CD22 CAR	https://ClinicalTrials.gov/show/NCT04088890
NCT04196413	GD2 CAR T Cells in Diffuse Intrinsic Pontine Gliomas(DIPG) & Spinal Diffuse Midline Glioma(DMG)	Glioma of Spinal Cord|Glioma of Brainstem	Drug: GD2 CAR T cells|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04196413
NCT04088864	CD22-CAR T Cells in Children and Young Adults With B Cell Malignancies	B Cell Lymphoma|Acute Lymphoblastic Leukemia, Pediatric|Lymphoma	Drug: Fludarabine|Drug: Cyclophosphamide|Drug: Autologous CD22 CAR T	https://ClinicalTrials.gov/show/NCT04088864
NCT04257578	Acalabrutinib and Anti-CD19 CAR T-cell Therapy for the Treatment of B-cell Lymphoma	B-Cell Non-Hodgkin Lymphoma|Diffuse Large B-Cell Lymphoma, Not Otherwise Specified|High Grade B-Cell Lymphoma|Primary Mediastinal (Thymic) Large B-Cell Lymphoma|Transformed Follicular Lymphoma to Diffuse Large B-Cell Lymphoma	Drug: Acalabrutinib|Biological: Axicabtagene Ciloleucel	https://ClinicalTrials.gov/show/NCT04257578
NCT03093168	BCMA Chimeric Antigen Receptor Expressing T Cells in Multiple Myeloma	Multiple Myeloma	Biological: Anti-BCMA CAR-T cells|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03093168
NCT03774654	CD19.CAR Allogeneic NKT for Patients With Relapsed or Refractory B-Cell Malignancies (ANCHOR)	Refractory B-Cell Non-Hodgkin Lymphoma|Refractory B-Cell Small Lymphocytic Lymphoma|Relapsed Adult ALL|Relapsed CLL|Relapsed Non Hodgkin Lymphoma	Genetic: CD19.CAR-aNKT cells|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03774654
NCT03943472	BCMA Chimeric Antigen Receptor Expressing T Cells Therapy for Relapsed/Refractory Multiple Myeloma	Multiple Myeloma	Biological: Anti-BCMA CAR-T cells|Drug: Fludarabine|Drug: Cyclophosphamide|Drug: Immune inhibitors	https://ClinicalTrials.gov/show/NCT03943472
NCT04083495	CD30 CAR for Relapsed/Refractory CD30+ T Cell Lymphoma	Peripheral T Cell Lymphoma	Biological: ATLCAR.CD30 T cells|Drug: Bendamustine|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04083495

FIG. 19-28

NCT Number	Title	Conditions	Interventions	URL
NCT03593109	A Single-center Clinical Study to Evaluate the Safety, Tolerability, and Efficacy of LCAR-L10D Cell Formulations Targeting CD19 and CD22 in Patients With CD19- and/or CD22-Positive Relapsed/Refractory B-cell Lymphoma	Lymphoma, B-Cell	Drug: Dual Specificity CD19 and CD22 CAR-T Cell Immunotherapy	https://ClinicalTrials.gov/show/NCT03593109
NCT03070327	BCMA Targeted CAR T Cells With or Without Lenalidomide for the Treatment of Multiple Myeloma	Multiple Myeloma	Biological: EGFRt/BCMA-4188z CAR T cell|Drug: Cyclophosphamide|Drug: Lenalidomide.	https://ClinicalTrials.gov/show/NCT03070327
NCT03244306	A Phase 1 Study of CD22-CAR TCell Immunotherapy for CD22+ Leukemia and Lymphoma	Leukemia	Biological: Patient-derived CD22-specific CAR T-cells also expressing an EGFRt	https://ClinicalTrials.gov/show/NCT03244306
NCT03598179	XLCART001 Treatment in Relapsed/Refractory/High-risk B-cell Malignancy Subjects	Lymphoma, B-Cell|Leukemia, B-cell	Biological: chimeric antigen receptor T cells	https://ClinicalTrials.gov/show/NCT03598179
NCT04007978	Anti-CD22 Chimeric Antigen Receptor (CAR)-Modified T Cell Therapy for Relapsed Refractory B-cell Malignancies	B Cell Lymphoma|Acute Lymphoblastic Leukemia	Genetic: Third generation CAR-T cells	https://ClinicalTrials.gov/show/NCT04007978
NCT04034446	CD19-CD22 Chimeric Antigen Receptor T (CAR-T) Cell for Treatment of B Cell Acute Lymphoblastic Leukemia (B-ALL)	Relapsed or Refractory B Cell Acute Lymphoblastic Leukemia	Biological: CD19-CD22 CAR-T cells	https://ClinicalTrials.gov/show/NCT04034446
NCT04513431	A Clinical Research of CAR T Cells Targeting CEA Positive Colorectal Cancer (CRC)	Stage III Colorectal Cancer|Colorectal Cancer Liver Metastasis	Biological: Anti-CEA-CAR T	https://ClinicalTrials.gov/show/NCT04513431
NCT03585517	Safety and Efficacy Evaluation of IM23 CAR-T Cells (IM23CAR-T)	AML	Drug: IM23	https://ClinicalTrials.gov/show/NCT03585517
NCT04100187	Immunotherapy With CD19 CAR T-cells for B-Cell Lymphoma	Lymphoma	Biological: Anti-CD19-CAR	https://ClinicalTrials.gov/show/NCT04100187
NCT01716364	Safety Study of Anti LewisY Chimeric Antigen Receptor in Myeloma, Acute Myeloid Leukemia or Myelodysplastic Syndrome	Multiple Myeloma|Acute Myeloid Leukaemia|Myelodysplastic Syndrome	Biological: Anti-LeY- scFv-CD28-¶ vector,.	https://ClinicalTrials.gov/show/NCT01716364
NCT03186118	Pilot Study of T-APCs Following CAR T Cell Immunotherapy for CD19+ Leukemia	CD 19+ Acute Leukemia	Biological: T-cell Antigen Presenting Cells expressing truncated CD19 (T-APC)	https://ClinicalTrials.gov/show/NCT03186118
NCT03915184	Clinical Trial to Evaluate CT053 in Patients With Relapsed and/or Refractory Multiple Myeloma (LUMMICAR STUDY 2)	Multiple Myeloma	Biological: CT053	https://ClinicalTrials.gov/show/NCT03915184

FIG. 19-29

NCT Number	Title	Conditions	Interventions	URL
NCT03430011	Study Evaluating the Safety and Efficacy of JCARH125 in Subjects With Relapsed and/or Refractory Multiple Myeloma	Multiple Myeloma	Biological: JCARH125|Biological: JCARH125 + anakinra	https://ClinicalTrials.gov/show/NCT03430011
NCT04650451	Safety and Activity Study of HER2-Targeted Dual Switch CAR-T Cells (BPX-603) in Subjects With HER2-Positive Solid Tumors	HER-2 Gene Amplification|HER2-positive Gastric Cancer|HER2-positive Breast Cancer|HER-2 Protein Overexpression|Solid Tumor, Adult	Biological: chimeric antigen receptor (CAR) T cell therapy	https://ClinicalTrials.gov/show/NCT04650451
NCT01865617	Laboratory Treated T Cells in Treating Patients With Relapsed or Refractory Chronic Lymphocytic Leukemia, Non-Hodgkin Lymphoma, or Acute Lymphoblastic Leukemia	CD19-Positive Neoplastic Cells Present|Recurrent Adult Acute Lymphoblastic Leukemia|Recurrent Chronic Lymphocytic Leukemia|Recurrent Diffuse Large B-Cell Lymphoma|Recurrent Mantle Cell Lymphoma|Recurrent Non-Hodgkin Lymphoma|Recurrent Small Lymphocytic Lymphoma|Refractory Acute Lymphoblastic Leukemia|Refractory Chronic Lymphocytic Leukemia|Refractory Diffuse Large B-Cell Lymphoma|Refractory Mantle Cell Lymphoma|Refractory Non-Hodgkin Lymphoma|Refractory Small Lymphocytic Lymphoma	Biological: Autologous Anti-CD19CAR-4-1BB-CD3zeta-EGFRt-expressing T Lymphocytes|Other: Laboratory Biomarker Analysis	https://ClinicalTrials.gov/show/NCT01865617
NCT03720496	Treatment of Refractory/Relapsed Non-Hodgkin Lymphoma With CD19-TriCART Cell Therapy	Non-hodgkin Lymphoma,B Cell	Biological: CD19-TriCAR-T	https://ClinicalTrials.gov/show/NCT03720496
NCT03497533	Treatment of Refractory/Relapsed Non-Hodgkin Lymphoma With TriCAR-T_CD19	Non-hodgkin Lymphoma,B Cell	Biological: TriCAR-T-CD19	https://ClinicalTrials.gov/show/NCT03497533
NCT03056339	Umbilical & Cord Blood (CB) Derived CAR-Engineered NK Cells for B Lymphoid Malignancies	B-Lymphoid Malignancies|Acute Lymphocytic Leukemia|Chronic Lymphocytic Leukemia|Non-hodgkin Lymphoma	Drug: Fludarabine|Drug: Cyclophosphamide|Drug: Mesna|Biological: iC9/CAR.19/IL15-Transduced CB-NK Cells|Drug: AP1903	https://ClinicalTrials.gov/show/NCT03056339
NCT02631044	Study Evaluating the Safety and Pharmacokinetics of JCAR017 in B-cell Non-Hodgkin Lymphoma (TRANSCEND-NHL-001)	Non-Hodgkin Lymphoma|Diffuse Large B Cell Lymphoma|Follicular Lymphoma|Mantle-cell Lymphoma|Primary Mediastinal B-cell Lymphoma	Biological: JCAR017 (lisocabtagene maraleucel) single-dose schedule|Biological: JCAR017 (lisocabtagene maraleucel) 2-dose schedule	https://ClinicalTrials.gov/show/NCT02631044
NCT04011293	A Clinical Study of Anti-CD19 Chimeric Antigen Receptor T-Cell injection (CNCT19) in the Treatment of Cluster of Differentiation 19 (CD19) Positive Relapsed or Refractory B Cell Malignancies	Relapsed or Refractory Hematological Malignancies	Biological: CNCT19	https://ClinicalTrials.gov/show/NCT04011293

FIG. 19-30

NCT Number	Title	Conditions	Interventions	URL
NCT02792114	T-Cell Therapy for Advanced Breast Cancer	Breast Cancer|Metastatic HER2-negative Breast	Drug: Cyclophosphamide|Biological: Mesothelin-targeted T cells|Drug: AP1903	https://ClinicalTrials.gov/show/NCT02792114
NCT04077866	B7-H3 CAR-T for Recurrent or Refractory Glioblastoma	Recurrent Glioblastoma|Refractory Glioblastoma	Drug: Temozolomide|Biological: B7-H3 CAR-T	https://ClinicalTrials.gov/show/NCT04077866
NCT04406610	CAR-T Cell Immunotherapy for GD2 Positive Glioma Patients	Glioma of Brain|CAR-T Cell Immunotherapy	Biological: GD2 CAR-T immunotherapy	https://ClinicalTrials.gov/show/NCT04406610
NCT03060356	Autologous T Cells Expressing MET scFv CAR (RNA CART-cMET)	Malignant Melanoma|Breast Cancer	Biological: T cells modified with RNA anti -cMET CAR	https://ClinicalTrials.gov/show/NCT03060356
NCT02277522	CD19 Redirected Autologous T Cells for Hodgkin Lymphoma	Hodgkin Lymphoma With no Available Curative Treatment Options Who Have a Limited Prognosis	Biological: RNA anti-CD19 CAR T cells	https://ClinicalTrials.gov/show/NCT02277522
NCT02729493	Study Evaluating the Efficacy and Safety With CAR-T for Liver Cancer	Liver Neoplasms	Biological: EPCAM-targeted CAR-T cells	https://ClinicalTrials.gov/show/NCT02729493
NCT02725125	Study Evaluating the Efficacy and Safety With CAR-T for Stomach Cancer	Stomach Neoplasms	Biological: EPCAM-targeted CAR-T cells	https://ClinicalTrials.gov/show/NCT02725125
NCT02735291	Study Evaluating the Efficacy and Safety With CAR-T for Recurrent or Refractory Acute Non T Lymphocyte Leukemia	Leukemia	Biological: CD19-targeted CAR-T cells	https://ClinicalTrials.gov/show/NCT02735291
NCT04213469	Quikin CD19-CART in Patients With r/r B-cell Lymphoma	B-cell Lymphoma	Biological: CD19-Specific Chimeric Antigen Receptor T cells with PD1 knockout	https://ClinicalTrials.gov/show/NCT04213469
NCT01475058	CD19 CAR T Cells for B Cell Malignancies After Allogeneic Transplant	Philadelphia Chromosome Negative Adult Precursor Acute Lymphoblastic Leukemia|Philadelphia Chromosome Positive Adult Precursor Acute Lymphoblastic Leukemia|Recurrent Adult Acute Lymphoblastic Leukemia|Recurrent Adult Diffuse Large Cell Lymphoma|Recurrent Adult Immunoblastic Large Cell Lymphoma|Recurrent Mantle Cell Lymphoma|Refractory Chronic Lymphocytic Leukemia	Biological: allogeneic cytomegalovirus-specific cytotoxic T lymphocytes	https://ClinicalTrials.gov/show/NCT01475058
NCT04812691	CD19-targeted CAR T Cells ï¼ˆJWCAR029ï¼‰ for Primary Refractory Diffuse Large B Cell Lymphoma	Diffuse Large B Cell Lymphoma	Biological: JWCAR029 (CD19-targeted Chimeric Antigen Receptor Cells)	https://ClinicalTrials.gov/show/NCT04812691
NCT02728882	Study Evaluating the Efficacy and Safety With CAR-T for Recurrent or Refractory Diffuse Large B Cell Lymphoma	Lymphoma	Biological: CD19-targeted CAR-T cells	https://ClinicalTrials.gov/show/NCT02728882
NCT00924326	CAR T Cell Receptor Immunotherapy for Patients With B-cell Lymphoma	Primary Mediastinal B-cell Lymphoma|Diffuse, Large B-cell Lymphoma|Diffuse Large B-Cell Lymphoma Transformed From Follicular Lymphoma|Mantle Cell	Drug: Fludarabine|Drug: Cyclophosphamide|Biological: Anti-cluster of differentiation 19 (CD19)-CAR PBL|Drug: Aldesleukin	https://ClinicalTrials.gov/show/NCT00924326

FIG. 19-31

NCT Number	Title	Conditions	Interventions	URL
NCT04163575	Immunotherapy With CD22 CAR T-cells for B-Cell Lymphoma, ALL and CLL	Leukemia|Lymphoma	Biological: :Anti-CD22-CAR	https://ClinicalTrials.gov/show/NCT04163575
NCT02893189	CAR19 Donor Lymphocytes for Relapsed CD19+ Malignancies Following Allogeneic Transplantation	CD19+ Malignancies: Relapse Post-allogeneic Transplant	Genetic: Infusion of modified CAR19 T-cells (4G7-CARD T-cells)	https://ClinicalTrials.gov/show/NCT02893189
NCT02546739	Immunotherapy With CD19 CAR T-cells for B-Cell Lymphoma, ALL and CLL	Leukemia|Lymphoma	Biological: Anti-CD19-CAR	https://ClinicalTrials.gov/show/NCT02546739
NCT02656147	Immunotherapy With CD19 CAR [3]T-cells for B-Cell Lymphoma, ALL and CLL	Leukemia|Lymphoma	Biological: Anti-CD19-CAR [3]T	https://ClinicalTrials.gov/show/NCT02656147
NCT03173417	Safety and Efficacy Evaluation of IM19 CAR-T Cells (IM19CAR-T)	Leukemia	Biological: IM19 CAR-T|Drug: fludarabine and cyclophosphamide	https://ClinicalTrials.gov/show/NCT03173417
NCT01886976	Treatment of Chemotherapy Refractory Multiple Myeloma by CART-138	Multiple Myeloma	Biological: CART-138 cells	https://ClinicalTrials.gov/show/NCT01886976
NCT03361748	Efficacy and Safety Study of bb2121 in Subjects With Relapsed and Refractory Multiple Myeloma	Multiple Myeloma	Biological: bb2121	https://ClinicalTrials.gov/show/NCT03361748
NCT04026737	Cardiovascular Effects of CART Cell Therapy	Leukemia|Lymphoma|Cardiotoxicity|Risk Factor, Cardiovascular|Immunotherapy		https://ClinicalTrials.gov/show/NCT04026737
NCT04562298	A Single-Center, Phase I Clinical Study to Evaluate the Safety, Tolerability, and Efficacy of LCAR-M23, a CAR-T Cell Therapy Targeting MSLN in Patients With Relapsed and Refractory Epithelial Ovarian Cancer	Epithelial Ovarian Cancer	Biological: LCAR-M23 cells	https://ClinicalTrials.gov/show/NCT04562298
NCT03356795	Intervention of CAR-T Against Cervical Cancer	Cervical Cancer	Biological: Cervical cancer-specific CAR-T cells	https://ClinicalTrials.gov/show/NCT03356795
NCT03081910	Autologous T-Cells Expressing a Second Generation CAR for Treatment of T-Cell Malignancies Expressing CD5 Antigen	T-cell Acute Lymphoblastic Lymphoma|T-non-Hodgkin Lymphoma|T-cell Acute Lymphoblastic Leukemia	Genetic: Autologous CD5.CAR/28zeta CAR T cells|Drug: Fludarabine|Drug: Cytoxan|Genetic: Allogeneic CD5.CAR/28zeta CAR T cells	https://ClinicalTrials.gov/show/NCT03081910
NCT02159716	CART-meso in Mesothelin Expressing Cancers	Metastatic Pancreatic (Ductal) Adenocarcinoma|Epithelial Ovarian Cancer|Malignant Epithelial Pleural Mesothelioma	Biological: CART-meso	https://ClinicalTrials.gov/show/NCT02159716
NCT03196830	CAR-T for R/R B-NHL	Relapsed Non Hodgkin Lymphoma|Refractory Non-Hodgkin Lymphoma|CAR - T CD19/CD20/CD22/CD30	Biological: CAR-T	https://ClinicalTrials.gov/show/NCT03196830
NCT03323944	CAR T Cell Immunotherapy for Pancreatic Cancer	Pancreatic Cancer|Cancer of the Pancreas	Biological: huCART-meso cells	https://ClinicalTrials.gov/show/NCT03323944

FIG. 19-32

NCT Number	Title	Conditions	Interventions	URL
NCT03054298	CAR T Cells in Mesothelin Expressing Cancers	Lung Adenocarcinoma|Ovarian Cancer|Peritoneal Carcinoma|Fallopian Tube Cancer|Mesotheliomas Pleural|Mesothelioma Peritoneum	Biological: huCART-meso cells	https://ClinicalTrials.gov/show/NCT03054298
NCT04803929	Clinical Study of Anti-ILT3 CAR-T Therapy for R/R AML(M4/M5)	AML M4|AML M5	Biological: anti-ILT3 CAR-T	https://ClinicalTrials.gov/show/NCT04803929
NCT03207178	Sequential Infusion of Anti-CD19 and Anti-CD20 CAR-T Cells Against Relapsed and Refractory B-cell Lymphoma	Recurrent or Refractory B Cell Malignancy	Biological: Mixed CD19/CD20 CAR-T Transfer	https://ClinicalTrials.gov/show/NCT03207178
NCT04677452	Dose Exploration Study OF JWCAR129, BCMA-Targeted CART for RRMM	Safety and Efficacy	Biological: JWCAR129	https://ClinicalTrials.gov/show/NCT04677452
NCT02030847	Study of Redirected Autologous T Cells Engineered to Contain Anti-CD19 Attached to TCR and 4-1BB Signaling Domains in Patients With Chemotherapy Resistant or Refractory Acute Lymphoblastic Leukemia	Patients With B Cell ALL, Relapsed or Refractory, With no Available Curative Treatment Options	Biological: CART-19	https://ClinicalTrials.gov/show/NCT02030847
NCT03638193	Study of Autologous T-cells in Patients With Metastatic Pancreatic Cancer	Pancreatic Cancer	Biological: CART-meso cells	https://ClinicalTrials.gov/show/NCT03638193
NCT03815383	A Study of BCMA-directed CAR-T Cells Treatment in Subjects With r/r Multiple Myeloma	Relapsed or Refractory Multiple Myeloma	Biological: C-CAR088	https://ClinicalTrials.gov/show/NCT03815383
NCT04134117	Tisagenlecleucel In Primary CNS Lymphoma	Primary CNS Lymphoma|Refractory Primary CNS Lymphoma|Relapsed Primary CNS Lymphoma	Biological: Tisagenlecleucel	https://ClinicalTrials.gov/show/NCT04134117
NCT04697940	Decitabine-primed Tandem CD19/CD20 CAR T Cells Treatment in r/r B-NHL	Relapse and Refractory B-cell Non-Hodgkin's Lymphoma|Decitabine-primed Tandem CD19/CD20 CAR T Cells	Biological: Decitabine-primed Tandem CAR19/20 engineered T cells	https://ClinicalTrials.gov/show/NCT04697940
NCT03751293	A Study of BCMA-directed CAR-T Cells Treatment in Subjects With r/r Multiple Myeloma	Relapsed or Refractory Multiple Myeloma	Biological: C-CAR088	https://ClinicalTrials.gov/show/NCT03751293
NCT04863066	Third-Generation CAR-T-cell Therapy in Individuals With HIV-1 Infection	HIV-1	Biological: CAR-T cells	https://ClinicalTrials.gov/show/NCT04863066
NCT04250324	Study of Safety and Efficacy of BZ019 in (R/R) Large B-cell Lymphoma	Large B-cell Lymphoma	Biological: BZ019	https://ClinicalTrials.gov/show/NCT04250324
NCT03993743	A Study of CD147-targeted CAR-T by Hepatic Artery Infusions for Very Advanced Hepatocellular Carcinoma	Advanced Hepatocellular Carcinoma	Biological: CD147-CART	https://ClinicalTrials.gov/show/NCT03993743

FIG. 19-33

NCT Number	Title	Conditions	Interventions	URL
NCT04045847	CD147-CART Cells in Patients With Recurrent Malignant Glioma.	Recurrent Glioblastoma|CD147 Positive	Biological: CD147-CART	https://ClinicalTrials.gov/show/NCT04045847
NCT04661384	Brain Tumor-Specific Immune Cells (IL13Ralpha2-CAR T Cells) for the Treatment of Leptomeningeal Glioblastoma, Ependymoma, or Medulloblastoma	Leptomeningeal Metastases	Biological: IL13Ralpha2-specific Hinge-optimized 4188-co-stimulatory CAR Truncated CD19-expressing Autologous T-Lymphocytes	https://ClinicalTrials.gov/show/NCT04661384
NCT03299738	A Study Evaluating Safety and Efficacy of C-CAR011 in Subjects With B-NHL	Refractory or Relapsed B-cell Non-Hodgkin Lymphoma	Biological: C-CAR011	https://ClinicalTrials.gov/show/NCT03299738
NCT03767725	Anti-BCMA or/and Anti-CD19 CART Cells Treatment of Relapsed Multiple Myeloma	Multiple Myeloma in Relapse	Biological: Treatment	https://ClinicalTrials.gov/show/NCT03767725
NCT04488354	Long-term Follow-up Study for Patients Treated With CLBR001 CAR-T	Relapsed/Refractory B-cell Lymphomas|Diffuse Large B-Cell Lymphoma (DLBCL)|Follicular Lymphoma (FL)|Chronic Lymphocytic Leukemia (CLL)|Marginal Zone Lymphoma (MZL)|Mantle Cell Lymphoma (MCL)|Small Lymphocytic Lymphoma (SLL)|Primary Mediastinal Large B Cell Lymphoma|Transformed Follicular Lymphoma	Combination Product: CLBR001 and SWI019	https://ClinicalTrials.gov/show/NCT04488354
NCT03090659	LCAR-B38M Cells in Treating Relapsed/Refractory (R/R) Multiple Myeloma	Refractory or Relapsed Multiple Myeloma	Biological: LCAR-B38M CAR-T cell injection	https://ClinicalTrials.gov/show/NCT03090659
NCT04599556	Clinical Trial for the Safety and Efficacy of Anti-CD7 CAR-T Cell Therapy for Patients With Relapsed or Refractory CD7 Positive Hematological Malignancy	CD7+ Acute Leukemia|CD7+ Lymphoma	Biological: anti-CD7 CAR-T	https://ClinicalTrials.gov/show/NCT04599556
NCT04412889	A Study of BCMA/CD19 Dual-Target CAR-T Cell Immunotherapy for Relapsed or Refractory MM	Multiple Myeloma	Biological: BCMA/CD19 dual-target CAR-T cell immunotherapy	https://ClinicalTrials.gov/show/NCT04412889
NCT03792633	Study of huCART19 for Very High-Risk (VHR) Subsets of Pediatric B-ALL	Acute Lymphoid Leukemia	Biological: huCART19	https://ClinicalTrials.gov/show/NCT03792633
NCT04182581	A Study of BCMA/CD19 Dual-Target CAR-T Cell Immunotherapy for Relapsed or Refractory Multiple Myeloma	Multiple Myeloma	Biological: BCMA/CD19 Dual-Target CAR-T	https://ClinicalTrials.gov/show/NCT04182581
NCT04276870	Phase 2 Trial of CD19 Redirected Autologous T Cells	Pediatric and Young Adult Patientswith Hypodiploid or t(17;19) B-ALL|Infants With Very High Risk KMT2A B-ALL|Patients With Central Nervous System Relapse Who Did Not Receive Cranial Radiation or Bone Marrow Transplantation	Biological: Murine CART19	https://ClinicalTrials.gov/show/NCT04276870

FIG. 19-34

NCT Number	Title	Conditions	Interventions	URL
NCT02744287	Safety and Activity Study of PSCA-Targeted CAR-T Cells (BPX-601) in Subjects With Selected Advanced Solid Tumors	Metastatic Castration-resistant Prostate Cancer|Metastatic Prostate Cancer|Metastatic Pancreatic Ductal Adenocarcinoma|Metastatic Pancreatic Cancer|Metastatic Pancreatic Adenocarcinoma	Biological: BPX-601|Drug: Rimiducid	https://ClinicalTrials.gov/show/NCT02744287
NCT04660929	CAR-macrophages for the Treatment of HER2 Overexpressing Solid Tumors	HER2-positive|Adenocarcinoma|Bile Duct Cancer|Biliary Tract Cancer|Bladder Cancer|Breast Cancer|Breast Neoplasm|Carcinoma, Ductal|Carcinoma, Hepatocellular|Cancer|Lung Cancer, Non-Small-Cell|Carcinoma, Ovarian Epithelial|Carcinoma, Small Cell|Carcinoma, Squamous|Carcinoma, Transitional Cell|Colorectal Cancer|Esophagogastric Junction Neoplasms|Inflammatory Breast Cancer|Stomach Neoplasms|Malignant Neoplasms|Ovarian Neoplasms|Pancreatic Cancer|HER2-positive Solid Tumors|HER2-positive Breast Cancer|HER2-positive Gastric Cancer|HER-2 Protein Overexpression|HER-2 Gene Amplification|Prostate Cancer|Head and Neck Cancer|Endometrial Cancer|Lung Cancer, Small Cell	Biological: CT-0508	https://ClinicalTrials.gov/show/NCT04660929
NCT03960060	A Study of CCT301-59 CAR T Therapy in Adult Subjects With Recurrent or Refractory Solid Tumors	Solid Tumor|Soft Tissue Sarcoma|Gastric Cancer|Pancreatic Cancer|Bladder Cancer	Biological: CCT301-59	https://ClinicalTrials.gov/show/NCT03960060
NCT03672305	Clinical Study on the Efficacy and Safety of c-Met/PD-L1 CAR-T Cell Injection in the Treatment of HCC	Primary Hepatocellular Carcinoma	Biological: c-Met/PD-L1 CAR-T cell injection	https://ClinicalTrials.gov/show/NCT03672305
NCT02924753	The Safety and Efficacy of CART-19 Cells in B-cell Acute Lymphoblastic Leukemia (B-ALL).	B-cell Acute Lymphoblastic Leukemia	Drug: Cyclophosphamide|Drug: Fludarabine|Biological: CART-19 cells	https://ClinicalTrials.gov/show/NCT02924753
NCT02465983	Pilot Study of Autologous T-cells in Patients With Metastatic Pancreatic Cancer	Pancreatic Cancer	Biological: CART-meso-19 T cells|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT02465983
NCT04553393	Decitabine-primed Tandem CD19/CD20 CAR T Cells Plus Epigenetic Agents in Aggressive r/r B-NHL With Huge Tumor Burden	Refractory or Relapsed Aggressive r/r B-NHL With Huge Tumor Burden	Drug: Chidamide|Drug: Decitabine|Drug: Chidamide and Decitabine|Biological: Decitabine-primed Tandem CAR19/20 engineered T cells	https://ClinicalTrials.gov/show/NCT04553393
NCT04601831	'Re-Priming' RT After Incomplete Response to CAR-T in R/R NHL	Non-Hodgkin Lymphoma	Radiation: Focal radiation therapy (RT)	https://ClinicalTrials.gov/show/NCT04601831
NCT04626765	CAR-T for Children With Relapsed and Refractory Acute Lymphoblastic Leukemia	Childhood Acute Lymphoblastic Leukemia	Drug: CD19 CAR-T|Drug: CD22 CAR-T|Drug: CD 19+22|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04626765

FIG. 19-35

NCT Number	Title	Conditions	Interventions	URL
NCT04119024	Gene Modified Immune Cells (IL13Ralpha2 CAR T Cells) After Conditioning Regimen for the Treatment of Stage IIIC or IV Melanoma	Clinical Stage IV Cutaneous Melanoma AJCC v8|IL13RA2 Positive|Metastatic Melanoma|Cutaneous Melanoma, Stage III|Cutaneous Melanoma, Stage IV	Drug: Cyclophosphamide|Drug: Fludarabine Phosphate|Biological: IL13Ralpha2-specific Hinge-optimized 4-1BB-co-stimulatory CAR/Truncated CD19-expressing Autologous TN/MEM Cells|Drug: Recombinant Interleukin-2	https://ClinicalTrials.gov/show/NCT04119024
NCT02903810	Combination Transfer of Î±CD19-TCRz-41BB and Î±CD22-TCRz-41BB CAR-T Cells for B-cell Hematologic Malignancy	Hematopoietic/Lymphoid Cancer	Biological: Mixed CAR-T Transfer	https://ClinicalTrials.gov/show/NCT02903810
NCT04384393	Safety and Efficacy of ThisCART19 in Patients With Refractory or Relapsed B Cell Malignancies	B Cell Malignancy	Biological: ThisCART19 cells	https://ClinicalTrials.gov/show/NCT04384393
NCT03752541	Efficacy and Safety Evaluation of BCMA-UCART	Multiple Myeloma	Biological: BCMA-UCART	https://ClinicalTrials.gov/show/NCT03752541
NCT03013712	A Clinical Research of CAR T Cells Targeting EpCAM Positive Cancer	Colon Cancer|Esophageal Carcinoma|Pancreatic Cancer|Prostate Cancer|Gastric Cancer|Hepatic Carcinoma	Biological: CAR-T cell immunotherapy	https://ClinicalTrials.gov/show/NCT03013712
NCT04440436	Assessment of Safety and Efficacy of IM19 for Recurrent or Refractory (R/R) Non-Hodgkin's Lymphoma(NHL) Patients	NHL	Drug: IM19 CAR-T Cells	https://ClinicalTrials.gov/show/NCT04440436
NCT02706782	A Study of Mesothelin Redirected Autologous T Cells for Advanced Pancreatic Carcinoma	Pancreatic Cancer	Drug: TAI-meso-CART	https://ClinicalTrials.gov/show/NCT02706782
NCT04626752	CAR-T Cells in Treating Patients With Relapsed or Refractory Multiple Myeloma	Relapsed or Refractory Multiple Myeloma	Drug: BCMA CAR-T|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04626752
NCT04511871	A Phase I Trial of CCT303-406 in Patients With Relapsed or Refractory HER2 Positive Solid Tumors	Solid Tumor|Gastric Cancer|Breast Cancer|Ovarian Cancer|Sarcoma	Biological: CCT303-406	https://ClinicalTrials.gov/show/NCT04511871
NCT03768310	CD19.CAR-multiVSTs for Patients With CD19+ B-ALL or NHL Undergoing Related Allogeneic HSCT (CARMA)	Non-hodgkin Lymphoma|Acute Lymphoblastic Leukemia	Biological: CD19.CAR-multiVST for Group A|Biological: CD19.CAR-multiVST for Group B	https://ClinicalTrials.gov/show/NCT03768310
NCT03130712	A Study of GPC3-targeted T Cells by Intratumor Injection for Advanced HCC (GPC3-CART)	Carcinoma, Hepatocellular	Drug: GPC3-CART cells	https://ClinicalTrials.gov/show/NCT03130712
NCT02992210	Study on GD2 Positive Solid Tumors by 4SCAR-GD2	Solid Tumor	Genetic: 4SCAR-GD2	https://ClinicalTrials.gov/show/NCT02992210
NCT03085173	A Trial of "Armored" CAR T Cells Targeting CD19 For Patients With Relapsed CD19+ Hematologic Malignancies	Chronic Lymphocytic Leukemia (CLL)|Relapsed|Refractory	Biological: EGFRt/19-28z/4-1BBL CAR T cells	https://ClinicalTrials.gov/show/NCT03085173

FIG. 19-36

NCT Number	Title	Conditions	Interventions	URL
NCT02876978	Anti-GPC3 CAR T for Recurrent or Refractory Lung Squamous Cell Carcinoma	Lung Squamous Cell Carcinoma	Genetic: CAR-GPC3 T Cells|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT02876978
NCT04053062	LIGHT-PSMA-CART in Treating Patients With Castrate-Resistant Prostate Cancer	Castrate-Resistant Prostate Cancer	Biological: LIGHT-PSMA-CART cells	https://ClinicalTrials.gov/show/NCT04053062
NCT03229876	Safety and Efficacy Evaluation of CD19-UCART	Acute Lymphoblastic Leukemia (ALL)|Non Hodgkin Lymphoma (NHL)	Biological: CD19-UCART	https://ClinicalTrials.gov/show/NCT03229876
NCT02735083	A Study to Evaluate the Long-term Safety of Patients With Advanced Lymphoid Malignancies Who Have Been Previously Administered With UCART19	Advanced Lymphoid Malignancies	Biological: UCART19 follow up	https://ClinicalTrials.gov/show/NCT02735083
NCT02685670	Competitive Transfer of Î±CD19-TCRz-CD28 and Î±CD19-TCRz-CD137 CAR-T Cells for B-cell Leukemia/Lymphoma	Hematopoietic/Lymphoid Cancer|Adult Acute Lymphoblastic Leukemia in Remission|B-cell Adult Acute Lymphoblastic Leukemia|B-cell Chronic Lymphocytic Leukemia|Recurrent Adult Diffuse Large Cell Lymphoma|Recurrent Grade 1 Follicular Lymphoma|Recurrent Grade 2 Follicular Lymphoma|Recurrent Grade 3 Follicular Lymphoma|Recurrent Mantle Cell Lymphoma|Refractory Chronic Lymphocytic Leukemia|Stage III Adult Diffuse Large Cell Lymphoma|Stage III Chronic Lymphocytic Leukemia|Stage III Grade 1 Follicular Lymphoma|Stage III Grade 2 Follicular Lymphoma|Stage III Grade 3 Follicular Lymphoma|Stage III Mantle Cell Lymphoma|Stage IV Adult Diffuse Large Cell Lymphoma|Stage IV Chronic Lymphocytic Leukemia|Stage IV Grade 1 Follicular Lymphoma|Stage IV Grade 2 Follicular Lymphoma|Stage IV Grade 3 Follicular Lymphoma|Stage IV Mantle Cell Lymphoma	Biological: anti-CD19 CAR-T|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT02685670
NCT03110640	Anti-CD19 CAR T Infusion Combined With Allogeneic Stem Cell Transplantation for B-cell Leukemia/Lymphoma	B-cell Adult Acute Lymphoblastic Leukemia|B-cell Chronic Lymphocytic Leukemia|Adult Acute Lymphoblastic Leukemia in Remission|Hematopoietic/Lymphoid Cancer|Refractory Chronic Lymphocytic Leukemia	Biological: anti-CD19 CAR-T|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03110640
NCT04534634	Study of IFN-Î± Combined With CAR-T Cell Therapy in Relapsed and Refractory Acute Lymphoblastic Leukemiaï¼ˆR/R-ALLï¼‰	B-cell Acute Lymphoblastic Leukemia	Combination Product: IFN-Î± combined with CAR-T cell therapy	https://ClinicalTrials.gov/show/NCT04534634
NCT04881240	Study of CD19-directed Allogeneic Memory T-cell Therapy for Relapsed/Refractory CD19+ Leukemia	Acute Lymphoblastic Leukemia, in Relapse|Acute Lymphoblastic Leukemia, Refractory|Pediatric ALL	Biological: CD19-CAR(Mem) T-cells|Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Mesna|Device: CliniMACS|Procedure: Leukapheresis	https://ClinicalTrials.gov/show/NCT04881240

FIG. 19-37

NCT Number	Title	Conditions	Interventions	URL
NCT03765177	CUC-1901 for the Treatment of Patients With Relapsed/Refractory CD19 Positive Hematologic Malignancies	Acute Lymphoblastic Leukemia|Non-Hodgkin's Lymphoma	Biological: CUC-1901	https://ClinicalTrials.gov/show/NCT03765177
NCT03338972	Immunotherapy With BCMA CAR-T Cells in Treating Patients With BCMA Positive Relapsed or Refractory Multiple Myeloma	Recurrent Plasma Cell Myeloma|Refractory Plasma Cell Myeloma	Biological: Autologous Anti-BCMA-CAR-expressing CD4+/CD8+ T-lymphocytes FCARH143|Drug: Cyclophosphamide|Drug: Fludarabine|Other: Laboratory Biomarker Analysis|Procedure: Leukapheresis	https://ClinicalTrials.gov/show/NCT03338972
NCT02715362	A Study of GPC3 Redirected Autologous T Cells for Advanced HCC	Carcinoma, Hepatocellular	Drug: TAI-GPC3-CART cells	https://ClinicalTrials.gov/show/NCT02715362
NCT02650999	Pembrolizumab in Patients Failing to Respond to or Relapsing After CAR T Cell Therapy for Relapsed or Refractory Lymphomas	CD19+ Diffuse Large B-cell Lymphomas|Follicular Lymphomas|Mantle Cell Lymphomas	Drug: Pembrolizumab	https://ClinicalTrials.gov/show/NCT02650999
NCT02794246	CART-19 Post-ASCT for Multiple Myeloma	Multiple Myeloma	Biological: CART-19 cells	https://ClinicalTrials.gov/show/NCT02794246
NCT02862704	A Study of MG7 Redirected Autologous T Cells for Advanced MG7 Positive Liver Metastases(MG7-CART)	Liver Metastases	Biological: MG7-CART	https://ClinicalTrials.gov/show/NCT02862704
NCT03366324	Anti-CD19 CAR-T Therapy Combine With HSCT to Treat MRD+ B-cell Malignancies	Acute Lymphoblastic Leukemia|B Cell Lymphoma	Genetic: Second generation CAR-T cells|Procedure: Hematological stem cell transplantation	https://ClinicalTrials.gov/show/NCT03366324
NCT04148430	A Study of Anakinra to Prevent or Treat Severe Side Effects for Patients Receiving CAR-T Cell Therapy	B Cell ALL|B-Cell Lymphoma|B-cell Non Hodgkin Lymphoma	Drug: Anakinra	https://ClinicalTrials.gov/show/NCT04148430
NCT03366350	Anti-CD19 CAR-T Therapy Bridging to HSCT for CD19+ B-Cell Malignancies	Acute Lymphoblastic Leukemia|B Cell Lymphoma	Procedure: Allogeneic hematological stem cell transplantation	https://ClinicalTrials.gov/show/NCT03366350
NCT03060343	Zeushield Cytotoxic T Lymphocytes (Z-CTLs) for Relapsed or Refractory Non Small Cell Lung Cancer (NSCLC)	Non-small Cell Lung Cancer	Biological: Zeushield Cytotoxic T Lymphocytes	https://ClinicalTrials.gov/show/NCT03060343
NCT01853631	Activated T-Cells Expressing 2nd or 3rd Generation CD19-Specific CAR, Advanced B-Cell NHL, ALL, and CLL (SAGAN)	Non-Hodgkin Lymphoma|Chronic Lymphocytic Leukemia|Acute Lymphocytic Leukemia	Biological: CD19 CAR T Cells|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT01853631
NCT03393936	Safety and Efficacy of CCT301 CAR-T in Adult Subjects With Recurrent or Refractory Stage IV Renal Cell Carcinoma	Renal Cell Carcinoma	Biological: CCT301-38|Biological: CCT301-59	https://ClinicalTrials.gov/show/NCT03393936

FIG. 19-38

NCT Number	Title	Conditions	Interventions	URL
NCT03103971	huCAR014 CAR-T Cells in Treating Adult Patients With Relapsed or Refractory B-Cell Non-Hodgkin Lymphoma or Acute Lymphoblastic Leukemia	Recurrent Adult Acute Lymphoblastic Leukemia|Recurrent B-Cell Non-Hodgkin Lymphoma|Recurrent Diffuse Large B-Cell Lymphoma|Recurrent Primary Mediastinal (Thymic) Large B-Cell Lymphoma|Refractory Adult Acute Lymphoblastic Leukemia|Refractory B-Cell Non-Hodgkin Lymphoma|Refractory Diffuse Large B-Cell Lymphoma|Refractory Primary Mediastinal (Thymic) Large B-Cell Lymphoma|Recurrent Transformed Non-Hodgkin Lymphoma|Recurrent High Grade B-Cell Lymphoma With MYC, BCL2, and BCL6 Rearrangements|Refractory High Grade B-Cell Lymphoma With MYC, BCL2, and BCL6 Rearrangements|Recurrent B Acute Lymphoblastic Leukemia|Recurrent Diffuse Large B-Cell Lymphoma, Not Otherwise Specified|Recurrent High Grade B-Cell Lymphoma With MYC and BCL2 or BCL6 Rearrangements|Refractory B Acute Lymphoblastic Leukemia|Refractory Diffuse Large B-Cell Lymphoma, Not Otherwise Specified|Refractory High Grade B-Cell Lymphoma With MYC and BCL2 or BCL6 Rearrangements	Biological: Autologous Human Anti-CD19CAR-4-1BB-CD3zeta-EGFRt-expressing CD4+/CD8+ T-lymphocytes|Drug: Cyclophosphamide|Drug: Fludarabine|Other: Laboratory Biomarker Analysis|Procedure: Leukapheresis|Other: Pharmacological Study	https://ClinicalTrials.gov/show/NCT03103971
NCT03620058	CART22 Alone or in Combination With huCART19 for ALL	Chemotherapy Resistant Acute Lymphoblastic Leukemia|Refractory Acute Lymphoblastic Leukemia	Biological: CART22-65s cells|Biological: huCART19 Cells	https://ClinicalTrials.gov/show/NCT03620058
NCT04287660	Study of BiRd Regimen Combined With BCMA CAR T-cell Therapy in Newly Diagnosed Multiple Myeloma (MM) Patients	Multiple Myeloma	Drug: clarithromycin, lenalidomide, dexamethasone and autologous BCMA-directed CAR T-cells	https://ClinicalTrials.gov/show/NCT04287660
NCT04815356	Phase I Study of Anti-CD22 Chimeric Receptor T Cells in Patients With Relapsed/Refractory Hairy Cell Leukemia and Variant	Hairy Cell Leukemia|Hairy Cell Leukemia Variant	Biological: CD22CART cell infusion	https://ClinicalTrials.gov/show/NCT04815356
NCT00881920	Kappa-CD28 T Lymphocytes, Chronic Lymphocytic Leukemia, B-cell Lymphoma or Multiple Myeloma, CHARKALL	Lymphoma|Myeloma|Leukemia	Biological: Kappa CD28 T cells	https://ClinicalTrials.gov/show/NCT00881920
NCT04381741	CD19 CAR-T Expressing IL7 and CCL19 Combined With PD1 mAb for Relapsed or Refractory Diffuse Large B Cell Lymphoma	Diffuse Large B-cell Lymphoma	Biological: CD19-7Ã—19 CAR-T plus PD1 monoclonal antibody	https://ClinicalTrials.gov/show/NCT04381741
NCT04499573	Bispecific CD19/CD22 CAR-T for Treatment of Children and Young Adults With r/r B-ALL	B-ALL	Drug: CD19/CD22 CAR-T	https://ClinicalTrials.gov/show/NCT04499573
NCT01460901	Study of Donor Derived, Multi-virus-specific, Cytotoxic T-Lymphocytes for Relapsed/Refractory Neuroblastoma	Neuroblastoma	Biological: GD2 CAR modified Tri-virus specific cytotoxic t-cells	https://ClinicalTrials.gov/show/NCT01460901

FIG. 19-39

NCT Number	Title	Conditions	Interventions	URL
NCT02159495	Genetically Modified T-cell Immunotherapy in Treating Patients With Relapsed/Refractory Acute Myeloid Leukemia and Persistent/Recurrent Blastic Plasmacytoid Dendritic Cell Neoplasm	Adult Acute Myeloid Leukemia in Remission|Acute Biphenotypic Leukemia|Early Relapse of Acute Myeloid Leukemia|Late Relapse of Acute Myeloid Leukemia|Recurrent Adult Acute Myeloid Leukemia|Secondary Acute Myeloid Leukemia|Blastic Plasmacytoid Dendritic Cell Neoplasm|Acute Myeloid Leukemia|Adult Acute Lymphoblastic Leukemia|Interleukin-3 Receptor Subunit Alpha Positive|Minimal Residual Disease|Refractory Acute Myeloid Leukemia|Untreated Adult Acute Myeloid Leukemia	Drug: cyclophosphamide|Biological: Autologous CD123CAR-CD28-CD3zeta-EGFRt-expressing T Lymphocytes|Other: laboratory biomarker analysis|Biological: Allogeneic CD123CAR-CD28-CD3zeta-EGFRt-expressing T-lymphocytes|Drug: Fludarabine Phosphate	https://ClinicalTrials.gov/show/NCT02159495
NCT02746952	Dose Escalation Study of UCART19 in Adult Patients With Relapsed / Refractory B-cell Acute Lymphoblastic Leukaemia	B-cell Acute Lymphoblastic Leukemia	Biological: UCART19	https://ClinicalTrials.gov/show/NCT02746952
NCT04467853	A Clinical Study to Evaluate CAR-T Cell-based Medicinal Product in the Treatment of Advanced Gastric Cancer	Gastric Cancer	Biological: LCAR-C18S cells	https://ClinicalTrials.gov/show/NCT04467853
NCT03890198	A Phase 1 Study of LCAR-C182A Cells in the Treatment of Advanced Gastric Cancer and Pancreatic Ductal Adenocarcinoma	Gastric Cancer|Pancreatic Ductal Adenocarcinoma	Biological: LCAR-C182A cells	https://ClinicalTrials.gov/show/NCT03890198
NCT03179007	CTLA-4 and PD-1 Antibodies Expressing MUC1-CAR-T Cells for MUC1 Positive Advanced Solid Tumor	Advanced Solid Tumor	Biological: Anti-CTLA-4/PD-1 expressing MUC1-CAR-T	https://ClinicalTrials.gov/show/NCT03179007
NCT03182803	CTLA-4 and PD-1 Antibodies Expressing Mesothelin-CAR-T Cells for Mesothelin Positive Advanced Solid Tumor	Advanced Solid Tumor	Biological: CTLA-4/PD-1 antibodies expressing mesoCAR-T	https://ClinicalTrials.gov/show/NCT03182803
NCT03182816	CTLA-4 and PD-1 Antibodies Expressing EGFR-CAR-T Cells for EGFR Positive Advanced Solid Tumor	Advanced Solid Tumor	Biological: anti-CTLA-4/PD-1 expressing EGFR-CAR-T	https://ClinicalTrials.gov/show/NCT03182816
NCT01864902	Treatment of Relapsed and/or Chemotherapy Refractory CD33 Positive Acute Myeloid Leukemia by CART-33	Relapsed Adult Myeloid Leukemia|Chemotherapy Refractory Adult Myeloid Leukemia	Biological: CART33 cells|Biological: anti-CD33 CART|Biological: anti-CD33 CAR T cells	https://ClinicalTrials.gov/show/NCT01864902
NCT04653493	CD19 Targeted CAR T Cell Therapy in Patients With Relapsed/ Refractory B Cell Acute Lymphoblastic Leukaemia (ALL)	Relapsed B Cell Acute Lymphoblastic Leukemia (ALL)|Refractory B Cell Acute Lymphoblastic Leukemia (ALL)	Biological: CD19 CAR engineered autologous T-cells|Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Mesna	https://ClinicalTrials.gov/show/NCT04653493

FIG. 19-40

NCT Number	Title	Conditions	Interventions	URL
NCT03579927	CAR.CD19-CD28-zeta-2A-iCasp9-IL15-Transduced Cord Blood NK Cells, High-Dose Chemotherapy, and Stem Cell Transplant in Treating Participants With B-cell Lymphoma	CD19 Positive|Mantle Cell Lymphoma|Recurrent Diffuse Large B-Cell Lymphoma|Recurrent Follicular Lymphoma|Refractory B-Cell Non-Hodgkin Lymphoma|Refractory Diffuse Large B-Cell Lymphoma|Refractory Follicular Lymphoma	Procedure: Autologous Hematopoietic Stem Cell Transplantation|Drug: Carmustine|Drug: Cytarabine|Drug: Etoposide|Biological: Filgrastim|Drug: Melphalan|Biological: Rituximab|Biological: Umbilical Cord Blood-derived Natural Killer Cells	https://ClinicalTrials.gov/show/NCT03579927
NCT03155191	Study of TBI-1501 for Relapsed or Refractory Acute Lymphoblastic Leukemia	Lymphoblastic Leukemia, Acute Adult	Biological: TBI-1501	https://ClinicalTrials.gov/show/NCT03155191
NCT04561557	Safety and Efficacy of CT103A Cells for Relapsed/Refractory Antibody-associated Idiopathic Inflammatory Diseases of the Nervous System	Autoimmune Diseases|Autoimmune Diseases of the Nervous System|Neuromyelitis Optica Spectrum Disorder	Biological: CT103A cells|Drug: Cyclophosphamide and fludarabine	https://ClinicalTrials.gov/show/NCT04561557
NCT01818323	Phase I Trial: T4 Immunotherapy of Head and Neck Cancer	Head and Neck Cancer	Other: Intra-tumoral T4 immunotherapy	https://ClinicalTrials.gov/show/NCT01818323
NCT02315612	Anti-CD22 Chimeric Receptor T Cells in Pediatric and Young Adults With Recurrent or Refractory CD22-expressing B Cell Malignancies	Follicular Lymphoma|ALL|NHL|Large Cell Lymphoma	Biological: CD22-CAR	https://ClinicalTrials.gov/show/NCT02315612
NCT04136275	CAR-37 T Cells in Hematologic Malignancies	Hematologic Malignancy|Leukemia|Lymphoma|Lymphoma, B-Cell|Lymphoma, T-Cell|Lymphoma, Non-Hodgkin	Biological: CAR-37 T cells	https://ClinicalTrials.gov/show/NCT04136275
NCT02782351	Humanized CAR-T Therapy for Treatment of B Cell Malignancy	Leukemia, Lymphocytic, Chronic, B-Cell	Biological: CAR-T	https://ClinicalTrials.gov/show/NCT02782351
NCT04789408	Study Evaluating the Safety of KITE-222 in Participants With Relapsed/Refractory Acute Myeloid Leukemia	Acute Myeloid Leukemia	Drug: Cyclophosphamide|Drug: Fludarabine|Biological: KITE-222	https://ClinicalTrials.gov/show/NCT04789408
NCT02535364	Study Evaluating the Efficacy and Safety of JCAR015 in Adult B-cell Acute Lymphoblastic Leukemia (B-ALL)	Acute Lymphoblastic Leukemia	Biological: JCAR015 (CD19-targeted CAR T cells)	https://ClinicalTrials.gov/show/NCT02535364
NCT04499339	A Phase I/IIa Clinical Trial to Assess Feasibility, Safety and Antitumor Activity of Autologous SLAMF7 CAR-T Cells in Multiple Myeloma	Multiple Myeloma	Drug: SLAMF7 CAR-T	https://ClinicalTrials.gov/show/NCT04499339
NCT03166878	A Study Evaluating UCART019 in Patients With Relapsed or Refractory CD19+ Leukemia and Lymphoma	B Cell Leukemia|B Cell Lymphoma	Biological: UCART019	https://ClinicalTrials.gov/show/NCT03166878
NCT02963038	CAR T Cells for Refractory B Cell Malignancy	B-Cell Leukemia|B-Cell Lymphoma	Biological: Autologous CD19-targeting CAR T cells	https://ClinicalTrials.gov/show/NCT02963038

FIG. 19-41

NCT Number	Title	Conditions	Interventions	URL
NCT03573700	Evaluation of CD19-Specific CAR Engineered Autologous T-Cells for Treatment of Relapsed/Refractory CD19+ Acute Lymphoblastic Leukemia	Acute Lymphoblastic Leukemia, in Relapse|Acute Lymphoblastic Leukemia, Refractory	Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Mesna|Device: CliniMACS|Biological: CD19- specific CAR engineered autologous T-cells (SJCAR19 product)	https://ClinicalTrials.gov/show/NCT03573700
NCT02028455	A Pediatric and Young Adult Trial of Genetically Modified T Cells Directed Against CD19 for Relapsed/Refractory CD19+ Leukemia	CD19+ Acute Leukemia	Biological: Patient Derived CD19 specific CAR T cells also expressing an EGFRt	https://ClinicalTrials.gov/show/NCT02028455
NCT04486872	An Exploratory Clinical Trial of Autologous Humanized Anti-cluster of Differentiation Antigen 19/20(CD19/CD20) Dual Specific CAR-T Cells Injection	Diffuse Large B Cell Lymphoma	Biological: Autologous humanized anti-CD19 and anti-CD20 dual specific CAR-T Cells	https://ClinicalTrials.gov/show/NCT04486872
NCT03980691	Effect of Chidamide Combined With CAT-T or TCR-T Cell Therapy on HIV-1 Latent Reservoir	HIV/AIDS	Biological: Chidamide with CAR-T or TCR-T cell therapy	https://ClinicalTrials.gov/show/NCT03980691
NCT03068416	CD19-targeting, 3rd Generation CAR T Cells for Refractory B Cells Malignancy	B-cell Leukemia|B-Cell Lymphoma	Biological: CAR T cells	https://ClinicalTrials.gov/show/NCT03068416
NCT03064269	CAR-T Therapy for Central Nervous System B-cell Acute Lymphocytic Leukemia	B-cell Acute Lymphocytic Leukemia	Biological: CD19 CAR-T cells	https://ClinicalTrials.gov/show/NCT03064269
NCT04303520	Anti-CD19/CD22 Bispecific CAR-T Cell Therapy for CD19-positive ALL	CD19-positive ALL	Biological: anti-CD19/CD22 CAR-T cells|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04303520
NCT03142646	Safety and Efficacy Evaluation of IM19 CAR-T Cells	Leukemia	Biological: IM19 CAR-T	https://ClinicalTrials.gov/show/NCT03142646
NCT03084380	Anti-GPC3 CAR-T for Treating GPC3-positive Advanced Hepatocellular Carcinoma (HCC)	Hepatocellular Carcinoma	Biological: Retroviral vector-transduced autologous T cells to express anti-GPC3 CARs|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03084380
NCT03814447	The Fourth Generation CART-cell Therapy for Refractory-Relapsed Ovarian Cancer	Ovarian Cancer	Drug: anti- MESO CAR-T cells|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03814447
NCT03271515	Immunotherapy With Bispecific CAR-T Cells for B Cell Lymphoma, ALL and CLL	Leukemia|Lymphoma	Biological: anti-CD19 anti-CD20 Bispecific CAR-T	https://ClinicalTrials.gov/show/NCT03271515
NCT02958384	A Clinical Research of LeY-Targeted CAR-T in Myeloid Malignancies	Myeloid Malignancies	Biological: Anti-LeY-CAR-transduced T cells	https://ClinicalTrials.gov/show/NCT02958384
NCT02958397	A Clinical Research of CD33-Targeted CAR-T in Myeloid Malignancies	Myeloid Malignancies	Biological: Anti-CD33-CAR-transduced T cells	https://ClinicalTrials.gov/show/NCT02958397

FIG. 19-42

NCT Number	Title	Conditions	Interventions	URL
NCT03101709	The Safety and Efficacy of CART-19 Cells in Relapse and Refractory Patients With CD19+ B-cell Lymphoma	B Cell Lymphoma	Drug: Cyclophosphamide | Drug: Fludarabine | Biological: CART-19	https://ClinicalTrials.gov/show/NCT03101709
NCT03879382	Anti-CD19/BCMA Bispecific CAR-T Cell Therapy for R/R POMES	POMES Syndrome | Relapsed and Refractory POMES Syndrome	Biological: anti-CD19/BCMA CAR-T cells | Drug: Fludarabine | Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03879382
NCT02937103	A Clinical Research of CD123-Targeted CAR-T in Myeloid Malignancies	Leukemia	Biological: Anti-CD123-CAR-transduced T cells	https://ClinicalTrials.gov/show/NCT02937103
NCT02710149	A Clinical Research of CD20-Targeted CAR-T in B Cell Malignancies	Leukemia | Lymphoma	Biological: Anti-CD20-CAR-transduced T cells	https://ClinicalTrials.gov/show/NCT02710149
NCT04008394	Anti-CD30 CAR-T Therapy in Patients With Refractory/Relapsed Lymphocyte Malignancies	Adult T-Cell Lymphoma/Leukaemia | Anaplastic Large Cell Lymphoma | Angioimmunoblastic T-cell Lymphoma | NK/T-cell Lymphoma | Peripheral T Cell Lymphoma | Hodgkin Lymphoma	Genetic: Anti-CD30 CAR T cells	https://ClinicalTrials.gov/show/NCT04008394
NCT03375619	Long-term Follow-up Study of Patients Receiving CAR-20/19-T Cells	Chronic Lymphocytic Leukemia | Lymphomas Non-Hodgkin's B-Cell | Lymphoma, Small Lymphocytic	Other: Long-Term Follow-Up of Participants who Received CAR-20/19-T cells	https://ClinicalTrials.gov/show/NCT03375619
NCT02954445	A Clinical Research of BCMA-Targeted CAR-T in B Cell Malignancies	Leukemia | Lymphoma | Multiple Myeloma	Biological: Anti-BCMA-CAR-transduced T cells	https://ClinicalTrials.gov/show/NCT02954445
NCT04627740	Anti-ALPP CAR-T Cells Immunotherapy for Ovarian and Endometrial Cancer	Ovarian Cancer | Endometrial Cancer	Drug: Retroviral vector-transduced autologous T cells to express anti-ALPP CARs	https://ClinicalTrials.gov/show/NCT04627740
NCT02958410	A Clinical Research of CD30-Targeted CAR-T in Lymphocyte Malignancies	Leukemia | Lymphoma	Biological: Anti-CD30-CAR-transduced T cells	https://ClinicalTrials.gov/show/NCT02958410
NCT03994705	Descartes-11 in Multiple Myeloma	Multiple Myeloma	Biological: Descartes-11 | Drug: Fludarabine | Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03994705
NCT03467256	CD19 T-CAR for Treatment of Children and Young Adults With r/r B-ALL	B-cell Acute Lymphoblastic Leukemia | Acute Lymphocytic Leukemia, Pediatric	Biological: Chimeric Antigen Receptor T-Cell Therapy | Drug: Fludarabine | Drug: Cyclophosphamide | Drug: Tocilizumab	https://ClinicalTrials.gov/show/NCT03467256
NCT03559439	CD19-targeting CAR T Cells in Relapsed or Refractory CD19 Positive B-cell Malignancies	B-cell Malignancy | B-cell Lymphoma | B-Cell Acute Lymphoblastic Leukaemia	Biological: CD19 CAR T	https://ClinicalTrials.gov/show/NCT03559439
NCT03542799	EGFR-IL12-CART Cells for Patients With Metastatic Colorectal Cancer	Metastatic Colorectal Cancer	Biological: EGFR IL12 CART	https://ClinicalTrials.gov/show/NCT03542799
NCT04626726	Adult B-ALL Treated by CART Cell Bridging Allogeneic Hematopoietic Stem Cell Transplantation	Adult B Acute Lymphoblastic Leukemia	Drug: CD19 CAR-T | Drug: CD22 CAR-T | Drug: CD19+CD22 CAR-T | Drug: Fludarabine | Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04626726
NCT04796675	Cord Blood Derived Anti-CD19 CAR-Engineered NK Cells for B Lymphoid Malignancies	Acute Lymphocytic Leukemia | Chronic Lymphocytic Leukemia | Non Hodgkin's Lymphoma	Drug: Fludarabine + Cyclophosphamide + CAR-NK-CD19 Cells	https://ClinicalTrials.gov/show/NCT04796675

FIG. 19-43

NCT Number	Title	Conditions	Interventions	URL
NCT04823091	Autologous Cells Derived Anti-CD7 CAR-Engineered T Cells for T Lymphoid Malignancies	T-Cell Lymphocytic Leukemia|T-Cell Chronic Lymphocytic Leukemia|T Cell Non-Hodgkin Lymphoma	Drug: Fludarabine + Cyclophosphamide + CAR7-T Cells	https://ClinicalTrials.gov/show/NCT04823091
NCT03152435	EGFR CART Cells for Patients With Metastatic Colorectal Cancer	EGFR-positive Colorectal Cancer	Biological: EGFR CART	https://ClinicalTrials.gov/show/NCT03152435
NCT04420754	Study of AIC100 in Relapsed/Refractory Thyroid Cancer	Anaplastic Thyroid Cancer|Relapsed/Refractory Poorly Differentiated Thyroid Cancer	Biological: AIC100 CAR T Cells	https://ClinicalTrials.gov/show/NCT04420754
NCT02935153	A Clinical Research of CD22-Targeted CAR-T in B Cell Malignancies	Leukemia|Lymphoma	Biological: Anti-CD22-CAR-transduced T cells	https://ClinicalTrials.gov/show/NCT02935153
NCT04404660	A Study of CD19 Targeted CAR T Cell Therapy in Adult Patients With Relapsed or Refractory B Cell Acute Lymphoblastic Leukaemia (ALL)	Relapsed or Refractory B Cell Acute Lymphoblastic Leukemia	Biological: AUTO1	https://ClinicalTrials.gov/show/NCT04404660
NCT02822326	Phase I Study of CD19-CAR-T2 Cells for Patients With Chemotherapy Resistant or Refractory CD19+ Acute Leukemia	Acute Leukemia	Biological: CD19-CAR-T2 Cells	https://ClinicalTrials.gov/show/NCT02822326
NCT03146533	CD19 CART Cells for Patients With Relapse and Refractory CD19+ B-cell Lymphoma.	B Cell Lymphoma	Drug: Fludarabine|Drug: Cyclophosphamide|Biological: CD19 CART	https://ClinicalTrials.gov/show/NCT03146533
NCT02737085	the Sequential Therapy of CD19-targeted and CD20-targeted CAR-T Cell Therapy for Diffuse Large B Cell Lymphoma(DLBCL)	Lymphoma, Large B-Cell, Diffuse	Biological: Anti-CD19 CAR-T cells and Anti-CD20 CAR-T cells	https://ClinicalTrials.gov/show/NCT02737085
NCT04503980	Î±PD1-MSLN-CAR T Cells for the Treatment of MSLN-positive Advanced Solid Tumors	Colorectal Cancer|Ovarian Cancer	Biological: Î±PD1-MSLN-CAR T cells	https://ClinicalTrials.gov/show/NCT04503980
NCT04489862	Î±PD1-MSLN-CAR T Cells for the Treatment of MSLN-positive Advanced Solid Tumors	Non-small-cell Lung Cancer|Mesothelioma	Biological: Î±PD1-MSLN-CAR T cells	https://ClinicalTrials.gov/show/NCT04489862
NCT04215016	Safety of Autologous Humanized Anti-CD19 and Anti-CD20 Dual Specific CAR-T Cells in Adult Patients With Diffuse Large B-cell Lymphoma	Relapsed or Refractory DLBCL Patients With Either CD19 or CD20 Positive	Biological: Autologous humanized anti-CD19 and anti-CD20 dual specific CAR-T Cells	https://ClinicalTrials.gov/show/NCT04215016
NCT02443831	CARPALL: Immunotherapy With CD19 CAR T-cells for CD19+ Haematological Malignancies	Acute Lymphoblastic Leukemia|Burkitt Lymphoma	Procedure: Leukapheresis|Drug: Lymphodepletion with fludarabine|Drug: Lymphodepletion with cyclophosphamide|Biological: CD19 CAR T-cells	https://ClinicalTrials.gov/show/NCT02443831
NCT02587689	Phase I/II Study of Anti-Mucin1 (MUC1) CAR T Cells for Patients With MUC1+ Advanced Refractory Solid Tumor	Hepatocellular Carcinoma|Non-small Cell Lung Cancer|Pancreatic Carcinoma|Triple-Negative Invasive Breast Carcinoma	Biological: anti-MUC1 CAR T Cells	https://ClinicalTrials.gov/show/NCT02587689
NCT02395250	Anti-GPC3 CAR T for Treating Patients With Advanced HCC	Hepatocellular Carcinoma	Biological: anti-GPC3 CAR T	https://ClinicalTrials.gov/show/NCT02395250

FIG. 19-44

NCT Number	Title	Conditions	Interventions	URL
NCT02331693	CAR T Cells in Treating Patients With Malignant Gliomas Overexpressing EGFR	Advanced Glioma	Biological: anti-EGFR CAR T	https://ClinicalTrials.gov/show/NCT02331693
NCT04678336	CD123 Redirected T Cells for AML in Pediatric Subjects	Acute Myeloid Leukemia, in Relapse|Acute Myeloid Leukemia, Pediatric|Acute Myeloid Leukemia, Refractory	Biological: CART123 cells; cyclophosphamide; fludarabine	https://ClinicalTrials.gov/show/NCT04678336
NCT03766126	Lentivirally Redirected CD123 Autologous T Cells in AML	Acute Myeloid Leukemia, in Relapse|Acute Myeloid Leukemia, Adult|Acute Myeloid Leukemia, Refractory	Biological: CART123 cells; cyclophosphamide; fludarabine	https://ClinicalTrials.gov/show/NCT03766126
NCT03574168	CD19-CAR-T Cells in Patients With R/R B-ALL	B-cell Acute Lymphoblastic Leukemia	Biological: CD19-CAR-T Cells	https://ClinicalTrials.gov/show/NCT03574168
NCT04186520	CAR-20/19-T Cells in Patients With Relapsed Refractory B Cell Malignancies	Non Hodgkin Lymphoma (NHL)|Mantle Cell Lymphoma (MCL)	Biological: 8/12-Day Production of Car-T Cells|Biological: 12-Day Production of Car-T Cells	https://ClinicalTrials.gov/show/NCT04186520
NCT03747965	Study of PD-1 Gene-knocked Out Mesothelin-directed CAR-T Cells With the Conditioning of PC in Mesothelin Positive Multiple Solid Tumors	Solid Tumor, Adult	Biological: Mesothelin-directed CAR-T cells	https://ClinicalTrials.gov/show/NCT03747965
NCT02623582	CD123 Redirected Autologous T Cells for AML	Relapsed or Refractory Acute Myeloid Leukemia	Biological: Autologous Anti-CD 123 CAR TCR/4-1BB-expressing T-lymphocytes|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT02623582
NCT02968472	A Phase I Trial of 4SCAR19 Cells in the Treatment of Relapsed and Refractory B Cell Leukemia	B Acute Lymphoblastic Leukemia	Genetic: prophylactic 4SCAR19 cells	https://ClinicalTrials.gov/show/NCT02968472
NCT03796390	Study Evaluating Safety and Efficacy of CAR-T Cells Targeting CD123 in Patients With Acute Myelocytic Leukemia	Acute Myelocytic Leukemia	Biological: CD123 CAR-T cells	https://ClinicalTrials.gov/show/NCT03796390
NCT03885076	Gamma Delta T Cells in AML	Acute Myeloid Leukemia	Procedure: Blood collection and bone marrow aspirate	https://ClinicalTrials.gov/show/NCT03885076
NCT03121625	CAR-T Therapy in Relapsed or Refractory Haematopoietic and Lymphoid Malignancies	Leukemia|Lymphoma	Biological: Autologous CAR-T	https://ClinicalTrials.gov/show/NCT03121625
NCT03312205	CAR-T Cells for Relapsed or Refractory Haematopoietic and Lymphoid Malignancies	Leukemia|Lymphoma|Multiple Myeloma of Bone (Diagnosis)	Biological: Autologous CAR-T cells	https://ClinicalTrials.gov/show/NCT03312205
NCT04390542	Intervention for Caregivers of Patients Undergoing HSCT or CAR T-cell Therapy	Blood Cancer	Behavioral: Psychoeducation	https://ClinicalTrials.gov/show/NCT04390542
NCT02794961	CD22 Targeting CAR-T Therapy Against B Cell Hematological Malignancies	Recurrent or Refractory B Cell Malignancy	Biological: CD22 CAR-T	https://ClinicalTrials.gov/show/NCT02794961
NCT04653649	CAR T-cells Against CD30 (HSP-CAR30) for Relapsed/ Refractory Hodgkin and T-cell Lymphoma.	Hodgkin Lymphoma, Adult|T Cell Lymphoma	Biological: HSP-CAR30	https://ClinicalTrials.gov/show/NCT04653649
NCT03258047	Novel Autologou CAR-T Therapy for Relapsed/Refractory B Cell Lymphoma	B Cell Lymphoma	Combination Product: CAR-T	https://ClinicalTrials.gov/show/NCT03258047

FIG. 19-45

NCT Number	Title	Conditions	Interventions	URL
NCT03191773	A Study of Anti-CD19 CAR-T Cell Immunotherapy for Refractory /Relapsed B Cell Malignancies	Acute Lymphocytic Leukemia|Chronic Lymphocytic Leukemia|Lymphoma	Combination Product: Drugs and anti-CD19 CAR transduced T cells	https://ClinicalTrials.gov/show/NCT03191773
NCT03318861	Study to Evaluate the Safety and Efficacy of KITE-585 in Participants With Relapsed/Refractory Multiple Myeloma	Relapsed/Refractory Multiple Myeloma	Genetic: KITE-585|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03318861
NCT03960840	CD19-specific CAR-T Cells in CLL/SLL and DLBCL	Chronic Lymphocytic Leukemia; Small Lymphocytic Lymphoma; Diffuse Large B-cell Lymphoma; Acute Lymphoblastic Leukemia	Drug: YTB323 and ibrutinib|Drug: YTB323 single agent	https://ClinicalTrials.gov/show/NCT03960840
NCT04795882	A New Study Evaluating the Activity of Modular CAR T for mYeloma	Multiple Myeloma	Biological: BCMA CAR T cells|Biological: BCMA/CD19 CAR T cells	https://ClinicalTrials.gov/show/NCT04795882
NCT02624258	Pilot Study of Non-Viral, RNA-Redirected Autologous T Cells in Patients With Refractory or Relapsed Hodgkin Lymphoma	Hodgkin Lymphoma	Biological: CD19 RNA redirected autologous T-cells (RNA CART19 cells)	https://ClinicalTrials.gov/show/NCT02624258
NCT03907527	Modified Immune Cells (Autologous CAR T Cells) in Treating Patients With Advanced, Recurrent Platinum Resistant Ovarian, Fallopian Tube or Primary Peritoneal Cancer	Carcinoma|Platinum-Resistant Ovarian Carcinoma|Platinum-Resistant Primary Peritoneal Carcinoma|Recurrent Fallopian Tube Carcinoma|Recurrent Ovarian Carcinoma|Recurrent Primary Peritoneal Carcinoma|Refractory Fallopian Tube Carcinoma|Refractory Ovarian Carcinoma|Refractory Primary Peritoneal Carcinoma|Stage III Fallopian Tube Cancer AJCC v8|Stage III Ovarian Cancer AJCC v8|Stage III Primary Peritoneal Cancer AJCC v8|Stage IIIA Fallopian Tube Cancer AJCC v8|Stage IIIA Ovarian Cancer AJCC v8|Stage IIIA Primary Peritoneal Cancer AJCC v8|Stage IIIA1 Fallopian Tube Cancer AJCC v8|Stage IIIA1 Ovarian Cancer AJCC v8|Stage IIIA2 Fallopian Tube Cancer AJCC v8|Stage IIIA2 Ovarian Cancer AJCC v8|Stage IIIB Fallopian Tube Cancer AJCC v8|Stage IIIB Ovarian Cancer AJCC v8|Stage IIIB Primary Peritoneal Cancer AJCC v8|Stage IIIC Fallopian Tube Cancer AJCC v8|Stage IIIC Ovarian Cancer AJCC v8|Stage IIIC Primary Peritoneal Cancer AJCC v8|Stage IV Fallopian Tube Cancer AJCC v8|Stage IV Ovarian Cancer AJCC v8|Stage IV Primary Peritoneal Cancer AJCC v8|Stage IVA Fallopian Tube Cancer AJCC v8|Stage IVA	Biological: PRGN-3005 UltraCAR-T cells	https://ClinicalTrials.gov/show/NCT03907527
NCT02666248	Long-term Follow-up of Subjects Exposed to Lentiviral-based CART-EGFRvIII Gene-modified Cellular Therapy Products in Cancer Studies	Subjects Entering into This Protocol Will be Followed for up to 15 Years After Initial CART-EGFRvIII Infusion		https://ClinicalTrials.gov/show/NCT02666248
NCT04155749	Master Protocol for the Phase 1 Study of Cell Therapies in Multiple Myeloma	Relapsed and Refractory Multiple Myeloma	Drug: CART-ddBCMA	https://ClinicalTrials.gov/show/NCT04155749

FIG. 19-46

NCT Number	Title	Conditions	Interventions	URL
NCT02965157	Pilot Study of Anti-CD20-CAR-engineered T Cells in Patients With Chemotherapy Resistant or Refractory CD20+ Lymphoma	Lymphoma, B-Cell	Biological: CART20	https://ClinicalTrials.gov/show/NCT02965157
NCT02713984	A Clinical Research of CAR T Cells Targeting HER2 Positive Cancer	Breast Cancer|Ovarian Cancer|Lung Cancer|Gastric Cancer|Colorectal Cancer|Glioma|Pancreatic Cancer	Biological: Anti-HER2 CAR-T	https://ClinicalTrials.gov/show/NCT02713984
NCT04503538	Telemedicine for Early Detection of Cytokine Release Syndrome and Neurotoxicity	Large B-cell Lymphoma|Diffuse Large B Cell Lymphoma|Primary Mediastinal Large B Cell Lymphoma|High-grade B-cell Lymphoma|Follicular Lymphoma	Other: Telemedicine visit	https://ClinicalTrials.gov/show/NCT04503538
NCT04670068	Phase I Study of Autologous CAR T-Cells Targeting the B7-H3 Antigen in Recurrent Epithelial Ovarian	Epithelial Ovarian Cancer	Drug: CAR.B7-H3|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04670068
NCT03050190	A Phase I/II Multiple Center Trial of 4SCAR19 Cells in the Treatment of Relapsed and Refractory B Cell Malignancies	B-cell Malignancies	Genetic: Therapeutic 4SCAR19 cells	https://ClinicalTrials.gov/show/NCT03050190
NCT02132624	CD19-targeting 3rd Generation CAR T Cells for Refractory B Cell Malignancy - a Phase I/IIa Trial.	B Cell Lymphoma|B Cell Leukemia	Biological: Autologous 3rd generation CD19-targeting CAR T cells	https://ClinicalTrials.gov/show/NCT02132624
NCT04008524	A Clinical Study of CAR-T Cells in the Treatment of Relapsed and Refractory Hematological Malignancies	Relapsed and Refractory Hematological Malignancies	Biological: CAR-T cells	https://ClinicalTrials.gov/show/NCT04008524
NCT04430530	4SCAR-T Therapy Post CD19-targeted Immunotherapy	CD19 Negative B-cell Malignancies	Biological: Infusion of 4SCAR-T specific to CD22/CD123/CD38/ CD10/CD20	https://ClinicalTrials.gov/show/NCT04430530
NCT04016129	CAR-T Immunotherapy Targeting CD19- ALL	B-cell Leukemia	Biological: 4SCAR-CD22/CD123/CD38/CD10/ CD20/TSLPR	https://ClinicalTrials.gov/show/NCT04016129
NCT04359784	Anakinra for the Prevention of Cytokine Release Syndrome and Neurotoxicity in Patients With B-Cell Lymphoma Receiving CD19-Targeted CAR-T Cell Therapy	B-Cell Non-Hodgkin Lymphoma	Biological: Anakinra|Biological: Axicabtagene Ciloleucel	https://ClinicalTrials.gov/show/NCT04359784
NCT03125577	Combination CAR-T Cell Therapy Targeting Hematological Malignancies	B-cell Malignancies	Biological: 4SCAR19 and 4SCAR22|Biological: 4SCAR19 and 4SCAR38|Biological: 4SCAR19 and 4SCAR20|Biological: 4SCAR19 and 4SCAR123|Biological: 4SCAR19 and 4SCAR70|Biological: 4SCAR19 and 4SCAR30	https://ClinicalTrials.gov/show/NCT03125577
NCT02546167	CART-BCMA Cells for Multiple Myeloma	Multiple Myeloma	Biological: CART-BCMA	https://ClinicalTrials.gov/show/NCT02546167

FIG. 19-47

NCT Number	Title	Conditions	Interventions	URL
NCT02030834	Phase IIa Study of Redirected Autologous T Cells Engineered to Contain Anti-CD19 Attached to TCRz and 4-Signaling Domains in Patients With Chemotherapy Relapsed or Refractory CD19+ Lymphomas	Non-Hodgkins Lymphoma (NHL) Patients, With CD19+B Cell Lymphomas	Biological: CART-19	https://ClinicalTrials.gov/show/NCT02030834
NCT04429438	Multi-CAR-T Cells Targeting B Cell Lymphomas	B Cell Lymphoma (BCL)	Biological: 4SCAR19 and 4SCAR20/22/70/PSMA/13/79b/GD2	https://ClinicalTrials.gov/show/NCT04429438
NCT03423706	Clinical Studies of New Model Haploidentical Hematopoietic Stem Cell Transplantation	CD19-chimeric Antigen Receptor T Cells|Relapsed and/or Refractory Acute Lymphoblastic Leukemia|the Haploidentical Hematopoietic Stem Cell Transplantation	Procedure: the new model of haplo-HSCT for r/r B-ALL	https://ClinicalTrials.gov/show/NCT03423706
NCT02215967	Study of T Cells Targeting B-Cell Maturation Antigen for Previously Treated Multiple Myeloma	Myeloma, Plasma-Cell|Myeloma-Multiple	Drug: Cyclophosphamide|Drug: Fludarabine|Biological: Anti-B-cell maturation antigen (BCMA) chimeric antigen receptor (CAR) T cells	https://ClinicalTrials.gov/show/NCT02215967
NCT04893031	Effect of Tocilizumab on Intensive Care Patients With COVID-19 Pneumonia, a Retrospective Cohort Study	Tocilizumab|COVID-19|Critical Care|Mortality	Drug: Tocilizumab	https://ClinicalTrials.gov/show/NCT04893031
NCT03601078	An Efficacy and Safety Study of bb2121 in Subjects With Relapsed and Refractory Multiple Myeloma and in Subjects With High-Risk Multiple Myeloma	Multiple Myeloma	Biological: bb2121	https://ClinicalTrials.gov/show/NCT03601078
NCT04442022	A Study of Rituximab-Gemcitabine-Dexamethasone-Platinum (R-GDP) With or Without Selinexor in Patients With Relapsed/Refractory Diffuse Large B-cell Lymphoma	Relapsed/Refractory Diffuse Large B-cell Lymphoma	Drug: Selinexor (combination therapy)|Drug: Placebo matching for Selinexor (combination therapy)|Drug: Rituximab (combination therapy)|Drug: Gemcitabine (combination therapy)|Drug: Dexamethasone (combination therapy)|Drug: Cisplatin (combination therapy)|Drug: Selinexor (continuous therapy)|Drug: Placebo matching for Selinexor (continuous therapy)	https://ClinicalTrials.gov/show/NCT04442022
NCT04051216	The SMART CART Study: Health Information Technology	Leukemia, Acute|Leukemia, Lymphoblastic	Behavioral: Education information system|Other: Activity monitor|Other: Interview|Other: Survey Administration|Other: Laboratory Biomarker Analysis	https://ClinicalTrials.gov/show/NCT04051216

FIG. 19-48

NCT Number	Title	Conditions	Interventions	URL
NCT02247609	Evaluation of 4th Generation Safety-designed CAR T Cells Targeting High-risk and Refractory B Cell Lymphomas	B-cell Lymphomas	Genetic: Anti-CD19 CAR T cells	https://ClinicalTrials.gov/show/NCT02247609
NCT04608487	Axi-cel in CNS Lymphoma	Lymphoma|Lymphoma Cns	Drug: Fludarabine|Drug: Cyclophosphamide|Biological: Axicabtagene Ciloleucel	https://ClinicalTrials.gov/show/NCT04608487
NCT03117751	Total Therapy XVII for Newly Diagnosed Patients With Acute Lymphoblastic Leukemia and Lymphoma	Acute Lymphoblastic Leukemia|Acute Lymphoblastic Lymphoma	Drug: Prednisone|Drug: Vincristine|Drug: Daunorubicin|Drug: Pegaspargase|Drug: ErwinaseÂ®|Drug: Cyclophosphamide|Drug: Cytarabine|Drug: Mercaptopurine|Drug: Dasatinib|Drug: Methotrexate|Drug: Blinatumomab|Drug: Ruxolitinib|Drug: Bortezomib|Drug: Dexamethasone|Drug: Doxorubicin|Drug: Etoposide|Drug: Clofarabine|Drug: Vorinostat|Drug: Idarubicin|Drug: Nelarabine|Drug: Thioguanine	https://ClinicalTrials.gov/show/NCT03117751
NCT04410900	Vaccine Responsiveness After CAR-T Cell Therapy	B-Cell Neoplasm	Biological: Wistar Rabies Virus Strain PM-1503-3M Vaccine|Procedure: Biospecimen Collection	https://ClinicalTrials.gov/show/NCT04410900
NCT04264039	Anti-CD19 U-CAR-T Cell Therapy for B Cell Hematologic Malignancies	B-cell Acute Lymphoblastic Leukemia|B-cell Lymphoma	Biological: anti-CD19 UCAR T cells|Drug: Fludarabine|Drug: Cytoxan|Drug: Melphalan	https://ClinicalTrials.gov/show/NCT04264039
NCT04747093	Induced-T Cell Like NK Cells for B Cell Malignancies	B Cell Leukemia|B Cell Lymphoma|B-cell Acute Lymphoblastic Leukemia|B-cell Lymphoma Recurrent|B-cell Lymphoma Refractory	Biological: CAR-ITNK cells	https://ClinicalTrials.gov/show/NCT04747093
NCT04264078	Anti-CD7 U-CAR-T Cell Therapy for T/NK Cell Hematologic Malignancies	T-cell Leukemia|T-cell Lymphoma	Biological: CD7 UCAR-T cells|Drug: Fludarabine|Drug: Cytoxan|Drug: Melphalan	https://ClinicalTrials.gov/show/NCT04264078
NCT04892433	Tissue Study in Patients Undergoing CAR-T Cell Therapy (CAR_21_01)	CAR-T Therapy Complications		https://ClinicalTrials.gov/show/NCT04892433
NCT03468153	Dual Specificity CD19 and CD22 CAR-T Cell Immunotherapy for CD19+CD22+ Relapsed and Refractory Lymphoma	Lymphoma	Biological: Dual Specificity CD19 and CD22 CAR-T Cell Immunotherapy	https://ClinicalTrials.gov/show/NCT03468153
NCT04432649	Targeting CD276 (B7-H3) Positive Solid Tumors by 4SCAR-276	Solid Tumor	Biological: 4SCAR-276	https://ClinicalTrials.gov/show/NCT04432649
NCT04571138	A Pediatric and Young Adult Trial of Genetically Modified T Cells Directed Against CD22 for Relapsed/Refractory Leukemia or Lymphoma	Leukemia|Lymphoma	Biological: SCRI-CAR22v2	https://ClinicalTrials.gov/show/NCT04571138

FIG. 19-49

NCT Number	Title	Conditions	Interventions	URL
NCT02274584	CAR T Cells Targeting CD30 Positive Lymphomas (4SCAR30273)	Lymphomas	Genetic: Anti-CD30 CAR T cells	https://ClinicalTrials.gov/show/NCT02274584
NCT03330691	A Feasibility and Safety Study of Dual Specificity CD19 and CD22 CAR-T Cell Immunotherapy for CD19+CD22+ Leukemia	Leukemia|Lymphoma	Biological: Patient-derived CD19- and CD22 specific CAR	https://ClinicalTrials.gov/show/NCT03330691
NCT03684889	CD19-specific CAR T Cells With a Fully Human Binding Domain for CD19+ Leukemia or Lymphoma	Leukemia|Lymphoma	Biological: SCRI-huCAR19v1|Biological: SCRI-huCAR19v2	https://ClinicalTrials.gov/show/NCT03684889
NCT03484702	Trial to Determine the Efficacy and Safety of JCAR017 in Adult Subjects With Aggressive B-Cell Non-Hodgkin Lymphoma	Lymphoma, Non-Hodgkin	Drug: JCAR017	https://ClinicalTrials.gov/show/NCT03484702
NCT02786511	Longterm Follow-up of Subjects Treated With bb2121	Multiple Myeloma	Drug: Safety and efficacy assessments	https://ClinicalTrials.gov/show/NCT02786511
NCT02721407	Anti-CD22 CAR-T Therapy for CD19-refractory or Resistant Lymphoma Patients	Recurrent Adult Diffuse Large Cell Lymphoma|Recurrent Follicular Lymphoma|Recurrent Mantle Cell Lymphoma|Stage III/IV Adult Diffuse Large Cell Lymphoma|Stage III/IV Follicular Lymphoma|Stage III/IV Mantle Cell Lymphoma	Drug: Retroviral vector-transduced autologous T cells to express CD22-specific CARs	https://ClinicalTrials.gov/show/NCT02721407
NCT03208556	Safety and Efficacy of iPD1 CD19 eCAR T Cells in Relapsed or Refractory B-cell Lymphoma	Relapsed or Refractory B-cell Lymphoma	Biological: iPD1 CD19 eCAR T cells|Drug: Fludarabine and cyclophosphamide	https://ClinicalTrials.gov/show/NCT03208556
NCT04557436	TT52CAR19 Therapy for B-cell Acute Lymphoblastic Leukaemia (B-ALL)	B Acute Lymphoblastic Leukemia	Drug: PBLTT52CAR19	https://ClinicalTrials.gov/show/NCT04557436
NCT04690595	Leukemia-Specific Immune Cells (BAFFR-CAR T Cells) for the Treatment of Relapsed or Refractory B-cell Acute Lymphoblastic Leukemia	Relapsed or Refractory B-cell Acute Lymphoblastic Leukemia	Biological: BAFFR-CAR T cells	https://ClinicalTrials.gov/show/NCT04690595
NCT04844866	Efficacy and Safety of MB-CART2019.1 vs. SoC in Lymphoma Patients	Diffuse Large B-cell Lymphoma	Genetic: MB-CART2019.1|Drug: R-GemOx or BR plus polatuzumab vedotin	https://ClinicalTrials.gov/show/NCT04844866
NCT03594162	Compassionate Use of CAR T Cells Targeting the CD19 Antigen and Containing the Inducible Caspase 9 Safety Switch	Acute Lymphoblastic Leukemia|Immune System Diseases|Immunoproliferative Disorders	Drug: iC9-CAR19 cells|Drug: AP1903|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03594162
NCT04483778	B7H3 CAR T Cell Immunotherapy for Recurrent/Refractory Solid Tumors in Children and Young Adults	Pediatric Solid Tumor|Germ Cell Tumor|Retinoblastoma|Hepatoblastoma|Wilms Tumor|Rhabdoid Tumor|Carcinoma|Osteosarcoma|Ewing Sarcoma|Rhabdomyosarcoma|Synovial Sarcoma|Clear Cell Sarcoma|Malignant Peripheral Nerve Sheath Tumors|Desmoplastic Small Round Cell Tumor|Soft Tissue Sarcoma|Neuroblastoma|Melanoma	Biological: second generation 4-1BBÎ¶ B7H3-EGFRt-DHFR|Biological: second generation 4-1BBÎ¶ B7H3-EGFRt-DHFR(selected) and a second generation 4-1BBÎ¶ CD19-Her2tG	https://ClinicalTrials.gov/show/NCT04483778

FIG. 19-50

NCT Number	Title	Conditions	Interventions	URL
NCT02652910	Memory-enriched CAR-T Cells Immunotherapy for B Cell Lymphoma	Recurrent Adult Diffuse Large Cell Lymphoma|Recurrent Follicular Lymphoma|Recurrent Mantle Cell Lymphoma|Stage III Adult Diffuse Large Cell Lymphoma|Stage III Follicular Lymphoma|Stage III Mantle Cell Lymphoma|Stage IV Adult Diffuse Large Cell Lymphoma|Stage IV Follicular Lymphoma|Stage IV Mantle Cell Lymphoma	Drug: CD19.CAR-T cells	https://ClinicalTrials.gov/show/NCT02652910
NCT03740256	Binary Oncolytic Adenovirus in Combination With HER2-Specific Autologous CAR VST, Advanced HER2 Positive Solid Tumors	Bladder Cancer|Head and Neck Squamous Cell Carcinoma|Cancer of the Salivary Gland|Lung Cancer|Breast Cancer|Gastric Cancer|Esophageal Cancer|Colorectal Cancer|Pancreatic Adenocarcinoma|Solid Tumor	Biological: CAdVEC	https://ClinicalTrials.gov/show/NCT03740256
NCT04684563	huCART19-IL18 in NHL/CLL Patients	Chronic Lymphocytic Leukemia|Non-Hodgkin Lymphoma	Biological: huCART19-IL18	https://ClinicalTrials.gov/show/NCT04684563
NCT03618381	EGFR806 CAR T Cell Immunotherapy for Recurrent/Refractory Solid Tumors in Children and Young Adults	Pediatric Solid Tumor|Germ Cell Tumor|Retinoblastoma|Hepatoblastoma|Wilms Tumor|Rhabdoid Tumor|Carcinoma|Osteosarcoma|Ewing Sarcoma|Rhabdomyosarcoma|Synovial Sarcoma|Clear Cell Sarcoma|Malignant Peripheral Nerve Sheath Tumors|Desmoplastic Small Round Cell Tumor|Soft Tissue Sarcoma|Neuroblastoma	Biological: second generation 4-1BBÎ¶ EGFR806-EGFRt|Biological: second generation 4-1BBÎ¶ EGFR806-EGFRt and a second generation 4-1BBÎ¶ CD19-Her2tG	https://ClinicalTrials.gov/show/NCT03618381
NCT02388828	CART-meso Long-term Follow-up	Subjects Who Have Received Lentiviral-based CART-meso Therapy	Biological: lentiviral-based CART meso therapy	https://ClinicalTrials.gov/show/NCT02388828
NCT02842320	Targeting Leukemic Stem Cell Expressing the IL-1RAP Protein in Chronic Myelogenous Leukemia (CML)	Chronic Myeloid Leukemia	Other: biological samples	https://ClinicalTrials.gov/show/NCT02842320
NCT03488160	CAR-T Treatment for Relapse / Refractory Type Safety and Effectiveness of Lymphoma	Lymphoma	Biological: CD19-targeted CAR-T cells	https://ClinicalTrials.gov/show/NCT03488160
NCT03492268	Safety and Efficacy Evaluation of BCMA-CART for Treating Multiple Myeloma	Multiple Myeloma	Biological: BCMA-CART	https://ClinicalTrials.gov/show/NCT03492268
NCT01722149	Re-directed T Cells for the Treatment (FAP)-Positive Malignant Pleural Mesothelioma	Malignant Pleural Mesothelioma	Genetic: Adoptive Transfer of re-directed T cells	https://ClinicalTrials.gov/show/NCT01722149
NCT03811457	Immunotherapy With CD19 CAR T-cells in Patients With Relapsed or Refractory CD19+ Leukemia and Lymphoma	Lymphoma Leukemia	Genetic: Welgenaleucel	https://ClinicalTrials.gov/show/NCT03811457
NCT03975907	Clinical Trial to Evaluate CT053 in Patients With Relapsed and/or Refractory Multiple Myeloma (LUMMICAR STUDY 1)	Multiple Myeloma	Biological: CAR-BCMA T Cells	https://ClinicalTrials.gov/show/NCT03975907
NCT03914885	Compassionate Use Re-Infusion of ATLCAR.CD30	Hodgkin Lymphoma, Adult	Genetic: ATLCAR.CD30|Drug: Bendamustine|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03914885
NCT03672318	Study of ATLCAR.CD138 Cells for Relapsed/Refractory Multiple Myeloma	Multiple Myeloma|Immune System Diseases	Drug: CAR138 T Cells	https://ClinicalTrials.gov/show/NCT03672318

FIG. 19-51

NCT Number	Title	Conditions	Interventions	URL
NCT04903080	HER2-specific CAR T Cells for Children With Ependymoma	Ependymoma	Biological: HER-2 Specific CAR T Cell	https://ClinicalTrials.gov/show/NCT04903080
NCT04314843	Study of Lenzilumab and Axicabtagene Ciloleucel in Participants With Relapsed or Refractory Large B-Cell Lymphoma	Relapsed/Refractory Large B-cell Lymphoma	Drug: Cyclophosphamide|Drug: Fludarabine|Biological: Lenzilumab|Biological: Axicabtagene Ciloleucel	https://ClinicalTrials.gov/show/NCT04314843
NCT03696784	Anti-CD19 CAR-T Cells With Inducible Caspase 9 Safety Switch for B-cell Lymphoma	Lymphoma|Lymphoma, B-Cell|Immune System Diseases|Immunoproliferative Disorders|Lymphatic Diseases	Biological: iC9-CAR19 T cells|Drug: Bendamustine|Drug: Fludarabine|Drug: AP1903|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03696784
NCT01626495	Phase I/IIA Study of CART19 Cells for Patients With Chemotherapy Resistant or Refractory CD19+ Leukemia and Lymphoma	B Cell Leukemia|B Cell Lymphoma	Biological: CART-19	https://ClinicalTrials.gov/show/NCT01626495
NCT04734678	Comparison of Tocilizumab Versus Tocilizumab/Infliximab in Patients With COVID-19-associated Cytokine Storm Syndrome	Covid19|Cytokine Storm|Corona Virus Infection	Drug: Tocilizumab|Drug: Infliximab	https://ClinicalTrials.gov/show/NCT04734678
NCT03226704	Leukapheresis for CAR or Adoptive Cell Therapy Manufacturing	Leukemia|Lymphoma|Acute Lymphoblastic Leukemia|Diffuse Large B-Cell Lymphoma|Non-Hodgkin's Lymphoma		https://ClinicalTrials.gov/show/NCT03226704
NCT03321123	MB-CART19.1 in Patients With R/R ALL	Precursor B-Lymphoblastic Lymphoma/Leukaemia Refractory	Drug: MB-CART19.1	https://ClinicalTrials.gov/show/NCT03321123
NCT03016377	Administration of Autologous CAR-T CD19 Antigen With Inducible Safety Switch in Patients With Relapsed/Refractory ALL	Acute Lymphoblastic Leukemia|Immune System Diseases|Immunoproliferative Disorders	Biological: iC9-CAR19 cells|Drug: Rimiducid|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03016377
NCT03605238	Treatment of Relapsed and/or Refractory AQP4-IgG Seropositive NMOSD by Tandem CAR T Cells Targeting CD19 and CD20	Neuromyelitis Optica Spectrum Disorder	Biological: Corticosteroids & tanCART19/20	https://ClinicalTrials.gov/show/NCT03605238
NCT03941626	Autologous CAR-T/TCR-T Cell Immunotherapy for Solid Malignancies	Esophagus Cancer|Hepatoma|Glioma|Gastric Cancer	Biological: CAR-T/TCR-T cells immunotherapy	https://ClinicalTrials.gov/show/NCT03941626
NCT03389035	Transposon-manipulated Allogeneic CARCIK-CD19 Cells in Pediatric and Adult Patients With r/r ALL Post HSCT	Acute Lymphoblastic Leukemia, in Relapse	Biological: CARCIK-CD19	https://ClinicalTrials.gov/show/NCT03389035
NCT03893019	MB-CART20.1 Melanoma	Melanoma (Skin)	Biological: MB-CART20.1	https://ClinicalTrials.gov/show/NCT03893019
NCT03638206	Autologous CAR-T/TCR-T Cell Immunotherapy for Malignancies	B-cell Acute Lymphoblastic Leukemia|Lymphoma|Myeloid Leukemia|Multiple Myeloma|Hepatoma|Gastric Cancer|Pancreatic Cancer|Mesothelioma|Colorectal Cancer|Esophagus Cancer|Lung Cancer|Glioma|Melanoma|Synovial Sarcoma|Ovarian Cancer|Renal Carcinoma	Biological: CAR-T cell immunotherapy	https://ClinicalTrials.gov/show/NCT03638206

FIG. 19-52

NCT Number	Title	Conditions	Interventions	URL
NCT04332913	Efficacy and Safety of Tocilizumab in the Treatment of SARS-Cov-2 Related Pneumonia	COVID-19 Pneumonia		https://ClinicalTrials.gov/show/NCT04332913
NCT03664635	MB-CART20.1 Lymphoma	Relapsed or Refractory B-cell Non-Hodgkin's Lymphoma|Non-Hodgkin's Lymphoma|B-cell Lymphoma Refractory|B-cell Lymphoma Recurrent	Biological: MB-CART20.1	https://ClinicalTrials.gov/show/NCT03664635
NCT03853616	MB-CART19.1 r/r CD19+ B-cell Malignancies (BCM)	Acute Lymphoblastic Leukemia Recurrent|B-cell Lymphoma Recurrent|B-cell Lymphoma Refractory|Chronic Lymphocytic Leukemia Recurrent|Chronic Lymphocytic Leukemia Refractory	Biological: MB-CART19.1	https://ClinicalTrials.gov/show/NCT03853616
NCT01318317	Genetically Engineered Lymphocyte Therapy After Peripheral Blood Stem Cell Transplant in Treating Patients With High-Risk, Intermediate-Grade, B-cell Non-Hodgkin Lymphoma	Recurrent Adult Diffuse Large Cell Lymphoma|Recurrent Adult Diffuse Mixed Cell Lymphoma|Recurrent Adult Diffuse Small Cleaved Cell Lymphoma|Recurrent Grade 3 Follicular Lymphoma|Recurrent Mantle Cell Lymphoma	Procedure: peripheral blood stem cell transplantation (PBSCT)|Biological: filgrastim|Genetic: polymerase chain reaction|Biological: rituximab|Biological: genetically engineered lymphocyte therapy|Other: laboratory biomarker analysis|Drug: plerixafor|Procedure: autologous hematopoietic stem cell transplantation	https://ClinicalTrials.gov/show/NCT01318317
NCT04419909	Retreatment With CTL019/CTL119	Lymphoma, B-Cell	Drug: CD19 redirected autologous T cells (CTL019 or CTL119 cells)	https://ClinicalTrials.gov/show/NCT04419909
NCT03274219	Study of bb21217 in Multiple Myeloma	Multiple Myeloma	Biological: bb21217	https://ClinicalTrials.gov/show/NCT03274219
NCT03289455	CD19 /22 CAR T Cells (AUTO3) for the Treatment of B Cell Acute Lymphoblastic Leukemia (ALL)	B Acute Lymphoblastic Leukemia|Recurrent Childhood Acute Lymphoblastic Leukemia|Refractory Childhood Acute Lymphoblastic Leukemia|B-cell Acute Lymphoblastic Leukemia	Biological: AUTO3 (CD19/22 CAR T cells	https://ClinicalTrials.gov/show/NCT03289455
NCT03287817	CD19/22 CAR T Cells (AUTO3) for the Treatment of Diffuse Large B Cell Lymphoma	Diffuse Large B Cell Lymphoma|Relapsed Diffuse Large B-Cell Lymphoma|Refractory Diffuse Large B-Cell Lymphoma|DLBCL	Biological: AUTO3	https://ClinicalTrials.gov/show/NCT03287817
NCT02625480	Study Evaluating Brexucabtagene Autoleucel (KTE-X19) in Pediatric and Adolescent Participants With Relapsed/Refractory B-precursor Acute Lymphoblastic Leukemia or Relapsed/Refractory B-Cell Non-Hodgkin Lymphoma	Acute Lymphoblastic Leukemia|Relapsed Non Hodgkin Lymphoma|Refractory Non-Hodgkin Lymphoma	Biological: Brexucabtagene Autoleucel (KTE-X19)|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT02625480
NCT04880434	Study to Evaluate the Efficacy of Brexucabtagene Autoleucel (KTE-X19) in Participants With Relapsed/Refractory Mantle Cell Lymphoma (Cohort 3)	Relapsed/Refractory Mantle Cell Lymphoma	Drug: Fludarabine|Drug: Cyclophosphamide|Biological: Brexucabtagene autoleucel	https://ClinicalTrials.gov/show/NCT04880434

FIG. 19-53

NCT Number	Title	Conditions	Interventions	URL
NCT04888442	Phase I Study of pCAR-19B in the Treatment of Adult CD19-positive Relapsed/Refractory B-ALL	Acute Lymphoblastic Leukemia, in Relapse|Refractory Acute Lymphoblastic Leukemia	Biological: pCAR-19B cells	https://ClinicalTrials.gov/show/NCT04888442
NCT03994913	Clinical Trial to Evaluate CD19 CAR T (CT032) in Patients With Relapsed and/or Refractory Non-Hodgkin's B Cell Lymphoma	Refractory B-Cell Non-Hodgkin Lymphoma|Relapsed B-cell Non-Hodgkin Lymphoma	Biological: CAR-CD19 T Cells	https://ClinicalTrials.gov/show/NCT03994913
NCT04720313	HB10101 Multiple Myeloma	Dose Escalation and Safety	Drug: CART BCMA	https://ClinicalTrials.gov/show/NCT04720313
NCT03661554	BCMA Nano Antibody CAR T Cells for Patients With Refractory and Relapsed Multiple Myeloma	Relapsed and Refractory Multiple Myeloma	Biological: BCMA CAR-T Cells	https://ClinicalTrials.gov/show/NCT03661554
NCT04295018	A Study of BCMA-directed CAR-T Cells Treatment in Subjects With r/r Multiple Myeloma	Multiple Myeloma	Drug: C-CAR088	https://ClinicalTrials.gov/show/NCT04295018
NCT02601313	Study to Evaluate the Efficacy of Brexucabtagene Autoleucel (KTE-X19) in Participants With Relapsed/Refractory Mantle Cell Lymphoma	Relapsed/Refractory Mantle Cell Lymphoma	Biological: brexucabtagene autoleucel|Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Axicabtagene Ciloleucel	https://ClinicalTrials.gov/show/NCT02601313
NCT02926833	Safety and Efficacy of KTE-C19 in Combination With Atezolizumab in Adults With Refractory Diffuse Large B-Cell Lymphoma (DLBCL)	Refractory Diffuse Large B Cell Lymphoma	Biological: KTE-C19|Biological: Atezolizumab|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT02926833
NCT04706936	Novel BCMA-targeted CAR-T Cell Therapy for Multiple Myeloma	Relapsed or Refractory Multiple Myeloma	Biological: anti-BCMA CAR-T|Drug: Cyclophosphamid|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT04706936
NCT04272151	Safety and Efficacy of BCMA-Targeted CAR-T Therapy for Relapsed/Refractory Multiple Myeloma	Multiple Myeloma|Multiple Myeloma in Relapse|Neoplasm, Plasma Cell	Biological: BCMA CAR-T cells	https://ClinicalTrials.gov/show/NCT04272151
NCT04271644	BCMA-Targeted CAR-T Cell Therapy for Relapsed/Refractory Multiple Myeloma	Multiple Myeloma|Neoplasm, Plasma Cell|Multiple Myeloma in Relapse	Biological: BCMA CAR-T cells	https://ClinicalTrials.gov/show/NCT04271644
NCT03690011	Cell Therapy for High Risk T-Cell Malignancies Using CD7-Specific CAR Expressed On Autologous T Cells	T-cell Acute Lymphoblastic Leukemia|T-cell Acute Lymphoblastic Lymphoma|T-non-Hodgkin Lymphoma	Genetic: CD7.CAR/28zeta CAR T cells|Drug: Fludarabine|Drug: Cytoxan	https://ClinicalTrials.gov/show/NCT03690011

FIG. 19-54

NCT Number	Title	Conditions	Interventions	URL
NCT03019055	Study of CAR-20/19-T Cells in Patients With Relapsed Refractory B Cell	Lymphoma, Non-Hodgkin|Lymphoma, B-Cell|Chronic Lymphocytic Leukemia|Small Lymphocytic Lymphoma	Biological: CAR-20/19-T cells (1.0 x10^5 CAR-20/19-T cells/kg)|Biological: CAR-20/19-T cells (2.5 x10^5 CAR-20/19-T cells/kg)|Biological: CAR-20/19-T cells (7.5 x10^5 CAR-20/19-T cells/kg)|Biological: CAR-20/19-T cells (2.5 x10^6 CAR-20/19-T cells/kg)	https://ClinicalTrials.gov/show/NCT03019055
NCT00889954	Her2 and TGFBeta Cytotoxic T Cells in Treatment of Her2 Positive Malignancy	HER2 Positive Malignancies	Biological: TGFBeta resistant HER2/EBV-CTLs	https://ClinicalTrials.gov/show/NCT00889954
NCT04322292	A Study of BCMA-directed CAR-T Cells Treatment in Subjects With r/r Multiple Myeloma	Multiple Myeloma	Drug: C-CAR088	https://ClinicalTrials.gov/show/NCT04322292
NCT04776330	a Clinical Research of BCMA-Targeted Prime CAR-T Cell Therapy in Relapsed/Refractory Multiple Myeloma	Multiple Myeloma|Neoplasm, Plasma Cell|Multiple Myeloma in Relapse	Biological: BCMA targeted prime CAR-T cells	https://ClinicalTrials.gov/show/NCT04776330
NCT04836507	Study of Efficacy and Safety of CRC01 in Adult Large B-cell Lymphoma Patients	Relapsed Large B-cell Lymphoma|Refractory Large B-cell Lymphoma|Diffuse Large B-cell Lymphoma (DLBCL)|Primary Mediastinal Large B-Cell Lymphoma (PMBCL)|High-grade B-cell Lymphoma|Transformed Follicular Lymphoma (TFL)	Biological: CRC01|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04836507
NCT02813252	Long-Term Follow-up Study for Patients Previously Treated With JCAR015	Acute Lymphoblastic Leukemia	Genetic: JCAR015	https://ClinicalTrials.gov/show/NCT02813252
NCT03642496	Clinical Study of ET019002-T Cell Therapy for Refractory/Relapsed B-Cell Malignancies	B-Cell Malignancies	Biological: Low dose ET019002- T Cells|Biological: Middle dose ET019002- T Cells|Biological: High dose ET019002- T Cells	https://ClinicalTrials.gov/show/NCT03642496
NCT04249947	P-PSMA-101 CAR-T Cells in the Treatment of Subjects With Metastatic Castration-Resistant Prostate Cancer (mCRPC)	Prostatic Neoplasms, Castration-Resistant|Neoplasms by Histologic Type|Neoplasms, Prostate|Prostate Cancer|Metastatic Castration-resistant Prostate Cancer|Neoplasms|Prostatic Neoplasms|Genital Neoplasms, Male|Urogenital Neoplasms|Neoplasms by Site|Prostatic Disease	Biological: P-PSMA-101 CAR-T cells|Drug: Rimiducid	https://ClinicalTrials.gov/show/NCT04249947
NCT04637503	4SCAR-T Therapy Targeting GD2, PSMA and CD276 for Treating Neuroblastoma	Neuroblastoma	Biological: GD2, PSMA and CD276 CAR-T cells	https://ClinicalTrials.gov/show/NCT04637503
NCT03958656	T-cells Expressing an Anti-SLAMF7 CAR for Treating Multiple Myeloma	Myeloma-Multiple|Myeloma, Plasma-Cell	Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Rimiducid|Biological: Anti-SLAMF7 CAR T cells	https://ClinicalTrials.gov/show/NCT03958656
NCT04556669	Anti-PD-L1 Armored Anti-CD22 CAR-T/CAR-TILs Targeting Patients With Solid Tumors	Solid Tumor, Adult|Cervical Cancer|Sarcoma|NSCLC	Biological: Autologous aPD-L1 armored anti-CD22 CAR T cells	https://ClinicalTrials.gov/show/NCT04556669

FIG. 19-55

NCT Number	Title	Conditions	Interventions	URL
NCT03602612	T Cells Expressing a Novel Fully-Human Anti-BCMA CAR for Treating Multiple Myeloma	Myeloma-Multiple|Myeloma, Plasma-Cell	Drug: Cyclophosphamide|Drug: Fludarabine|Biological: Anti-BCMA CAR T cells	https://ClinicalTrials.gov/show/NCT03602612
NCT01430390	In Vitro Expanded Allogeneic Epstein-Barr Virus Specific Cytotoxic T-Lymphocytes (EBV-CTLs) Genetically Targeted to the CD19 Antigen in B-cell Malignancies	Acute Lymphocytic Leukemia|Lymphoma	Biological: Biological/Genetically Modified T cells|Drug: Cyclophosphamide-based chemotherapy	https://ClinicalTrials.gov/show/NCT01430390
NCT03288493	P-BCMA-101 Tscm CAR-T Cells in the Treatment of Patients With Multiple Myeloma (MM)	Multiple Myeloma	Biological: P-BCMA-101 CAR-T cells|Drug: Rimiducid	https://ClinicalTrials.gov/show/NCT03288493
NCT03579888	CD19-Specific T Cells Post AlloSCT	B Acute Lymphoblastic Leukemia With t(v;11q23.3); KMT2A Rearranged|Recurrent B Acute Lymphoblastic Leukemia|Recurrent Chronic Lymphocytic Leukemia|Recurrent Diffuse Large B-Cell Lymphoma, Not Otherwise Specified|Recurrent Mantle Cell Lymphoma|Recurrent Non-Hodgkin Lymphoma|Recurrent Ph-Like Acute Lymphoblastic Leukemia|Recurrent Primary Mediastinal (Thymic) Large B-Cell Cell Lymphoma|Recurrent Small Lymphocytic Lymphoma|Refractory B Acute Lymphoblastic Leukemia|Refractory Chronic Lymphocytic Leukemia|Refractory Diffuse Large B-Cell Lymphoma, Not Otherwise Specified|Refractory Mantle Cell Lymphoma|Refractory Non-Hodgkin Lymphoma|Refractory Ph-Like Acute Lymphoblastic Leukemia|Refractory Primary Mediastinal (Thymic) Large B-Cell Cell Lymphoma|Refractory Small Lymphocytic Lymphoma	Biological: Autologous CD19-CD8-CD28-CD3zeta-CAR-mbIL15-HER1t T Cells|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03579888
NCT03563326	Intraperitoneal Infusion of EpCAM CAR-T Cell in Advanced Gastric Cancer With Peritoneal Metastasis (WCH-GC-CART)	Neoplasm, Stomach|Metastases, Neoplasm|Neoplasm Seeding	Biological: CAR-T cells targeting EpCAM|Biological: Chemotherapy	https://ClinicalTrials.gov/show/NCT03563326
NCT03436771	Long-term Follow-up Study for Patients Previously Treated With a Juno CAR T-Cell Product	Non Hodgkin Lymphoma|Multiple Myeloma|Chronic Lymphocytic Leukemia|Diffuse Large B Cell Lymphoma|Mantle Cell Lymphoma|Follicular Lymphoma	Genetic: JCAR017|Genetic: JCARH125	https://ClinicalTrials.gov/show/NCT03436771
NCT04613557	Safety, Activity and Cell Kinetics of CYAD-211 in Patients With Relapsed or Refractory Multiple Myeloma	Relapse/Refractory Multiple Myeloma	Biological: CYAD-211|Drug: Endoxan|Drug: Fludara	https://ClinicalTrials.gov/show/NCT04613557
NCT04167696	Study in Relapsed/Refractory Acute Myeloid Leukemia or Myelodysplastic Syndrome Patients to Determine the Recommended Dose of CYAD-02	Acute Myeloid Leukemia|Myelodysplastic Syndrome	Biological: CYAD-02|Drug: ENDOXAN|Drug: Fludara	https://ClinicalTrials.gov/show/NCT04167696

FIG. 19-56

NCT Number	Title	Conditions	Interventions	URL
NCT04162756	Study of Brexucabtagene Autoleucel (KTE-X19) for the Treatment of Individuals With Relapsed/Refractory B-Cell Malignancies	Relapse/Refractory Mantle Cell Lymphoma	Biological: Brexucabtagene Autoleucel (KTE-X19)|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04162756
NCT03761056	Efficacy and Safety of Axicabtagene Ciloleucel as First-Line Therapy in Participants With High-Risk Large B-Cell Lymphoma	B-cell Lymphoma	Biological: Axicabtagene Ciloleucel|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03761056
NCT03624036	Safety and Tolerability of Brexucabtagene Autoleucel (KTE-X19) in Adults With Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma	Relapsed/Refractory Chronic Lymphocytic Leukemia and Relapsed/Refractory Small Lymphocytic Lymphoma	Biological: brexucabtagene autoleucel (KTE-X19)|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03624036
NCT04355780	Immunologic Features of Respiratory Failure in Pediatric Hematopoietic Cell Transplantation (HCT) Recipients and Pediatric Oncology Patients	Respiratory Failure|Respiratory Disease		https://ClinicalTrials.gov/show/NCT04355780
NCT04405778	A Study of TAK-102 in Adult With Previously-Treated Solid Tumors	Solid Tumors	Biological: TAK-102	https://ClinicalTrials.gov/show/NCT04405778
NCT02348216	Safety and Efficacy of KTE-C19 in Adults With Refractory Aggressive Non Hodgkin Lymphoma	Refractory Diffuse Large B Cell Lymphoma (DLBCL)|Relapsed Diffuse Large B-Cell Lymphoma|Transformed Follicular Lymphoma (TFL)|Primary Mediastinal B-cell Lymphoma (PMBCL)|High Grade B-cell Lymphoma (HGBCL)	Biological: Axicabtagene Ciloleucel|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT02348216
NCT04109482	Trial to Evaluate the Safety and Efficacy of MB-102 in Patients With BPDCN.	Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)	Biological: MB-102|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04109482
NCT04163302	Safety and Efficiency Study of CD19-PD1-CART Cell in Relapsed/Refractory B Cell Lymphoma	Lymphoma, B-Cell	Biological: CD19-PD1-CART Cell	https://ClinicalTrials.gov/show/NCT04163302
NCT04236011	BCMA and CD19 Targeted Fast Dual CAR-T for BCMA+ Refractory/Relapsed Multiple Myeloma	Multiple Myeloma	Biological: GC012F injection	https://ClinicalTrials.gov/show/NCT04236011
NCT01860937	T-Lymphocytes Genetically Targeted to the B-Cell Specific Antigen CD19 in Pediatric and Young Adult Patients With Relapsed B-Cell Acute Lymphoblastic Leukemia	Relapsed B-Cell Acute Lymphoblastic Leukemia	Procedure: leukapheresis or collection of PBMCs|Drug: cyclophosphamide based chemotherapy regimens|Biological: modified T cells	https://ClinicalTrials.gov/show/NCT01860937
NCT04002401	Safety and Efficacy of Axicabtagene Ciloleucel in Combination With Rituximab in Participants With Refractory Large B-Cell Lymphoma	Refractory Large B-cell Lymphoma	Biological: Axicabtagene Ciloleucel|Drug: Rituximab|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04002401

FIG. 19-57

NCT Number	Title	Conditions	Interventions	URL
NCT03704298	Safety and Efficacy of Axicabtagene Ciloleucel in Combination With Utomilumab in Adults With Refractory Large B-cell Lymphoma	Relapsed/Refractory Large B-cell Lymphoma	Drug: Cyclophosphamide|Drug: Fludarabine|Biological: Axicabtagene Ciloleucel|Biological: Utomilumab	https://ClinicalTrials.gov/show/NCT03704298
NCT03391466	Efficacy of Axicabtagene Ciloleucel Compared to Standard of Care Therapy in Subjects With Relapsed/Refractory Diffuse Large B Cell Lymphoma	Relapsed/Refractory Diffuse Large B-Cell Lymphoma (DLBCL)	Biological: Axicabtagene Ciloleucel|Drug: Platinum-containing salvage chemotherapy (eg, R-ICE) followed by high dose therapy (eg, BEAM) and autologous stem cell transplant in responders.|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03391466
NCT04074330	A Study of TAK-981 Given With Rituximab in Adults With Relapsed or Refractory CD20-Positive Non-Hodgkin Lymphoma	Lymphoma, Non-Hodgkin	Drug: TAK-981|Drug: Rituximab	https://ClinicalTrials.gov/show/NCT04074330
NCT04162119	Safety and Efficiency Study of BCMA-PD1-CART Cells in Relapsed/Refractory Multiple Myeloma	Multiple Myeloma	Biological: BCMA-PD1-CART Cell	https://ClinicalTrials.gov/show/NCT04162119
NCT03271632	Multi-CAR T Cell Therapy in the Treatment of Multiple Myeloma	Multiple Myeloma	Biological: CAR T cells	https://ClinicalTrials.gov/show/NCT03271632
NCT02917083	CD30 CAR T Cells, Relapsed CD30 Expressing Lymphoma (RELY-30)	Hodgkin's Lymphoma|Non-Hodgkin Lymphoma	Genetic: CAR T Cells|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT02917083
NCT04429451	PSMA-specific CAR-T Cell Therapy	PSMA Positive Tumors or Tumor Tissues	Biological: 4SCAR-PSMA T cells	https://ClinicalTrials.gov/show/NCT04429451
NCT04617704	BCMA and CD19 Targeted Fast Dual CART for Chromosomal Abnomalities High-risk BCMA+ Multiple Myeloma	Multiple Myeloma	Biological: GC012F injection	https://ClinicalTrials.gov/show/NCT04617704
NCT04234061	Clinical Trial to Assess The Efficacy and Safety of the Combination of Tisagenlecleucel And Ibrutinib in Mantle Cell Lymphoma	Mantle Cell Lymphoma Recurrent	Combination Product: ibrutinib and Tisagenlecleucel	https://ClinicalTrials.gov/show/NCT04234061
NCT03389230	Memory-Enriched T Cells in Treating Patients With Recurrent or Refractory Grade III-IV Glioma	Glioblastoma|Malignant Glioma|Recurrent Glioma|Refractory Glioma|WHO Grade III Glioma	Biological: HER2(EQ)BBÎ¶/CD19t+ T cells|Other: Laboratory Biomarker Analysis|Procedure: Leukapheresis	https://ClinicalTrials.gov/show/NCT03389230
NCT03483103	Lisocabtagene Maraleucel (JCAR017) as Second-Line Therapy (TRANSCEND-PILOT-017006)	Lymphoma, Non-Hodgkin|Lymphoma, Nonhodgkin|Lymphoma, B-Cell|Lymphoma, Large B-Cell, Diffuse	Biological: lisocabtagene maraleucel	https://ClinicalTrials.gov/show/NCT03483103

FIG. 19-58

NCT Number	Title	Conditions	Interventions	URL
NCT03310619	A Safety and Efficacy Trial of JCAR017 Combinations in Subjects With Relapsed/Refractory B-cell Malignancies (PLATFORM)	Lymphoma, Non-Hodgkin|Lymphoma, Large B-Cell, Diffuse|Lymphoma, Follicular	Biological: JCAR017|Drug: Durvalumab|Drug: CC-122|Drug: Ibrutinib|Drug: CC-220|Drug: Relatlimab|Drug: Nivolumab|Drug: CC-99282	https://ClinicalTrials.gov/show/NCT03310619
NCT03744676	A Safety Trial of Lisocabtagene Maraleucel (JCAR017) for Relapsed and Refractory (R/R) B-cell Non-Hodgkin Lymphoma (NHL) in the Outpatient Setting (TRANSCEND-OUTREACH-007)	Lymphoma, Non-Hodgkin|Lymphoma|Lymphoma, B-Cell|Lymphoma, Large B-Cell, Diffuse|Neoplasms|Neoplasms by Histologic Type|Lymphoproliferative Disorders|Lymphatic Diseases|Immunoproliferative Disorders|Immune System Disorder	Biological: lisocabtagene maraleucel	https://ClinicalTrials.gov/show/NCT03744676
NCT03601442	CTL019 Out of Specification MAP for ALL or DLBCL Patients	Acute Lymphoblastic Leukemia (ALL)|Diffuse Large B-cell Lymphoma (DLBCL)	Biological: CTL019	https://ClinicalTrials.gov/show/NCT03601442
NCT03568461	Efficacy and Safety of Tisagenlecleucel in Adult Patients With Refractory or Relapsed Follicular Lymphoma	Follicular Lymphoma	Biological: tisagenlecleucel	https://ClinicalTrials.gov/show/NCT03568461
NCT02445248	Study of Efficacy and Safety of CTL019 in Adult DLBCL Patients	Diffuse Large B-cell Lymphoma (DLBCL)	Biological: CTL019	https://ClinicalTrials.gov/show/NCT02445248
NCT02858310	E7 TCR T Cells for Human Papillomavirus-Associated Cancers	Papillomavirus Infections|Cervical Intraepithelial Neoplasia|Carcinoma In Situ|Vulvar Neoplasms|Vulvar Diseases	Biological: E7 TCR cells|Drug: Aldesleukin|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT02858310
NCT03181126	A Study of Venetoclax in Combination With Navitoclax and Chemotherapy in Subjects With Relapsed/Refractory Acute Lymphoblastic Leukemia or Relapsed/Refractory Lymphoblastic Lymphoma	Acute Lymphoblastic Leukemia (ALL)|Lymphoblastic Lymphoma	Drug: Navitoclax|Drug: Chemotherapy|Drug: Venetoclax	https://ClinicalTrials.gov/show/NCT03181126
NCT02208362	Genetically Modified T-cells in Treating Patients With Recurrent or Refractory Malignant Glioma	Recurrent Glioblastoma|Recurrent Malignant Glioma|Recurrent WHO Grade II Glioma|Recurrent WHO Grade III Glioma|Refractory Glioblastoma|Refractory Malignant Glioma|Refractory WHO Grade II Glioma|Refractory WHO Grade III Glioma	Biological: IL13Ralpha2-specific Hinge-optimized 4-1BB-co-stimulatory CAR/Truncated CD19-expressing Autologous TN/MEM Cells|Biological: IL13Ralpha2-specific Hinge-optimized 41BB-co-stimulatory CAR Truncated CD19-expressing Autologous T-Lymphocytes|Other: Laboratory Biomarker Analysis|Procedure: Magnetic Resonance Imaging|Procedure: Magnetic Resonance Spectroscopic Imaging|Other: Quality-of-Life Assessment	https://ClinicalTrials.gov/show/NCT02208362

FIG. 19-59

NCT Number	Title	Conditions	Interventions	URL
NCT02303821	Study of Carfilzomib in Combination With Induction Chemotherapy in Children With Relapsed or Refractory Acute Lymphoblastic Leukemia	Acute Lymphoblastic Leukemia (ALL)	Drug: Carfilzomib | Drug: Dexamethasone | Drug: Mitoxantrone | Drug: PEG-asparaginase | Drug: Vincristine | Drug: Intrathecal (IT) Methotrexate | Drug: Intrathecal Triple Therapy (Intrathecal Cytarabine, Hydrocortisone, and Methotrexate) | Drug: 6-Mercaptopurine | Drug: Cyclophosphamide | Drug: Cytarabine | Drug: Daunorubicin	https://ClinicalTrials.gov/show/NCT02303821
NCT04456959	InO - A Retrospective Study of UK Patients With Leukaemia	Precursor Cell Lymphoblastic Leukemia-Lymphoma	Drug: Inotuzumab Ozogamicin	https://ClinicalTrials.gov/show/NCT04456959
NCT03648372	A Study of TAK-981 in Participants With Relapsed/Refractory Solid Tumors or Non-Hodgkin Lymphoma (NHL)	Neoplasms | Lymphoma | Hematologic Neoplasms	Drug: TAK-981	https://ClinicalTrials.gov/show/NCT03648372
NCT01188343	Study of Japanese Encephalitis Chimeric Virus Vaccine Given With Measles-Mumps-Rubella Vaccine in Taiwanese Toddlers	Japanese Encephalitis | Measles | Mumps | Rubella	Biological: Japanese encephalitis chimeric virus: Measles, mumps, and rubella live attenuated virus	https://ClinicalTrials.gov/show/NCT01188343
NCT03651128	Efficacy and Safety Study of bb2121 Versus Standard Regimens in Subjects With Relapsed and Refractory Multiple Myeloma (RRMM)	Multiple Myeloma	Biological: bb2121 | Drug: Daratumumab | Drug: Pomalidomide | Drug: Dexamethasone | Drug: Bortezomib | Drug: Ixazomib | Drug: Lenalidomide | Drug: Carfilzomib | Drug: Elotuzumab	https://ClinicalTrials.gov/show/NCT03651128
NCT04539366	Testing a New Immune Cell Therapy, GD2-Targeted Modified T-cells (GD2CART), in Children, Adolescents, and Young Adults With Relapsed/Refractory Osteosarcoma and Neuroblastoma, The GD2-CAR PERSIST Trial	Recurrent Neuroblastoma | Recurrent Osteosarcoma | Refractory Neuroblastoma | Refractory Osteosarcoma	Drug: Cyclophosphamide | Drug: Fludarabine Phosphate | Biological: GD2-CAR-expressing Autologous T-lymphocytes	https://ClinicalTrials.gov/show/NCT04539366
NCT01644565	Safety Study of Chimeric Vaccine to Prevent ETEC Diarrhea	Escherichia Coli Infection	Biological: Recombinant fimbrial adhesin dsc14CfaE sCTA2/LTB5 | Biological: Recombinant fimbrial adhesin dscCfaE | Biological: Modified E. coli heat labile enterotoxin LTR192G	https://ClinicalTrials.gov/show/NCT01644565
NCT02580747	Treatment of Relapsed and/or Chemotherapy Refractory Advanced Malignancies by CART-meso	Malignant Mesothelioma | Pancreatic Cancer | Ovarian Tumor | Triple Negative Breast Cancer | Endometrial Cancer | Other Mesothelin Positive Tumors	Biological: anti-meso-CAR vector transduced T cells	https://ClinicalTrials.gov/show/NCT02580747

FIG. 19-60

NCT Number	Title	Conditions	Interventions	URL
NCT01935843	Treatment of Chemotherapy Refractory Human Epidermalgrowth Factor Receptor-2(HER-2) Positive Advanced Solid Tumors	Advanced HER-2 Positive Solid Tumors|Chemotherapy Refactory|HER-2 Antibody Inhibitor Therapy Refactory	Biological: CART-HER-2	https://ClinicalTrials.gov/show/NCT01935843
NCT01869166	Treatment of Chemotherapy Refractory EGFR(Epidermal Growth Factor Receptor) Positive Advanced Solid Tumors (CART-EGFR)	Advanced EGFR-positive Solid Tumors	Biological: CART-EGFR	https://ClinicalTrials.gov/show/NCT01869166
NCT02541370	Treatment of Relapsed and/or Chemotherapy Refractory Advanced Malignancies by CART133	Liver Cancer|Pancreatic Cancer|Brain Tumor|Breast Cancer|Ovarian Tumor|Colorectal Cancer|Acute Myeloid and Lymphoid Leukemias	Biological: anti-CD133-CAR vector-transduced T cells	https://ClinicalTrials.gov/show/NCT02541370
NCT01864889	Treatment of Relapsed and/or Chemotherapy Refractory B-cell Malignancy by CART19	Hematopoietic/Lymphoid Cancer|Adult Acute Lymphoblastic Leukemia in Remission|B-cell Adult Acute Lymphoblastic Leukemia|B-cell Chronic Lymphocytic Leukemia|Prolymphocytic Leukemia|Recurrent Adult Diffuse Large Cell Lymphoma|Recurrent Grade 1 Follicular Lymphoma|Recurrent Grade 2 Follicular Lymphoma|Recurrent Grade 3 Follicular Lymphoma|Recurrent Mantle Cell Lymphoma|Refractory Chronic Lymphocytic Leukemia|Stage III Adult Diffuse Large Cell Lymphoma|Stage III Chronic Lymphocytic Leukemia|Stage III Grade 1 Follicular Lymphoma|Stage III Grade 2 Follicular Lymphoma|Stage III Grade 3 Follicular Lymphoma|Stage III Mantle Cell Lymphoma|Stage IV Adult Diffuse Large Cell Lymphoma|Stage IV Chronic Lymphocytic Leukemia|Stage IV Grade 1 Follicular Lymphoma|Stage IV Grade 2 Follicular Lymphoma|Stage IV Grade 3 Follicular Lymphoma|Stage IV Mantle Cell Lymphoma	Biological: anti-CD19-CAR vector-transduced T cells	https://ClinicalTrials.gov/show/NCT01864889
NCT00291447	111In-ch806 in Patients With Advanced Tumours Expressing the 806 Antigen	Neoplasms	Biological: ch806	https://ClinicalTrials.gov/show/NCT00291447
NCT02772822	A Study Comparing the Efficiency and Safety of S-CHOP(Cyclophosphamide, Hydroxydaunomycin, Oncovin, and Prednisone) Versus R-CHOP in Untreated CD20(Cluster of Differentiation Antigen 20)-Positive DLBCL Patients	Diffuse Large B Cell Lymphoma	Drug: SCT400 plus CHOP|Drug: Rituximab plus CHOP	https://ClinicalTrials.gov/show/NCT02772822
NCT00433446	S0354, Anti-IL-6 Chimeric Monoclonal Antibody in Patients With Metastatic Prostate Cancer That Did Not Respond to Hormone Therapy	Prostate Cancer	Biological: CNTO 328	https://ClinicalTrials.gov/show/NCT00433446

FIG. 19-61

NCT Number	Title	Conditions	Interventions	URL
NCT00735644	Study of ChimeriVaxâ„¢-Japanese Encephalitis Vaccine in Toddlers in Thailand and the Philippines	Japanese Encephalitis|Hepatitis A	Biological: Japanese encephalitis vaccine|Biological: Japanese encephalitis vaccine (Acambis)|Biological: Hepatitis A vaccine	https://ClinicalTrials.gov/show/NCT00735644
NCT03196414	Study of T Cells Targeting CD138/BCMA/CD19/More Antigens (CART-138/BCMA/19/More) for Chemotherapy Refractory and Relapsed Multiple Myeloma	Multiple Myeloma	Biological: CART-138/BCMA/19/more	https://ClinicalTrials.gov/show/NCT03196414
NCT01140373	Adoptive Transfer of Autologous T Cells Targeted to Prostate Specific Membrane Antigen (PSMA) for the Treatment of Castrate Metastatic Prostate Cancer (CMPC)	Prostate Cancer	Biological: engineered autologous T cells|Drug: cyclophosphamide	https://ClinicalTrials.gov/show/NCT01140373
NCT02973672	Phase I of SGM-101 in Patients With Cancer of the Colon, Rectum or Pancreas	Colon Cancer|Rectum Cancer|Pancreas Cancer|Metastatic Colorectal Cancer|Recurrent Colorectal Carcinoma	Drug: SGM-101	https://ClinicalTrials.gov/show/NCT02973672
NCT01040000	QUILT-3.019: Phase 2 Study of NPC-1C Chimeric Monoclonal Antibody to Treat Pancreatic and Colorectal Cancer	Metastatic Pancreatic Cancer|Metastatic Colorectal Cancer	Drug: NPC-1C/NEO-102	https://ClinicalTrials.gov/show/NCT01040000
NCT01493453	A Phase I Study of CD19 Specific T Cells in CD19 Positive Malignancy	CD19 Positive Non-Hodgkin Lymphoma	Genetic: aCD19z cells, IL2, pre conditioning Cyclophosphamide & Fludarabine	https://ClinicalTrials.gov/show/NCT01493453
NCT01044069	Precursor B Cell Acute Lymphoblastic Leukemia (B-ALL) Treated With Autologous T Cells Genetically Targeted to the B Cell Specific Antigen CD19	Leukemia|Acute Lymphoblastic Leukemia	Biological: gene-modified T cells targeted	https://ClinicalTrials.gov/show/NCT01044069

FIG. 20-1

NCT Number	Title	Conditions	Interventions	URL
NCT04729543	MAGE-C2 TCR T Cell Trial to Treat Melanoma and Head and Neck Cancer	Melanoma|Melanoma, Uveal|Head and Neck Cancer	Biological: Adoptive therapy with autologous MC2 TCR T cells	https://ClinicalTrials.gov/show/NCT04729543
NCT03925896	Phase I Trial of LMP2 Antigen-specific TCR T-cell Therapy for Recurrent and Metastatic NPC Patients	Nasopharyngeal Carcinoma	Drug: LMP2 Antigen-specific TCR T cells	https://ClinicalTrials.gov/show/NCT03925896
NCT04476251	E7 TCR T Cell Induction Immunotherapy for Stage IIB-IVA Cervical Cancer	Uterine Cervical Neoplasms	Biological: E7 TCR	https://ClinicalTrials.gov/show/NCT04476251
NCT02654821	Study With T-cel Receptor Gene Therapy in Metastatic Melanoma	Stage IV Skin Melanoma|Eye; Melanoma	Biological: TCR transduced T-cells|Procedure: Biopsy|Procedure: Blood taking	https://ClinicalTrials.gov/show/NCT02654821
NCT04368182	AFP Specific T Cell Receptor Transduced T Cells Injection(C-TCR055) in Unresectable Hepatocellular Carcinoma	Hepatocellular Carcinoma	Biological: Autologous C-TCR055	https://ClinicalTrials.gov/show/NCT04368182
NCT04015336	E7 TCR Cell Induction Immunotherapy for Stage II and Stage III HPV-Associated Oropharyngeal Cancer	Papillomavirus Infections|Oropharyngeal Neoplasms	Biological: E7 TCR	https://ClinicalTrials.gov/show/NCT04015336
NCT04044950	A Phase II Study of Neoadjuvant E7 TCR T Cell Immunotherapy for Borderline Resectable and Unresectable Stage I HPV-Associated Oropharyngeal Cancer	Papillomavirus Infections|Oropharyngeal Neoplasms	Biological: E7 TCR	https://ClinicalTrials.gov/show/NCT04044950
NCT03326921	HA-1 T TCR T Cell Immunotherapy for the Treatment of Patients With Relapsed or Refractory Acute Leukemia After Donor Stem Cell Transplant	Myelomonocytic Leukemia|Recurrent Acute Biphenotypic Leukemia|Recurrent Acute Undifferentiated Leukemia|Recurrent Childhood Acute Lymphoblastic Leukemia|Recurrent Childhood Acute Myeloid Leukemia|Refractory Acute Lymphoblastic Leukemia|Refractory Adult Acute Lymphoblastic Leukemia|Blast Phase Chronic Myelogenous Leukemia, BCR-ABL1 Positive|Recurrent Blastic Plasmacytoid	Biological: CD8+ and CD4+ Donor Memory T-cells-expressing HA1-Specific TCR|Drug: Fludarabine|Other: Laboratory Biomarker Analysis	https://ClinicalTrials.gov/show/NCT03326921
NCT03971747	AFP Specific T Cell Receptor Transduced T Cells Injection(C-TCR055) in Unresectable Hepatocellular Carcinoma	Hepatocellular Carcinoma	Biological: AFP Specific T Cell Receptor T Cells	https://ClinicalTrials.gov/show/NCT03971747
NCT04677088	TCR-Redirected T Cell Treatment in Patients With Recurrent HBV-related Hepatocellular Carcinoma Post Liver Transplantation	Recurrent Hepatocellular Carcinoma	Biological: TCR-T cells	https://ClinicalTrials.gov/show/NCT04677088
NCT03778814	TCR-T Cell for Immunotherapy of Lung Cancer and Other Solid Tumors	Nonsmall Cell Lung Cancer|Solid Tumor, Adult	Biological: TCR-T cells	https://ClinicalTrials.gov/show/NCT03778814

FIG. 20-2

NCT Number	Title	Conditions	Interventions	URL
NCT02550535	A Phase I/II Study of Gene-modified WT1 TCR Therapy in MDS & AML Patients	Myelodysplastic Syndromes (MDS)|Acute Myeloid Leukaemia (AML)	Genetic: Autologous WT1 TCR transduced T cells	https://ClinicalTrials.gov/show/NCT02550535
NCT04411134	E7 TCR T Cell Immunotherapy for High-Grade Cervical Intraepithelial Neoplasia	Cervical Intraepithelial Neoplasia	Biological: E7 TCR	https://ClinicalTrials.gov/show/NCT04411134
NCT02988258	Study of Adoptive Immunotherapy With Donor-derived CMV-specific T Cells for Recipients of Allo-HSCT	Haematological Malignancies|CMV Infection	Genetic: CMV-TCR transduced donor-derived T cells	https://ClinicalTrials.gov/show/NCT02988258
NCT04146298	Mutant KRAS G12V-specific TCR Transduced T Cell Therapy for Advanced Pancreatic Cancer	Pancreatic Cancer|Pancreatic Neoplasms|Pancreatic Ductal Adenocarcinoma|Advanced Cancer	Drug: Cyclophosphamide|Drug: Fludarabine|Biological: Mutant KRAS G12V-specific TCR transduced autologous T cells|Drug: Anti-PD-1 monoclonal antibody	https://ClinicalTrials.gov/show/NCT04146298
NCT03462316	NY-ESO-1-specific T Cell Receptor (TCR) T Cell in Sarcoma	Bone Sarcoma|Soft Tissue Sarcoma	Biological: NY-ESO-1ï¼ˆTCR Affinity Enhancing Specific T cell Therapyï¼‰	https://ClinicalTrials.gov/show/NCT03462316
NCT03029273	NY-ESO-1 TCR ï¼ˆTAEST16001ï¼‰for Patients With Advanced NSCLC	Lung Cancer, Nonsmall Cell, Recurrent	Drug: Cyclophosphamide and Fludarabine|Biological: Anti-NY-ESO-1 TCR transduced T cells	https://ClinicalTrials.gov/show/NCT03029273
NCT03899415	TCR-Redirected T Cells Therapy in Patient With HBV Related HCC	Hepatocellular Carcinoma	Biological: TCR redirected T cells	https://ClinicalTrials.gov/show/NCT03899415
NCT03047811	The Study of Targeted NY-ESO-1 T Cell Receptor (TCR) Genetic Modified Autologous T Cells Treatment of Advanced Solid Tumors	Advanced Malignant Solid Tumors	Other: TCR - T cell therapy	https://ClinicalTrials.gov/show/NCT03047811
NCT03937791	Immunotherapy With E7 T Cell Receptor T Cells for Vulvar High-Grade Squamous Intraepithelial Lesions	Squamous Intraepithelial Lesions of Vulva|Neoplasms, Squamous Cell|Vulvar HSIL	Biological: E7 T Cell Receptor (TCR)	https://ClinicalTrials.gov/show/NCT03937791
NCT03648697	EBV-TCR-Tï¼ˆYT-E001ï¼‰for Patients With EBV-positive Recurrent or Metastatic NPC	Nasopharyngeal Carcinoma	Biological: EBV-TCR-T (YT-E001) cells	https://ClinicalTrials.gov/show/NCT03648697
NCT02686372	TCR-Redirected T Cell Infusions to Prevent Hepatocellular Carcinoma Recurrence Post Liver Transplantation	Hepatocellular Carcinoma	Other: Biological: HBV antigen specific TCR redirected T cell	https://ClinicalTrials.gov/show/NCT02686372
NCT01810120	Trial to Assess the Efficacy of a TCR Alfa Beta Depleted Graft in Pediatric Affected by ALL or AML and Receiving an HSCT	Acute Lymphoblastic Leukemia|Leukemia Acute Myeloid - AML|Non-Hodgkin Lymphoma|Myelodysplastic Syndromes	Biological: TCR alfa beta T cell depletion	https://ClinicalTrials.gov/show/NCT01810120
NCT04153279	CMV-TCR-T Cells for CM Virus Infection After HSCT	CMV Infection or Reactivation After Allogenic HSCT	Biological: CMV-TCR-T cells	https://ClinicalTrials.gov/show/NCT04153279
NCT03197025	Immunotherapy With E6 T Cell Receptor (TCR) T Cells for Vulvar High-Grade Squamous Intraepithelial Lesions	Human Papillomavirus|HPV-16|High Grade Squamous Intraepithelial Lesion	Drug: Aldesleukin|Biological: E6 T Cell Receptor (TCR)	https://ClinicalTrials.gov/show/NCT03197025

FIG. 20-3

NCT Number	Title	Conditions	Interventions	URL
NCT02719782	A Study of TCR-Redirected T Cell Infusion in Subject With Recurrent HBV-related HCC Post Liver Transplantation	Recurrent Hepatocellular Carcinoma	Biological: Biological: TCR-T	https://ClinicalTrials.gov/show/NCT02719782
NCT04156217	EBV-TCR-T Cells for EB Virus Infection After HSCT	EBV Emia and EBV Positive PTLD After Allogenic HSCT	Biological: EBV-TCR-T cells	https://ClinicalTrials.gov/show/NCT04156217
NCT01621724	WT1 TCR Gene Therapy for Leukaemia: A Phase I/II Safety and Toxicity Study	Acute Myeloid Leukaemia|Chronic Myeloid Leukaemia	Genetic: WT1 TCR-transduced T cells	https://ClinicalTrials.gov/show/NCT01621724
NCT03575767	Characteristics and Dynamics of TCR Repertoire in Patients With Hematological Malignancies After Allo-HSCT	Hematologic Neoplasms|Hematopoietic Stem Cell Transplantation|Graft Vs Host Disease|Recurrence	Other: Myeloablative Hematopoietic Stem Cell Transplantation	https://ClinicalTrials.gov/show/NCT03575767
NCT02327351	TCR Alpha/Beta Depletion for HSCT From Haploidentical and Unrelated Donors in the Treatment of PID	Primary Immune Deficiency Disorder|Hematopoietic Stem Cell Transplantation	Other: Biological: TCR alfa beta T cell depletion	https://ClinicalTrials.gov/show/NCT02327351
NCT04139057	EBV-Specific Anti-PD1 TCR-T Cells in the Treatment of EBV-Positive NHSCC	Head and Neck Squamous Cell Carcinoma	Drug: EBV-specific TCR-T cell with anti-PD1 auto-secreted element	https://ClinicalTrials.gov/show/NCT04139057
NCT04356469	TCR Alpha Beta T-cell Depleted Haploidentical HCT in the Treatment of Non-Malignant Hematological Disorders in Children	Hemoglobinopathy (Disorder)|Severe Aplastic Anemia|Bone Marrow Failure Syndrome	Biological: Haploidentical Hematopoietic Cell Transplantation	https://ClinicalTrials.gov/show/NCT04356469
NCT04414046	TCR Alpha Beta T-cell Depleted Haploidentical HCT in the Treatment of Primary Immunodeficiency and Inherited Metabolic Disorders in Children	Primary Immune Deficiency Disorders|Metabolic Disease	Biological: Haploidentical Hematopoietic Cell Transplantation	https://ClinicalTrials.gov/show/NCT04414046
NCT03980691	Effect of Chidamide Combined With CAT-T or TCR-T Cell Therapy on HIV-1 Latent Reservoir	HIV/AIDS	Biological: Chidamide with CAR-T or TCR-T cell therapy	https://ClinicalTrials.gov/show/NCT03980691
NCT03891706	Individualized Tumor Specific TCR-T Cells in the Treatment of Advanced Solid Tumors	Solid Tumor	Drug: tumor-specific TCR-T cells|Drug: Interleukin-2|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03891706
NCT03578406	HPV-E6-Specific Anti-PD1 TCR-T Cells in the Treatment of HPV-Positive NHSCC or Cervical Cancer	Cervical Cancer|Head and Neck Squamous Cell Carcinoma	Drug: HPV E6-specific TCR-T cells	https://ClinicalTrials.gov/show/NCT03578406
NCT04745403	Redirected HBV-Specific T Cells in Patients With HBV-related HCC (SAFE-T-HBV)	Hepatocellular Carcinoma	Drug: mRNA HBV/TCR T-cells	https://ClinicalTrials.gov/show/NCT04745403
NCT01694472	Clinical Safety and Preliminary Efficacy of MAGE-A4 TCR Gene-Modified T Cells to Treat Malignant Tumors	Malignant Solid Tumors	Biological: MAGE-A4 TCR Gene-Modified T Cells	https://ClinicalTrials.gov/show/NCT01694472
NCT02200718	A Study of NeuroVaxâ„¢, a Novel Therapeutic TCR Peptide Vaccine for Pediatric Multiple Sclerosis	Multiple Sclerosis	Biological: NeuroVax|Biological: IFA Incompiete Freund's Adjuvant	https://ClinicalTrials.gov/show/NCT02200718
NCT04509726	LMP2-Specific IL12-secreting TCR-T Cells in the Treatment of EBV-Positive Metastatic/Refractory Nasopharyngeal Carcinoma	Nasopharyngeal Carcinoma	Drug: LMBP2-specific TCR-T cell with IL12 auto-secreting element	https://ClinicalTrials.gov/show/NCT04509726

FIG. 20-4

NCT Number	Title	Conditions	Interventions	URL
NCT01982266	A Prospective, Multicenter, Single Arm Feasibility Study of the Safety and Performance of GRADIONâ„¢ Hip Total Cartilage Replacement (TCR)â„¢ in the Treatment of Degenerative Joint Disease of the Hip	Degenerative Joint Disease of the Hip	Device: GRADIONâ„¢ Hip Total Cartilage Replacement (TCR)â„¢	https://ClinicalTrials.gov/show/NCT01982266
NCT03747484	Gene-Modified Immune Cells (FH-MCVA2TCR) in Treating Patients With Metastatic or Unresectable Merkel Cell Cancer	Other Skin	Biological: Autologous MCPyV-specific HLA-A02-restricted TCR-transduced CD4+ and CD8+ T-cells FH-MCVA2TCR|Drug: Avelumab|Biological: Pembrolizumab|Radiation: Radiation Therapy	https://ClinicalTrials.gov/show/NCT03747484
NCT02858310	E7 TCR T Cells for Human Papillomavirus-Associated Cancers	Papillomavirus Infections|Cervical Intraepithelial Neoplasia|Carcinoma In Situ|Vulvar Neoplasms|Vulvar Diseases	Biological: E7 TCR cells|Drug: Aldesleukin|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT02858310
NCT02775292	Gene-Modified T Cells, Vaccine Therapy, and Nivolumab in Treating Patients With Stage IV or Locally Advanced Solid Tumors Expressing NY-ESO-1	Adult Solid Neoplasm|Childhood Solid Neoplasm|Metastatic Neoplasm	Biological: Aldesleukin|Drug: Cyclophosphamide|Drug: Fludarabine Phosphate|Other: Laboratory Biomarker Analysis|Biological: Nivolumab|Biological: NY-ESO-1 Reactive TCR Retroviral Vector Transduced Autologous PBL|Biological: NY-ESO-1(157-165) Peptide-pulsed Autologous Dendritic Cell Vaccine|Procedure: Positron Emission Tomography	https://ClinicalTrials.gov/show/NCT02775292
NCT04809766	Mesothelin-Specific T-Cells (FH-TCR-TÁ´sÊŸÉ´) for the Treatment of Metastatic Pancreatic Ductal Adenocarcinoma	Metastatic Pancreatic Ductal Adenocarcinoma|Stage IV Pancreatic Cancer AJCC v8	Biological: Autologous Mesothelin-specific TCR-T Cells|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT04809766
NCT03431311	T Cell Receptor Based Therapy of Metastatic Colorectal Cancer	Colorectal Cancer	Biological: Adoptive Cell Therapy (ACT)	https://ClinicalTrials.gov/show/NCT03431311
NCT03717480	Ex Vivo TCR Î±Î²Â² T Cell Depletion for Graft-Versus-Host Disease Prophylaxis in Mismatched Donor Peripheral Blood Stem Cell Transplantation for Hematologic Malignancies	Hematologic Malignancy	Device: ClinicMACs	https://ClinicalTrials.gov/show/NCT03717480
NCT04614571	T Cell Receptor (TCR) Sequencing and Transcriptional Profiling in Adult Celiac Disease Patients Undergoing Gluten Challenge	Celiac Disease	Dietary Supplement: Gluten Powder	https://ClinicalTrials.gov/show/NCT04614571
NCT00910650	Study of Gene Modified Immune Cells in Patients With Advanced Melanoma	Metastatic Melanoma	Biological: F5 TCR transgenic cells and MART-1 peptide pulsed dendritic cells|Drug: non-myeloablative conditioning chemotherapy	https://ClinicalTrials.gov/show/NCT00910650

FIG. 20-5

NCT Number	Title	Conditions	Interventions	URL
NCT04464889	HA-1H TCR T Cell for Relapsed/Persistent Hematologic Malignancies After Allogeneic Stem Cell Transplantation	Acute Myeloid Leukemia|Acute Lymphoid Leukemia|Myelodysplastic Syndromes|Myeloproliferative Disorders|Chronic Myeloid Leukemia|Myelofibrosis|Multiple Myeloma|Malignant Lymphoma	Drug: MDG1021 dose 1|Drug: MDG1021 dose 2|Drug: MDG1021 dose 3|Drug: MDG1021 optimal dose	https://ClinicalTrials.gov/show/NCT04464889
NCT03545815	Study of CRISPR-Cas9 Mediated PD-1 and TCR Gene-knocked Out Mesothelin-directed CAR-T Cells in Patients With Mesothelin Positive Multiple Solid Tumors.	Solid Tumor, Adult	Biological: anti-mesothelin CAR-T cells	https://ClinicalTrials.gov/show/NCT03545815
NCT03503968	TCR Modified T Cells MDG1011 in High Risk Myeloid and Lymphoid Neoplasms	Safety|Tolerability|Feasibility|Treatment Efficacy	Drug: MDG1011|Other: investigator Choice therapy	https://ClinicalTrials.gov/show/NCT03503968
NCT03240861	Genetically Engineered PBMC and PBSC Expressing NY-ESO-1 TCR After a Myeloablative Conditioning Regimen to Treat Patients With Advanced Cancer	HLA-A*0201 Positive Cells Present|Locally Advanced Malignant Neoplasm|NY-ESO-1 Positive|Unresectable Malignant Neoplasm|Sarcoma	Other: 18F-FHBG|Biological: Aldesleukin|Drug: Busulfan|Biological: Cellular Therapy|Procedure: Computed Tomography|Biological: Filgrastim|Drug: Fludarabine|Procedure: Leukapheresis|Drug: Plerixafor|Procedure: Positron Emission Tomography	https://ClinicalTrials.gov/show/NCT03240861
NCT03941626	Autologous CAR-T/TCR-T Cell Immunotherapy for Solid Malignancies	Esophagus Cancer|Hepatoma|Glioma|Gastric Cancer	Biological: CAR-T/TCR-T cells immunotherapy	https://ClinicalTrials.gov/show/NCT03941626
NCT03228368	The Predicted Potential of Quantitative T Cell Repertoire(TCR) in Anti-PD-L1 Treatment in NSCLC Patients	Non-Small Cell Lung Cancer	Drug: Atezolizumab (MPDL3280A)	https://ClinicalTrials.gov/show/NCT03228368
NCT00393029	Phase II Study of Metastatic Cancer That Overexpresses P53 Using Lymphodepleting Conditioning Followed by Infusion of Anti-P53 TCR-Gene Engineered Lymphocytes	Anti-p53 TCR-Gene	Biological: anti-protein 53 or tumor protein 53 (p53) T-cell receptor transduced peripheral blood lymphocytes|Biological: aldesleukin|Biological: filgrastim|Drug: cyclophosphamide|Drug: fludarabine phosphate	https://ClinicalTrials.gov/show/NCT00393029
NCT03506802	TCR Genetically Engineered PBMC and PBSC After Melphalan Conditioning Regimen in Treating Participants With Relapsed and Refractory Multiple Myeloma	HLA-A*0201 Positive Cells Present|NY-ESO-1 Positive Tumor Cells Present|Recurrent Plasma Cell Myeloma|Refractory Plasma Cell Myeloma	Radiation: 18F-FHBG|Biological: Aldesleukin|Biological: Cellular Therapy|Procedure: Computed Tomography|Biological: Filgrastim|Other: Laboratory Biomarker Analysis|Drug: Lenalidomide|Procedure: Leukapheresis|Drug: Melphalan|Drug: Plerixafor|Procedure: Positron Emission Tomography	https://ClinicalTrials.gov/show/NCT03506802
NCT04878484	Evaluate TCRT-ESO-A2 Autologous T Cells Expressing TCR Specific for NY-ESO-1 in Subjects With Advanced Solid Tumors	Advanced Solid Tumor	Biological: TCRT-ESO-A2	https://ClinicalTrials.gov/show/NCT04878484

FIG. 20-6

NCT Number	Title	Conditions	Interventions	URL
NCT03691376	Genetically Engineered Cells (NY-ESO-1 TCR Engineered T Cells and HSCs) After Melphalan Conditioning Regimen in Treating Patients With Recurrent or Refractory Ovarian, Fallopian Tube, or Primary Peritoneal Cancer	Fallopian Tube Carcinoma | Platinum-Resistant Ovarian Carcinoma | Platinum-Resistant Primary Peritoneal Carcinoma | Platinum-Sensitive Fallopian Tube Carcinoma | Platinum-Sensitive Ovarian Carcinoma | Platinum-Sensitive Primary Peritoneal Carcinoma | Recurrent Fallopian Tube Carcinoma | Recurrent Ovarian Carcinoma | Recurrent Primary Peritoneal Carcinoma | Refractory Fallopian Tube Carcinoma | Refractory Ovarian	Biological: Aldesleukin | Biological: Autologous NY-ESO-1-specific CD8-positive T Lymphocytes | Other: Cellular Therapy | Drug: Melphalan	https://ClinicalTrials.gov/show/NCT03691376
NCT00509496	Phase II Study of Metastatic Melanoma With Lymphodepleting Conditioning and Anti-gp100:154-162 TCR Gene Engineered Lymphocytes	Skin Cancer | Melanoma	Drug: fludarabine phosphate | Drug: cyclophosphamide | Biological: aldesleukin | Biological: autologous anti-gp 100:154-162 T-cell receptor gene-engineered tumor infiltrating lymphocytes | Biological: autologous anti-gp 100:154-162 T-cell receptor gene-engineered peripheral blood lymphocytes	https://ClinicalTrials.gov/show/NCT00509496
NCT02457650	T Cell Receptor-transduced T Cells Targeting NY-ESO-1 for Treatment of Patients With NY-ESO-1- Expressing Malignancies	Bladder Carcinoma | Breast Cancer | Esophagus Carcinoma | Lung Cancer | Melanoma | Multiple Myeloma | Neuroblastoma | Ovarian Cancer | Synovial Sarcoma | Other Metastatic Solid Cancers	Drug: Cyclophosphamide | Drug: Fludarabine | Biological: Anti-NY ESO-1 TCR-transduced T cells	https://ClinicalTrials.gov/show/NCT02457650
NCT01967823	T Cell Receptor Immunotherapy Targeting NY-ESO-1 for Patients With NY-ESO-1 Expressing Cancer	Melanoma | Meningioma | Breast Cancer | Non-Small Cell Lung Cancer | Hepatocellular Cancer	Biological: Anti-NY ESO-1 mTCR PBL | Drug: Cyclophosphamide | Drug: Fludarabine | Drug: Aldesleukin	https://ClinicalTrials.gov/show/NCT01967823

FIG. 20-7

NCT Number	Title	Conditions	Interventions	URL
NCT04639245	Genetically Engineered Cells (MAGE-A1-specific T Cell Receptor-transduced Autologous T-cells) and Atezolizumab for the Treatment of Metastatic Triple Negative Breast Cancer, Urothelial Cancer, or Non-small Cell Lung Cancer	Anatomic Stage IV Breast Cancer AJCC v8|Metastatic Lung Non-Small Cell Carcinoma|Metastatic Malignant Solid Neoplasm|Metastatic Triple-Negative Breast Carcinoma|Metastatic Urothelial Carcinoma|Prognostic Stage IV Breast Cancer AJCC v8|Stage IV Lung Cancer AJCC v8|Stage IVA Lung Cancer AJCC v8|Stage IVB Lung Cancer AJCC v8	Drug: Atezolizumab|Drug: Cyclophosphamide|Drug: Fludarabine|Biological: MAGE-A1-specific T Cell Receptor-transduced Autologous T-cells|Biological: PD1 Inhibitor	https://ClinicalTrials.gov/show/NCT04639245
NCT03301168	Study of Gene Modified Donor T-cells Following TCR Alpha Beta Positive Depleted Stem Cell Transplant	Acute Lymphoblastic Leukemia|Leukemia, Acute Myeloid (AML), Child|Lymphoma, Non-Hodgkin|Myelodysplastic Syndromes|Primary Immune Deficiency Disorder|Osteopetrosis|Cytopenia|Hemoglobinopathy in Children|Anemia, Aplastic	Biological: BPX-501 T cells|Drug: Rimiducid	https://ClinicalTrials.gov/show/NCT03301168
NCT03939585	Preemptive Infusion of Donor Lymphocytes Depleted of TCR + T Cells + CD19+ B Cells Following ASCT	Allogeneic Stem Cell Transplant Candidate|Acute Myeloid/Lymphoblastic Leukemia|Myelodysplastic Syndrome|Myeloproliferative Neoplasm|Lymphoproliferative Disorders	Biological: Cellular therapy product	https://ClinicalTrials.gov/show/NCT03939585

FIG. 20-8

NCT Number	Title	Conditions	Interventions	URL
NCT02065869	Safety Study of Gene Modified Donor T-cells Following TCR Alpha Beta Depleted Stem Cell Transplant	Acute Lymphoblastic Leukemia|Leukemia, Acute Myeloid (AML), Child|Lymphoma, Non-Hodgkin|Myelodysplastic Syndrome|Primary Immunodeficiency|Anemia, Aplastic|Osteopetrosis|Hemoglobinopathies|Cytopenia|Fanconi Anemia|Diamond Blackfan Anemia|Thalassemia|Anemia, Sickle Cell	Biological: BPX-501 T cells|Drug: rimiducid	https://ClinicalTrials.gov/show/NCT02065869
NCT03391791	Long Term Follow up of Subjects Exposed to Genetically Engineered T Cell Receptors	Solid and Hematological Malignancies	Genetic: Genetically engineered T Cell Receptors	https://ClinicalTrials.gov/show/NCT03391791
NCT00509288	Phase II Study of Metastatic Melanoma With Lymphodepleting Conditioning and Infusion of Anti-MART-1 F5 TCR-Gene-Engineered Lymphocytes	Melanoma|Skin Cancer	Biological: autologous anti-MART-1 F5 T-cell receptor|Drug: Cyclophosphamide|Drug: Fludarabine|Biological: Aldesleukin|Biological: autologous anti-MART-1 F5 T-cell receptor gene-engineered tumor infiltrating lymphocytes	https://ClinicalTrials.gov/show/NCT00509288
NCT03354390	HERV-E TCR Transduced Autologous T Cells in People With Metastatic Clear Cell Renal Cell Carcinoma	Kidney Cancer	Biological: cell infusion	https://ClinicalTrials.gov/show/NCT03354390
NCT02030847	Study of Redirected Autologous T Cells Engineered to Contain Anti-CD19 Attached to TCR and 4-1BB Signaling Domains in Patients With Chemotherapy Resistant or Refractory Acute Lymphoblastic Leukemia	Patients With B Cell ALL, Relapsed or Refractory, With no Available Curative Treatment Options	Biological: CART-19	https://ClinicalTrials.gov/show/NCT02030847
NCT00991224	Redirected High Affinity Gag-Specific Autologous T Cells for HIV Gene Therapy	HIV Infections	Biological: WT-gag-TCR modified T cells|Biological: Î±/6-gag-TCR modified T cells|Other: STI or Drug Holiday	https://ClinicalTrials.gov/show/NCT00991224
NCT03047746	Unrelated And Partially Matched Related Donor PSCT w/ TCR Î±Î²Â² Depletion for Patients With BMF	Acquired Aplastic Anemia|Paroxysmal Nocturnal Hemoglobinuria|Inherited Bone Marrow Failure Syndromes	Device: CliniMACs	https://ClinicalTrials.gov/show/NCT03047746
NCT03019809	A Trial of Plerixafor/G-CSF as Additional Agents for Conditioning Before TCR Alpha/Beta Depleted HSCT in WAS Patients	Wiskott-Aldrich Syndrome|Hematopoietic Stem Cell Transplantation|Graft Failure	Biological: G-CSF for Conditioning before HSCT.|Biological: Plerixafor for Conditioning before HSCT.	https://ClinicalTrials.gov/show/NCT03019809

FIG. 20-9

NCT Number	Title	Conditions	Interventions	URL
NCT02280811	T Cell Receptor Immunotherapy Targeting HPV-16 E6 for HPV-Associated Cancers	Vaginal Cancer|Cervical Cancer|Anal Cancer|Penile Cancer|Oropharyngeal Cancer	Drug: Fludarabine|Drug: Cyclophosphamide|Biological: E6 TCR|Drug: Aldesleukin	https://ClinicalTrials.gov/show/NCT02280811
NCT04194190	A Single Patient Will be Treated With Individual Patient TCR-Transduced PBL		Drug: Individual Patient TCR-Transduced PBL	https://ClinicalTrials.gov/show/NCT04194190
NCT02153905	T Cell Receptor Immunotherapy Targeting MAGE-A3 for Patients With Metastatic Cancer Who Are HLA-A*01 Positive	Breast Cancer|Cervical Cancer|Renal Cancer|Melanoma|Bladder Cancer	Drug: Aldesleukin|Drug: Fludarabine|Drug: Cyclophosphamide|Biological: Anti-MAGE-A3 human leukocyte antigen serotype within HLA-A A serotype group (HLA-A* 01)-restricted T-cell receptor (TCR)	https://ClinicalTrials.gov/show/NCT02153905
NCT02057159	A Study of NeuroVaxâ„¢, a Therapeutic TCR Peptide Vaccine for SPMS of Multiple Sclerosis	Secondary Progress Multiple Sclerosis|Multiple Sclerosis	Biological: NeuroVax|Biological: IFA Placebo	https://ClinicalTrials.gov/show/NCT02057159
NCT00610311	Anti-gp100 Cells Plus ALVAC gp100 Vaccine to Treat Advanced Melanoma	Metastatic Melanoma|Skin Cancer	Drug: cyclophosphamide|Drug: fludarabine phosphate|Biological: Aldesleukin|Biological: ALVAC gp100 Vaccine|Biological: anti-gp100:154-162 Tcell receptor (TCR) peripheral blood lymphocyte (PBL)	https://ClinicalTrials.gov/show/NCT00610311
NCT02070406	Gene-Modified T Cells, Vaccine Therapy, and Ipilimumab in Treating Patients With Locally Advanced or Metastatic Malignancies	Unspecified Adult Solid Tumor, Protocol Specific	Drug: cyclophosphamide|Drug: fludarabine phosphate|Biological: NY-ESO-1 reactive TCR retroviral vector transduced autologous PBL|Biological: dendritic cell vaccine therapy|Biological: aldesleukin|Radiation: fludeoxyglucose F 18|Procedure: positron emission tomography|Other: laboratory biomarker analysis	https://ClinicalTrials.gov/show/NCT02070406
NCT02149706	A Study of NeuroVaxâ„¢, a Novel Therapeutic TCR Peptide Vaccine for SPMS of Multiple Sclerosis	Multiple Sclerosis	Biological: NeuroVax|Biological: IFA Incomplete Freund's Adjuvant	https://ClinicalTrials.gov/show/NCT02149706
NCT04616482	Therapeutic Nutrition With Technology in Primary Care	Diet Modification	Behavioral: Digital therapeutic carbohydrate restriction (TCR) program	https://ClinicalTrials.gov/show/NCT04616482
NCT00612222	Anti-MART-1 F5 Cells Plus ALVAC MART-1 Vaccine to Treat Advanced Melanoma	Metastatic Melanoma|Skin Cancer	Biological: autologous anti-MART-1 F5 T-cell receptor gene-engineered peripheral blood lymphocytes|Biological: ALVAC MART-1 Vaccine|Biological: aldesleukin|Drug: cyclophosphamide|Drug: fludarabine phosphate	https://ClinicalTrials.gov/show/NCT00612222
NCT02111850	T Cell Receptor Immunotherapy Targeting MAGE-A3 for Patients With Metastatic Cancer Who Are HLA-DP0401 Positive	Cervical Cancer|Renal Cancer|Urothelial Cancer|Melanoma|Breast Cancer	Biological: Anti-MAGE-A3-DP4 TCR PBL|Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Aldesleukin	https://ClinicalTrials.gov/show/NCT02111850
NCT00923390	Phase 1/2 Study of Metastatic Renal Cancer Using T-Cells Transduced With a T-Cell Receptor Which Recognizes TRAIL Bound to the DR4 Receptor	Renal Cancer|Kidney Cancer	Genetic: 2G-1 TCR Retroviral Vector-Transduced lyn|Drug: Aldesleukin|Drug: Cyclophosphamide|Drug: Fludarabine|Drug: (PG13-A(F/K-F-SGSG-T2a-B (opt) (2G-1 TCR) retroviral vector-transduced lymphocyte	https://ClinicalTrials.gov/show/NCT00923390

FIG. 20-10

NCT Number	Title	Conditions	Interventions	URL
NCT01273181	MAGE-A3/12 Metastatic Cancer Treatment With Anti-MAGE-A3/12 TCR-Gene Engineered Lymphocytes	Metastatic Cancer|Metastatic Renal Cancer|Metastatic Melanoma	Biological: PG13-MAGE-A3 TCR9W11 (anti-MAGE-A3/12 TCR) Transduced Autologous Peripheral Blood Lymphocytes|Drug: Aldesleukin|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT01273181
NCT02623582	CD123 Redirected Autologous T Cells for AML	Relapsed or Refractory Acute Myeloid Leukemia	Biological: Autologous Anti-CD 123 CAR TCR/4-1BB-expressing T-lymphocytes|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT02623582
NCT04379466	Effector and Regulatory T Cell Receptor Repertoire Analyses in Patients Affected by COVID-19	COVID-19		https://ClinicalTrials.gov/show/NCT04379466
NCT02366546	Investigator Initiated Phase 1 Study of TBI-1301	Solid Tumors	Drug: TBI-1301|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT02366546
NCT04665388	LANDscape MApping of Epitopes and T Cell Receptors for Selected Cancers	Solid Tumor		https://ClinicalTrials.gov/show/NCT04665388
NCT02096614	Investigator Initiated Phase 1 Study of TBI-1201	Solid Tumors	Drug: TBI-1201|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT02096614
NCT00670748	Chemotherapy Followed by ESO-1 Lymphocytes and Aldesleukin to Treat Metastatic Cancer	Metastatic Melanoma|Metastatic Renal Cell Cancer|Metastatic Cancer	Biological: Anti-NY ESO-1 T-cell receptor PBL|Drug: aldesleukin|Drug: Cyclophosphamide|Drug: fludarabine phosphate|Biological: ALVAC NY ESO-1 vaccine	https://ClinicalTrials.gov/show/NCT00670748
NCT01697527	Gene and Vaccine Therapy in Treating Patients With Advanced Malignancies	Malignant Neoplasm	Biological: aldesleukin|Drug: fludarabine phosphate|Drug: cyclophosphamide|Other: laboratory biomarker analysis|Biological: NY-ESO-1 reactive TCR retroviral vector transduced autologous PBL|Biological: dendritic cell vaccine therapy|Radiation: fludeoxyglucose F 18|Procedure: positron emission tomography	https://ClinicalTrials.gov/show/NCT01697527
NCT02869217	Study of TBI-1301 (NY-ESO-1 Specific TCR Gene Transduced Autologous T Lymphocytes) in Patients With Solid Tumors	NY-ESO-1 Expressing Solid Tumors in HLA-A2 Positive Patients|Synovial Sarcoma|Melanoma|Esophageal Cancer|Ovarian Cancer|Lung Cancer|Bladder Cancer|Liver Cancer	Drug: Cyclophosphamide|Biological: TBI-1301|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT02869217
NCT01350401	Phase I/II Study to Assess the Safety and Activity of Enhanced TCR Transduced Autologous T Cells in Metastatic Melanoma	Melanoma	Genetic: Autologous genetically modified T cells, NY-ESO-1á¶¢Â²âµâ¹T	https://ClinicalTrials.gov/show/NCT01350401
NCT01306188	Prognostic Value of Divpenia and CD4 Count in Relapsed Breast or Lung Cancer Patients	Breast Cancer|Lung Cancer	Biological: Breast cancer cohort|Biological: Lung cancer cohort	https://ClinicalTrials.gov/show/NCT01306188
NCT01350401	Phase I/II Study to Assess the Safety and Activity of Enhanced TCR Transduced Autologous T Cells in Metastatic Melanoma	Melanoma	Genetic: Autologous genetically modified T cells, NY-ESO-1á¶¢Â²âµâ¹T	https://ClinicalTrials.gov/show/NCT01350401

FIG. 20-11

NCT Number	Title	Conditions	Interventions	URL
NCT01306188	Prognostic Value of Divpenia and CD4 Count in Relapsed Breast or Lung Cancer Patients	Breast Cancer|Lung Cancer	Biological: Breast cancer cohort|Biological: Lung cancer cohort	https://ClinicalTrials.gov/show/NCT01306188
NCT02646839	KIR Favorable Mismatched Haplo Transplant and KIR Polymorphism in ALL/AML/MDS Allo-HCT Children	Acute Lymphoblastic Leukemia|Acute Myeloid Leukemia|Myelodysplastic Syndromes	Device: CliniMacs TCR alpha-beta-Biotin system	https://ClinicalTrials.gov/show/NCT02646839
NCT04102436	Non-Viral TCR Gene Therapy	Glioblastoma|Non-Small Cell Lung Cancer|Breast Cancer|Gastrointestinal/Genitourinary Cancer|Ovarian Cancer	Drug: Fludarabine|Drug: Cyclophosphamide|Drug: Aldesleukin|Biological: Sleeping Beauty Transposed PBL	https://ClinicalTrials.gov/show/NCT04102436
NCT02652468	TCR-ⅈ±/ⅈ² and CD19 Depleted Stem Cell Grafts From Haplo Donors for HSCT in Relapsed Lymphoma	Lymphoma	Drug: Fludarabine Phosphate|Drug: Mesna|Drug: Cyclophosphamide|Radiation: Total nodal irradiation|Biological: T Cell-Depleted Hematopoietic Stem Cell Transplantation|Procedure: Allogeneic Hematopoietic Stem Cell Transplantation|Procedure: Peripheral Blood Stem Cell Transplantation|Drug: Mycophenolate Mofetil|Drug: Tacrolimus|Biological: Rituximab	https://ClinicalTrials.gov/show/NCT02652468
NCT03159585	To Evaluate the Efficacy of NY-ESO-1-specific T Cell Receptor Affinity Enhancing Specific T Cell in Solid Tumors	Liver Cancer Stage IV|Gastric Cancer Stage IV|Esophageal Cancer, Stage IV|Bone and Soft Tissue Tumors|Breast Cancer Stage IV|Bladder Carcinoma Stage IV|Prostate Carcinoma Stage IV|Thyroid Cancer Stage IV|Ovarian Cancer Stage IV|Solid Tumor	Drug: TAEST16001	https://ClinicalTrials.gov/show/NCT03159585
NCT03638206	Autologous CAR-T/TCR-T Cell Immunotherapy for Malignancies	B-cell Acute Lymphoblastic Leukemia|Lymphoma|Myeloid Leukemia|Multiple Myeloma|Hepatoma|Gastric Cancer|Pancreatic Cancer|Mesothelioma|Colorectal Cancer|Esophagus Cancer|Lung Cancer|Glioma|Melanoma|Synovial Sarcoma|Ovarian Cancer|Renal Carcinoma	Biological: CAR-T cell immunotherapy	https://ClinicalTrials.gov/show/NCT03638206

FIG. 20-12

NCT Number	Title	Conditions	Interventions	URL
NCT02337595	Memory T-cell Infusion to Improve Immunity After TCR-alpha/Beta Depleted Hematopoietic Stem Cell Transplantation	Precursor T-Cell Lymphoblastic Leukemia-Lymphoma|Leukemia, Myeloid, Acute|Immune Deficiency Disease|Bone Marrow Failure Syndromes|Opportunistic Infections|Graft vs Host Disease	Biological: CD45RA-depleted peripheral blood mononuclear cells	https://ClinicalTrials.gov/show/NCT02337595
NCT04680416	Tissue Collection to ID TCRs From Renal Clear Cell Carcinoma Patients Responding to Immune Checkpoint Inhibitors	Renal Clear Cell Carcinoma		https://ClinicalTrials.gov/show/NCT04680416
NCT04249830	Stem Cell Transplant From Donors After Alpha Beta Cell Depletion in Children and Young Adults	Hematologic Diseases	Biological: Allogeneic Stem Cell Transplant|Device: CliniMACS TCR $\alpha\beta$ Reagent Kit and CliniMACS CD19	https://ClinicalTrials.gov/show/NCT04249830
NCT00923806	Gene Therapy Using Anti-CEA Cells to Treat Metastatic Cancer	Metastatic Cancer	Biological: PG13-CEA_TCR (Anti-CEA TCR PBL)|Drug: Aldesleukin	https://ClinicalTrials.gov/show/NCT00923806
NCT02062359	T Cell Receptor Immunotherapy Targeting NY-ESO-1 for Patients With NY-ESO-1 Expressing Melanoma	Metastatic Cancer|Metastatic Melanoma	Biological: Anti-NY ESO-1 T cell receptor (TCR) cluster of differentiation 62L (CD62L)+ cells|Drug: Aldesleukin|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT02062359
NCT02743611	Safety & Activity of Controllable PRAME-TCR Therapy in Previously Treated AML/MDS or Metastatic Uveal Melanoma	Acute Myeloid Leukemia|Myelodysplastic Syndrome|Uveal Melanoma	Biological: BPX-701|Drug: Rimiducid	https://ClinicalTrials.gov/show/NCT02743611
NCT01029366	CART19 to Treat B-Cell Leukemia or Lymphoma That Are Resistant or Refractory to Chemotherapy	mphoid Cancer|Adult Acute Lymphoblastic Leukemia in Remission|B-cell Adult Acute Lymphoblastic Leukemia|B-cell Chronic Lymphocytic Leukemia|Prolymphocytic Leukemia|Recurrent Adult Diffuse Large Cell Lymphoma|Recurrent Grade 1 Follicular Lymphoma|Recurrent Grade 2 Follicular Lymphoma|Recurrent Grade 3 Follicular Lymphoma|Recurrent Mantle Cell Lymphoma|Refract	Biological: CART-19	https://ClinicalTrials.gov/show/NCT01029366

FIG. 20-13

NCT Number	Title	Conditions	Interventions	URL
NCT04520711	Study of Adoptively Transferred, Gene-engineered T Cells With CD40 Activation and PD-1 Blockade in Incurable Cancers	Malignant Epithelial Neoplasms	Biological: TCR-transduced T cells | Drug: CDX-1140 | Drug: Pembrolizumab	https://ClinicalTrials.gov/show/NCT04520711
NCT04323657	TC-110 T Cells in Adults With Relapsed or Refractory Non-Hodgkin Lymphoma or Acute Lymphoblastic Leukemia	Non Hodgkin Lymphoma | Acute Lymphoblastic Leukemia | Diffuse Large B Cell Lymphoma | Primary Mediastinal Large B Cell Lymphoma | Mantle Cell Lymphoma | Follicular Lymphoma	Drug: TC-110 T Cells | Drug: Fludarabine | Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04323657
NCT03907852	Phase 1/2 Trial of Gavo-cel (TC-210) in Patients With Advanced Mesothelin-Expressing Cancer	Mesothelioma | Mesothelioma, Malignant | Mesothelioma; Pleura | Mesotheliomas Pleural | Mesothelioma Peritoneum | Cholangiocarcinoma | Cholangiocarcinoma Recurrent | Ovarian Cancer | Non Small Cell Lung Cancer | Non Small Cell Lung Cancer Metastatic	Drug: gavo-cel | Drug: fludarabine | Drug: cyclophosphamide | Biological: anti-PD1	https://ClinicalTrials.gov/show/NCT03907852
NCT01892293	CT Antigen TCR-Engineered T Cells for Myeloma	Multiple Myeloma	Drug: Treatment with NY-ESO-1c259-modified T cells	https://ClinicalTrials.gov/show/NCT01892293
NCT04536922	Administration of Autologous T-Cells Genetically Engineered to Express T-Cell Receptors Reactive Against Mutated or Viral Neoantigens in a Patient With Metastatic Cancer Plus the Administration of Pembrolizumab	Metastatic HPV-16 Positive Squamous Cell Anal Cancer	Drug: Cyclophosphamide | Drug: Fludarabine | Drug: Aldesleukin | Drug: Pembrolizumab (KEYTRUDA(R)) | Biological: Individual Patient TCR-Transduced PBL	https://ClinicalTrials.gov/show/NCT04536922
NCT01352286	Redirected Auto T Cells for Advanced Myeloma	Multiple Myeloma	Genetic: Autologous Genetically modified T cells	https://ClinicalTrials.gov/show/NCT01352286
NCT00704938	Gene-Modified Lymphocytes, High-Dose Aldesleukin, and Vaccine Therapy in Treating Patients With Progressive or Recurrent Metastatic Cancer	Kidney Cancer | Melanoma (Skin) | Unspecified Adult Solid Tumor, Protocol Specific	Biological: aldesleukin | Biological: anti-p53 T-cell receptor-transduced peripheral blood lymphocytes | Biological: autologous dendritic cell-adenovirus p53 vaccine | Biological: filgrastim | Drug: cyclophosphamide | Drug: fludarabine phosphate	https://ClinicalTrials.gov/show/NCT00704938

FIG. 20-14

NCT Number	Title	Conditions	Interventions	URL
NCT02650986	Gene-Modified T Cells With or Without Decitabine in Treating Patients With Advanced Malignancies Expressing NY-ESO-1	Tube Carcinoma | Advanced Malignant Solid Neoplasm | Advanced Melanoma | Advanced Ovarian Carcinoma | Advanced Primary Peritoneal Carcinoma | Advanced Synovial Sarcoma | Clinical Stage III Cutaneous Melanoma AJCC v8 | Clinical Stage IV Cutaneous Melanoma AJCC v8 | Metastatic Fallopian Tube Carcinoma | Metastatic Melanoma | Metastatic Ovarian Carcinoma | Metastatic Primary Peritoneal	Drug: Cyclophosphamide | Drug: Decitabine | Other: Laboratory Biomarker Analysis | Procedure: Leukapheresis | Biological: TGFbDNRII-transduced Autologous Tumor Infiltrating Lymphocytes	https://ClinicalTrials.gov/show/NCT02650986
NCT03399448	NY-ESO-1-redirected CRISPR (TCRendo and PD1) Edited T Cells (NYCE T Cells)	Multiple Myeloma | Melanoma | Synovial Sarcoma | Myxoid/Round Cell Liposarcoma	Biological: NY-ESO-1 redirected autologous T cells with CRISPR edited endogenous TCR and PD-1 | Drug: Cyclophosphamide | Drug: Fludarabine | Device: NY-ESO-1 expression testing	https://ClinicalTrials.gov/show/NCT03399448
NCT02774291	Anti-ESO (Cancer/Test Antigen) mTCR-transduced Autologous Peripheral Blood Lymphocytes and Combination Chemotherapy in Treating Patients With Metastatic Cancer That Expresses NY-ESO-1	HLA-A2 Positive Cells Present | Metastatic Malignant Neoplasm | Metastatic Malignant Neoplasm in the Brain	Biological: Aldesleukin | Biological: Anti-thyroglobulin mTCR-transduced Autologous Peripheral Blood Lymphocytes | Drug: Cyclophosphamide | Biological: Filgrastim | Drug: Fludarabine Phosphate | Other: Laboratory Biomarker Analysis	https://ClinicalTrials.gov/show/NCT02774291
NCT03297697	Minimal Residual Disease in Peripheral T-cell Lymphoma	Peripheral T Cell Lymphoma	Procedure: Tumor biopsy | Procedure: Peripheral blood draw | Procedure: Lymphotrack TCR clonality assay	https://ClinicalTrials.gov/show/NCT03297697
NCT01567891	CT Antigen TCR-redirected T Cells for Ovarian Cancer.	Ovarian Cancer	Biological: NYESO-1c259 T cells	https://ClinicalTrials.gov/show/NCT01567891
NCT03970382	A Study of Gene Edited Autologous Neoantigen Targeted TCR T Cells With or Without Anti-PD-1 in Patients With Solid Tumors	Solid Tumor	Biological: NeoTCR-P1 adoptive cell therapy | Biological: nivolumab | Biological: IL-2	https://ClinicalTrials.gov/show/NCT03970382
NCT03579875	T Cell Receptor Î±/Î² TCD HCT in Patients With Fanconi Anemia	Fanconi Anemia | Severe Aplastic Anemia | Myelodysplastic Syndromes	Drug: Total Body Irradiation (TBI) (Plan 1) | Drug: Cyclophosphamide (CY) (Plan 1) | Drug: Fludarabine (FLU) | Drug: Methylprednisolone (MP) | Device: Donor mobilized PBSC infusion | Drug: G-CSF | Drug: Cyclophosphamide (CY) (Plan 2) | Drug: Rituximab | Drug: Busulfan	https://ClinicalTrials.gov/show/NCT03579875
NCT03412877	Administration of Autologous T-Cells Genetically Engineered to Express T-Cell Receptors Reactive Against Neoantigens in People With Metastatic Cancer	Endocrine Tumors | Non-Small Cell Lung Cancer | Ovarian Cancer | Breast Cancer | Gastrointestinal/Genitourinary Cancer | Neuroendocrine Tumors	Drug: Cyclophosphamide | Drug: Fludarabine | Drug: Aldesleukin | Biological: Individual Patient TCR-Transduced PBL | Drug: Pembrolizumab (KEYTRUDA)	https://ClinicalTrials.gov/show/NCT03412877

FIG. 20-15

NCT Number	Title	Conditions	Interventions	URL
NCT03441100	TCR-engineered T Cells in Solid Tumors: IMA202-101	Solid Tumor, Adult|Cancer|Hepatocellular Carcinoma|Hepatocellular Cancer|Nonsmall Cell Lung Cancer|Liver Cancer|Lung Cancer	Drug: IMA202 Product|Device: IMA_Detect	https://ClinicalTrials.gov/show/NCT03441100
NCT03247309	TCR-engineered T Cells in Solid Tumors (ACTengine IMA201-101)	Solid Tumor|Cancer|Head and Neck Squamous Cell Carcinoma|Non-small Cell Lung Cancer	Biological: IMA201 Product|Diagnostic Test: IMA_Detect	https://ClinicalTrials.gov/show/NCT03247309
NCT01457131	Modified White Blood Cells That Secrete IL-2 and Express a Protein That Targets the ESO-1tumor Protein for Metastatic Cancer	Metastatic Cancer|Metastatic Melanoma|Metastatic Renal Cancer	Drug: Fludarabine|Drug: Cyclophosphamide|Other: IL-12 &amp, Anti-NY ESO1 TCR PBL	https://ClinicalTrials.gov/show/NCT01457131
NCT00001350	Study of Autoimmune Lymphoproliferative Syndrome (ALPS)	Benign Lymphoproliferative Disorder		https://ClinicalTrials.gov/show/NCT00001350
NCT03686124	TCR-engineered T Cells in Solid Tumors	Refractory Cancer|Recurrent Cancer|Solid Tumor, Adult|Cancer	Biological: IMA203 Product|Device: IMADetect|Drug: Atezolizumab	https://ClinicalTrials.gov/show/NCT03686124
NCT00411723	Safety Study of RTL1000 (Recombinant T Cell Receptor Ligand) in Subjects With Multiple Sclerosis	Multiple Sclerosis, Chronic Progressive|Multiple Sclerosis, Relapsing-Remitting	Drug: RTL1000 (recombinant T cell receptor ligand)|Drug: RTL1000 Placebo	https://ClinicalTrials.gov/show/NCT00411723
NCT00923195	Radiation, Chemotherapy, Vaccine and Anti-MART-1 and Anti-gp100 Cells for Patients With Metastatic Melanoma	Melanoma|Skin Cancer	Drug: MART-1: 26-35(27L) Peptide|Drug: Montanide ISA 51 VG|Drug: gp100:154-162 Peptide|Procedure: Radiation|Drug: Aldesleukin|Drug: Fludarabine|Drug: Cyclophosphamide|Genetic: Anti-gp 100:154 TCR PBL|Genetic: Anti-MART-1 F5 TCR PBL	https://ClinicalTrials.gov/show/NCT00923195
NCT00753051	Treat Clozapine (CLZ)-Resistant Schizophrenia Comparing CLZ + Haloperidol vs. CLZ + Electroconvulsive Therapy (ECT)	Schizophrenia	Drug: clozapine+haloperidol|Drug: clozapine,electroconvulsive therapy	https://ClinicalTrials.gov/show/NCT00753051
NCT03996018	T-cell Responses to Concurrent HIV and Herpesvirus Infections	HIV|HIV Infections	Other: T-cell lymphocyte responses	https://ClinicalTrials.gov/show/NCT03996018
NCT00499070	Assessing Immune Function in Young Patients With Cytopenia That Did Not Respond to Treatment	Dyskeratosis Congenita|Fanconi Anemia|Myelodysplastic Syndromes|Pearson Marrow-pancreas Syndrome|Shwachman-diamond Syndrome	Genetic: polymerase chain reaction|Other: flow cytometry|Other: immunologic technique|Procedure: biopsy	https://ClinicalTrials.gov/show/NCT00499070
NCT03139370	Safety and Efficacy of MAGE-A3/A6 T Cell Receptor Engineered T Cells (KITE-718) in HLA-DPB1*04:01 Positive Adults With Advanced Cancers	Solid Tumor	Drug: KITE-718|Drug: Cyclophosphamide|Drug: Fludarabine|Device: MAGE - A3/A6 Screening Test	https://ClinicalTrials.gov/show/NCT03139370

FIG. 20-16

NCT Number	Title	Conditions	Interventions	URL
NCT04135092	Single Patient Protocol: A Phase II Study Using the Administration of Autologous T-Cells Genetically Engineered to Express T-Cell Receptors Reactive Against Mutated Neoantigens in a Patient With Metastatic Cancer Plus the Administration of Pembrolizumab		Biological: Individual Patient TCR Transduced PBL|Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Aldesleukin|Drug: Pembrolizumab	https://ClinicalTrials.gov/show/NCT04135092
NCT03709706	Pilot Immunotherapy Study With Autologous T-cells Specific for NY-ESO-1/ LAGE-1a-positive Advanced NSCLC Either Alone or in Combination With Pembrolizumab	Neoplasms	Drug: letetresgene autoleucel|Drug: Pembrolizumab	https://ClinicalTrials.gov/show/NCT03709706
NCT02820259	Therapeutic Drug Monitoring of Tacrolimus Biliary Concentrations for Liver-transplanted Patients (STABiLE)	Biliary Concentration of Tacrolimus	Drug: Tacrolimus	https://ClinicalTrials.gov/show/NCT02820259
NCT04806347	Alpha/Beta T-cell Depleted Blood-forming Stem Cell Transplant From Related or Unrelated Donors for Blood Diseases in Children and Young Adults	Blood Disease	Biological: TCRÎ±Î²+/CD19+ depleted Hematopoietic stem cell (HSC) graft|Device: CliniMACSÂ® System	https://ClinicalTrials.gov/show/NCT04806347
NCT04746209	Blinatumomab After TCR Alpha Beta/CD19 Depleted HCT	B-cell Acute Lymphoblastic Leukemia|B-cell Childhood Acute Lymphoblastic Leukemia|B-Cell ALL, Childhood	Device: Alpha/Beta T-cell and B-cell depleted HCT|Drug: Blinatumomab	https://ClinicalTrials.gov/show/NCT04746209
NCT02870244	Adoptive T Cell Immunotherapy for Advanced Melanoma Using Engineered Lymphocytes	Melanoma	Biological: Escalating Doses	https://ClinicalTrials.gov/show/NCT02870244
NCT03615144	TCR Alpha Beta T-cell and CD19 B-cell Depleted Peripheral Blood Stem Cell Transplantation Using the CliniMACS System for Patients With Non-Malignant Hematologic Disorders From Matched or Mismatched, Related or Unrelated Donors	Non-Malignant Hematologic Disorders	Drug: Melphalan|Drug: Thiotepa|Drug: Clofarabine|Drug: Fludarabine|Drug: Anti-Thymocyte Globulin (Rabbit) (ThymoglobulinÂ®)|Procedure: CliniMACS reagents	https://ClinicalTrials.gov/show/NCT03615144
NCT03236558	The Role of the Thymus in Type I Diabetes.	Type1 Diabetes	Procedure: Blood collection	https://ClinicalTrials.gov/show/NCT03236558
NCT03603002	Pathologic and Immunologic Response After Ablative Radiation in Lung Cancer	Non-small Cell Lung Cancer Stage I	Diagnostic Test: Post-SABR Biopsy	https://ClinicalTrials.gov/show/NCT03603002
NCT02508038	Alpha/Beta CD19+ Depleted Haploidentical Transplantation + Zometa for Pediatric Hematologic Malignancies and Solid Tumors	Acute Myeloid Leukemia|Acute Lymphoblastic Leukemia|Hodgkin Lymphoma|Non-Hodgkin Lymphoma|Myelodysplastic Syndrome|Myeloproliferative Syndrome|Rhabdomyosarcoma|Ewing Sarcoma|Primitive Neuroectodermal Tumor|Osteosarcoma|Neuroblastoma	Procedure: TCRÎ±Î²+/CD19+ depleted Haploidentical HSCT|Drug: Zoledronate	https://ClinicalTrials.gov/show/NCT02508038

FIG. 20-17

NCT Number	Title	Conditions	Interventions	URL
NCT03250325	Study of TBI-1301 (NY-ESO-1 T Cell Receptor Gene Transduced Autologous T Lymphocytes) in Patients With Synovial Sarcoma	Synovial Sarcoma	Biological: TBI-1301|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03250325
NCT02040337	Sequencing T-cells in Type I Diabetes Mellitus	Diabetes Mellitus, Type 1|Diabetes Mellitus, Type 2		https://ClinicalTrials.gov/show/NCT02040337
NCT03422224	ALLoreactive T-Cell receptOr RePertoire in kidnEy tranSplantation	Renal Transplant Rejection|Immune Repertoire|Transplant; Complication, Rejection|Alloreactivity	Diagnostic Test: Mixed lymphocyte reaction	https://ClinicalTrials.gov/show/NCT03422224
NCT01218867	CAR T Cell Receptor Immunotherapy Targeting VEGFR2 for Patients With Metastatic Cancer	Metastatic Cancer|Metastatic Melanoma|Renal Cancer	Biological: Anti-VEGFR2 CAR CD8 plus PBL|Drug: Cyclophosphamide|Biological: Aldesleukin|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT01218867
NCT01586403	Transfer of Genetically Engineered Lymphocytes in Melanoma Patients	Melanoma	Biological: Dose 1|Biological: Dose 2|Biological: Dose 3|Biological: Dose 4	https://ClinicalTrials.gov/show/NCT01586403
NCT00087594	A Study of PEGASYS (Peginterferon Alfa-2a (40KD)) in Combination With Copegus (Ribavirin) in Patients With Chronic Hepatitis C (CHC) Enrolled in a Methadone Maintenance Treatment Program.	Hepatitis C, Chronic	Drug: peginterferon alfa-2a [Pegasys]|Drug: ribavirin	https://ClinicalTrials.gov/show/NCT00087594
NCT04526509	Master Protocol to Assess the Safety and Dose of First Time in Human Next Generation Engineered T Cells in NY-ESO-1 and/or LAGE-1a Positive Advanced Solid Tumors	Neoplasms	Drug: GSK3901961|Drug: GSK3845097|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04526509
NCT03745326	Administering Peripheral Blood Lymphocytes Transduced With a Murine T-Cell Receptor Recognizing the G12D Variant of Mutated RAS in HLA-A*11:01 Patients	Gastrointestinal Cancer|Pancreatic Cancer|Gastric Cancer|Colon Cancer|Rectal Cancer	Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Aldesleukin|Biological: anti-KRAS G12D mTCR PBL	https://ClinicalTrials.gov/show/NCT03745326
NCT03190941	Administering Peripheral Blood Lymphocytes Transduced With a Murine T-Cell Receptor Recognizing the G12V Variant of Mutated RAS in HLA-A*11:01 Patients	Pancreatic Cancer|Gastric Cancer|Gastrointestinal Cancer|Colon Cancer|Rectal Cancer	Drug: Cyclophosphamide|Drug: Fludarabine|Biological: Anti-KRAS G12V mTCR PBL|Drug: Aldesleukin	https://ClinicalTrials.gov/show/NCT03190941
NCT02390739	Administering Peripheral Blood Lymphocytes Transduced With a Murine T-Cell Receptor Recognizing Human Thyroglobulin to People With Thyroglobulin Expressing Thyroid Cancer	Metastatic Thyroid Cancer	Drug: Aldesleukin|Drug: Fludarabine|Drug: Cyclophosphamide|Biological: Anti-Thyroglobulin mTCR PBL	https://ClinicalTrials.gov/show/NCT02390739
NCT04364828	NGS Diagnostic in COVID-19 Hosts - Genetic Cause Relating to the Course of Disease Progression	COVID-19	Genetic: Whole Genome Analysis|Genetic: T-cell receptor (TCR) repertoire|Genetic: SARS-CoV-2 viral composition	https://ClinicalTrials.gov/show/NCT04364828
NCT03145545	Expanded Access Protocol Using Alpha/Beta T and CD19+ Depleted PBSC	Leukemia|Bone Marrow Failure Syndrome|Immunodeficiencies	Device: Apha/beta T and CD19+ cell depletion using CliniMACS device	https://ClinicalTrials.gov/show/NCT03145545

FIG. 20-18

NCT Number	Title	Conditions	Interventions	URL
NCT02277522	CD19 Redirected Autologous T Cells for Hodgkin Lymphoma	Hodgkin Lymphoma With no Available Curative Treatment Options Who Have a Limited Prognosis	Biological: RNA anti-CD19 CAR T cells	https://ClinicalTrials.gov/show/NCT02277522
NCT00085930	Blood T-Cells and EBV Specific CTLs Expressing GD-2 Specific Chimeric T Cell Receptors to Neuroblastoma Patients	Neuroblastoma	Biological: EBV specific CTLs	https://ClinicalTrials.gov/show/NCT00085930
NCT01583686	CAR T Cell Receptor Immunotherapy Targeting Mesothelin for Patients With Metastatic Cancer	Cervical Cancer|Pancreatic Cancer|Ovarian Cancer|Mesothelioma|Lung Cancer	Drug: Fludarabine|Biological: Anti-mesothelin chimeric T cell receptor (CAR) transduced peripheral blood lymphocytes (PBL)|Drug: Cyclophosphamide|Drug: Aldesleukin	https://ClinicalTrials.gov/show/NCT01583686
NCT02748902	Exploratory Study of Efficacy and Safety of Ingenol Mebutate 0.05% Gel for Common Warts on the Hands.	Verruca Vulgaris|Common Warts	Drug: ingenol mebutate 0.05% gel	https://ClinicalTrials.gov/show/NCT02748902
NCT03733249	Long Term Follow-up Study for Patients Enrolled on the BP-004 Clinical Study	Acute Lymphoblastic Leukemia|Leukemia, Acute Myeloid (AML), Child|Lymphoma, Non-Hodgkin|Myelodysplastic Syndromes|Primary Immunodeficiency|Anemia, Aplastic|Hemoglobinopathies|Cytopenia|Fanconi Anemia|Diamond Blackfan Anemia|Thalassemia|Anemia, Sickle Cell	Drug: Rimiducid|Biological: rivogenlecleucel	https://ClinicalTrials.gov/show/NCT03733249
NCT03639844	BPX-501 T Cells Infused Post Stem Cell Transplant in Pediatrics With Non-Malignant Disorders Ineligible for BPU004 Study	Hurler Syndrome|Inherited Metabolic Disorder|Lysosomal Storage Disorder|Metachromatic Leukodystrophy|Inborn Errors of Metabolism	Biological: rivogenlecleucel|Drug: rimiducid	https://ClinicalTrials.gov/show/NCT03639844
NCT01747486	Dose Optimization Trial of CD19 Redirected Autologous T Cells	Adult Patients Who Have Relapsed or Refractory CLL (3rd Line) or SLL	Biological: CART-19	https://ClinicalTrials.gov/show/NCT01747486
NCT02624258	Pilot Study of Non-Viral, RNA-Redirected Autologous T Cells in Patients With Refractory or Relapsed Hodgkin Lymphoma	Hodgkin Lymphoma	Biological: CD19 RNA redirected autologous T-cells (RNA CART19 cells)	https://ClinicalTrials.gov/show/NCT02624258
NCT04640987	Stem Cell Transplant From Donors After Alpha Beta Cell Depletion in Children and Adults With T-allo10 Cells Addback	Hematologic Diseases	Biological: Allogeneic Stem Cell Transplant|Device: CliniMACS Prodigy System|Drug: T-allo10 cells addback	https://ClinicalTrials.gov/show/NCT04640987

FIG. 20-19

NCT Number	Title	Conditions	Interventions	URL
NCT03017131	Genetically Modified T Cells and Decitabine in Treating Patients With Recurrent or Refractory Ovarian, Primary Peritoneal, or Fallopian Tube Cancer	Recurrent Fallopian Tube Carcinoma|Recurrent Ovarian Carcinoma|Recurrent Primary Peritoneal Carcinoma	Biological: Aldesleukin|Drug: Cyclophosphamide|Drug: Decitabine|Biological: Genetically Engineered NY-ESO-1-specific T Lymphocytes|Other: Laboratory Biomarker Analysis	https://ClinicalTrials.gov/show/NCT03017131
NCT01154387	Evaluating Safety and Efficacy of TOL101 Induction Versus Anti-Thymocyte Globulin to Prevent Kidney Transplant Rejection	End Stage Renal Disease|Renal Transplant	Drug: Anti-Thymocyte Globulin|Drug: TOL101|Drug: Steroids|Drug: Tacrolimus|Drug: Mycophenolate mofetil (MMF)	https://ClinicalTrials.gov/show/NCT01154387
NCT01551043	Allo CART-19 Protocol	Acute Lymphocytic Leukemia	Biological: CART-19	https://ClinicalTrials.gov/show/NCT01551043
NCT03336567	Perceptions of Cell and Gene Therapies (CGT) for the Treatment of Cancer	Neoplasms	Other: Telephonic interview	https://ClinicalTrials.gov/show/NCT03336567
NCT04558736	Haploidentical HCT for Severe Aplastic Anemia	Aplastic Anemia|Bone Marrow Failure Syndrome|Dyskeratosis Congenita	Drug: Anti-Thymocyte Globulin (Rabbit)|Drug: Fludarabine|Drug: Cyclophosphamide|Drug: Mesna|Drug: G-CSF|Radiation: Total Lymphoid Irradiation (TLI)|Device: CliniMACS|Biological: HPC, A Infusion|Biological: CD45RA-depleted DLI	https://ClinicalTrials.gov/show/NCT04558736
NCT00852527	Evaluation of VA's Traumatic Brain Injury (TBI) Clinical Reminder and Comprehensive TBI Evaluation (CTBIE)	Traumatic Brain Injury		https://ClinicalTrials.gov/show/NCT00852527
NCT03587376	Characterization of T-Cell Response in Participants Previously Treated With JNJ-54861911 (Atabecestat)	Alzheimer Disease	Drug: Atabecestat	https://ClinicalTrials.gov/show/NCT03587376
NCT02588612	Letetresgene Autoleucel Engineered T Cells in NY-ESO -1 Positive Advanced Non-Small Cell Lung Cancer (NSCLC)	Neoplasms	Drug: letetresgene autoleucel (GSK3377794)|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT02588612
NCT03634683	A Study of LioCyx in Patient With Recurrent HBV-related HCC Post Liver Transplantation	Recurrent Hepatocellular Carcinoma	Biological: LioCyx	https://ClinicalTrials.gov/show/NCT03634683
NCT01700192	Efficacy and Safety Study of SCH 900237/MK-8237 in Children and Adults With House Dust Mite-Induced Allergic Rhinitis/Rhinoconjunctivitis (P05607)	Rhinitis, Allergic, Perennial|Rhinitis, Allergic, Nonseasonal	Biological: MK-8237 tablets|Biological: Placebo tablets|Drug: Rescue Medication: Self-Injectable Epinephrine|Drug: Rescue Medication: Loratadine tablets|Drug: Rescue Medication: Olopatadine ophthalmic drops|Drug: Rescue Medication: Mometasone furoate nasal spray	https://ClinicalTrials.gov/show/NCT01700192
NCT03912831	Safety and Efficacy of KITE-439 in HLA-A*02:01+ Adults With Relapsed/Refractory HPV16+ Cancers	Human Papillomavirus (HPV) 16+ Relapsed/Refractory Cancer	Drug: KITE-439|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT03912831
NCT04245124	Validation of Cognitive Enhancement Techniques for Mild Traumatic Brain Injury	Mild Traumatic Brain Injury	Other: Strategic Memory Advanced Reasoning Training|Other: Traditional Cognitive Rehabilitation	https://ClinicalTrials.gov/show/NCT04245124
NCT04402892	COVID-19: SARS-CoV-2 Specific Memory B and T-CD4+ Cells	COVID-19|SARS-CoV-2 Infection	Other: 35 ml blood, 5 tubes LITHIUM HEPARINATE at each time (hospitalized Patients)|Other: 35 ml blood, 5 tubes LITHIUM HEPARINATE at each time (cured Patients)	https://ClinicalTrials.gov/show/NCT04402892

FIG. 20-20

NCT Number	Title	Conditions	Interventions	URL
NCT02055521	Search Tolerance Signature in Vascularised Composite Allograft	Hand and Face Allotransplantation	Procedure: Blood sample, biopsy	https://ClinicalTrials.gov/show/NCT02055521
NCT04650724	Clinical Study of T Cell Infusion Targeting BCMA Chimeric Antigen Receptor	Multiple Myeloma	Drug: T cell infusion agent targeting BCMA chimeric antigen receptor	https://ClinicalTrials.gov/show/NCT04650724
NCT01982890	Telomeres and T-cell Receptor Excision Circles (TRECs) From Peripheral Blood in Normal Subjects Over Time	Telomere Length in Healthy Controls	Other: Control	https://ClinicalTrials.gov/show/NCT01982890
NCT04858828	Investigation on Predictive Molecular Markers of Efficacy for Front-line Immunochemotherapy in Advanced NSCLC	Biomarkers		https://ClinicalTrials.gov/show/NCT04858828
NCT04447053	Sequential Belimumab and T-cell Based Therapy in SLE	Systemic Lupus Erythematosus	Drug: Belimumab Injection [Benlysta]	https://ClinicalTrials.gov/show/NCT04447053
NCT03649529	Treatment of Malignant Melanoma With GPA-TriMAR-T Cell Therapy	Malignant Melanoma	Biological: GPA-TriMAR-T	https://ClinicalTrials.gov/show/NCT03649529
NCT02770820	Laboratory-Treated (Central Memory/Naive) CD8+ T Cells in Treating Patients With Newly Diagnosed or Relapsed Acute Myeloid Leukemia	Acute Myeloid Leukemia|EBV-Positive Neoplastic Cells Present|HLA-A*0201 Positive Cells Present|Blasts Under 5 Percent of Bone Marrow Nucleated Cells|Elevated WT1	Biological: Aldesleukin|Biological: Autologous WT1-TCRc4 Gene-transduced CD8-positive Tcm/Tn Lymphocytes|Other: Laboratory Biomarker Analysis	https://ClinicalTrials.gov/show/NCT02770820
NCT03132792	AFPá¶¡œÂ³Â²T in Advanced HCC	Hepatocellular Cancer|AFP Expressing Tumors	Genetic: Autologous genetically modified AFPá¶¡œÂ³Â²T cells	https://ClinicalTrials.gov/show/NCT03132792
NCT03392545	Combination of Immunization and Radiotherapy for Malignant Gliomas (InSituVac1)	High Grade Glioma|Glioblastoma|Glioma of Brainstem|Glioma, Malignant	Combination Product: Combined immune adjuvants and radiation	https://ClinicalTrials.gov/show/NCT03392545
NCT04636047	NGS-based Comprehensive Genomic ctDNA Panel in NSCLC With Immunotherapy	Lung Cancer	Other: The method of gene mutation detection	https://ClinicalTrials.gov/show/NCT04636047
NCT04494893	ImmuneRACE - Immune Response Action to COVID-19 Events	Covid19		https://ClinicalTrials.gov/show/NCT04494893
NCT04906382	Tislelizumab for the Treatment of Recurrent Mismatch Repair Deficient Endometrial Cancer	Lynch Syndrome|Recurrent Endometrial Carcinoma|Recurrent Endometrial Clear Cell Adenocarcinoma|Recurrent Uterine Corpus Carcinosarcoma|Mismatch Repair Deficiency|Recurrent Endometrial Cancer|Metastatic Endometrial Cancer	Procedure: Biopsy|Drug: Carboplatin|Drug: Paclitaxel|Biological: Tislelizumab	https://ClinicalTrials.gov/show/NCT04906382
NCT00706992	Anti-MART-1 F5 Lymphocytes to Treat High-Risk Melanoma Patients	Melanoma	Biological: ALVAC-MART-1 vaccine|Biological: MART-1:26-35(27L) peptide vaccine|Biological: Aldesleukin|Biological: autologous anti-MART-1 F5 T-cell receptor gene-engineered peripheral blood lymphocytes|Biological: incomplete Freund's adjuvant	https://ClinicalTrials.gov/show/NCT00706992

FIG. 20-21

NCT Number	Title	Conditions	Interventions	URL
NCT04201873	Pembrolizumab and a Vaccine (ATL-DC) for the Treatment of Surgically Accessible Recurrent Glioblastoma	Recurrent Glioblastoma	Biological: Dendritic Cell Tumor Cell Lysate Vaccine | Biological: Pembrolizumab | Other: Placebo Administration | Drug: Poly ICLC	https://ClinicalTrials.gov/show/NCT04201873
NCT04692948	TAA6 Cell Injection In The Treatment of Patients With Relapsed / Refractory Acute Myeloid Leukemia	CAR | Acute Myeloid Leukemia	Other: Chimeric antigen receptor T cells (car-t)	https://ClinicalTrials.gov/show/NCT04692948
NCT02636855	Screening Protocol for Tumor Antigen Expression Profiling and HLA Typing for Eligibility Determination	Solid and Hematological Malignancies		https://ClinicalTrials.gov/show/NCT02636855
NCT03409796	Assessment of Immune Activation and Tolerance in Celiac Disease During Gluten Challenge	Celiac Disease	Dietary Supplement: Gluten	https://ClinicalTrials.gov/show/NCT03409796
NCT04318964	TAEST16001 in the Treatment of Soft Tissue Sarcoma	Soft Tissue Sarcoma	Biological: TAEST16001 cells	https://ClinicalTrials.gov/show/NCT04318964
NCT00091104	Cyclophosphamide and Fludarabine Followed by Vaccine Therapy, Gene-Modified White Blood Cell Infusions, and Aldesleukin in Treating Patients With Metastatic Melanoma	Melanoma (Skin)	Biological: MART-1:27-35 peptide vaccine | Biological: aldesleukin | Biological: filgrastim | Biological: incomplete Freund's adjuvant | Biological: therapeutic autologous lymphocytes | Biological: therapeutic tumor infiltrating lymphocytes | Drug: cyclophosphamide | Drug: fludarabine phosphate | Procedure: autologous hematopoietic stem cell transplantation | Procedure: in vitro-treated peripheral blood stem cell transplantation | Radiation: total-body irradiation	https://ClinicalTrials.gov/show/NCT00091104
NCT00085462	Gene-Modified White Blood Cells Followed By Interleukin-2 and Vaccine Therapy in Treating Patients With Metastatic Melanoma	Melanoma (Skin)	Biological: aldesleukin | Biological: filgrastim | Biological: gp100-fowlpox vaccine | Biological: therapeutic autologous lymphocytes | Biological: therapeutic tumor infiltrating lymphocytes | Drug: cyclophosphamide | Drug: fludarabine phosphate	https://ClinicalTrials.gov/show/NCT00085462
NCT01284504	Effect of Celecoxib on Perioperative Inflammatory Response in Colon Cancer	Colorectal Cancer | Colon Cancer	Drug: Celecoxib | Other: placebo	https://ClinicalTrials.gov/show/NCT01284504

FIG. 20-22

NCT Number	Title	Conditions	Interventions	URL
NCT02408016	Genetically Modified T Cells in Treating Patients With Stage III-IV Non-small Cell Lung Cancer or Mesothelioma	Malignant Mesothelioma|HLA-A*0201 Positive Cells Present|Recurrent Non-Small Cell Lung Carcinoma|Recurrent Pleural Malignant Mesothelioma|Stage III Non-Small Cell Lung Cancer AJCC v7|Stage III Pleural Malignant Mesothelioma AJCC v7|Stage IIIA Non-Small Cell Lung Cancer AJCC v7|Stage IIIB Non-Small Cell Lung Cancer AJCC v7|Stage IV Non-Small Cell Lung Cancer AJCC v7|Stage IV Pleural Malignant	Biological: Aldesleukin|Biological: Autologous WT1-TCRc4 Gene-transduced CD8-positive Tcm/Tn Lymphocytes|Drug: Cyclophosphamide|Other: Laboratory Biomarker Analysis|Procedure: Therapeutic Conventional Surgery	https://ClinicalTrials.gov/show/NCT02408016
NCT01370213	NK Cell Based Non-Myeloablative Transplantation in Acute Myeloid Diseases	Acute Myeloid Leukemia|Myelodysplastic Syndrome	Drug: Preparative Regimen|Biological: NK Cells|Drug: Interleukin-2|Biological: CD34 Graft/Anti-thymocyte globulin|Biological: Donor TCR Î±/Î²-depleted Graft/ATG	https://ClinicalTrials.gov/show/NCT01370213
NCT03453801	The Role of CD4+ Memory Phenotype, Memory, and Effector T Cells in Vaccination and Infection	Influenza|Healthy	Biological: FluzoneÂ®|Biological: FluMistÂ®	https://ClinicalTrials.gov/show/NCT03453801
NCT03156101	A Clinical Study Evaluating the Safety and Efficacy of BinD19 Treatment in R/R ALL and Lymphoma Subjects	Relapsed B-cell Acute Lymphoblastic Leukemia|Refractory B-cell Acute Lymphoblastic Leukemia|Relapsed i¾Refractory B-cell Lymphoma	Biological: BinD19	https://ClinicalTrials.gov/show/NCT03156101
NCT03265106	A Clinical Study Evaluating the Safety and Efficacy of BinD19 Treatment in Childhood R/R ALL and Lymphoma Subjects	Relapsed B-cell Acute Lymphoblastic Leukemia, Childhood|Refractory B-cell Acute Lymphoblastic Leukemia, Childhood|Relapsed/Refractory B-cell Lymphoma, Childhood	Biological: BinD19	https://ClinicalTrials.gov/show/NCT03265106
NCT04222595	FluPRINT Study: Characterisation of the Immune and Transcriptional Response to LAIV	Immunization	Other: Fluenz Tetra nasal spray suspension	https://ClinicalTrials.gov/show/NCT04222595
NCT02571166	HSV529 Vaccine in HSV-2 Seropositive Adults	Herpes Simplex Virus 2	Biological: HSV529|Drug: Valacyclovir	https://ClinicalTrials.gov/show/NCT02571166

FIG. 20-23

NCT Number	Title	Conditions	Interventions	URL
NCT01640301	Laboratory-Treated T Cells in Treating Patients With High-Risk Relapsed Acute Myeloid Leukemia, Myelodysplastic Syndrome, or Chronic Myelogenous Leukemia Previously Treated With Donor Stem Cell Transplant	Recurrent Adult Acute Myeloid Leukemia|Recurrent Childhood Acute Myeloid Leukemia|Secondary Acute Myeloid Leukemia|Therapy-Related Acute Myeloid Leukemia|Donor|Hematopoietic Cell Transplant Recipient|HLA-A*0201 Positive Cells Present|Recurrent Acute Myeloid Leukemia	Biological: Aldesleukin|Drug: Cyclophosphamide|Drug: Fludarabine Phosphate|Other: Laboratory Biomarker Analysis|Biological: WT1-Sensitized Allogeneic T-Lymphocytes	https://ClinicalTrials.gov/show/NCT01640301
NCT02340845	Bromelain, Comosain as a New Drug for Treating and Preventing Various Types of Cancer in the Humans	Cancer	Biological: Bromelain and Comosain	https://ClinicalTrials.gov/show/NCT02340845
NCT02942173	CD45RA Depleted T-cell Infusion for Prevention of Infections After TCRab/CD19-depleted Allo-HSCT	Leukemia|Lymphoma|Myelodysplastic Syndromes|GvHD|Opportunistic Infections|Graft-versus-Host Disease	Biological: CD45RA-depleted peripheral blood mononuclear cells	https://ClinicalTrials.gov/show/NCT02942173
NCT04534322	Expanded Access Program for Melphalan Flufenamide (Melflufen) in Triple Class Refractory Multiple Myeloma	Relapsed and/or Refractory Multiple Myeloma	Drug: Melphalan Flufenamide|Drug: Dexamethasone	https://ClinicalTrials.gov/show/NCT04534322
NCT03738228	Atezolizumab Before and/or With Chemoradiotherapy in Immune System Activation in Patients With Node Positive Stage IB2, II, IIIB, or IVA Cervical Cancer	Cervical Adenocarcinoma|Cervical Adenosquamous Carcinoma|Cervical Squamous Cell Carcinoma, Not Otherwise Specified|Stage IB2 Cervical Cancer AJCC v8|Stage II Cervical Cancer AJCC v8|Stage IIA Cervical Cancer AJCC v8|Stage IIA1 Cervical Cancer AJCC v8|Stage IIA2 Cervical Cancer AJCC v8|Stage IIB Cervical Cancer AJCC v8|Stage IIIB Cervical Cancer AJCC v8|Stage IVA Cervical Cancer AJCC v8	Drug: Atezolizumab|Radiation: Brachytherapy|Drug: Cisplatin|Radiation: Radiation Therapy	https://ClinicalTrials.gov/show/NCT03738228

FIG. 20-24

NCT Number	Title	Conditions	Interventions	URL
NCT04877613	GFRÎ±4 CAR T Cells in MTC Patients	Metastatic Medullary Thyroid Cancer	Drug: single dose of CART-GFRa4 cells | Drug: Fludarabine | Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04877613
NCT03369353	Precision Diagnostics in Inflammatory Bowel Disease, Cellular Therapy and Transplantation (The PREDICT Trial)	Graft Vs Host Disease | Inflammatory Bowel Diseases | Functional Gastrointestinal Disorders		https://ClinicalTrials.gov/show/NCT03369353
NCT03365661	QUILT-3.034: Non-Myeloablative TCRa/b Deplete Haplo HSCT With Post ALT-803 for AML	High-Risk Acute Myeloid Leukemia | Treatment-Related Acute Myeloid Leukemia | Secondary Acute Myeloid Leukemia | Myelodysplastic Syndrome	Biological: ALT-803	https://ClinicalTrials.gov/show/NCT03365661
NCT04646837	Mechanism of Response to IMFINZI Neoadjuvant Therapy in Non-small Cell Lung Cancer Patients Based on Multiple-omics Models	Non-small Cell Lung Cancer	Drug: Durvalumab | Drug: Albumin Paclitaxel | Drug: Carboplatin/Cisplatin	https://ClinicalTrials.gov/show/NCT04646837
NCT02617108	Intrauterine Balloon and Postoperative Estrogen Therapy in the Prevention of Adhesion Reformation After Hysteroscopic Adhesiolysis	Uterine Septum	Device: Foley balloon	https://ClinicalTrials.gov/show/NCT02617108
NCT02809560	Detection of Cav1 Calcium Channels in Inflammatory Cells of Asthmatic Children	Asthma	Procedure: Induced sputum method using hypertonic serum	https://ClinicalTrials.gov/show/NCT02809560
NCT03391778	Long Term Follow-Up of Subjects Exposed to GSK3377794	Neoplasms	Genetic: GSK3377794 (NY-ESO-1á¶œÂ²âµâ³ T)	https://ClinicalTrials.gov/show/NCT03391778
NCT02133196	T Cell Receptor Immunotherapy for Patients With Metastatic Non-Small Cell Lung Cancer	Advanced Non-Small Cell Lung Cancer | Squamous Cell Carcinoma | Advanced NSCLC | Adenosquamous Carcinoma | Adenocarcinomas	Drug: Aldesleukin | Drug: Fludarabine | Drug: Cyclophosphamide | Biological: Young TIL	https://ClinicalTrials.gov/show/NCT02133196
NCT03397186	Immune Changes Following Trabectedin in Patients With Metastatic or Unresectable Sarcoma	Myxoid Liposarcoma | Round Cell Liposarcoma | Stage III Soft Tissue Sarcoma AJCC v7 | Stage IV Soft Tissue Sarcoma AJCC v7 | Metastatic Soft Tissue Sarcoma | Unresectable Soft Tissue Sarcoma	Procedure: Biopsy | Other: Laboratory Biomarker Analysis | Drug: Trabectedin	https://ClinicalTrials.gov/show/NCT03397186

FIG. 20-25

NCT Number	Title	Conditions	Interventions	URL
NCT03849651	TCRÎ±Î²-depleted Progenitor Cell Graft With Additional Memory T-cell DLI, Plus Selected Use of Blinatumomab, in Naive T-cell Depleted Haploidentical Donor Hematopoietc Cell Transplantation for Hematologic Malignancies	Acute Lymphoblastic Leukemia (ALL)|Acute Myeloid Leukemia (AML)|Myelodysplastic Syndromes (MDS)|NK-Cell Leukemia|Hodgkin Lymphoma|Non Hodgkin Lymphoma (NHL)|Juvenile Myelomonocytic Leukemia (JMML)|Chronic Myeloid Leukemia (CML)	Drug: Cyclophosphamide|Biological: Fludarabine|Drug: Thiotepa|Drug: Melphalan|Biological: G-csf|Drug: Mesna|Device: CliniMACS|Biological: ATG (rabbit)|Drug: Blinatumomab|Biological: TCRÎ±/Î²+|Biological: CD19+|Biological: CD45RA-depleted DLI	https://ClinicalTrials.gov/show/NCT03849651
NCT03953599	CD19-Synthetic T Cell Antigen Receptor(STAR)-T in B-cell Malignancies Patients	B Cell Malignancy	Biological: CD19-STAR-T cells	https://ClinicalTrials.gov/show/NCT03953599
NCT00924326	CAR T Cell Receptor Immunotherapy for Patients With B-cell Lymphoma	Primary Mediastinal B-cell Lymphoma|Diffuse, Large B-cell Lymphoma|Diffuse Large B-Cell Lymphoma Transformed From Follicular Lymphoma|Mantle Cell	Drug: Fludarabine|Drug: Cyclophosphamide|Biological: Anti-cluster of differentiation 19 (CD19)-CAR PBL|Drug: Aldesleukin	https://ClinicalTrials.gov/show/NCT00924326
NCT02719405	Impact of Infant Formula on Resolution of Cow's Milk Allergy	Milk Allergy	Dietary Supplement: Lactobacillus GG|Dietary Supplement: Extensively Hydrolyzed Casein Formula|Dietary Supplement: Amino Acid Formula	https://ClinicalTrials.gov/show/NCT02719405
NCT03118687	Human Immunome Program	Healthy	Other: Biospecimen and survey collection	https://ClinicalTrials.gov/show/NCT03118687
NCT01454596	CAR T Cell Receptor Immunotherapy Targeting EGFRvIII for Patients With Malignant Gliomas Expressing EGFRvIII	Malignant Glioma|Glioblastoma|Brain Cancer|Gliosarcoma	Biological: Epidermal growth factor receptor(EGFRv)III Chimeric antigen receptor (CAR) transduced PBL|Drug: Aldesleukin|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT01454596
NCT01209676	IMCgp100 in Advanced Unresectable Melanoma	Melanoma|Advanced Disease|Unresectable	Drug: IMCgp100 injection	https://ClinicalTrials.gov/show/NCT01209676
NCT03568058	Personalized Immunotherapy in Adults With Advanced Cancers Immunotherapy in Adults With Advanced Cancers	Advanced Cancer	Drug: personalized vaccine|Drug: Pembrolizumab	https://ClinicalTrials.gov/show/NCT03568058
NCT03551795	Clinical Research on Comprehensive Treatment of Tuberculosis With Malignant Solid Tumor	Malignant Solid Tumor	Biological: infusion of iNKT cells	https://ClinicalTrials.gov/show/NCT03551795
NCT01723306	Phase II/Pilot Study of 2nd Generation Anti-CEA Designer T Cells in Adenocarcinomas	Metastatic Cancers	Genetic: Gene Modified T Cells	https://ClinicalTrials.gov/show/NCT01723306
NCT02570308	A Study of the Intra-Patient Escalation Dosing Regimen With IMCgp100 in Patients With Advanced Uveal Melanoma	Uveal Melanoma	Drug: IMCgp100	https://ClinicalTrials.gov/show/NCT02570308

FIG. 20-26

NCT Number	Title	Conditions	Interventions	URL
NCT02776813	Study of ACTR087 in Subjects With Relapsed or Refractory B-cell Lymphoma	Lymphoma	Biological: ACTR087|Biological: rituximab	https://ClinicalTrials.gov/show/NCT02776813
NCT04713163	COVID-19 Vaccine Induced Immunity	Covid19	Drug: covid19 vaccine	https://ClinicalTrials.gov/show/NCT04713163
NCT03267641	Prospective Cohort Study on the Clinical Trajectory of Resected Hepatocellular Carcinoma	Hepatocellular Carcinoma		https://ClinicalTrials.gov/show/NCT03267641
NCT02135406	CART-19 for Multiple Myeloma	Multiple Myeloma	Biological: CART-19 T cells	https://ClinicalTrials.gov/show/NCT02135406
NCT02546167	CART-BCMA Cells for Multiple Myeloma	Multiple Myeloma	Biological: CART-BCMA	https://ClinicalTrials.gov/show/NCT02546167
NCT02030834	Phase IIa Study of Redirected Autologous T Cells Engineered to Contain Anti-CD19 Attached to TCRz and 4-Signaling Domains in Patients With Chemotherapy Relapsed or Refractory CD19+ Lymphomas	Non-Hodgkins Lymphoma (NHL) Patients, With CD19+B Cell Lymphomas	Biological: CART-19	https://ClinicalTrials.gov/show/NCT02030834
NCT02711696	Randomized Clincal Trial on the Effect of a Restricted Gluten Contamination Elimination Diet Among Celiacs [GluCED]	Celiac Disease	Behavioral: GCED, Gluten Contamination Elimination Diet	https://ClinicalTrials.gov/show/NCT02711696
NCT03093688	Clinical Safty and Efficacy Study of Infusion of iNKT Cells and CD8+T Cells in Patients With Advanced Solid Tumor	Non-small Cell Lung Cancer|Small Cell Lung Cancer|Pancreas Cancer|Hepatocellular Carcinoma|Gastric Cancer|Renal Cell Carcinoma	Biological: Infusion of iNKT cells and CD8+T cells	https://ClinicalTrials.gov/show/NCT03093688
NCT02681302	Check Point Inhibition After Autologous Stem Cell Transplantation in Patients at High Risk of Post Transplant Recurrence	Multiple Myeloma|Lymphoma	Drug: Ipilimumab|Drug: Nivolumab	https://ClinicalTrials.gov/show/NCT02681302
NCT02840110	Long-Term Follow-Up Study of Subjects Treated With ACTR T Cell Product	B Cell Lymphomas|Multiple Myeloma|Solid Tumor|HER-2 Protein Overexpression	Other: ACTR T Cell Product	https://ClinicalTrials.gov/show/NCT02840110
NCT00622232	A Rollover Study for Subjects Who Completed Participation in the VRX496-USA-05-002 Trial	HIV Infections	Genetic: VRX496-transduced autologous CD4 T cells	https://ClinicalTrials.gov/show/NCT00622232
NCT03921047	Characterization of T-cell Repertoire in Patients With Acute Myeloid Leukemia Undergoing Donor Stem Cell Transplant	Acute Myeloid Leukemia	Procedure: Biospecimen Collection|Other: Laboratory Biomarker Analysis	https://ClinicalTrials.gov/show/NCT03921047
NCT02333760	Long Term Safety Follow up of Haematopoietic Stem Cell Gene Therapy for the Wiskott Aldrich Syndrome	Wiskott-Aldrich Syndrome	Genetic: Autologous CD34+ cells transduced with WASP lentiviral vector	https://ClinicalTrials.gov/show/NCT02333760
NCT03515551	Safety and Efficacy of IMCnyeso in Advanced NY-ESO-1 and/or LAGE-1A Positive Cancers	Select Advanced Solid Tumors	Drug: IMCnyeso	https://ClinicalTrials.gov/show/NCT03515551
NCT01921036	The Effects of Combined Exercise Training on Exercise Capacity in Cardiac Rehabilitation	Coronary Artery Disease	Procedure: traditional cardiac rehabilitation|Procedure: combined exercise	https://ClinicalTrials.gov/show/NCT01921036
NCT04556474	[Trial of device that is not approved or cleared by the U.S. FDA]			https://ClinicalTrials.gov/show/NCT04556474
NCT00004178	Gene Therapy in Treating Patients With Cancer	Cancer	Biological: therapeutic autologous lymphocytes	https://ClinicalTrials.gov/show/NCT00004178

FIG. 20-27

NCT Number	Title	Conditions	Interventions	URL
NCT04783038	Determining The Impact Of Distance Reiki On Patient Reported QOL And Immunity Among Multiple Myeloma Patients	Multiple Myeloma|Autologous Stem Cell Transplant	Other: Distance Reiki|Other: Sham distance Reiki	https://ClinicalTrials.gov/show/NCT04783038
NCT02661659	A Phase Ib Trial of a Maintenance Multipeptide Vaccine (S-588210) in Patients With Unresectable Malignant Pleural Mesothelioma Without Progression After First-Line Chemotherapy	Malignant Pleural Mesothelioma (MPM)	Biological: Multipeptide vaccine S-588210	https://ClinicalTrials.gov/show/NCT02661659
NCT01211262	Study to Assess the Tolerability of a Bispecific Targeted Biologic IMCgp100 in Malignant Melanoma	Malignant Melanoma	Drug: IMCgp100	https://ClinicalTrials.gov/show/NCT01211262
NCT01036399	Study of Lenalidomide (Revlimid) in Patients With Relapsed/Refractory Peripheral T-cell Lymphoma (PTCL) Patients	Peripheral T-cell Lymphoma	Drug: Lenalidomide	https://ClinicalTrials.gov/show/NCT01036399
NCT04790409	Sintilimab Combined With Anlotinib in Advanced NSCLC With Uncommon Mutations	Lung Cancer	Drug: PD-1 inhibitor and anlotinib	https://ClinicalTrials.gov/show/NCT04790409
NCT02244450	Generalized Neonatal Screening of Severe Combined Immunodeficiencies	Severe Combined Immunodeficiency, Atypical	Biological: SCID screening	https://ClinicalTrials.gov/show/NCT02244450
NCT03559803	A Prospective Study of Monitoring Immune Response in Locally Advanced Cervix Cancer	Cervical Cancer	Drug: Cisplatin	https://ClinicalTrials.gov/show/NCT03559803
NCT02702427	Virus-specific ImmunoTherapy Following Allogeneic Stem Cell Transplantation	Cytomegalovirus Infection|Adenovirus Infection	Biological: virus-specific T-Cells	https://ClinicalTrials.gov/show/NCT02702427
NCT01884168	Study of Gene Expression Profiling and Immunological Mechanism Affects the Response of Immunotherapy	Malignant Tumor	Biological: Dc-CIK immunotherapy	https://ClinicalTrials.gov/show/NCT01884168
NCT02941744	A Clinical Trial: Adjuvant Low-dose Ipilimumab + Nivolumab After Resection of Melanoma Macrometastases	Stage IIIC Skin Melanoma|Stage IV Skin Melanoma	Drug: nivolumab|Drug: ipilimumab	https://ClinicalTrials.gov/show/NCT02941744
NCT00019136	Gene Therapy and Biological Therapy in Treating Patients With Ovarian Epithelial Cancer	Ovarian Cancer	Biological: MOv-gamma chimeric receptor gene|Biological: aldesleukin|Biological: therapeutic allogeneic lymphocytes	https://ClinicalTrials.gov/show/NCT00019136
NCT02472704	Lymphocytic Enteritis and Suspected Coeliac Disease: Gluten vs Placebo	Celiac Disease|Non-celiac Gluten Sensitivity	Dietary Supplement: Gluten challenge|Dietary Supplement: Placebo challenge	https://ClinicalTrials.gov/show/NCT02472704
NCT03541083	Blinatumomab Added to Prephase and Consolidation Therapy in Precursor B-acute Lymphoblastic Leukemia in Adults.	ALL, Adult	Drug: Blinatumomab	https://ClinicalTrials.gov/show/NCT03541083
NCT01050296	Molecular Analysis Of Solid Tumors	Pediatric Solid Tumors		https://ClinicalTrials.gov/show/NCT01050296
NCT04411043	Observatory of Prolymphocytic Leukemia T	Prolymphocytic Leukemia|T-cell Leukemia	Behavioral: Molecular caracterization	https://ClinicalTrials.gov/show/NCT04411043
NCT00341146	Molecular Genetics Study of Nasopharyngeal Carcinoma: Characterization of NCP Susceptibility Gene(s)	Nasopharyngeal Carcinoma		https://ClinicalTrials.gov/show/NCT00341146
NCT03709719	Blinatumomab in High-risk B-cell Precursor Acute Lymphoblastic Leukemia	Acute Lymphoblastic Leukemia, Adult B-Cell	Drug: Blinatumomab Injection	https://ClinicalTrials.gov/show/NCT03709719
NCT04729452	Characterisation of the Immune Response to SARS-CoV-2	Covid19	Other: blood test	https://ClinicalTrials.gov/show/NCT04729452

FIG. 20-28

NCT Number	Title	Conditions	Interventions	URL
NCT02980146	Impact of HLA-E Overexpression by Tumor Cells on the Biology of TIL in Colorectal Cancer	ColoRectal Cancer	Other: Non interventional study	https://ClinicalTrials.gov/show/NCT02980146
NCT03166878	A Study Evaluating UCART019 in Patients With Relapsed or Refractory CD19+ Leukemia and Lymphoma	B Cell Leukemia|B Cell Lymphoma	Biological: UCART019	https://ClinicalTrials.gov/show/NCT03166878
NCT03038334	Magnesium Sulfate for the Improvement of Cognition in Patients With Alzheimer Disease	Alzheimer Disease	Dietary Supplement: Magnesium sulfate	https://ClinicalTrials.gov/show/NCT03038334
NCT03644043	Evidence Amyloid Scan EEG Study	Alzheimer Disease|Dementia Frontal|Mild Cognitive Impairment	Device: EEG scan	https://ClinicalTrials.gov/show/NCT03644043
NCT03038282	Effects of Chromium on Insulin Resistance in Alzheimer Disease Patients	Alzheimer Disease	Dietary Supplement: Chromium Chloride|Other: Individual Exercise	https://ClinicalTrials.gov/show/NCT03038282
NCT00172666	Decoy Receptor 3 (DcR3) Polymorphisms in Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE)	Rheumatoid Arthritis|Systemic Lupus Erythematosus		https://ClinicalTrials.gov/show/NCT00172666
NCT02889861	IMCgp100-401 Rollover Study	Malignant Melanoma	Drug: IMCgp100	https://ClinicalTrials.gov/show/NCT02889861
NCT02102893	Gastroenteral-Pancreatic Neuroendocrine Tumors in Taiwan	This Study Plans to Include 600 GEP-NET Patients.		https://ClinicalTrials.gov/show/NCT02102893
NCT03209245	House Dust Mite Injection Immunotherapy in Elderly Patients.	Allergen Immunotherapy in Elderly Patients	Biological: Purethal Mites|Other: placebo injection|Diagnostic Test: monitoring of allergen specific IgE|Diagnostic Test: monitoring of allergen specific IgG4	https://ClinicalTrials.gov/show/NCT03209245
NCT01384201	Confocal Endomicroscopy Detection of Gastric Preneoplasia and Neoplasia	Gastric Intestinal Metaplasia		https://ClinicalTrials.gov/show/NCT01384201
NCT03523429	PETHEMA-BLIN-01/PET069014 (BLIN-01)	Philadelphia Chromosome-negative or BCR-ABL-negative, CD19-positive ALL	Drug: blinatumomab	https://ClinicalTrials.gov/show/NCT03523429
NCT00396695	Neuroimmunological Model of Traumatic Memory	Stress Disorders, Post-Traumatic	Procedure: Blood test	https://ClinicalTrials.gov/show/NCT00396695
NCT04908514	A Clinical Trial to Evaluate the Safety, Tolerability, and Efficacy of Subjects With Plaque Psoriasis	Plaque Psoriasis	Drug: ADX-629	https://ClinicalTrials.gov/show/NCT04908514
NCT02590328	Neonatal Screening of Severe Combined Immunodeficiencies	Severe Combined Immunodeficiency|Neonatal Screening		https://ClinicalTrials.gov/show/NCT02590328
NCT00924287	Gene Therapy Using Anti-Her-2 Cells to Treat Metastatic Cancer	Metastatic Cancer	Drug: in vitro tumor reactive, chimeric T cell receptor (CAR) gene-transduced PBL plus IV aldesleukin|Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Mesna	https://ClinicalTrials.gov/show/NCT00924287
NCT03088904	Genetic and Environmental Factors in the Response to Influenza Vaccination	Influenza|Healthy	Biological: FluMistÂ® Quadrivalent|Biological: FluzoneÂ® Quadrivalent vaccine	https://ClinicalTrials.gov/show/NCT03088904
NCT04262466	Safety and Efficacy of IMC-F106C as a Single Agent and in Combination With Checkpoint Inhibitors	Select Advanced Solid Tumors	Drug: IMC-F106C|Drug: anti-PD(L)1	https://ClinicalTrials.gov/show/NCT04262466
NCT01231841	Anti-thymocyte Globulin and Cyclosporine as First-Line Therapy in Treating Patients With Severe Aplastic Anemia	Aplastic Anemia	Drug: cyclosporine|Biological: anti-thymocyte globulin	https://ClinicalTrials.gov/show/NCT01231841

FIG. 20-29

NCT Number	Title	Conditions	Interventions	URL
NCT01207388	Confirmatory Phase II Study of Blinatumomab (MT103) in Patients With Minimal Residual Disease of B-precursor Acute Lymphoblastic Leukemia (ALL)	B-cell Acute Lymphoblastic Leukemia	Drug: Blinatumomab	https://ClinicalTrials.gov/show/NCT01207388
NCT04622423	Advanced Therapies for Liver Metastases	Pancreatic Ductal Adenocarcinoma (PDAC)|Colorectal Cancer (CRC)|Liver Metastasis	Other: Observational study	https://ClinicalTrials.gov/show/NCT04622423
NCT04034225	Addition of SNS-301 to Checkpoint Inhibitor Treatment in Metastatic/Recurrent SCCHN	Squamous Cell Carcinoma of the Head and Neck	Drug: SNS-301|Drug: Pembrolizumab	https://ClinicalTrials.gov/show/NCT04034225
NCT01020396	Bioequivalence of Metronidazole Gel, 0.75% in the Treatment of Bacterial Vaginosis	Bacterial Vaginosis	Drug: Metronidazole	https://ClinicalTrials.gov/show/NCT01020396
NCT01906632	Gene Expression Profiling of Malignant Tumor Predict the Therapeutic Response of DC-CIK Immunotherapy	Malignant Tumor	Biological: DC-CIK Immunotherapy	https://ClinicalTrials.gov/show/NCT01906632
NCT03325465	Neoadjuvant Pembrolizumab + Epacadostat Prior to Curative Surgical Care for Squamous Cell Carcinoma of the Head and Neck	Squamous Cell Carcinoma of the Head and Neck	Drug: Pembrolizumab|Drug: Epacadostat	https://ClinicalTrials.gov/show/NCT03325465
NCT00894842	Study of a Neurocognition Enhancing Agent in Patients With Schizophrenia	Schizophrenia	Drug: Pregnenolone|Drug: Placebo	https://ClinicalTrials.gov/show/NCT00894842
NCT04337515	A Feasibility Study Using CLINIMACSÂ® for Alpha/Beta T-Cell Depletion in Stem Cell Transplant	Graft Vs Host Disease|Graft-versus-host-disease	Device: CliniMacsÂ®	https://ClinicalTrials.gov/show/NCT04337515
NCT03397355	Monitoring the Changes of Tumor-related Biomarkers Before and After Pulmonary Nodule Biopsy.	Lung Cancer		https://ClinicalTrials.gov/show/NCT03397355
NCT03070392	Safety and Efficacy of IMCgp100 Versus Investigator Choice in Advanced Uveal Melanoma	Uveal Melanoma	Biological: IMCgp100|Drug: Dacarbazine|Biological: Ipilimumab|Biological: Pembrolizumab	https://ClinicalTrials.gov/show/NCT03070392
NCT04206943	Study of CD19 Specific Chimeric Antigen Receptor Positive T Cells (CAR-T) in ALL and NHL	Acute Lymphoblastic Leukemia|Non Hodgkin Lymphoma	Biological: Car-T Cell Therapy	https://ClinicalTrials.gov/show/NCT04206943
NCT04406272	V8-111 in Surgically Accessible Recurrent/Progressive GBM	Glioblastoma|Recurrent Glioblastoma	Drug: VB11|Procedure: Surgery|Other: Placebo|Drug: Bevacizumab	https://ClinicalTrials.gov/show/NCT04406272
NCT04691713	CD276 CAR-T for Patients With Advanced CD276+ Solid Tumors	CAR|Solid Tumor	Drug: Targeting CD276 autologous chimeric antigen receptor T cells	https://ClinicalTrials.gov/show/NCT04691713
NCT04691349	CAR-T for r/r Malignant Tumors in Children	CAR-T|Child, Only|Malignant Tumor	Drug: CAR-T	https://ClinicalTrials.gov/show/NCT04691349
NCT03132922	MAGE-A4á¶ceÂ¹Â°Â³Â²T for Multi-Tumor	Urinary Bladder Cancer|Melanoma|Head and Neck Cancer|Ovarian Cancer|Non-Small Cell Lung Cancer|Esophageal Cancer|Gastric Cancer|Synovial Sarcoma|Myxoid Round Cell Liposarcoma|Gastroesophageal Junction	Genetic: Autologous genetically modified MAGE-A4á¶ceÂ¹Â°Â³Â²T cells|Radiation: Autologous genetically modified MAGE-A4c1032T cells combined with low dose radiation	https://ClinicalTrials.gov/show/NCT03132922
NCT02370212	Interval Training Plus Creatine Effects on Performance and Glucose Tolerance	Healthy	Dietary Supplement: Creatine|Dietary Supplement: Placebo|Other: High intensity interval training	https://ClinicalTrials.gov/show/NCT02370212

FIG. 20-30

NCT Number	Title	Conditions	Interventions	URL
NCT04405154	A Study of Concomitant Camrelizumab With Chemoradiation for Locally Advanced Head and Neck Cancer	Head and Neck Neoplasms	Biological: Camrelizumab | Drug: Cisplatin | Radiation: IMRT or VMAT	https://ClinicalTrials.gov/show/NCT04405154
NCT00871481	Laboratory-Treated T Cells and Ipilimumab in Treating Patients With Metastatic Melanoma	Recurrent Melanoma | Stage IV Melanoma	Biological: ipilimumab | Drug: cyclophosphamide | Procedure: biopsy | Biological: aldesleukin | Other: immunohistochemistry staining method | Genetic: polymerase chain reaction | Other: immunoenzyme technique | Biological: therapeutic cytotoxic T lymphocytes	https://ClinicalTrials.gov/show/NCT00871481
NCT01077531	Safety, Pharmacodynamics and Pharmacokinetics of GSK2136525 Repeat Dose in Rheumatoid Arthritis	Arthritis, Rheumatoid	Drug: Otelixizumab | Drug: Matching placebo	https://ClinicalTrials.gov/show/NCT01077531
NCT03619551	Conditioning SCID Infants Diagnosed Early	SCID	Drug: Busulfan | Device: Cell processing for TCRÎ±Î²+/CD19+ depletion	https://ClinicalTrials.gov/show/NCT03619551
NCT04844489	Study of the Humoral Response to SARS-CoV-2 Variants and of the Cellular Response After Vaccination Against COVID-19 in Immunocompromised People	Autoimmune or Autoinflammatory Diseases | HIV | Multiple Sclerosis | Solid Tumors or Cancers | Solid Organ Transplant	Other: Blood samples for the study of the humoral response to SARS-CoV-2 variants and of the cellular response after vaccination against COVID-19	https://ClinicalTrials.gov/show/NCT04844489
NCT01863888	Effect of Teriflunomide on Immune Cell Subsets in the Blood of Patients With Multiple Sclerosis	Multiple Sclerosis	Drug: teriflunomide HMR1726 | Drug: cholestyramine | Drug: charcoal	https://ClinicalTrials.gov/show/NCT01863888
NCT01430390	In Vitro Expanded Allogeneic Epstein-Barr Virus Specific Cytotoxic T-Lymphocytes (EBV-CTLs) Genetically Targeted to the CD19 Antigen in B-cell Malignancies	Acute Lymphocytic Leukemia | Lymphoma	Biological: Biological/Genetically Modified T cells | Drug: Cyclophosphamide-based chemotherapy	https://ClinicalTrials.gov/show/NCT01430390
NCT03335605	Improving the Diagnosis of Common Variable Immune Deficiency	CVI - Common Variable Immunodeficiency		https://ClinicalTrials.gov/show/NCT03335605
NCT03340155	Mechanisms of Action of Photo(Chemo)Therapy in Skin Diseases	Psoriasis | Cutaneous T Cell Lymphoma | Lymphoproliferative Disorders | Eczema | Lichen Planus | Prurigo | Pruritus | Polymorphic Light Eruption | Graft Vs Host Disease | Mastocytosis | Vitiligo	Other: Photo(chemo)therapy	https://ClinicalTrials.gov/show/NCT03340155
NCT04523376	Pilot Study P8SCT With TCRab Depletion For Hemoglobinopathies	Sickle Cell Disease | Thalassemia Major	Device: CliniMACS	https://ClinicalTrials.gov/show/NCT04523376
NCT00113464	Developing Newborn Screening for Infants With Primary Immunodeficiency	Immune System Diseases		https://ClinicalTrials.gov/show/NCT00113464
NCT04913519	A Phase 1 Study of TDM-105795 Topical Solution in Male Subjects With Androgenetic Alopecia (AGA)	Alopecia, Androgenetic	Drug: TDM-105795 | Drug: Placebo	https://ClinicalTrials.gov/show/NCT04913519
NCT01355965	Autologous Redirected RNA Meso-CIR T Cells	Malignant Pleural Mesothelioma	Biological: Autologous T cells	https://ClinicalTrials.gov/show/NCT01355965

FIG. 20-31

NCT Number	Title	Conditions	Interventions	URL
NCT02319226	Toward Immune Biomarkers for Tolerance and GvHD in Humans	Bone Marrow Transplantation|Graft vs Host Disease|Hematopoietic Stem Cell Transplantation	Other: Transplantation from an HLA-identical sibling donor	https://ClinicalTrials.gov/show/NCT02319226
NCT01440413	Study of the Response to a Neoadjuvant Chemotherapy Based on the Antitumor Immune Response in Localized Breast Cancer	Breast Cancer	Biological: Blood and tumor sample	https://ClinicalTrials.gov/show/NCT01440413
NCT01175239	Gene Therapy for X-linked Severe Combined Immunodeficiency (SCID-X1)	X-linked Severe Combined Immunodeficiency	Genetic: Single infusion of autologous CD34+ cells transduced with the self-inactivating (SIN) gammaretroviral vector pSRS11.EFS.IL2RG.pre	https://ClinicalTrials.gov/show/NCT01175239
NCT03973333	Safety and Efficacy of IMC-C103C as Monotherapy and in Combination With Atezolizumab	Select Advanced Solid Tumors	Drug: IMC-C103C|Drug: Atezolizumab	https://ClinicalTrials.gov/show/NCT03973333
NCT02028819	Compassionate Use of Ibalizumab for the Treatment of HIV Infection	Human Immunodeficiency Virus (HIV)	Drug: Dolutegravir Sodium Monohydrate|Drug: Ibalizumab	https://ClinicalTrials.gov/show/NCT02028819
NCT04195932	Exercise as a Modulator of Immune Risk Factors for Ischemic Heart Disease	Heart Diseases	Other: Exercise training	https://ClinicalTrials.gov/show/NCT04195932
NCT00560794	Phase II Study of the BiTEÂ® Blinatumomab (MT103) in Patients With Minimal Residual Disease of B-precursor Acute Lymphoblastic Leukemia (ALL)	Acute Lymphoblastic Leukemia	Biological: Blinatumomab (MT103)	https://ClinicalTrials.gov/show/NCT00560794
NCT04326751	Evolution of Multiple Primary Lung Cancer (Evolution)	Multiple Primary Lung Cancers|Lung Cancer|Non Small Cell Lung Cancer		https://ClinicalTrials.gov/show/NCT04326751
NCT00845416	Newborn Screening for Severe Combined Immunodeficiency (SCID) in a High-Risk Population	Severe Combined Immunodeficiency|T Cell Lymphocytopenia		https://ClinicalTrials.gov/show/NCT00845416
NCT03587285	A Pilot Study of Hormonal Therapy Combined With Central Memory T Cells (Tcm) for Patients With Advanced Prostate Cancer	Prostatic Neoplasms	Biological: Tcm+ Goserelin acetate+ Bicalutamide|Biological: Tcm+Goserelin acetate+Abiraterone acetate	https://ClinicalTrials.gov/show/NCT03587285
NCT01174875	Growing Up in Singapore Towards Healthy Outcomes	Metabolic Diseases|Neurological and Mental Health Conditions		https://ClinicalTrials.gov/show/NCT01174875
NCT04727151	TAC T-cells for the Treatment of HER2-positive Solid Tumors	HER2-Positive Solid Tumors	Biological: TAC01-HER2	https://ClinicalTrials.gov/show/NCT04727151
NCT03407170	Immunologic Determinants of Response to Pembrolizumab (MK-3475) in Advanced Melanoma (MK-3475-161/KEYNOTE-161)	Advanced Melanoma	Biological: pembrolizumab	https://ClinicalTrials.gov/show/NCT03407170
NCT04864379	Clinical Study of a Personalized Neoantigen Cancer Vaccine Combined With Anti-PD-1 and RFA in Patients With Solid Tumors	Advanced Malignant Solid Tumor	Biological: iNeo-Vac-P01|Other: GM-CSF|Drug: PD-1|Procedure: RFA	https://ClinicalTrials.gov/show/NCT04864379
NCT03880279	Autologous TAC T Cells Targeting CD19 in R/R Large B-Cell Lymphoma	Lymphoma, B-Cell	Biological: TAC01-CD19	https://ClinicalTrials.gov/show/NCT03880279
NCT04134325	Study of PD-1 Inhibitors After CD30.CAR T Cell Therapy in Relapsed/Refractory Hodgkin Lymphoma	Relapsed Hodgkin Lymphoma|Refractory Hodgkin Lymphoma	Biological: Nivolumab|Biological: Pembrolizumab	https://ClinicalTrials.gov/show/NCT04134325

FIG. 20-32

NCT Number	Title	Conditions	Interventions	URL
NCT04354038	Host and Bacterial Mechanisms During Cystic Fibrosis Pulmonary Exacerbations	Cystic Fibrosis		https://ClinicalTrials.gov/show/NCT04354038
NCT03697824	Clinical Trial of Safety, Tolerability and Antitumor Activity of Genetically Engineered T Cells in Combination With Anti-Cancer Agents in Relapsed and Refractory Synovial Sarcoma Expressing New York Esophageal Antigen-1 (NY-ESO-1) and/or LAGE-1a	Neoplasms	Drug: GSK3377794|Drug: Pembrolizumab|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03697824
NCT02799901	Nivolumab Plus Radiotherapy in Advanced Melanoma	Melanoma	Biological: Nivolumab|Radiation: hypofractionned radiotherapy	https://ClinicalTrials.gov/show/NCT02799901
NCT00545493	Efficacy of Tacrolimus and I.V.-Immunoglobulins in Rasmussen Encephalitis	Rasmussen Encephalitis	Drug: Tacrolimus|Drug: i.v. immunoglobulins	https://ClinicalTrials.gov/show/NCT00545493
NCT03802955	Study of ADG106 With Advanced or Metastatic Solid Tumors and/or Non-Hodgkin Lymphoma	Solid Tumor|Non-Hodgkin Lymphoma	Drug: ADG106	https://ClinicalTrials.gov/show/NCT03802955
NCT00694551	PSMA and TARP Peptide Vaccine With Poly IC-LC Adjuvant in HLA-A2 (+) Patients With Elevated PSA After Initial Definitive Treatment	Prostate Cancer	Biological: Peptide Vaccine|Drug: Poly IC-LC	https://ClinicalTrials.gov/show/NCT00694551
NCT03707093	Study of CD137 Agonist ADG106 With Advanced or Metastatic Solid Tumors and/or Non-Hodgkin Lymphoma	Solid Tumors, Non-Hodgkin Lymphoma	Drug: ADG106	https://ClinicalTrials.gov/show/NCT03707093
NCT04145232	Aimmune - Artificial Intelligence Algorithm for Identification of Immunogenic Neoepitopes of Cancer to Predict and Boost Patient's Response to Immunotherapies.	Non Small Cell Lung Cancer|Neoepitopes|Neoantigens|Immunotherapy|Next Generation Sequencing (NGS)|Personalized Neoantigen Cancer Vaccine	Biological: Collection of biopsy (FFPE), blood (PBMC) and stool	https://ClinicalTrials.gov/show/NCT04145232
NCT03878589	Understanding Cognition, Oxytocin & Pain in Elders	Knee Osteoarthritis|Osteoarthritis	Drug: Oxytocin (OT)|Drug: Placebo (P)	https://ClinicalTrials.gov/show/NCT03878589
NCT00785967	Immune Responses in Patients Treated With Raltegravir	HIV Infections	Biological: Various vaccines	https://ClinicalTrials.gov/show/NCT00785967
NCT04397900	Blood Collection Study From COVID-19 Convalescents Previously Hospitalized to Identify Immunogenic Viral Epitopes	Identify the Viral Epitopes of Memory CD8 T Cells From Individuals That Have Recovered From SARS-CoV-2 Infection|Determine Which SARS-CoV-2 Proteins Are Frequently Recognized by T Cells in Patients With Varying HLA Types		https://ClinicalTrials.gov/show/NCT04397900

FIG. 20-33

NCT Number	Title	Conditions	Interventions	URL
NCT02706392	Genetically Modified T-Cell Therapy in Treating Patients With Advanced ROR1+ Malignancies	Lymphoid Cell Neoplasm|Malignant Solid Neoplasm|Metastatic Lung Non-Small Cell Carcinoma|Metastatic Triple-Negative Breast Carcinoma|Recurrent Acute Lymphoblastic Leukemia|Recurrent Mantle Cell Lymphoma|Refractory Chronic Lymphocytic Leukemia|Stage III Lung Non-Small Cell Cancer AJCC v7|Stage IIIA Lung Non-Small Cell Cancer AJCC v7|Stage IIIB Lung Non-Small Cell Cancer AJCC v7|Stage IV Breast	Other: Laboratory Biomarker Analysis|Biological: ROR1 CAR-specific Autologous T-Lymphocytes	https://ClinicalTrials.gov/show/NCT02706392
NCT03904069	Study Evaluating the Safety, Tolerability, and Efficacy of FLT3 CAR-T AMG 553 in FLT3-positive Relapsed/Refractory AML	Relapsed/Refractory Acute Myeloid Leukemia	Drug: AMG 553	https://ClinicalTrials.gov/show/NCT03904069
NCT02210741	Next-generation Sequencing (NGS) of Peripheral Blood Immune Repertoire in Graves' Disease	Graves Disease		https://ClinicalTrials.gov/show/NCT02210741
NCT04362293	Reduced Intensity Transplantation for Severe Sickle Cell Disease	Sickle Cell Disease	Drug: hydroxyurea, azathioprine, alemtuzumab, thioptepa, low dose total body irradiation and sirolimus|Drug: hydroxyurea, azathioprine, alemtuzumab, thiotepa, plerixafor, low dose total body irradiation, cyclophosphamide and sirolimus	https://ClinicalTrials.gov/show/NCT04362293
NCT01260532	The Association of Costimulatory Molecules and PPAR-polymorphisms With Autoimmune Thyroid Disease in Taiwan	AITd Patients With Different Polymorphisms		https://ClinicalTrials.gov/show/NCT01260532
NCT00001688	A Pilot Study of the Immunologic Reconstitution in HIV-1 Infected Children Receiving Highly Active Antiretroviral Therapy With Combination Ritonavir, Nevirapine and Stavudine	HIV Infection	Drug: Ritonavir|Drug: Nevirapine|Drug: Stavudine	https://ClinicalTrials.gov/show/NCT00001688
NCT04340401	Total Neoadjuvant Treatment Plus SHR1210 for High-risk Rectal Cancer and Biomarker Screening Base on Neoantigen	Rectal Cancer	Drug: SHR-1210|Drug: Oxaliplatin|Drug: Capecitabine|Radiation: Intensity modulated radiotherapy|Procedure: Total mesorectal excision	https://ClinicalTrials.gov/show/NCT04340401
NCT00081783	Xcellerated T CellsTM for Non-Hodgkin's Lymphoma (NHL) Patients	Non-Hodgkin's Lymphoma	Drug: Xcellerated T Cells	https://ClinicalTrials.gov/show/NCT00081783
NCT00327496	Cytotoxicity Induced by Tumor Lysate Pulsed Dendritic Cells Against Autologous Hepatocellular Carcinoma Cells	Carcinoma, Hepatocellular	Biological: DC vaccine	https://ClinicalTrials.gov/show/NCT00327496

FIG. 20-34

NCT Number	Title	Conditions	Interventions	URL
NCT01410019	Gene Therapy for X-linked Severe Combined Immunodeficiency	X-linked Severe Combined Immunodeficiency	Other: Gene transfer	https://ClinicalTrials.gov/show/NCT01410019
NCT04065776	Evaluation of Hippocampal-Avoidance Using Proton Therapy in Low-Grade Glioma	Glioma|Pilocytic Astrocytoma|Pilomyxoid Astrocytoma|Pleomorphic Xanthoastrocytoma|Ganglioglioma|Optic Pathway Glioma|Diffuse Astrocytoma	Radiation: Hippocampal-avoidance proton therapy	https://ClinicalTrials.gov/show/NCT04065776
NCT00678886	Trial of Otelixizumab for Adults With Newly Diagnosed Type 1 Diabetes Mellitus (Autoimmune): DEFEND-1	Diabetes Mellitus, Type 1	Biological: otelixizumab infusion plus physician determined standard of care|Biological: placebo infusion plus physician determined standard of care	https://ClinicalTrials.gov/show/NCT00678886
NCT04422314	ImmuneSense Lyme Study	Lyme Disease	Diagnostic Test: T-Detect Lyme	https://ClinicalTrials.gov/show/NCT04422314
NCT04482699	RAPA-501-Allo Therapy of COVID-19-ARDS	Severe COVID-19 Disease	Biological: RAPA-501-Allo off-the-shelf Therapy of COVID-19|Other: Placebo	https://ClinicalTrials.gov/show/NCT04482699
NCT04207320	Haploidentical Hematopoietic Stem Cell Transplantation (HSCT) for Patients With Severe Sickle Cell Disease	Sickle Cell Disease	Device: İ±Î²+ T-cell depletion with Miltenyi CliniMACS system	https://ClinicalTrials.gov/show/NCT04207320
NCT02219165	Efficacy of IntraVenous ImmunoGlobulins in Toxic Shock Syndromes: a Paediatric Pilot Study	Toxic Shock Syndrome	Drug: Intravenous human immunoglobulin|Drug: Albumin	https://ClinicalTrials.gov/show/NCT02219165
NCT02466217	Phenomics in Autoimmune and Inflammatory Diseases	Healthy Volunteer|Rheumatoid Arthritis|Ankylosing Spondylitis|Systemic Lupus Erythematosus/Antiphospholipid Syndrome|FMF|Cryopyrin-Associated Periodic Syndromes/TNF-receptor Associated Periodic Syndrome|Vasculitis|Uveitis|Myositis|Crohn's Disease|Ulcerative Rectocolitis|Type 1 Diabetes|Unclassified IAD Knee and/or Hip Arthritis, Muscular Dystrophy	Other: 1: AID groups|Other: 2: Control groups	https://ClinicalTrials.gov/show/NCT02466217
NCT02889016	Neurobiologic, Immunologic, and Rheumatologic Markers in Youth With PANS	Pediatric Acute-Onset Neuropsychiatric Syndrome|Pediatric Autoimmune Neuropsychiatric Disorders Associated With Streptococcal Infections|PANS|PANDAS		https://ClinicalTrials.gov/show/NCT02889016
NCT00342134	Immunological Mechanisms of Hematopoietic Stem Cell Transplantation in Multiple Sclerosis	Multiple Sclerosis	Procedure: Stem Cell Transplanataion	https://ClinicalTrials.gov/show/NCT00342134

FIG. 20-35

NCT Number	Title	Conditions	Interventions	URL
NCT01982487	Vaccine Therapy and IDO1 Inhibitor INCB024360 in Treating Patients With Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer Who Are in Remission	Tube Cancer|Recurrent Ovarian Epithelial Cancer|Recurrent Primary Peritoneal Cavity Cancer|Stage IA Fallopian Tube Cancer|Stage IA Ovarian Epithelial Cancer|Stage IA Primary Peritoneal Cavity Cancer|Stage IB Fallopian Tube Cancer|Stage IB Ovarian Epithelial Cancer|Stage IB Primary Peritoneal Cavity Cancer|Stage IC Fallopian Tube Cancer|Stage IC Ovarian Epithelial Cancer|Stage IC Primary Peritoneal Cavity	Biological: ALVAC(2)-NY-ESO-1 (M)/TRICOM vaccine|Drug: IDO1 inhibitor INCB024360|Other: laboratory biomarker analysis|Other: pharmacological study	https://ClinicalTrials.gov/show/NCT01982487
NCT02166905	DEC-205/NY-ESO-1 Fusion Protein CDX-1401, Poly ICLC, and IDO1 Inhibitor INCB024360 in Treating Patients With Ovarian, Fallopian Tube, or Primary Peritoneal Cancer in Remission	Fallopian Tube Carcinoma|Ovarian Carcinoma|Primary Peritoneal Carcinoma	Biological: DEC-205/NY-ESO-1 Fusion Protein CDX-1401|Drug: Epacadostat|Other: Laboratory Biomarker Analysis|Other: Pharmacological Study|Drug: Poly ICLC	https://ClinicalTrials.gov/show/NCT02166905
NCT02535078	Phase 1b/2 Study of the Combination of IMCgp100 With Durvalumab and/or Tremelimumab in Cutaneous Melanoma	Malignant Melanoma	Drug: IMCgp100|Drug: durvalumab|Drug: tremelimumab	https://ClinicalTrials.gov/show/NCT02535078
NCT04658303	Evolution of Metabolic and Immune Dysfunction in In-transit Melanoma	Melanoma	Other: Pimonidazole	https://ClinicalTrials.gov/show/NCT04658303
NCT00001941	Anti-Tac for Treatment of Leukemia	HTLV-I Infection|T Cell Leukemia	Biological: daclizumab	https://ClinicalTrials.gov/show/NCT00001941
NCT02618109	Identification of New Immune Factors Specific of Relapse in Childhood B Lineage Acute Lymphoblastic Leukemia	B Acute Lymphoblastic Leukemia|Leukemia Relapse	Biological: Collection of blood samples	https://ClinicalTrials.gov/show/NCT02618109
NCT03948763	A Study of mRNA-5671/V941 as Monotherapy and in Combination With Pembrolizumab (V941-001)	Neoplasms|Carcinoma, Non-Small-Cell Lung|Pancreatic Neoplasms|Colorectal Neoplasms	Biological: V941|Biological: Pembrolizumab	https://ClinicalTrials.gov/show/NCT03948763
NCT02761122	Implication of Human Papillomavirus (HPV) in Lichen Physiopathology in Human (HPVLichen)	Lichen Planus	Procedure: Human biological samples	https://ClinicalTrials.gov/show/NCT02761122
NCT01744223	Safety Study of Gene Modified Donor T-cells Following Partially Mismatched Stem Cell Transplant	Acute Lymphoblastic Leukemia|Acute Myelogenous Leukemia|Lymphoma|Myelodysplastic Syndromes	Biological: BPX-501 dose 1|Drug: Rimiducid|Biological: BPX-501 dose 2|Biological: BPX-501 dose 3|Biological: BPX-501 dose 4|Procedure: SCT	https://ClinicalTrials.gov/show/NCT01744223

FIG. 20-36

NCT Number	Title	Conditions	Interventions	URL
NCT00839436	Interleukin-7 (CYT107) Treatment of Idiopathic CD4 Lymphocytopenia: Expansion of CD4 T Cells (ICICLE)	Idiopathic CD4+ T-Lymphocytopenia	Drug: CYT107	https://ClinicalTrials.gov/show/NCT00839436
NCT04451980	The HIV, Adipose Tissue Immunology, and Metabolism Study	Hiv|Diabetes Mellitus, Type 2	Procedure: Subcutaneous adipose tissue biopsy|Radiation: CT scan|Diagnostic Test: Oral glucose tolerance test|Diagnostic Test: Blood collection	https://ClinicalTrials.gov/show/NCT04451980
NCT04369963	The Healthy Endoscopy Study	Inflammatory Bowel Diseases|Functional Gastrointestinal Disorders	Procedure: Esophagogastroduodenoscopy and Colonoscopy with Biopsies	https://ClinicalTrials.gov/show/NCT04369963
NCT00924001	Chemotherapy Followed by Infusion of DMF5 Cells to Treat Metastatic Melanoma	Melanoma|Malignant Melanoma|Melanoma, Experimental	Drug: DMF5 Melanoma Reactive TIL|Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Aldesleukin	https://ClinicalTrials.gov/show/NCT00924001
NCT03578185	Genomic Analysis to Identify a Predictive Biomarker for Immunotherapy	Lung Cancer		https://ClinicalTrials.gov/show/NCT03578185
NCT01883804	Effect of Methyldopa on MHC Class II Antigen Presentation in Type 1 Diabetes	Diabetes Mellitus, Type 1	Drug: Methyldopa	https://ClinicalTrials.gov/show/NCT01883804
NCT04697940	Decitabine-primed Tandem CD19/CD20 CAR T Cells Treatment in r/r B-NHL	Relapase and Refractory B-cell Non-Hodgkin's Lymphoma|Decitabine-primed Tandem CD19/CD20 CAR T Cells	Biological: Decitabine-primed Tandem CAR19/20 engineered T cells	https://ClinicalTrials.gov/show/NCT04697940
NCT00213629	myoARRAY and TcLandscape Analysis for the Diagnosis of Inflammatory Myopathies	Polymyositis|Dermatomyositis	Other: transcriptome analysis|Other: T cell repertoire analysis	https://ClinicalTrials.gov/show/NCT00213629
NCT01192464	EBV CTLs Expressing CD30 Chimeric Receptors For CD 30+ Lymphoma	Hodgkin's Lymphoma|Non-Hodgkin's Lymphoma	Drug: autologous CAR.CD30 EBV specific-CTLs	https://ClinicalTrials.gov/show/NCT01192464
NCT00597441	Phase I Study of Umbilical Cord Blood Transplantation Followed by Third Party Thymus Transplantation	Stem Cell Transplantation	Biological: Thymic Transplantation for Recipients of UCB transplant	https://ClinicalTrials.gov/show/NCT00597441
NCT01413022	FOLFIRINOX Plus PF-04136309 in Patients With Borderline Resectable and Locally Advanced Pancreatic Adenocarcinoma	Pancreatic Neoplasms	Drug: Oxaliplatin|Drug: Irinotecan|Drug: Leucovorin|Drug: Fluorouracil|Other: laboratory biomarker analysis|Other: flow cytometry|Other: immunohistochemistry staining method|Other: pharmacological study|Drug: PF-04136309	https://ClinicalTrials.gov/show/NCT01413022
NCT03680560	Study of ACTR T Cell Product in Combination With Trastuzumab in Subjects With HER2-Positive Advanced Solid Tumor Cancers	Solid Tumor|HER-2 Protein Overexpression	Biological: ACTR T Cell Product|Drug: Trastuzumab	https://ClinicalTrials.gov/show/NCT03680560
NCT01114503	A Safety and Tolerability Study of Otelixizumab in Thyroid Eye Disease	Graves Ophthalmopathy	Drug: Otelixizumab - low dose|Drug: Otelixizumab - medium low dose|Drug: Otelixizumab - medium high dose|Drug: Otelixizumab - high dose|Drug: Otelixizumab|Drug: Methylprednisolone	https://ClinicalTrials.gov/show/NCT01114503
NCT04549142	Immune Tolerance Dysfunction in Pregnancy Due to Ambient Air Pollution Exposure	Air Pollution|Pregnancy	Other: There is no intervention	https://ClinicalTrials.gov/show/NCT04549142

FIG. 20-37

NCT Number	Title	Conditions	Interventions	URL
NCT00324623	Cyclophosphamide and Fludarabine Followed by Cellular Adoptive Immunotherapy and Vaccine Therapy in Patients With Metastatic Melanoma	Melanoma (Skin)	Biological: Melan-A VLP vaccine, IMP321 adjuvant|Biological: adoptive immunotherapy|Biological: therapeutic autologous lymphocytes|Drug: cyclophosphamide|Drug: fludarabine phosphate	https://ClinicalTrials.gov/show/NCT00324623
NCT04354584	Compartmental Inflammation in Mechanically Ventilated Patients With COVID-19	COVID-19|Respiratory Failure		https://ClinicalTrials.gov/show/NCT04354584
NCT00379119	Effect of Androgen Blockade Therapy on Thymus Function in Older Patients Who Have Undergone Radical Prostatectomy for Localized Prostate Cancer	Prostate Cancer	Other: diagnostic laboratory biomarker analysis|Other: flow cytometry|Other: physiologic testing|Procedure: computed tomography	https://ClinicalTrials.gov/show/NCT00379119
NCT00471887	Ticilimumab (CP-675,206) in Treating Patients With Stage IIIC or Stage IV Melanoma	Melanoma (Skin)	Biological: CP-675,206	https://ClinicalTrials.gov/show/NCT00471887
NCT03795610	Window of Opportunity Study of IPI-549 in Patients With Locally Advanced HPV+ and HPV- Head and Neck Squamous Cell Carcinoma	Head and Neck Squamous Cell Carcinoma|Head and Neck Cancer|Head and Neck Carcinoma|Head and Neck Cancer Stage IV|Head and Neck Cancer Stage III|HPV-Related Carcinoma|HPV-Related Malignancy|HPV-Related Squamous Cell Carcinoma	Drug: IPI-549	https://ClinicalTrials.gov/show/NCT03795610
NCT04903795	Bispecific T Cell Engager BRiTE for Patients With Grade IV Malignant Glioma	Malignant Glioma|Glioblastoma	Drug: hEGFRvIII-CD3 (BRiTE)|Biological: Activated Cell Therapy	https://ClinicalTrials.gov/show/NCT04903795
NCT03396575	Brain Stem Gliomas Treated With Adoptive Cellular Therapy During Focal Radiotherapy Recovery Alone or With Dose-intensified Temozolomide (Phase I)	Diffuse Intrinsic Pontine Glioma (DIPG)|Brain Stem Glioma	Biological: TTRNA-DC vaccines with GM-CSF|Biological: TTRNA-xALT|Drug: Cyclophosphamide + Fludarabine Lymphodepletive Conditioning|Drug: Dose-Intensified TMZ|Drug: Td vaccine|Biological: Autologous Hematopoietic Stem Cells (HSC)	https://ClinicalTrials.gov/show/NCT03396575
NCT03129061	Study to Evaluate Immunological Response to PD-1 Inhibition in Squamous Cell Carcinoma of the Head and Neck (SCCHN)	Squamous Cell Carcinoma of the Head and Neck	Drug: [18F]F-AraG PET Scan, baseline + post anti-PD-1 therapy.	https://ClinicalTrials.gov/show/NCT03129061
NCT00520130	Chemotherapy and Unrelated Donor Stem Cell Transplantation for Patients With Cancers of the Blood and Immune System	Myelodysplastic Syndrome|Hodgkin's Lymphoma|Non-Hodgkin's Disease|Acute Leukemia|Multiple Myeloma	Biological: Rituximab|Drug: Cyclosporine|Drug: Allogenic stem cell transplant (ASCT)|Drug: Conditioning Chemotherapy|Drug: TMS|Drug: FLAG|Drug: EPOCH-F|Biological: Alemtuzumab	https://ClinicalTrials.gov/show/NCT00520130

FIG. 20-38

NCT Number	Title	Conditions	Interventions	URL
NCT04445844	INCMGA00012 and Pelareorep for the Treatment of Metastatic Triple Negative Breast Cancer, IRENE Study	Anatomic Stage IV Breast Cancer AJCC v8|Locally Advanced Breast Carcinoma|Metastatic Triple-Negative Breast Carcinoma|Prognostic Stage IV Breast Cancer AJCC v8|Triple-negative Breast Cancer	Biological: Pelareorep|Other: Quality-of-Life Assessment|Other: Questionnaire Administration|Biological: Retifanlimab	https://ClinicalTrials.gov/show/NCT04445844
NCT02846376	Single Agent and Combined Inhibition After Allogeneic Stem Cell Transplant	Acute Myeloid Leukemia and Myelodysplastic Syndrome	Drug: Nivolumab|Drug: Ipilimumab	https://ClinicalTrials.gov/show/NCT02846376
NCT03159845	Zinc as Enhancer in Immune Recovery After Stem Cell Transplantation for Hematological Malignancies	Stem Cell Transplant Complications	Drug: Zinc Sulfate Oral Product|Drug: Levofloxacin 500Mg Oral Tablet|Drug: Fluconazole 200mg tab|Drug: Acyclovir 400 MG	https://ClinicalTrials.gov/show/NCT03159845
NCT04792437	Research on Precise Immune Prevention and Treatment of Glioma Based on Multi-omics Sequencing Data	Transcriptomics|Radiomics|Glioma	Procedure: surgery	https://ClinicalTrials.gov/show/NCT04792437
NCT01911065	T Cell Responses to Varicella Zoster Virus (VZV) Vaccine SLVP020	Herpes Zoster	Biological: Zostavaxâ„¢	https://ClinicalTrials.gov/show/NCT01911065
NCT01583972	Efficacy of Newborn Vitamin A Supplementation in Improving Immune Function	Vitamin A Deficiency	Dietary Supplement: retinyl palmitate|Dietary Supplement: Placebo	https://ClinicalTrials.gov/show/NCT01583972
NCT04224558	Stem Cell Transplantation in Crohn's Disease	Crohn Disease	Drug: Mesna|Drug: Cyclophosphamide|Drug: Filgrastim|Procedure: Apheresis catheter placement|Procedure: Leukapheresis|Drug: Fludarabine|Drug: Methylprednisolone|Drug: Diphenhydramine|Drug: Acetaminophen|Drug: anti-thymocyte globulin (rabbit)|Drug: lymphocyte immune globulin|Biological: Peripheral Blood Stem Cell Infusion|Drug: Cytoxan	https://ClinicalTrials.gov/show/NCT04224558
NCT00439465	Adoptive Cellular Immunotherapy Following Autologous Peripheral Blood Stem Cell Transplantation for Multiple Myeloma	Myeloma|Transplant-eligible Patients	Biological: Ex-vivo expanded effector cells	https://ClinicalTrials.gov/show/NCT00439465
NCT04626440	Research on the Heterogeneity of Taiwanese Breast Cancer Patients by Next Generation Sequencing (NGS) Tools	Next Generation Sequencing (NGS)|Breast Cancer	Procedure: Diagnostic stage or the Clinical outcome	https://ClinicalTrials.gov/show/NCT04626440
NCT03877250	Analysis of Biopsy Specimens to Study Responses to PD-1 or PD-L1 Therapies	Non Small Cell Lung Cancer	Diagnostic Test: Pre-Treatment Biopsy|Diagnostic Test: On-Treatment Biopsy|Diagnostic Test: Biopsy at Disease Progression|Diagnostic Test: Peripheral Blood-Based Studies	https://ClinicalTrials.gov/show/NCT03877250
NCT03601286	Lentiviral Gene Therapy for X-linked Severe Combined Immunodeficiency	Severe Combined Immunodeficiency, X-Linked	Drug: Lentiviral vector transduced CD34+ cells	https://ClinicalTrials.gov/show/NCT03601286

FIG. 20-39

NCT Number	Title	Conditions	Interventions	URL
NCT00621452	Genetically Engineered Lymphocytes, Cyclophosphamide, and Aldesleukin in Treating Patients With Relapsed or Refractory Mantle Cell Lymphoma or Indolent B-Cell Non-Hodgkin Lymphoma	Lymphocytic Leukemia|Extranodal Marginal Zone B-cell Lymphoma of Mucosa-associated Lymphoid Tissue|Nodal Marginal Zone B-cell Lymphoma|Recurrent Grade 1 Follicular Lymphoma|Recurrent Grade 2 Follicular Lymphoma|Recurrent Mantle Cell Lymphoma|Recurrent Marginal Zone Lymphoma|Recurrent Small Lymphocytic Lymphoma|Refractory Chronic Lymphocytic Leukemia|Splenic Marginal Zone	Biological: therapeutic autologous lymphocytes|Drug: cyclophosphamide|Biological: aldesleukin|Genetic: polymerase chain reaction|Genetic: gene rearrangement analysis|Procedure: lymph node biopsy|Biological: genetically engineered lymphocyte therapy|Procedure: bone marrow aspiration|Other: flow cytometry|Other: laboratory biomarker analysis|Other: enzyme-linked immunosorbent assay	https://ClinicalTrials.gov/show/NCT00621452
NCT04708535	Adaptive Immune Response in Visceral and Subcutaneous Fat: Role in Human Insulin Resistance	Insulin Resistance|Insulin Sensitivity|Obesity|Inflammation		https://ClinicalTrials.gov/show/NCT04708535
NCT01670994	QUILT-3.020: A Study of ALT-801 in Patients With Relapsed or Refractory Multiple Myeloma	Relapsed or Refractory Multiple Myeloma	Biological: ALT-801	https://ClinicalTrials.gov/show/NCT01670994
NCT01625260	A Study of ALT-801 in Patients With Bacillus Calmette-Guerin (BCG) Failure Non-Muscle Invasive Bladder Cancer	Non-muscle Invasive Bladder Cancer	Biological: ALT-801|Drug: Gemcitabine	https://ClinicalTrials.gov/show/NCT01625260
NCT02055196	Genetically Modified Stem Cells and Irinotecan Hydrochloride in Treating Patients With Recurrent High-Grade Gliomas	Adult Anaplastic Astrocytoma|Adult Anaplastic Oligodendroglioma|Adult Giant Cell Glioblastoma|Adult Glioblastoma|Adult Gliosarcoma|Recurrent Adult Brain Tumor	Biological: carboxylesterase-expressing allogeneic neural stem cells|Drug: irinotecan hydrochloride|Other: laboratory biomarker analysis	https://ClinicalTrials.gov/show/NCT02055196
NCT01326871	A Study of ALT-801 in Combination With Cisplatin and Gemcitabine in Muscle Invasive or Metastatic Urothelial Cancer	Transitional Cell Carcinoma of Bladder|Urethra Cancer|Ureter Cancer|Malignant Tumor of Renal Pelvis	Drug: Cisplatin|Drug: Gemcitabine|Biological: ALT-801	https://ClinicalTrials.gov/show/NCT01326871
NCT01029873	QUILT-2.008: Study of ALT-801 With Cisplatin in Patients With Metastatic Melanoma	Metastatic Melanoma	Drug: Cisplatin|Biological: ALT-801	https://ClinicalTrials.gov/show/NCT01029873
NCT00496860	Safety and Efficacy Study of ALT-801 to Treat Progressive Metastatic Malignancies	Progressive Metastatic Malignancies	Biological: ALT-801	https://ClinicalTrials.gov/show/NCT00496860

FIG. 20-40

NCT Number	Title	Conditions	Interventions	URL
NCT02737046	Belinostat Therapy With Zidovudine for Adult T-Cell Leukemia-Lymphoma	Adult T-cell Leukemia-Lymphoma|ATLL	Drug: Belinostat|Drug: Zidovudine|Drug: Interferon-Alfa-2b|Drug: Pegylated Interferon-Alfa-2b	https://ClinicalTrials.gov/show/NCT02737046
NCT04562623	Prospective Study of Immune Alterations in Operable Breast and Ovarian Carcinoma	Ovarian Carcinoma|Breast Carcinoma		https://ClinicalTrials.gov/show/NCT04562623
NCT02923180	Neoadjuvant Enoblituzumab (MGA271) in Men With Localized Intermediate and High-Risk Prostate Cancer	Prostate Cancer	Drug: Enoblituzumab	https://ClinicalTrials.gov/show/NCT02923180
NCT03168464	Radiation and Immune Checkpoints Blockade in Metastatic NSCLC (BMS # CA209-632)	Non Small Cell Lung Cancer Metastatic	Drug: Ipilimumab|Drug: Nivolumab|Radiation: Radiation therapy	https://ClinicalTrials.gov/show/NCT03168464
NCT04215471	NeoAdjuvant Therapy With Immunoreagent (SHR-1316) for Resectable Oesophageal Squamous Cell carciNoma	Oesophageal Squamous Cell Carcinoma	Drug: PD-L1 Antibody SHR-1316	https://ClinicalTrials.gov/show/NCT04215471
NCT01750879	Tolerance Following Peanut Oral Immunotherapy	Peanut Allergy	Drug: Peanut Flour|Drug: Oat Flour	https://ClinicalTrials.gov/show/NCT01750879
NCT04052334	Lymphodepletion Plus Adoptive Cell Therapy With High Dose IL-2 in Adolescent and Young Adult Patients With Soft Tissue Sarcoma	Sarcoma	Drug: TIL|Drug: Interleukin-2|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT04052334
NCT01215682	Vitamin D Supplementation and Upper Respiratory Tract Infections in Adolescent Swimmers	Upper Respiratory Tract Infections	Dietary Supplement: vitamin D|Dietary Supplement: placebo	https://ClinicalTrials.gov/show/NCT01215682
NCT04042415	Calorie Restriction in Multiple Sclerosis	Multiple Sclerosis, Relapsing-Remitting|Caloric Restriction	Other: Caloric restriction|Other: Caloric restriction without cow's milk and gluten	https://ClinicalTrials.gov/show/NCT04042415
NCT03491683	INO-5401 and INO-9012 Delivered by Electroporation (EP) in Combination With Cemiplimab (REGN2810) in Newly-Diagnosed Glioblastoma (GBM)	Glioblastoma	Biological: INO-5401|Biological: INO-9012|Biological: Cemiplimab|Radiation: Radiation Therapy|Drug: Temozolomide	https://ClinicalTrials.gov/show/NCT03491683
NCT04355780	Immunologic Features of Respiratory Failure in Pediatric Hematopoietic Cell Transplantation (HCT) Recipients and Pediatric Oncology Patients	Respiratory Failure|Respiratory Disease		https://ClinicalTrials.gov/show/NCT04355780
NCT03168438	Letetresgene Autoleucel Engineered T Cells Alone and in Combination With Pembrolizumab in NY-ESO-1 Positive Multiple Myeloma	Neoplasms	Drug: Letetresgene autoleucel|Drug: Letetresgene autoleucel with pembrolizumab|Drug: Fludarabine|Drug: Cyclophosphamide|Drug: Pembrolizumab	https://ClinicalTrials.gov/show/NCT03168438
NCT02992743	Letetresgene Autoleucel Engineered T Cells in NY-ESO-1 Positive Participants With Advanced Myxoid/ Round Cell Liposarcoma	Neoplasms	Drug: letetresgene autoleucel (GSK3377794)|Drug: Cyclophosphamide|Drug: Fludarabine	https://ClinicalTrials.gov/show/NCT02992743
NCT01827579	Infusion of Depleted T Cells Following Unrelated Donor Stem Cell Transplant (ICAT)	Haematological Malignancies	Biological: CD25/71 allodepleted donor T-cells	https://ClinicalTrials.gov/show/NCT01827579

FIG. 20-41

NCT Number	Title	Conditions	Interventions	URL
NCT02921269	Atezolizumab and Bevacizumab in Treating Patients With Recurrent, Persistent, or Metastatic Cervical Cancer	Cervical Adenocarcinoma|Cervical Adenosquamous Carcinoma|Cervical Squamous Cell Carcinoma, Not Otherwise Specified|Recurrent Cervical Carcinoma|Stage IV Cervical Cancer AJCC v6 and v7|Stage IVA Cervical Cancer AJCC v6 and v7|Stage IVB Cervical Cancer AJCC v6 and v7	Drug: Atezolizumab|Biological: Bevacizumab|Other: Laboratory Biomarker Analysis	https://ClinicalTrials.gov/show/NCT02921269
NCT01339000	Improving the Immune System With Human IL-7 Vaccine in Older Subjects Who Have Had Chemotherapy	Breast Cancer|Colon Cancer|Bladder Cancer	Drug: Glycosylated Recombinant Human Interleukin-7|Biological: Diphtheria/Tetanus Vaccine|Biological: Polio Vaccine|Biological: Pneumococcal Vaccine|Biological: Hepatitis A Vaccine|Biological: Hepatitis B Vaccine	https://ClinicalTrials.gov/show/NCT01339000
NCT03318900	T-Cell Infusion, Aldesleukin, and Utomilumab in Treating Patients With Recurrent Ovarian Cancer	COL6A3 Positive|HLA-A*0201 Positive Cells Present|PRAME Positive|Recurrent Ovarian Carcinoma	Biological: Aldesleukin|Drug: CD8-Positive T-Lymphocyte|Drug: Cyclophosphamide|Procedure: Leukapheresis|Biological: Utomilumab	https://ClinicalTrials.gov/show/NCT03318900
NCT02015819	Genetically Modified Neural Stem Cells, Flucytosine, and Leucovorin for Treating Patients With Recurrent High-Grade Gliomas	Adult Anaplastic Astrocytoma|Adult Anaplastic Oligodendroglioma|Adult Giant Cell Glioblastoma|Adult Glioblastoma|Adult Gliosarcoma|Recurrent Adult Brain Tumor|Anaplastic Oligoastrocytoma	Biological: E. coli CD-expressing genetically modified neural stem cells|Drug: flucytosine|Drug: leucovorin calcium|Other: pharmacological study|Other: laboratory biomarker analysis	https://ClinicalTrials.gov/show/NCT02015819
NCT01446016	Chloroquine With Taxane Chemotherapy for Advanced or Metastatic Breast Cancer After Anthracycline Failure (CAT)	Breast Neoplasms|Breast Cancer	Drug: Taxane|Drug: Docetaxel|Drug: Abraxane|Drug: Ixabepilone	https://ClinicalTrials.gov/show/NCT01446016
NCT03628859	BIOREN (Predictive BIOmarkers in Metastatic RENal Cancer)	Renal Cancer Metastatic	Biological: Immunological and tumour characterization	https://ClinicalTrials.gov/show/NCT03628859

FIG. 20-42

NCT Number	Title	Conditions	Interventions	URL
NCT03425461	Anti-SEMA4D Monoclonal Antibody VX15/2503 With Nivolumab or Ipilimumab in Treating Patients With Stage III or IV Melanoma	Metastatic Melanoma|Stage III Cutaneous Melanoma AJCC v7|Stage IIIA Cutaneous Melanoma AJCC v7|Stage IIIB Cutaneous Melanoma AJCC v7|Stage IIIC Cutaneous Melanoma AJCC v7|Stage IV Cutaneous Melanoma AJCC v6 and v7	Biological: Anti-SEMA4D Monoclonal Antibody VX15/2503|Biological: Ipilimumab|Other: Laboratory Biomarker Analysis|Biological: Nivolumab|Other: Pharmacological Study	https://ClinicalTrials.gov/show/NCT03425461
NCT04588038	NT-I7 for the Treatment of Recurrent Squamous Cell Carcinoma of Head and Neck Undergoing Surgery	Recurrent Head and Neck Squamous Cell Carcinoma|Recurrent Hypopharyngeal Squamous Cell Carcinoma|Recurrent Laryngeal Squamous Cell Carcinoma|Recurrent Oral Cavity Squamous Cell Carcinoma|Recurrent Oropharyngeal Squamous Cell Carcinoma|Resectable Oropharyngeal Squamous Cell Carcinoma	Biological: Efineptakin alfa	https://ClinicalTrials.gov/show/NCT04588038
NCT03584828	Tele-Cardiac Rehabilitation Program	Heart Diseases	Behavioral: Tele Cardiac Rehabilitation	https://ClinicalTrials.gov/show/NCT03584828
NCT04086290	National Danish Protocol. Surgery+ SBRT for M1 Prostate Cancer Patients	Prostate Cancer Metastatic	Procedure: RARP|Radiation: SBRT|Drug: ADT	https://ClinicalTrials.gov/show/NCT04086290
NCT00004918	Vaccine Therapy Plus Immune Adjuvant in Treating Patients With Chronic Myeloid Leukemia, Acute Myeloid Leukemia, or Myelodysplastic Syndrome	Accelerated Phase Chronic Myelogenous Leukemia|Adult Acute Myeloid Leukemia in Remission|Chronic Phase Chronic Myelogenous Leukemia|Previously Treated Myelodysplastic Syndromes|Refractory Anemia With Excess Blasts|Refractory Anemia With Excess Blasts in Transformation|Relapsing Chronic Myelogenous Leukemia	Biological: PR1 leukemia peptide vaccine|Drug: Montanide ISA 51 VG|Biological: sargramostim|Other: laboratory biomarker analysis	https://ClinicalTrials.gov/show/NCT00004918

FIG. 20-43

NCT Number	Title	Conditions	Interventions	URL
NCT03030352	Promoting Children's Mental Health: The Effects of a Parenting Program	Child Development	Behavioral: How-to Parenting Program	https://ClinicalTrials.gov/show/NCT03030352
NCT03714490	MRI Simulation-guided Boost in Short-course Preoperative Radiotherapy for Unresectable Rectal Cancer	Rectal Neoplasms	Radiation: SCPRT plus neoadjuvant chemotherapy|Radiation: long course chemoradiation	https://ClinicalTrials.gov/show/NCT03714490
NCT04532944	The Energetic Origin of Neurodegeneration in MS	Multiple Sclerosis	Diagnostic Test: imaging of energy dysfunction	https://ClinicalTrials.gov/show/NCT04532944
NCT03879876	Safety and Efficacy Study of Human T Lymphoid Progenitor (HTLP) Injection After Partially HLA Compatible Allogeneic Hematopoietic Stem Cell Transplantation in SCID Patients	Pediatric Patients|Any Type of Severe Combined Immunodeficiency (SCID)|Partial HLA Incompatible Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)	Drug: Human T Lymphoid Progenitor (HTLP) injection	https://ClinicalTrials.gov/show/NCT03879876
NCT02375711	Immunosenescence and Hepatitis B Virus (HBV) Vaccine Efficacy in Chronic Renal Disease Patient	Chronic Renal Disease	Biological: Blood sample	https://ClinicalTrials.gov/show/NCT02375711
NCT02864082	A Safety and Tolerability Study of Topical PAT-001 in Congenital Ichthyosis	Congenital Ichthyosis	Drug: PAT-001, 0.1%|Drug: PAT-001, 0.2%|Drug: Vehicle	https://ClinicalTrials.gov/show/NCT02864082
NCT02682238	A Safety, Tolerability and Preliminary Efficacy Study of BBI-4000 Gel in Subjects With Palmar Hyperhidrosis	Hyperhidrosis	Drug: BBI-4000, 15%|Other: Vehicle gel	https://ClinicalTrials.gov/show/NCT02682238
NCT01368107	Study Evaluating Impact of IL-7 on CD4 Lymphopenia, Risks of Severe Haematological Toxicity and Tumor Progression in Metastatic Breast Cancer Patients	Metastatic Breast Cancer	Drug: placebo|Drug: interleukin 7	https://ClinicalTrials.gov/show/NCT01368107
NCT03978624	Window of Opportunity Study of Pembrolizumab Alone and in Combinations in Bladder Cancer	Bladder Cancer	Drug: Pembrolizumab|Drug: Entinostat	https://ClinicalTrials.gov/show/NCT03978624
NCT03223155	Concurrent or Sequential Immunotherapy and Radiation Therapy in Patients With Metastatic Lung Cancer	Stage IV Small Cell Lung Cancer	Drug: Nivolumab|Drug: Ipilimumab|Radiation: Stereotactic body radiation therapy	https://ClinicalTrials.gov/show/NCT03223155
NCT00451321	TRX4 Monoclonal Antibody in Type 1 Diabetes (T1 DM)	Diabetes Mellitus, Type 1	Drug: Otelixizumab	https://ClinicalTrials.gov/show/NCT00451321
NCT02010203	A Phase 1/2 Study of HS-410 in Patients With Non-Muscle Invasive Bladder Cancer After TURBT	Bladder Cancer	Biological: HS-410|Biological: Placebo|Biological: BCG	https://ClinicalTrials.gov/show/NCT02010203
NCT01460160	Pediatric Philadelphia Positive Acute Lymphoblastic Leukemia	Leukemia, Pediatric	Drug: Dasatinib	https://ClinicalTrials.gov/show/NCT01460160
NCT03953794	Inflammatory Bowel Disease Tracker (IBD Tracker)	Inflammatory Bowel Diseases|Ulcerative Colitis|Crohn Disease	Device: Fitbit Charge 3	https://ClinicalTrials.gov/show/NCT03953794
NCT01280955	Donor Enhancement With Plerixafor Post Myeloablative Allogeneic Transplant	Failure of Bone Marrow Graft	Drug: Plerixafor	https://ClinicalTrials.gov/show/NCT01280955
NCT03341143	Fecal Microbiota Transplant (FMT) in Melanoma Patients	Melanoma	Drug: Fecal Microbiota Transplant with Pembrolizumab	https://ClinicalTrials.gov/show/NCT03341143
NCT04373200	Human Ab Response & immunoMONItoring of COVID-19 Patients	SARS-CoV-2 Coronavirus|Acute Respiratory Distress Syndrome	Biological: Blood samples collection|Other: Saliva collection	https://ClinicalTrials.gov/show/NCT04373200

FIG. 20-44

NCT Number	Title	Conditions	Interventions	URL
NCT01536054	Sirolimus and Vaccine Therapy in Treating Patients With Stage II-IV Ovarian Epithelial, Fallopian Tube, or Primary Peritoneal Cavity Cancer	Tube Cancer|Recurrent Ovarian Epithelial Cancer|Recurrent Primary Peritoneal Cavity Cancer|Stage IIA Fallopian Tube Cancer|Stage IIA Ovarian Epithelial Cancer|Stage IIA Primary Peritoneal Cavity Cancer|Stage IIB Fallopian Tube Cancer|Stage IIB Ovarian Epithelial Cancer|Stage IIB Primary Peritoneal Cavity Cancer|Stage IIC Fallopian Tube Cancer|Stage IIC Ovarian Epithelial Cancer|Stage IIC Primary Peritoneal Cavity	Biological: ALVAC(2)-NY-ESO-1 (M)/TRICOM vaccine|Drug: sirolimus|Other: laboratory biomarker analysis|Biological: sargramostim	https://ClinicalTrials.gov/show/NCT01536054
NCT03618641	CMP-001 in Combo With Nivolumab in Stage IIIB/C/D Melanoma Patients With Clinically Apparent Lymph Node Disease	Melanoma|Lymph Node Cancer	Drug: CMP-001|Biological: Nivolumab	https://ClinicalTrials.gov/show/NCT03618641
NCT00301990	Bevacizumab and Interleukin-2 in Treating Patients With Metastatic Kidney Cancer	Kidney Cancer	Biological: aldesleukin|Biological: bevacizumab	https://ClinicalTrials.gov/show/NCT00301990
NCT03249870	Study of Inotuzumab Ozogamicin Combined to Chemotherapy in Older Patients With Philadelphia Chromosome-negative CD22+ B-cell Precursor ALL	Acute Lymphoblastic Leukemia (ALL) - Philadelphia Chromosome (Ph)-Negative CD22+ B-cell Precursor (BCP)	Drug: Inotuzumab ozogamicin (INO)	https://ClinicalTrials.gov/show/NCT03249870
NCT04714983	DNX-2440 for Resectable Colorectal Liver Metastasis	Liver Metastases|Liver Metastasis Colon Cancer|Colorectal Cancer|Breast Cancer|Gastric Cancer|Periampullary Cancer|Melanoma|Renal Cell Cancer|Sarcoma|Squamous Cell Carcinoma|Gastrointestinal Stromal Tumors	Biological: DNX-2440	https://ClinicalTrials.gov/show/NCT04714983
NCT04495894	Pre-Incisional Ketorolac for Patients Undergoing Surgery for Non-Small Cell Lung Cancer and Renal Cell Carcinoma	Non-small Cell Lung Cancer|Renal Cell Carcinoma	Drug: Preoperative Ketorolac	https://ClinicalTrials.gov/show/NCT04495894
NCT03167151	Pembrolizumab in Intermediate Risk Recurrent Non-muscle Invasive Bladder Cancer (NMIBC)	Non-muscle Invasive Bladder Cancer (NMIBC)	Drug: Pembrolizumab	https://ClinicalTrials.gov/show/NCT03167151

FIG. 20-45

NCT Number	Title	Conditions	Interventions	URL
NCT04102150	Valemetostat Tosylate (DS-3201b) Phase 2 Study in Relapsed or Refractory Adult T-cell Leukemia/Lymphoma	Adult T-cell Leukemia/Lymphoma	Drug: Valemetostat Tosylate	https://ClinicalTrials.gov/show/NCT04102150
NCT04196491	A Study to Evaluate the Safety of bb2121 in Subjects With High Risk, Newly Diagnosed Multiple Myeloma (NDMM)	Multiple Myeloma	Biological: bb2121 carfilzomib | Drug: Fludarabine | Drug: Cyclophosphamide | Drug: Lenalidomide	https://ClinicalTrials.gov/show/NCT04196491
NCT03927898	Phase II Study of Toripalimab Plus Stereotactic Body Radiotherapy in Colorectal Cancer Patients With Oligometastasis	Metastatic Colorectal Cancer	Drug: Toripalimab | Radiation: Stereotactic Body Radiotherapy	https://ClinicalTrials.gov/show/NCT03927898
NCT04765462	Allogeneic Î³Î´ T Cell Therapy for Treatment of Patients With Advanced Solid Cancers	Advanced Solid Tumour	Biological: Allogeneic Î³Î´ T cells	https://ClinicalTrials.gov/show/NCT04765462
NCT04553393	Decitabine-primed Tandem CD19/CD20 CAR T Cells Plus Epigenetic Agents in Aggressive r/r B-NHL With Huge Tumor Burden	Refractory or Relapsed Aggressive r/r B-NHL With Huge Tumor Burden	Drug: Chidamide | Drug: Decitabine | Drug: Chidamide and Decitabine | Biological: Decitabine-primed Tandem CAR19/20 engineered T cells	https://ClinicalTrials.gov/show/NCT04553393
NCT03971214	PD-1 Inhibitors Consolidation in Extensive-stage Small Cell Lung Cancer	Extensive-stage Small Cell Lung Cancer | Radiotherapy | Immunotherapy	Drug: PD-1 inhibitor JS-001	https://ClinicalTrials.gov/show/NCT03971214
NCT02116270	Accelerated Immunosenescence and Chronic Kidney Disease	Renal Failure	Biological: Blood sample	https://ClinicalTrials.gov/show/NCT02116270
NCT04286815	Gene Therapy for X Linked Severe Combined Immunodeficiency	Gene Therapy	Device: Lentiviral Vector Gene Therapy	https://ClinicalTrials.gov/show/NCT04286815
NCT04330118	Origin and Function of Eosinophilic Polynuclear During DRESS Syndrome	Drug Hypersensitivity | DRESS Syndrome		https://ClinicalTrials.gov/show/NCT04330118
NCT04394884	Pathogenesis of BTK-mediated Hyper-Inflammatory Responses in COVID-19 (RESPOND)	COVID-19		https://ClinicalTrials.gov/show/NCT04394884
NCT04888611	Neoadjuvant PD-1 Antibody Alone or Combined With DC Vaccines for Recurrent Glioblastoma	Recurrent Glioblastoma	Biological: Camrelizumab plus GSC-DCV | Biological: Camrelizumab plus Placebo	https://ClinicalTrials.gov/show/NCT04888611
NCT01488552	Gemcitabine+Nab-paclitaxel and FOLFIRINOX and Molecular Profiling for Patients With Advanced Pancreatic Cancer	Stage IV Pancreatic Cancer	Drug: Gemcitabine | Drug: nab-paclitaxel | Drug: FOLFIRINOX | Genetic: Immunohistochemistry (IHC) Analysis | Drug: Metformin | Drug: mFOLFIRI	https://ClinicalTrials.gov/show/NCT01488552
NCT02741323	Impact of CCR5 Blockade in HIV+ Kidney Transplant Recipients	HIV Infections | Kidney Diseases	Drug: Maraviroc | Drug: Placebo	https://ClinicalTrials.gov/show/NCT02741323
NCT02014506	Haploidentical Allogeneic Hematopoietic Stem Cell Transplantation in Children and Adolescents	Haploidentical Hematopoietic Stem Cell Transplantation | Malignant Disease | Non-malignant Disease	Drug: Fludarabine | Drug: Cyclophosphamide | Biological: anti-thymocyte globulin | Biological: filgrastim | Radiation: Total body irradiation | Procedure: TCRÎ±Î²-depleted hematopoietic cell transplantation | Device: CliniMACS	https://ClinicalTrials.gov/show/NCT02014506
NCT04133948	Multicenter Phase 1b Trial Testing the Neoadjuvant Combination of Domatinostat, Nivolumab and Ipilimumab in IFN-gamma Signature-low and IFN-gamma Signature-high RECIST 1.1-measurable Stage III Cutaneous or Unknown Primary Melanoma	Malignant Melanoma Stage III	Drug: Domatinostat | Drug: Nivolumab | Drug: Ipilimumab	https://ClinicalTrials.gov/show/NCT04133948

FIG. 20-46

NCT Number	Title	Conditions	Interventions	URL
NCT03312244	Pyridostigmine as Immunomodulator in People Living With HIV	HIV-1-infection|CD4+ T Lymphocytopenia|Immune Deficiency|Immunosenescence	Drug: Pyridostigmine Bromide|Drug: Placebo	https://ClinicalTrials.gov/show/NCT03312244
NCT00361101	A Study of AMD11070 in HIV-infected Patients Carrying X4-tropic Virus	HIV Infections|X4 Tropic Virus	Drug: AMD11070	https://ClinicalTrials.gov/show/NCT00361101
NCT03827967	Trial of PalloV-CC in Colon Cancer	Colon Cancer	Biological: PalloV-CC	https://ClinicalTrials.gov/show/NCT03827967
NCT03784014	Molecular Profiling of Advanced Soft-tissue Sarcomas	Soft Tissue Sarcoma	Drug: Nilotinib|Drug: Ceritinib|Drug: Capmatinib|Drug: Lapatinib|Drug: Trametinib|Combination Product: Trametinib and Dabrafenib|Combination Product: Olaparib and Durvalumab|Drug: Palbociclib|Drug: Glasdegib|Drug: TAS-120|Other: Next Generation sequencing exome	https://ClinicalTrials.gov/show/NCT03784014
NCT01607216	Functional and Lymphocytic Markers of Respiratory Morbidity in Hyperoxic Preemies	Prematurity|Symptomatic Respiratory Disease|Bronchopulmonary Dysplasia		https://ClinicalTrials.gov/show/NCT01607216
NCT01343043	A Pilot Study of Genetically Engineered NY-ESO-1 Specific NY-ESO-1á¶œÂ²âµâ¹T in HLA-A2+ Patients With Synovial Sarcoma	Neoplasms	Biological: NY-ESO-1(c259)T Cells	https://ClinicalTrials.gov/show/NCT01343043
NCT01066377	PRIMAGE (Probiotics, Immunity and Ageing)	Influenza	Dietary Supplement: Prebiotic and probiotic mix	https://ClinicalTrials.gov/show/NCT01066377
NCT03967223	Master Protocol to Assess the Safety and Antitumor Activity of Genetically Engineered T Cells in NY-ESO-1 and/or LAGE-1a Positive Solid Tumors	Neoplasms	Drug: letetresgene autoleucel (lete-cel, GSK3377794)|Drug: Fludarabine|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT03967223
NCT02989064	MAGE-A10á¶œâ·â¹â¶T for Urothelial Cancer, Melanoma or Head and Neck Cancers	Urothelial Carcinoma|Head and Neck Cancer|Melanoma|Bladder Urothelial Carcinoma	Genetic: Autologous genetically modified MAGE A10á¶œâ·â¹â¶T cells	https://ClinicalTrials.gov/show/NCT02989064
NCT02592577	MAGE A10á¶œâ·â¹â¶T for Advanced NSCLC	Non-Small Cell Lung Cancer|Carcinoma	Biological: Autologous Genetically modified T cells, MAGEA10á¶œâ·â¹â¶T	https://ClinicalTrials.gov/show/NCT02592577
NCT02876510	ACTolog in Patients With Solid Cancers	Cancer|Solid Tumor	Drug: Fludarabine|Drug: Cyclophosphamide|Biological: IMA101 product|Biological: Recombinant human interleukin-2|Diagnostic Test: IMADetect|Drug: Atezolizumab	https://ClinicalTrials.gov/show/NCT02876510
NCT03260712	Pembrolizumab in Biliary Tract Cancer	Biliary Tract Cancer|Metastatic Cancer|Advanced Cancer|Gallbladder Cancer	Drug: Pembrolizumab|Drug: Cisplatin|Drug: Gemcitabine	https://ClinicalTrials.gov/show/NCT03260712
NCT03738800	A Safety, Efficacy and Systemic Exposure Study of CD5789 Cream in Adults and Adolescents With Lamellar Ichthyosis	Lamellar Ichthyosis	Drug: CD5789 Cream 200 Âµg/g|Drug: CD5789 Cream 100 Âµg/g|Drug: CD5789 Cream Vehicle	https://ClinicalTrials.gov/show/NCT03738800
NCT02842021	Efficacy and Safety of Product S2G6T-1in Patients With Symptomatic Inflammatory Interdigital Tinea Pedis	Tinea Pedis	Drug: S2G6T-1|Drug: S2G6T-2|Drug: S2G6T-3|Drug: S2G6T-4	https://ClinicalTrials.gov/show/NCT02842021
NCT02630901	Multiple Ascending Dose Study of PRX003 in Subjects With Psoriasis	Psoriasis	Drug: PRX003|Other: Placebo	https://ClinicalTrials.gov/show/NCT02630901

FIG. 20-47

NCT Number	Title	Conditions	Interventions	URL
NCT00816413	Donor Stem Cell Transplant, Pentostatin, and Total-Body Irradiation in Treating Patients With Hematological Cancer	Chronic Myeloproliferative Disorders|Leukemia|Lymphoma|Myelodysplastic Syndromes|Nonmalignant Neoplasm	Drug: cyclosporine|Drug: mycophenolate mofetil|Drug: pentostatin|Genetic: cytogenetic analysis|Genetic: fluorescence in situ hybridization|Genetic: protein analysis|Other: flow cytometry|Other: immunoenzyme technique|Other: laboratory biomarker analysis|Other: reduced-intensity transplant conditioning procedure|Procedure: nonmyeloablative allogeneic hematopoietic stem cell transplantation|Procedure: peripheral blood stem cell transplantation (PBSC)|Radiation: total-body irradiation	https://ClinicalTrials.gov/show/NCT00816413
NCT03139981	A Study To Evaluate ASN002 In Subjects With Atopic Dermatitis	Dermatitis, Atopic|Dermatitis Eczema|Dermatitis, Eczematous	Drug: ASN002|Drug: Placebo Oral Tablet	https://ClinicalTrials.gov/show/NCT03139981
NCT03349060	Study to Evaluate Efficacy and Safety of PF-04965842 in Subjects Aged 12 Years And Older With Moderate to Severe Atopic Dermatitis	Dermatitis, Atopic	Drug: PF-04965842 100 mg|Drug: PF-04965842 200 mg|Drug: Placebo	https://ClinicalTrials.gov/show/NCT03349060
NCT03259620	A Study to Evaluate the Safety and Efficacy of CLS006 Versus Vehicle in Subjects 2 Years of Age or Older With Cutaneous Common Warts	Cutaneous Common Warts	Drug: CLS006|Drug: CLS006 Vehicle	https://ClinicalTrials.gov/show/NCT03259620
NCT03721172	Apremilast as a Direct Treatment for Mild-to-moderate Plaque Psoriasis Versus Placebo: an Analysis of Clinical Safety and Efficacy	Psoriasis	Drug: Apremilast|Other: Placebo	https://ClinicalTrials.gov/show/NCT03721172
NCT02611804	A Randomized, Double-Blind, Parallel-Group, Vehicle-Controlled, Multicenter Study Comparing Diclofenac Sodium Gel, 3% to SolarazeÂ® Gel, 3% in the Treatment of Actinic Keratosis on the Face or Bald Scalp	Actinic Keratosis	Drug: Diclofenac sodium|Drug: Placebo	https://ClinicalTrials.gov/show/NCT02611804
NCT02303821	Study of Carfilzomib in Combination With Induction Chemotherapy in Children With Relapsed or Refractory Acute Lymphoblastic Leukemia	Acute Lymphoblastic Leukemia (ALL)	Drug: Carfilzomib|Drug: Dexamethasone|Drug: Mitoxantrone|Drug: PEG-asparaginase|Drug: Vincristine|Drug: Intrathecal (IT) Methotrexate|Drug: Intrathecal Triple Therapy (Intrathecal Cytarabine, Hydrocortisone, and Methotrexate)|Drug: 6-Mercaptopurine|Drug: Cyclophosphamide|Drug: Cytarabine|Drug: Daunorubicin	https://ClinicalTrials.gov/show/NCT02303821
NCT03443024	A Study of Lebrikizumab (LY3650150) in Participants With Moderate-to-Severe Atopic Dermatitis	Atopic Dermatitis	Biological: Lebrikizumab|Drug: Placebo	https://ClinicalTrials.gov/show/NCT03443024
NCT02780167	Study To Evaluate Pf-04965842 In Subjects With Moderate To Severe Atopic Dermatitis	Atopic Dermatitis	Drug: PF-04965842|Drug: Placebo	https://ClinicalTrials.gov/show/NCT02780167
NCT03127956	A Long-term Safety Study of Olumacostat Glasaretil Gel in Subjects With Acne Vulgaris	Acne Vulgaris	Drug: Olumacostat Glasaretil Gel, 5.0%	https://ClinicalTrials.gov/show/NCT03127956

FIG. 20-48

NCT Number	Title	Conditions	Interventions	URL
NCT03073486	A Study of Olumacostat Glasaretil Gel in Subjects With Acne Vulgaris	Acne Vulgaris	Drug: Olumacostat Glasaretil Gel, 5.0%|Other: Olumacostat Glasaretil Gel, Vehicle	https://ClinicalTrials.gov/show/NCT03073486
NCT04015700	Neoantigen-based Personalized DNA Vaccine in Patients With Newly Diagnosed, Unmethylated Glioblastoma	Glioblastoma	Biological: Personalized neoantigen DNA vaccine supplied by Geneos Therapeutics|Device: CELLECTRAÄ®2000 EP Device supplied by Geneos Therapeutics|Drug: Plasmid encoded IL-12	https://ClinicalTrials.gov/show/NCT04015700
NCT02640625	Improving Prognosis in HIV Infection	Human Immunodeficiency Virus	Dietary Supplement: Probiotic compound	https://ClinicalTrials.gov/show/NCT02640625
NCT03449108	LN-145 or LN-145-S1 in Treating Patients With Relapsed or Refractory Ovarian Cancer, Anaplastic Thyroid Cancer, Osteosarcoma, or Other Bone and Soft Tissue Sarcomas	Sarcoma|Dedifferentiated Chondrosarcoma|Giant Cell Tumor of Bone|Malignancy in Giant Cell Tumor of Bone|Malignant Solid Neoplasm|Ovarian Carcinosarcoma|Platinum-Resistant Ovarian Carcinoma|Poorly Differentiated Thyroid Gland Carcinoma|Recurrent Osteosarcoma|Recurrent Ovarian Carcinoma|Refractory Osteosarcoma|Soft Tissue Sarcoma|Thyroid Gland Anaplastic Carcinoma|Thyroid Gland Squamous	Biological: Aldesleukin|Biological: Autologous Tumor Infiltrating Lymphocytes LN-145|Drug: Autologous Tumor Infiltrating Lymphocytes LN-145-S1|Drug: Cyclophosphamide|Drug: Fludarabine|Other: Quality-of-Life Assessment|Other: Questionnaire Administration	https://ClinicalTrials.gov/show/NCT03449108
NCT03969446	Pembrolizumab and Decitabine in Treating Patients With Acute Myeloid Leukemia or Myelodysplastic Syndrome That is Newly-Diagnosed, Recurrent, or Refractory	Acute Myeloid Leukemia|High Risk Myelodysplastic Syndrome|Recurrent Acute Myeloid Leukemia|Recurrent High Risk Myelodysplastic Syndrome|Refractory Acute Myeloid Leukemia|Refractory High Risk Myelodysplastic Syndrome|Secondary Acute Myeloid Leukemia|Therapy-Related Acute Myeloid Leukemia	Drug: Decitabine|Biological: Pembrolizumab	https://ClinicalTrials.gov/show/NCT03969446
NCT02716233	A French Protocol for the Treatment of Acute Lymphoblastic Leukemia (ALL) in Children and Adolescents	Acute Lymphoblastic Leukemia	Drug: pegaspargase 1250 IU/m2 x 2|Drug: pegaspargase 2500 IU/m2 x 1	https://ClinicalTrials.gov/show/NCT02716233

FIG. 20-49

NCT Number	Title	Conditions	Interventions	URL
NCT04419467	Vascular Endothelial Growth Factor-B (VEGF-B) Blockade With the Monoclonal Antibody CSL346 in Subjects With Diabetic Kidney Disease	Diabetic Kidney Disease (DKD)	Biological: CSL346|Drug: Placebo	https://ClinicalTrials.gov/show/NCT04419467
NCT03921021	Phase 2 Study of Telomelysin (OBP-301) in Combination With Pembrolizumab in Esophagogastric Adenocarcinoma	Esophagogastric Adenocarcinoma	Drug: Telomelysin	https://ClinicalTrials.gov/show/NCT03921021
NCT03361800	Window of Opportunity Trial of Entinostat in Patients With Newly Diagnosed Stage I-IIIC,TNBC	Breast Cancer|Invasive Breast Cancer|ER-Negative PR-Negative HER2-Negative Breast Cancer	Drug: Entinostat	https://ClinicalTrials.gov/show/NCT03361800
NCT02965716	Talimogene Laherparepvec and Pembrolizumab in Treating Patients With Stage III-IV Melanoma	Advanced Melanoma|Recurrent Melanoma|Stage III Cutaneous Melanoma AJCC v7|Stage IIIA Cutaneous Melanoma AJCC v7|Stage IIIB Cutaneous Melanoma AJCC v7|Stage IIIC Cutaneous Melanoma AJCC v7|Stage IV Cutaneous Melanoma AJCC v6 and v7|Unresectable Melanoma	Biological: Pembrolizumab|Biological: Talimogene Laherparepvec	https://ClinicalTrials.gov/show/NCT02965716
NCT04911621	Adjuvant Dendritic Cell Immunotherapy for Pediatric Patients With High-grade Glioma or Diffuse Intrinsic Pontine Glioma	High Grade Glioma|Diffuse Intrinsic Pontine Glioma	Biological: Dendritic cell vaccination + temozolomide-based chemoradiation|Biological: Dendritic cell vaccination +- conventional next-line treatment	https://ClinicalTrials.gov/show/NCT04911621
NCT04930055	Immune Responses in Oncology Patients to Novel Coronavirus Vaccines (IROC)	Cancer	Biological: COVID-19 Vaccination	https://ClinicalTrials.gov/show/NCT04930055
NCT01712945	Keratinocyte Growth Factor to Prevent Autoimmunity After Alemtuzumab Treatment of Multiple Sclerosis	Multiple Sclerosis	Drug: Palifermin|Drug: Alemtuzumab	https://ClinicalTrials.gov/show/NCT01712945
NCT00521339	Apremilast Safety and PK Study in Recalcitrant Plaque Psoriasis	Psoriasis-Type Psoriasis|Plaque-Type Psoriasis	Drug: Apremilast	https://ClinicalTrials.gov/show/NCT00521339
NCT00217763	European Study of 3APS in Mild to Moderate Alzheimer's Disease Patients	Alzheimer's Disease	Drug: 3APS	https://ClinicalTrials.gov/show/NCT00217763

FIG. 20-50

NCT Number	Title	Conditions	Interventions	URL
NCT03357757	Avelumab With Valproic Acid in Virus-associated Cancer	Cancer That is Associated With a Chronic Viral Infection|p16 Positive SCCHN|Squamous Cell Carcinoma of the Cervix|p16 Positive Squamous Cell Carcinoma of the Vagina or Vulva|p16 Positive Squamous Cell Carcinoma of the Penis|p16 Positive Squamous Cell Carcinoma of the Anus or Anal Canal|EBER Positive NPC|EBER Positive Hodgkins and Non-Hodgkins Lymphona	Drug: Valproic Acid|Biological: Avelumab	https://ClinicalTrials.gov/show/NCT03357757
NCT03082534	Pembrolizumab Combined With Cetuximab for Treatment of Recurrent/Metastatic Head & Neck Squamous Cell Carcinoma	HNSCC|Lip SCC|Oral Cavity Cancer|Oropharynx Cancer|Larynx Cancer|Hypopharynx Cancer|Nasopharynx Cancer|Sinonasal Carcinoma|Cutaneous Squamous Cell Carcinoma|Head and Neck Neoplasms|Head and Neck Cancer|Head and Neck Squamous Cell Carcinoma	Drug: Pembrolizumab, Cetuximab	https://ClinicalTrials.gov/show/NCT03082534
NCT04858607	Humoral and Cellular Immune Response to COVID-19 Vaccines in Immunocompromised and Healthy Individuals	Covid19|Immunosuppression	Diagnostic Test: Blood sample|Diagnostic Test: Saliva sample	https://ClinicalTrials.gov/show/NCT04858607
NCT03615105	Donor Stem Cell Transplantation Using $\alpha\beta$+/$CD19$+ T-lymphocyte Depleted Grafts From HLA Mismatched Donors	Acute Lymphoid Leukemia (ALL)|Acute Myeloid Leukemia (AML)|Chronic Myeloid Leukemia (CML)|Hodgkin Lymphoma|Non-Hodgkin Lymphoma|Chronic Lymphocytic Leukemia	Radiation: Hyperfractionated total body irradiation|Drug: Thiotepa|Drug: Cyclophosphamide|Drug: Busulfan|Drug: Fludarabine|Drug: Melphalan|Drug: Clofarabine|Procedure: HPC(A) stem cell allograft|Drug: Rituximab|Device: Rabbit antithymocyte globulin	https://ClinicalTrials.gov/show/NCT03615105

FIG. 20-51

NCT Number	Title	Conditions	Interventions	URL
NCT01757639	Ipilimumab in Treating Patients With Relapsed or Refractory High-Risk Myelodysplastic Syndrome or Acute Myeloid Leukemia	Acute Myeloid Leukemia Arising From Previous Myelodysplastic Syndrome|Chronic Myelomonocytic Leukemia|Myelodysplastic Syndrome|Previously Treated Myelodysplastic Syndrome|Recurrent Adult Acute Myeloid Leukemia|Secondary Myelodysplastic Syndrome	Biological: Ipilimumab|Other: Laboratory Biomarker Analysis	https://ClinicalTrials.gov/show/NCT01757639
NCT00852618	Intensive Viral Dynamics Substudy of A5248	HIV Infections|Treatment Naive		https://ClinicalTrials.gov/show/NCT00852618
NCT02963610	Phase I/II Study of Lenalidomide Plus Pembrolizumab in Patients With Solid Tumors With Expansion in Non-small Cell Lung Cancer	Relapsed or Refractory Solid Tumors|Nonsmall Cell Lung Cancer	Drug: Lenalidomide|Drug: Pembrolizumab	https://ClinicalTrials.gov/show/NCT02963610
NCT02027610	Vitamin A, Stool Microbiota and Vaccine Response in Bangladeshi Infants	Vitamin A Deficiency		https://ClinicalTrials.gov/show/NCT02027610
NCT03601455	Radiation Therapy and Durvalumab With or Without Tremelimumab in Treating Participants With Unresectable, Locally Advanced, or Metastatic Bladder Cancer	Bladder Urothelial Carcinoma|Stage IV Bladder Cancer AJCC v8|Stage IVA Bladder Cancer AJCC v8|Stage IVB Bladder Cancer AJCC v8	Biological: Durvalumab|Radiation: External Beam Radiation Therapy|Biological: Tremelimumab	https://ClinicalTrials.gov/show/NCT03601455
NCT03634332	Second-line Study of PEGPH20 and Pembro for HA High Metastatic PDAC	Pancreatic Ductal Adenocarcinoma|Pancreatic Cancer|Pancreatic Neoplasms	Drug: PEGPH20|Biological: Pembrolizumab	https://ClinicalTrials.gov/show/NCT03634332
NCT02536794	MEDI4736 and Tremelimumab in Treating Patients With Metastatic HER2 Negative Breast Cancer	Estrogen Receptor Negative|Estrogen Receptor Positive|HER2/Neu Negative|Recurrent Breast Carcinoma|Stage IV Breast Cancer	Biological: Anti-B7H1 Monoclonal Antibody MEDI4736|Other: Laboratory Biomarker Analysis|Other: Pharmacological Study|Biological: Tremelimumab	https://ClinicalTrials.gov/show/NCT02536794
NCT01579318	Phase II Intratumoral IL12 Plasmid Electroporation in Cutaneous Lymphoma	Cutaneous T Cell Lymphomas (CTCL)|Mycosis Fungoides (MF)	Biological: Tavokinogene Telseplasmid (tavo)|Device: OncoSec Medical System (OMS)	https://ClinicalTrials.gov/show/NCT01579318

FIG. 20-52

NCT Number	Title	Conditions	Interventions	URL
NCT02978625	Talimogene Laherparepvec and Nivolumab in Treating Patients With Refractory Lymphomas or Advanced or Refractory Non-melanoma Skin Cancers	Carcinoma|Adnexal Carcinoma|Anaplastic Large Cell Lymphoma, ALK-Negative|Anaplastic Large Cell Lymphoma, ALK-Positive|Apocrine Carcinoma|Cylindrocarcinoma|Digital Papillary Adenocarcinoma|Endocrine Mucin-Producing Sweat Gland Carcinoma|Extramammary Paget Disease|Extraocular Cutaneous Sebaceous Carcinoma|Hidradenocarcinoma|Keratoacanthoma|Malignant Sweat Gland Neoplasm|Merkel Cell Carcinoma|Microcy	Other: Laboratory Biomarker Analysis|Biological: Nivolumab|Biological: Talimogene Laherparepvec	https://ClinicalTrials.gov/show/NCT02978625
NCT04301076	Testing the Addition of an Anti-cancer Drug, Lenalidomide, to the Usual Combination Chemotherapy Treatment ("EPOCH") for Adult T-Cell Leukemia-Lymphoma (ATL)	Acute Adult T-Cell Leukemia/Lymphoma|Adult T-Cell Leukemia/Lymphoma|Chronic Adult T-Cell Leukemia/Lymphoma|HTLV-1 Infection	Drug: Cyclophosphamide|Drug: Doxorubicin Hydrochloride|Drug: Etoposide|Drug: Lenalidomide|Drug: Prednisone|Drug: Vincristine Sulfate	https://ClinicalTrials.gov/show/NCT04301076
NCT02860559	Safety and Early Efficacy Study of TBX-1400 in Patients With Severe Combined Immunodeficiency	Severe Combined Immunodeficiency	Biological: TBX-1400	https://ClinicalTrials.gov/show/NCT02860559
NCT02981914	Pilot Study of Pembrolizumab Treatment for Disease Relapse After Allogeneic Stem Cell Transplantation	Classical Hodgkin Lymphoma|B-cell Non-Hodgkin Lymphoma|Acute Myeloid Leukemia|Myelodysplastic Syndromes	Drug: Pembrolizumab	https://ClinicalTrials.gov/show/NCT02981914
NCT02215707	A Clinical Trial of the PfSPZ Vaccine Administered by Direct Venous Inoculation in Healthy Malaria-NaÃ¯ve Adults: Heterologous vs. Homologous Controlled Human Malaria Infection and Reduction in Number of Doses	Malaria	Biological: PfSPZ Vaccine	https://ClinicalTrials.gov/show/NCT02215707
NCT03852823	Study of Recombinant Human Anti-PD-1 Monoclonal Antibody in Patients With Advanced Tumours	Advanced Solid Tumours|Cervical Cancer|Malignant Mesothelioma|Lymphoma|Non-Small-Cell Lung Cancer	Drug: SG001	https://ClinicalTrials.gov/show/NCT03852823

FIG. 20-53

NCT Number	Title	Conditions	Interventions	URL
NCT04300244	Nivolumab and Ipilimumab +/- UV1 Vaccination as Second Line Treatment in Patients With Malignant Mesothelioma	Cancer|Cancer, Lung|Cancer of Lung|Mesothelioma|Mesothelioma; Lung|Mesothelioma; Pleura|Mesothelioma Pleural	Biological: UV1 vaccine + leukine|Biological: ipilimumab|Biological: nivolumab	https://ClinicalTrials.gov/show/NCT04300244
NCT03812549	Safety and Tolerability Evaluation of Sintilimab in Combination With Radiation in Stage IV NSCLC Patients	Stage IV NSCLC	Drug: Sintilimab|Radiation: stereotactic body radiation therapy|Radiation: Low Dose Radiotherapy	https://ClinicalTrials.gov/show/NCT03812549
NCT04120454	Ramucirumab and Pembrolizumab for the Treatment of EGFR Mutant Recurrent or Metastatic Non-small Cell Lung Cancer	Metastatic Lung Non-Small Cell Carcinoma|Recurrent Lung Non-Small Cell Carcinoma|Stage IV Lung Cancer AJCC v8|Stage IVA Lung Cancer AJCC v8|Stage IVB Lung Cancer AJCC v8	Biological: Pembrolizumab|Biological: Ramucirumab	https://ClinicalTrials.gov/show/NCT04120454
NCT03526185	A Pilot Study Using Short-Term Cultured Anti-Tumor Autologous Lymphocytes	Metastatic Melanoma	Drug: Tumor Infiltrating Lymphocytes|Drug: Nivolumab and Ipilimumab	https://ClinicalTrials.gov/show/NCT03526185
NCT04630353	A Study HB-201 in Patients With Newly Diagnosed HPV16+ Oropharynx or Locally Advanced Cervical Cancer	HPV 16+ Confirmed Oropharynx Cancer and Cervical Cancer	Drug: HB-201 IT|Drug: HB-201 IV	https://ClinicalTrials.gov/show/NCT04630353
NCT01479296	Evaluating the Immune Response to a rAd5 HIV Vaccine Administered in Three Different Ways in Healthy, HIV-Uninfected Adults	HIV Infections	Biological: VRC rAd5 vaccine (rAd5 gag-pol/env A/B/C)|Biological: rAd5 env A|Biological: rAd5 env B|Biological: rAd5 env C|Biological: rAd5 gag-pol|Biological: Placebo Vaccine	https://ClinicalTrials.gov/show/NCT01479296
NCT03007147	Imatinib Mesylate and Combination Chemotherapy in Treating Patients With Newly Diagnosed Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia	Acute Lymphoblastic Leukemia|B Acute Lymphoblastic Leukemia|Mixed Phenotype Acute Leukemia|T Acute Lymphoblastic Leukemia	Procedure: Allogeneic Hematopoietic Stem Cell Transplantation|Drug: Cyclophosphamide|Drug: Cytarabine|Drug: Daunorubicin Hydrochloride|Drug: Dexamethasone|Drug: Dexrazoxane Hydrochloride|Drug: Doxorubicin|Drug: Etoposide|Biological: Filgrastim|Drug: Ifosfamide|Drug: Imatinib Mesylate|Other: Laboratory Biomarker Analysis|Drug: Leucovorin Calcium|Drug: Mercaptopurine|Drug: Methotrexate|Drug: Methylprednisolone|Drug: Pegaspargase|Drug: Prednisolone|Other: Questionnaire Administration|Drug: Therapeutic Hydrocortisone|Drug: Thioguanine|Drug: Vincristine Sulfate	https://ClinicalTrials.gov/show/NCT03007147

FIG. 20-54

NCT Number	Title	Conditions	Interventions	URL
NCT03389802	Phase I Study of APX005M in Pediatric CNS Tumors	Glioblastoma Multiforme|High-grade Astrocytoma NOS|CNS Primary Tumor, Nos|Ependymoma, NOS|Diffuse Intrinsic Pontine Gliomas (DIPG)|Medulloblastoma	Biological: APX005M treatment for recurrent or refractory primary malignant CNS tumor patients|Biological: APX005M treatment for newly diagnosed DIPG patients	https://ClinicalTrials.gov/show/NCT03389802
NCT02129075	CDX-1401 and Poly-ICLC Vaccine Therapy With or Without CDX-301 in Treating Patients With Stage IIB-IV Melanoma	Cutaneous Melanoma|Mucosal Melanoma|Ocular Melanoma|Stage IIB Cutaneous Melanoma AJCC v6 and v7|Stage IIC Cutaneous Melanoma AJCC v6 and v7|Stage III Cutaneous Melanoma AJCC v7|Stage IIIA Cutaneous Melanoma AJCC v7|Stage IIIB Cutaneous Melanoma AJCC v7|Stage IIIC Cutaneous Melanoma AJCC v7|Stage IV Cutaneous Melanoma AJCC v6 and v7	Biological: DEC-205/NY-ESO-1 Fusion Protein CDX-1401|Other: Laboratory Biomarker Analysis|Biological: Neoantigen-based Melanoma-Poly-ICLC Vaccine|Other: Pharmacological Study|Biological: Recombinant Flt3 Ligand	https://ClinicalTrials.gov/show/NCT02129075
NCT03220022	Ibrutinib, Rituximab, Etoposide, Prednisone, Vincristine Sulfate, Cyclophosphamide, and Doxorubicin Hydrochloride in Treating Patients With HIV-Positive Stage II-IV Diffuse Large B-Cell Lymphomas	AIDS-Related Lymphoma|Ann Arbor Stage II Diffuse Large B-Cell Lymphoma|Ann Arbor Stage III Diffuse Large B-Cell Lymphoma|Ann Arbor Stage IV Diffuse Large B-Cell Lymphoma	Drug: Cyclophosphamide|Drug: Doxorubicin Hydrochloride|Drug: Etoposide|Biological: Filgrastim|Drug: Ibrutinib|Other: Laboratory Biomarker Analysis|Biological: Pegfilgrastim|Other: Pharmacological Study|Drug: Prednisone|Biological: Rituximab|Drug: Vincristine Sulfate	https://ClinicalTrials.gov/show/NCT03220022
NCT01976182	Prospective, Multicentric, Phase II Randomized Controlled Trial on Two Parallel Groups Comparing the Efficacy of Two Immunosuppressive Drugs (Methotrexate, Cyclophosphamide) in Large Granular Lymphocytes Leukemia	Large Granular Lymphocytes Leukemia	Drug: Methotrexate|Drug: Cyclophosphamide	https://ClinicalTrials.gov/show/NCT01976182
NCT03083158	Immunity to Hepatitis B Vaccine	Hepatitis B|Immunization; Infection	Drug: Hepatitis B vaccine	https://ClinicalTrials.gov/show/NCT03083158
NCT00086359	Comparison of Anti-HIV Drug Combinations to Prevent Mother-to-Child Transmission of HIV	HIV Infections	Drug: Abacavir sulfate, lamivudine, and zidovudine|Drug: Lamivudine/zidovudine|Drug: Lopinavir/ritonavir	https://ClinicalTrials.gov/show/NCT00086359
NCT03475134	TIL-ACT After NMA Chemo With IL-2 and Nivo Rescue in Metastatic Melanoma (mMEL)	Metastatic Melanoma	Other: TIL|Drug: Cyclophosphamide|Drug: Fludarabine|Drug: Interleukin-2|Drug: Nivolumab	https://ClinicalTrials.gov/show/NCT03475134

FIG. 20-55

NCT Number	Title	Conditions	Interventions	URL
NCT04659486	Adolescents With COVID-19/MIS-C at HCFMUSP	Covid19|Corona Virus Infection|SARS (Severe Acute Respiratory Syndrome)|SARS-CoV Infection	Behavioral: Home-based exercise training	https://ClinicalTrials.gov/show/NCT04659486
NCT02869295	A Phase 1/2 Multicenter Dose Escalation and Expansion Study Of NKTR-214 In Subjects With Locally Advanced Or Metastatic Solid Tumors	Unspecified Adult Solid Tumor, Protocol Specific	Drug: NKTR-214	https://ClinicalTrials.gov/show/NCT02869295
NCT04810910	Personalized Neoantigen Vaccine in Pancreatic Cancer Patients Following Surgical Resection and Adjuvant Chemotherapy	Resectable Pancreatic Cancer	Biological: iNeo-Vac-P01|Other: GM-CSF	https://ClinicalTrials.gov/show/NCT04810910
NCT03662815	Clinical Study of a Personalized Neoantigen Cancer Vaccine in Treating Patients With Advanced Malignant Tumor	Advanced Malignant Solid Tumor	Biological: iNeo-Vac-P01|Other: GM-CSF	https://ClinicalTrials.gov/show/NCT03662815
NCT03645148	Clinical Study of a Personalized Neoantigen Cancer Vaccine in Treating Patients With Advanced Pancreatic Cancer	Pancreatic Cancer|Pancreatic Carcinoma	Biological: iNeo-Vac-P01|Other: GM-CSF	https://ClinicalTrials.gov/show/NCT03645148
NCT02775851	Pembrolizumab in Treating Patients With Desmoplastic Melanoma That Can or Cannot Be Removed by Surgery	Desmoplastic Melanoma	Biological: Pembrolizumab|Procedure: Therapeutic Conventional Surgery	https://ClinicalTrials.gov/show/NCT02775851
NCT04193189	B-Enhancement of HBV Vaccination in Persons Living With HIV (BEe-HiVe): Evaluation of HEPLISAV-B	HIV Infection|Hepatitis B	Biological: HEPLISAV-B|Biological: ENGERIX-B	https://ClinicalTrials.gov/show/NCT04193189
NCT03739996	Long-Acting Cabotegravir Plus VRC-HIVMAB075-00-AB (VRC07-523LS) for Viral Suppression in Adults Living With HIV-1	HIV Infections	Drug: Oral Cabotegravir (CAB)|Drug: Nucleoside Reverse Transcriptase Inhibitors (NRTIs)|Drug: Long-Acting Injectable Cabotegravir (CAB LA)|Biological: VRC07-523LS|Drug: Standard of Care (SOC) Oral ART	https://ClinicalTrials.gov/show/NCT03739996
NCT03705169	Pharmacokinetics of SAR441236	HIV-1-infection	Biological: SAR441236|Biological: Placebo|Drug: Antiretroviral treatment	https://ClinicalTrials.gov/show/NCT03705169
NCT03635788	The LATITUDE Study: Long-Acting Therapy to Improve Treatment SUccess in Daily LifE	HIV Infections	Drug: Standard of Care (SOC) Oral ART|Drug: Oral RPV|Drug: Oral CAB|Drug. RPV-LA Loading Dose|Drug: CAB-LA Loading Dose|Drug: RPV-LA Maintenance Dose|Drug: CAB-LA Maintenance Dose	https://ClinicalTrials.gov/show/NCT03635788
NCT03560258	HIV-1-Gag Conserved-Element DNA Vaccine as Therapeutic Vaccination in HIV-Infected Persons With Viral Suppression on Antiretroviral Therapy	HIV Infections	Biological: p24CE1/2 pDNA vaccine|Biological: p24CE1/2 pDNA vaccine admixed with full-length p55^gag pDNA vaccine|Biological: Full-length p55^gag pDNA vaccine|Biological: Placebo	https://ClinicalTrials.gov/show/NCT03560258
NCT03003676	A Pilot Study of Sequential ONCOS-102, an Engineered Oncolytic Adenovirus Expressing GMCSF, and Pembrolizumab in Patients With Advanced or Unresectable Melanoma Progressing After Programmed Cell Death Protein 1 (PD1) Blockade	Advanced or Unresectable Melanoma Progressing After PD1 Blockade	Biological: ONCOS-102|Drug: Cyclophosphamide|Drug: Pembrolizumab	https://ClinicalTrials.gov/show/NCT03003676

FIG. 20-56

NCT Number	Title	Conditions	Interventions	URL
NCT04375527	Binimetinib and Nivolumab for the Treatment of Locally Advanced Unresectable or Metastatic BRAF V600 Wildtype Melanoma	Cutaneous Melanoma AJCC v8|Clinical Stage IV Cutaneous Melanoma AJCC v8|Locally Advanced Cutaneous Melanoma|Metastatic Cutaneous Melanoma|Pathologic Stage III Cutaneous Melanoma AJCC v8|Pathologic Stage IIIA Cutaneous Melanoma AJCC v8|Pathologic Stage IIIB Cutaneous Melanoma AJCC v8|Pathologic Stage IIIC Cutaneous Melanoma AJCC v8|Pathologic	Drug: Binimetinib|Biological: Nivolumab|Other: Questionnaire Administration	https://ClinicalTrials.gov/show/NCT04375527
NCT03123055	A Study of B-701 in Combination With Pembrolizumab in Treatment of Locally Advanced or Metastatic Urothelial Cell Carcinoma	Locally Advanced or Metastatic Urothelial Cell Carcinoma|Urinary Bladder Disease|Urological Diseases	Drug: B-701|Drug: Pembrolizumab	https://ClinicalTrials.gov/show/NCT03123055
NCT02344290	Evaluating the Use of Pitavastatin to Reduce the Risk of Cardiovascular Disease in HIV-Infected Adults	HIV Infections|Cardiovascular Diseases	Drug: Pitavastatin|Drug: Placebo	https://ClinicalTrials.gov/show/NCT02344290
NCT01949116	Safety and Effectiveness of Low-Dose Methotrexate for Reducing Inflammation in HIV-Infected Adults on ARV Medications	HIV Infections	Drug: LDMTX|Drug: Placebo|Dietary Supplement: Folic acid	https://ClinicalTrials.gov/show/NCT01949116
NCT01266616	Safety of and Immune Response to an Investigational HIV-1 Vaccine With or Without Interleukin-12 (IL-12) in HIV-1 Infected Adults	HIV Infections	Biological: Profectus HIV MAG pDNA vaccine|Biological: IL-12|Other: Placebo	https://ClinicalTrials.gov/show/NCT01266616
NCT01482767	Evaluating the Effectiveness of Boceprevir, Pegylated-Interferon Alfa 2b and Ribavirin in Treating Hepatitis C Virus (HCV) Infection in Adults With HIV and HCV Infection	HIV Infections|Hepatitis C	Drug: Pegylated-Interferon Alfa 2b (PEG-IFN)|Drug: Ribavirin (RBV)|Drug: Boceprevir (BOC)	https://ClinicalTrials.gov/show/NCT01482767
NCT00660972	Study of Viral Load Decay Rates in HIV Infected Participants Starting Treatment With Raltegravir (RAL) and Emtricitabine/Tenofovir Disoproxil Fumarate (TDF)	HIV Infections	Drug: Raltegravir|Drug: Emtricitabine/tenofovir disoproxil fumarate	https://ClinicalTrials.gov/show/NCT00660972
NCT00537394	Optimizing Treatment for Treatment-Experienced, HIV-Infected People	HIV Infections	Drug: Enfuvirtide|Drug: Raltegravir|Drug: Darunavir|Drug: Tipranavir|Drug: Etravirine|Drug: Maraviroc	https://ClinicalTrials.gov/show/NCT00537394
NCT04212416	Leflunomide in Treating Patients With Steroid Dependent Chronic Graft Versus Host Disease	Chronic Graft Versus Host Disease|Steroid Refractory Graft Versus Host Disease	Drug: Leflunomide	https://ClinicalTrials.gov/show/NCT04212416

FIG. 21A

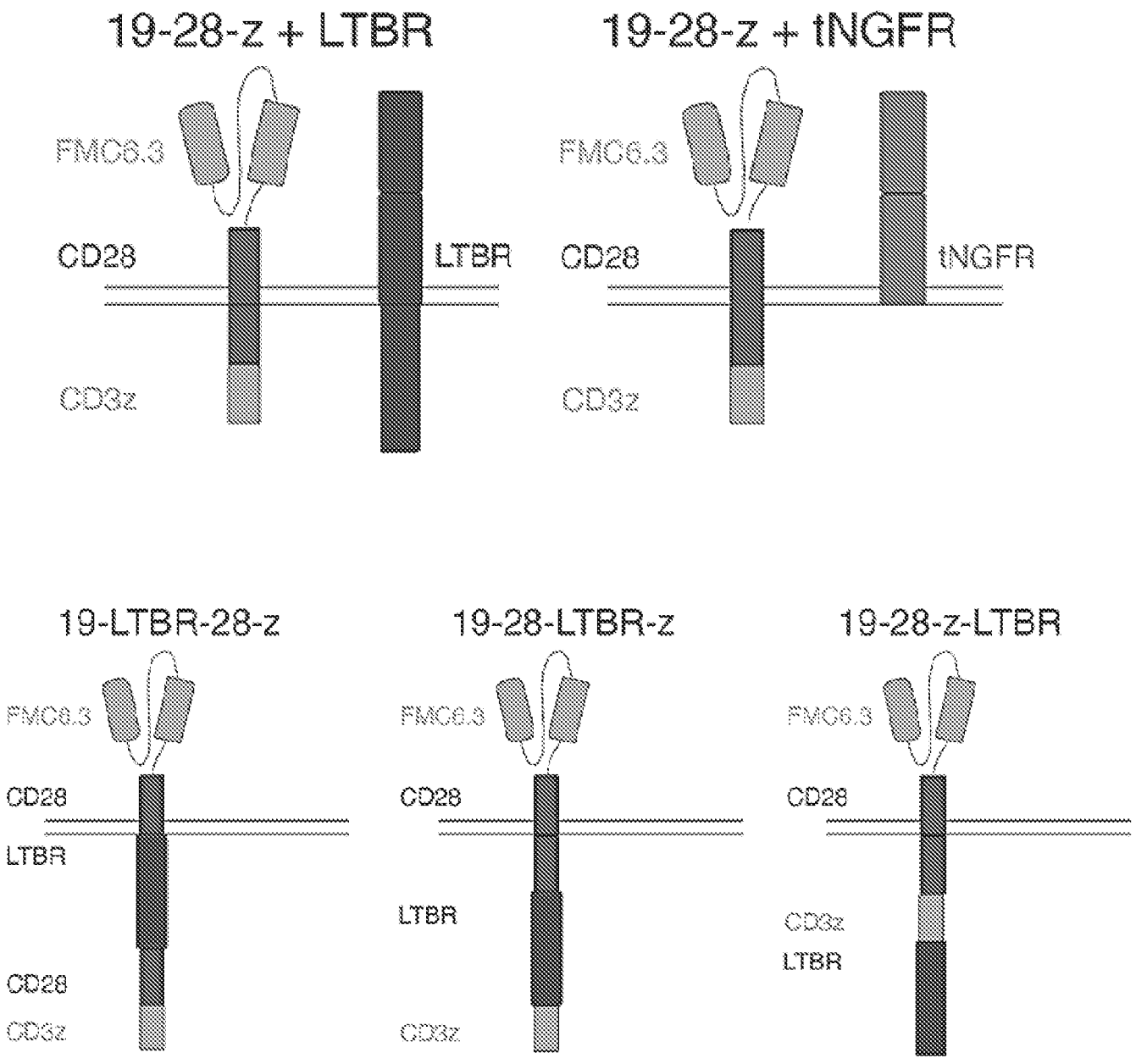

19-28-z + LTBR
FMC6.3
CD28
LTBR
CD3z
19-28-z + tNGFR
FMC6.3
CD28
tNGFR
CD3z
19-LTBR-28-z
FMC6.3
CD28
LTBR
CD28
CD3z
19-28-LTBR-z
FMC6.3
CD28
LTBR
CD3z
19-28-z-LTBR
FMC6.3
CD28
CD3z
LTBR

FIG. 21B

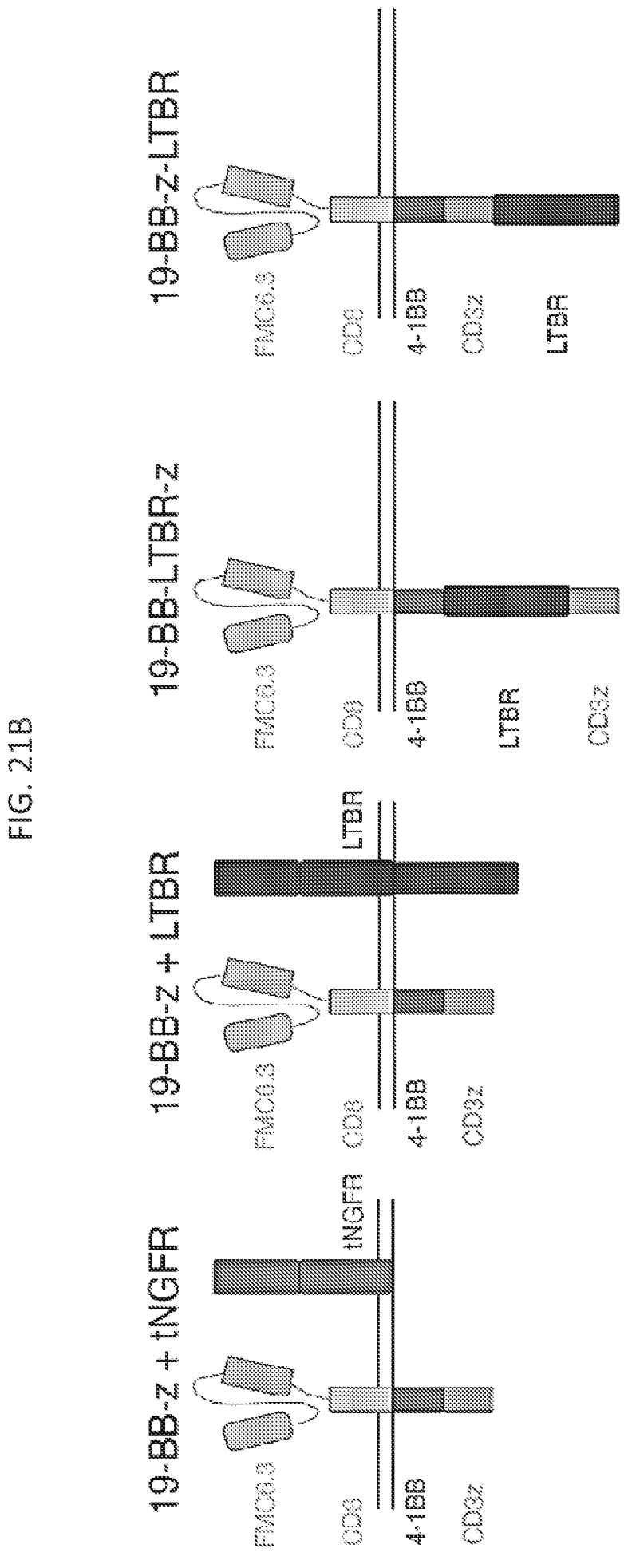

19-BB-z + tNGFR
FMC63
CD8
tNGFR
4-1BB
CD3z
19-BB-z + LTBR
FMC63
CD8
LTBR
4-1BB
CD3z
19-BB-LTBR-z
FMC63
CD8
4-1BB
LTBR
CD3z
19-BB-z-LTBR
FMC63
CD8
4-1BB
CD3z
LTBR

FIG. 21C

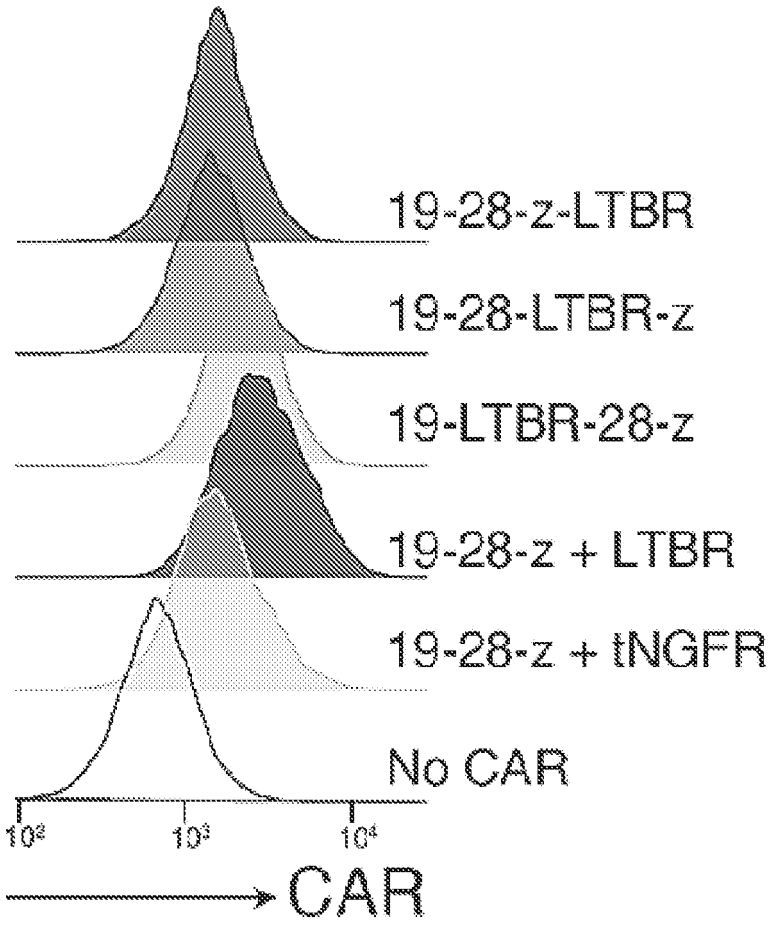


FIG. 21D

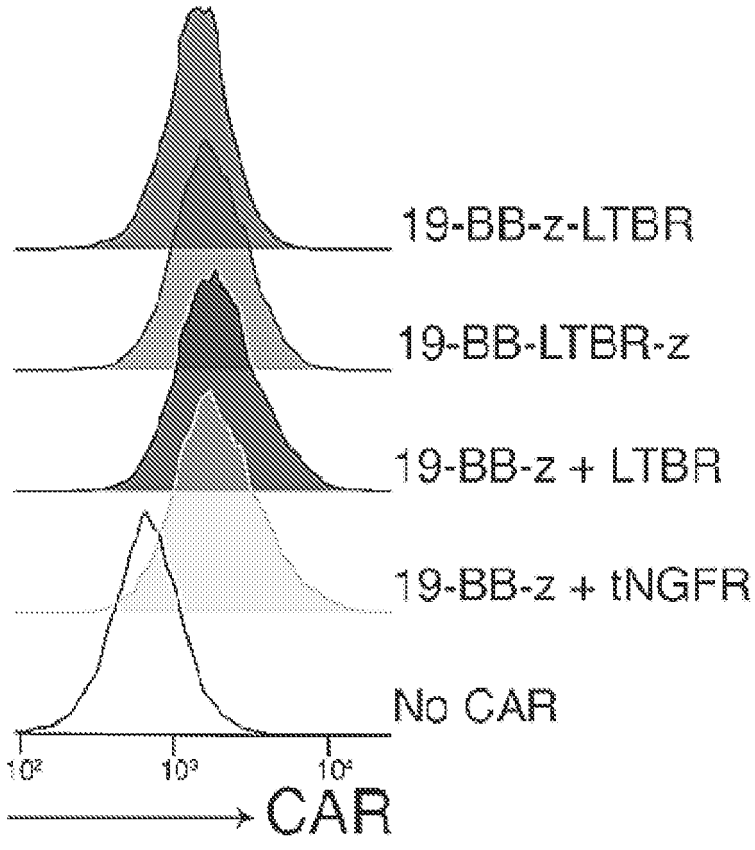


FIG. 21E

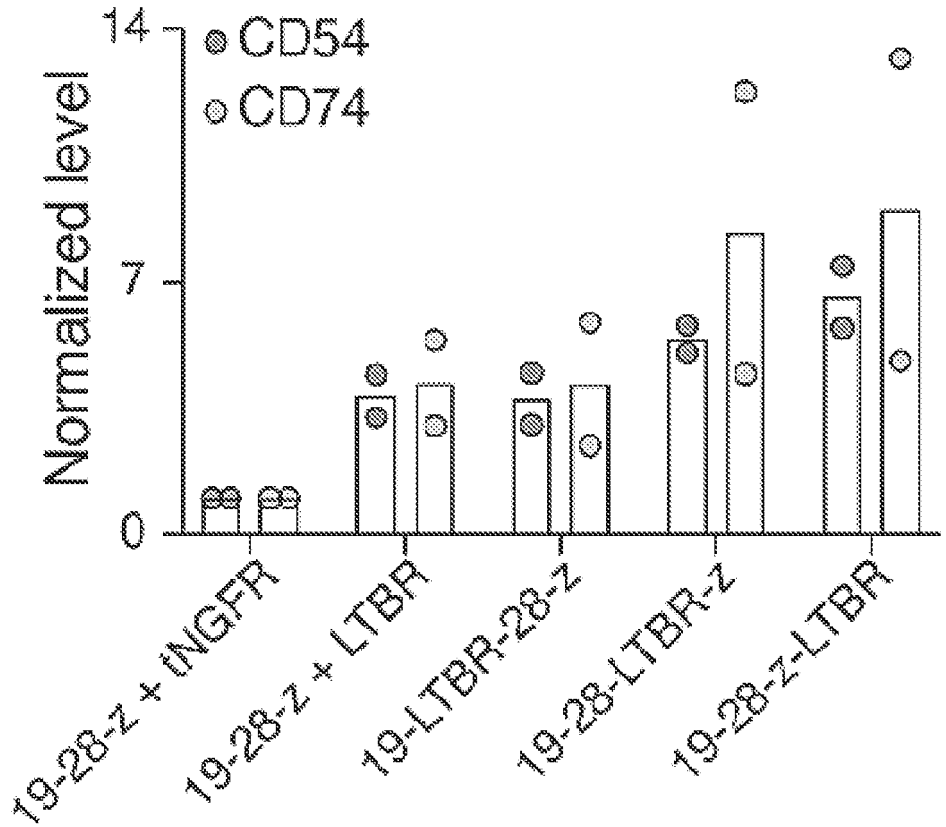


FIG. 21F

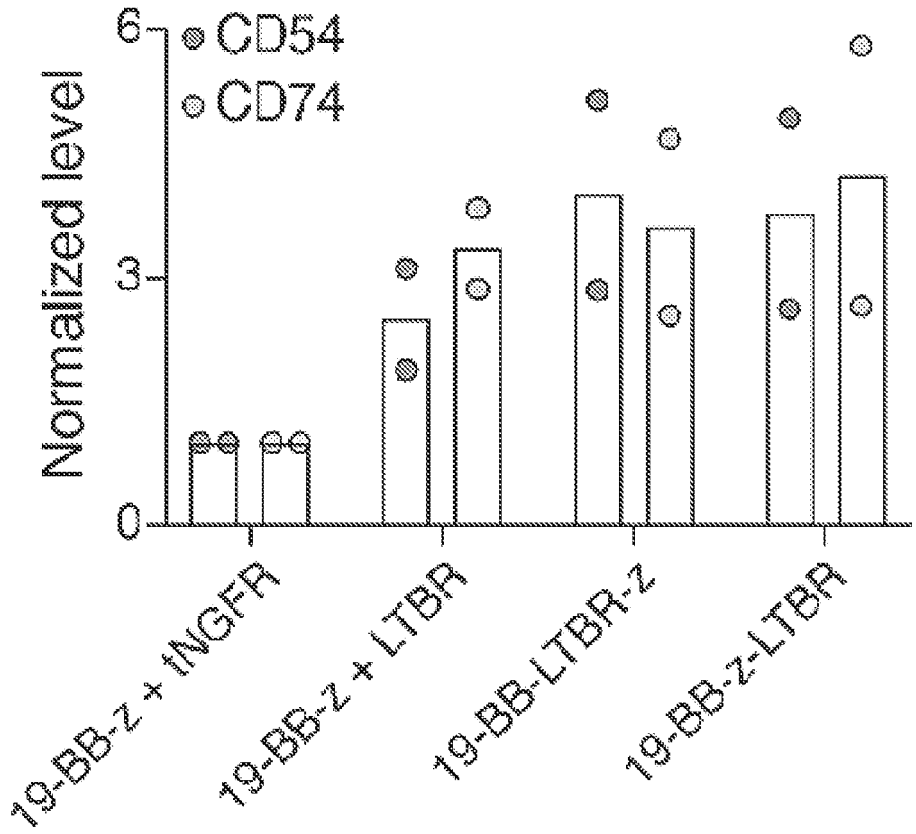


FIG. 21G

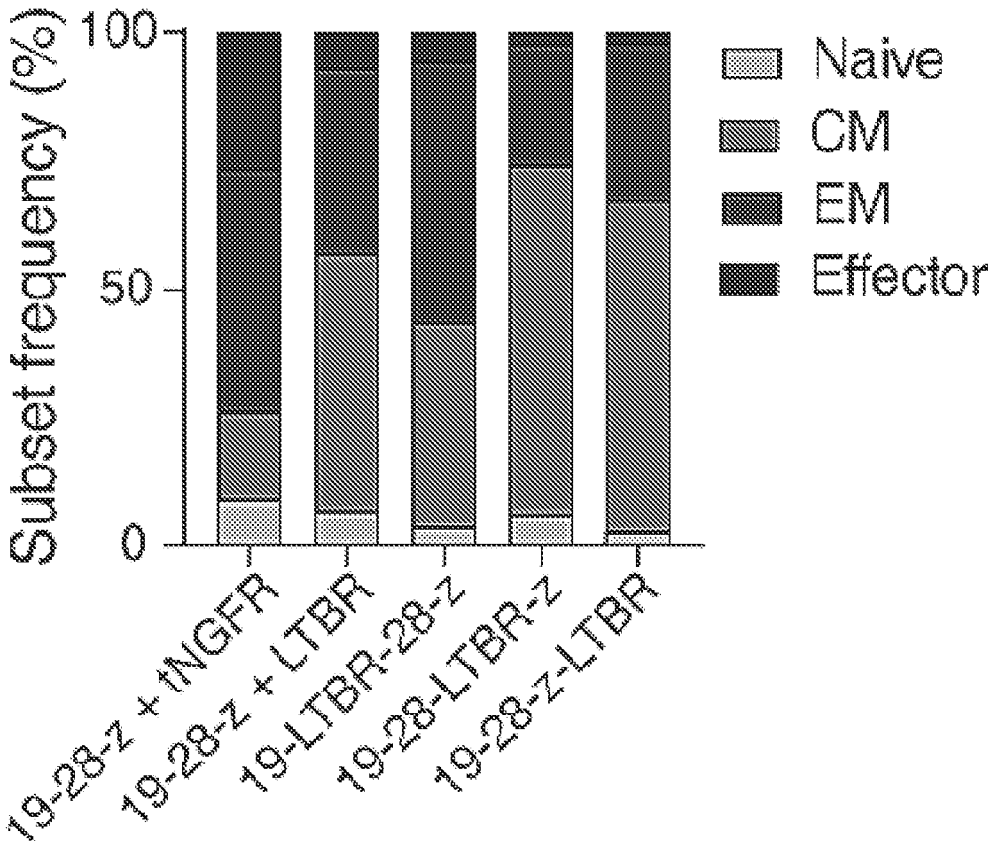


FIG. 21H

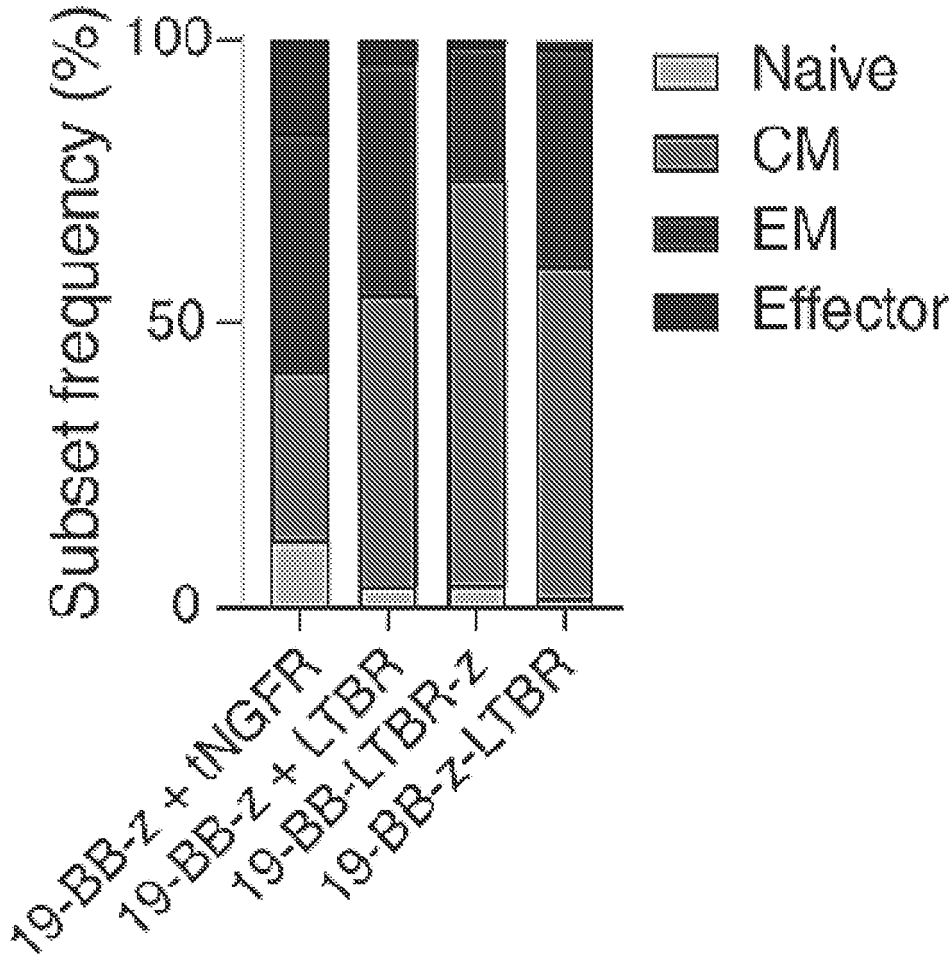


FIG. 21I

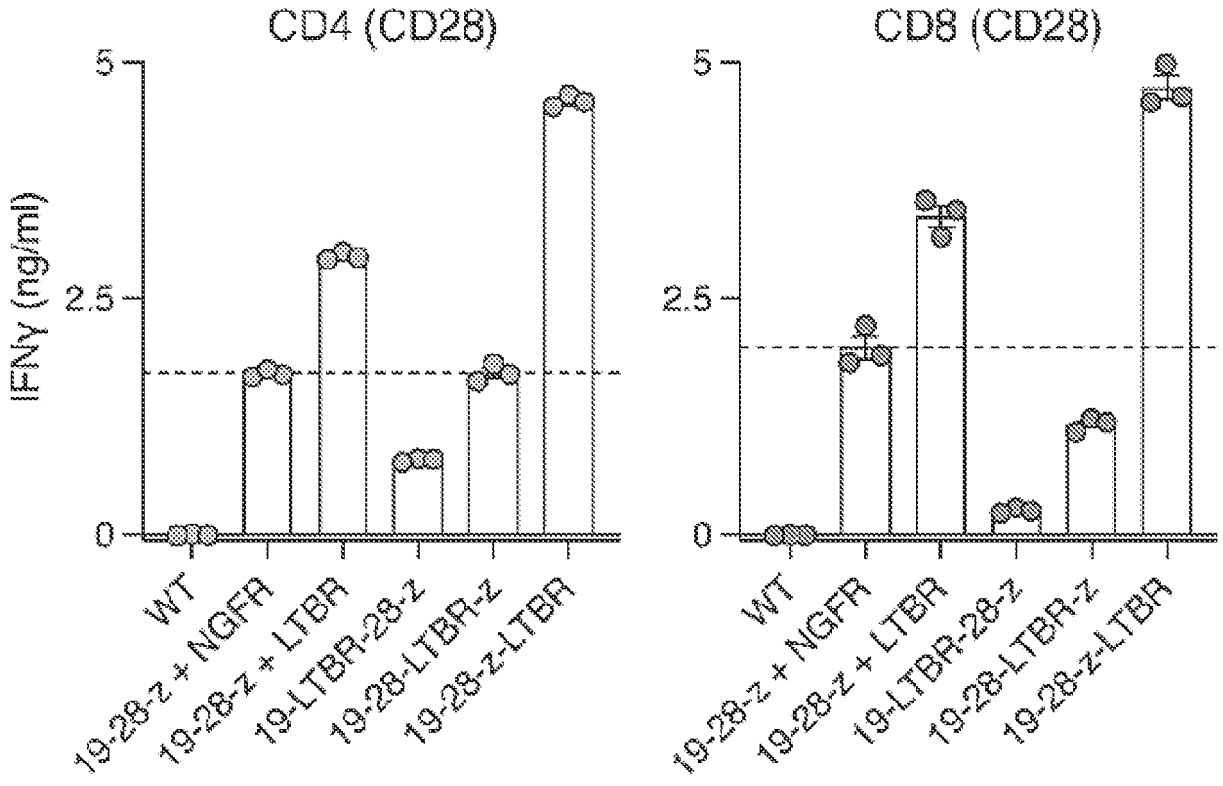


FIG. 21J

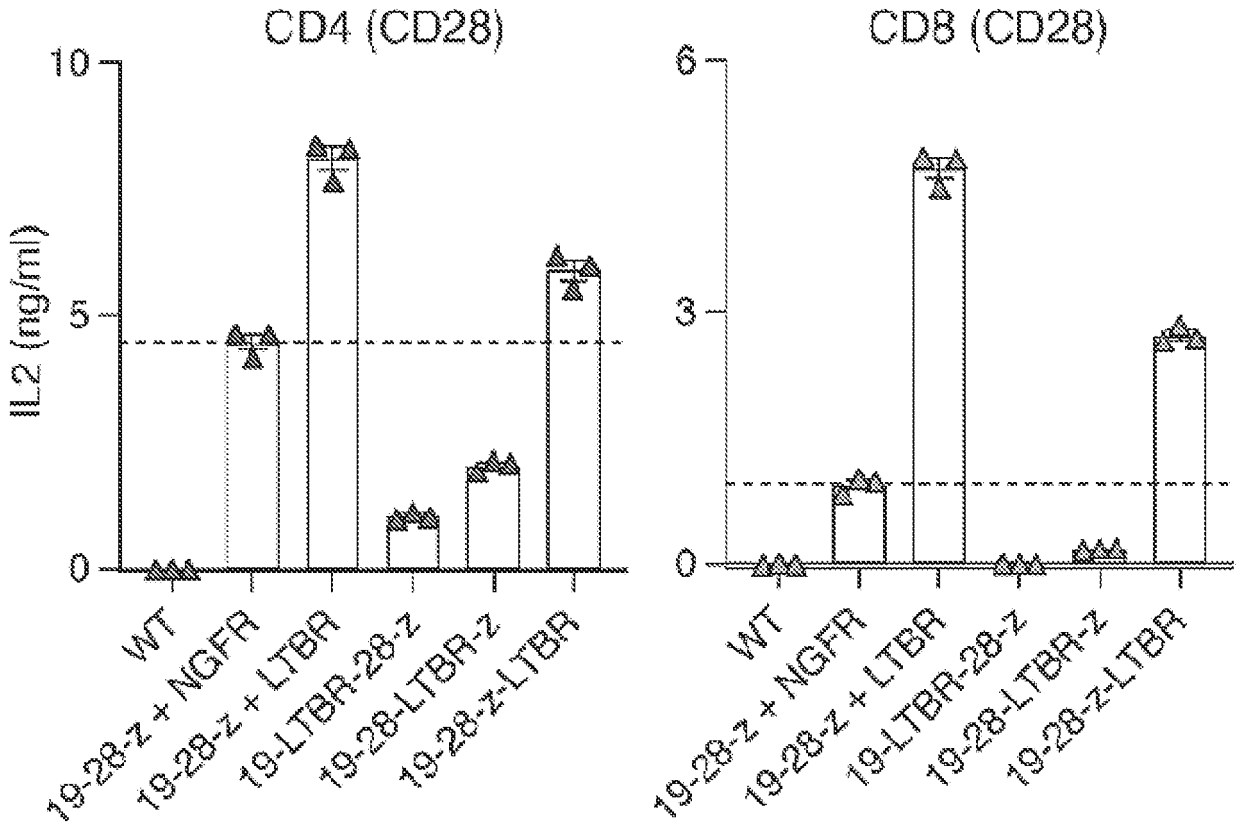


FIG. 21K

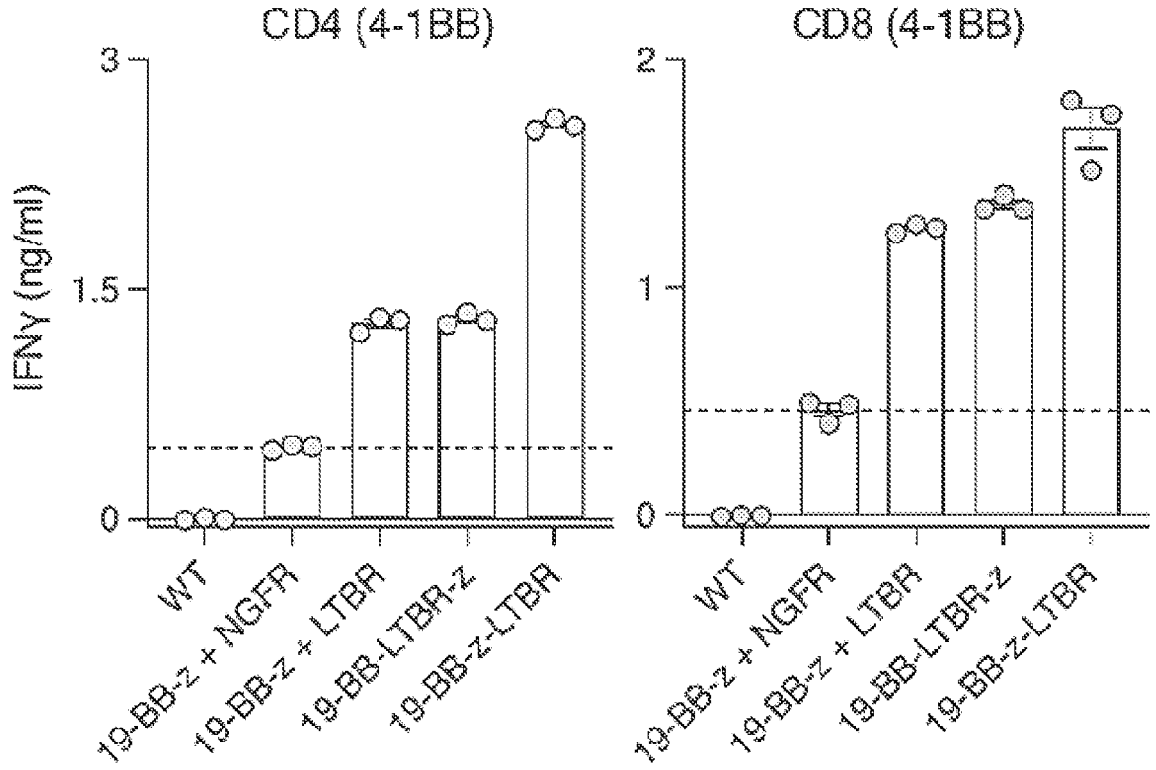
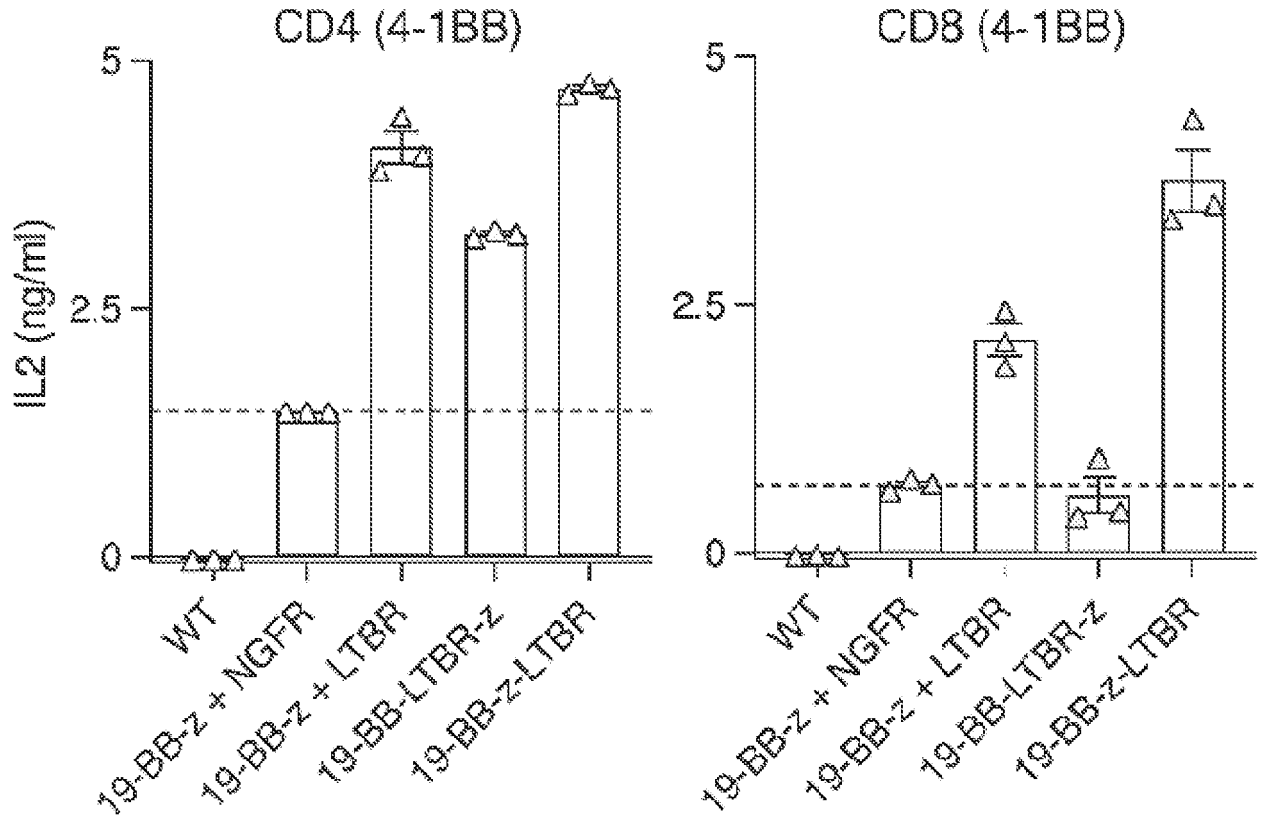


FIG. 21L



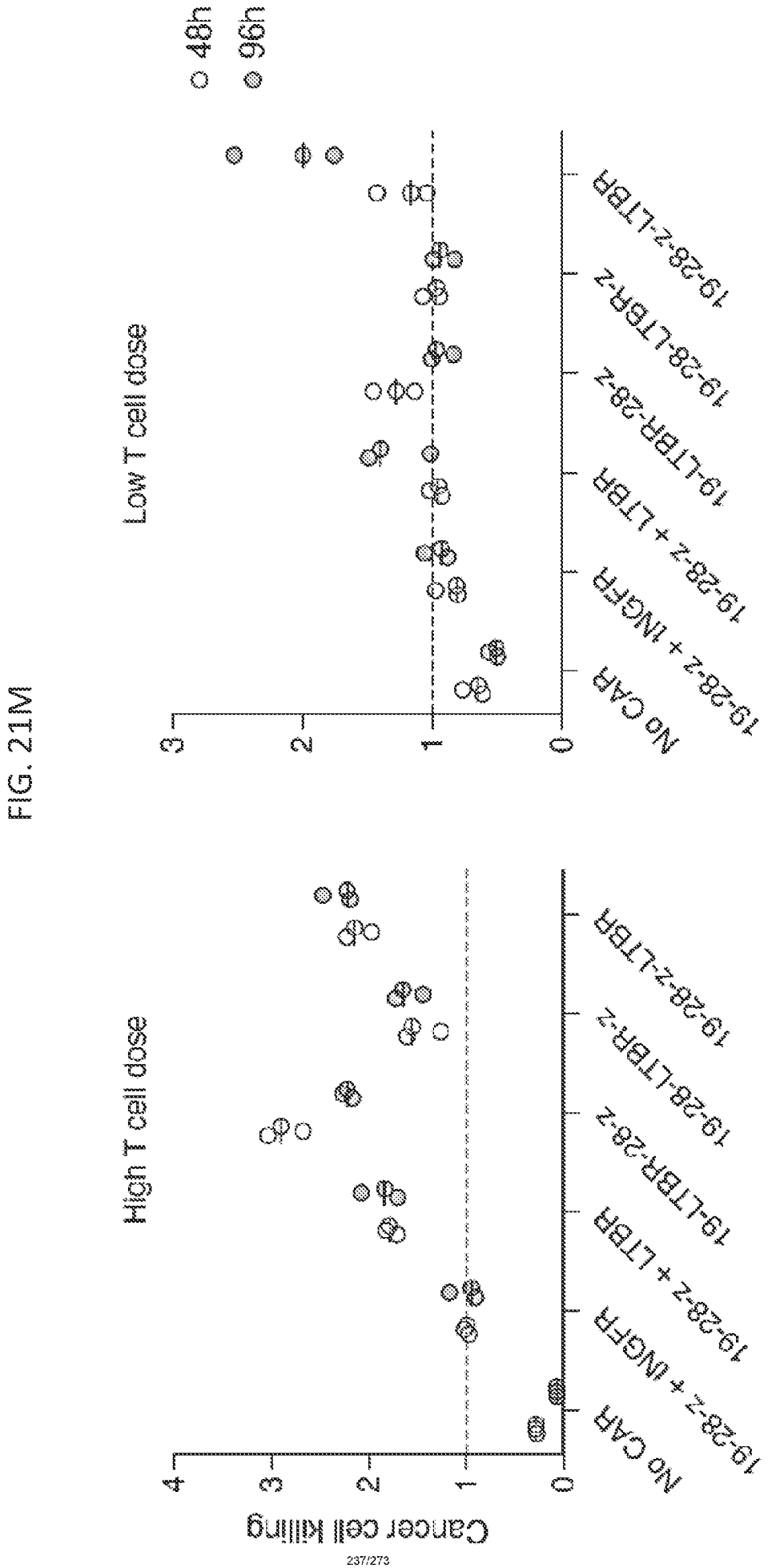

48h
96h
Low T cell dose
High T cell dose
Cancer cell killing
0
1
2
3
4
No CAR
19-28-z + iNGFR
19-28-z + LTBR
19-LTBR-28-z
19-28-LTBR-z
19-28-z-LTBR

FIG. 21M

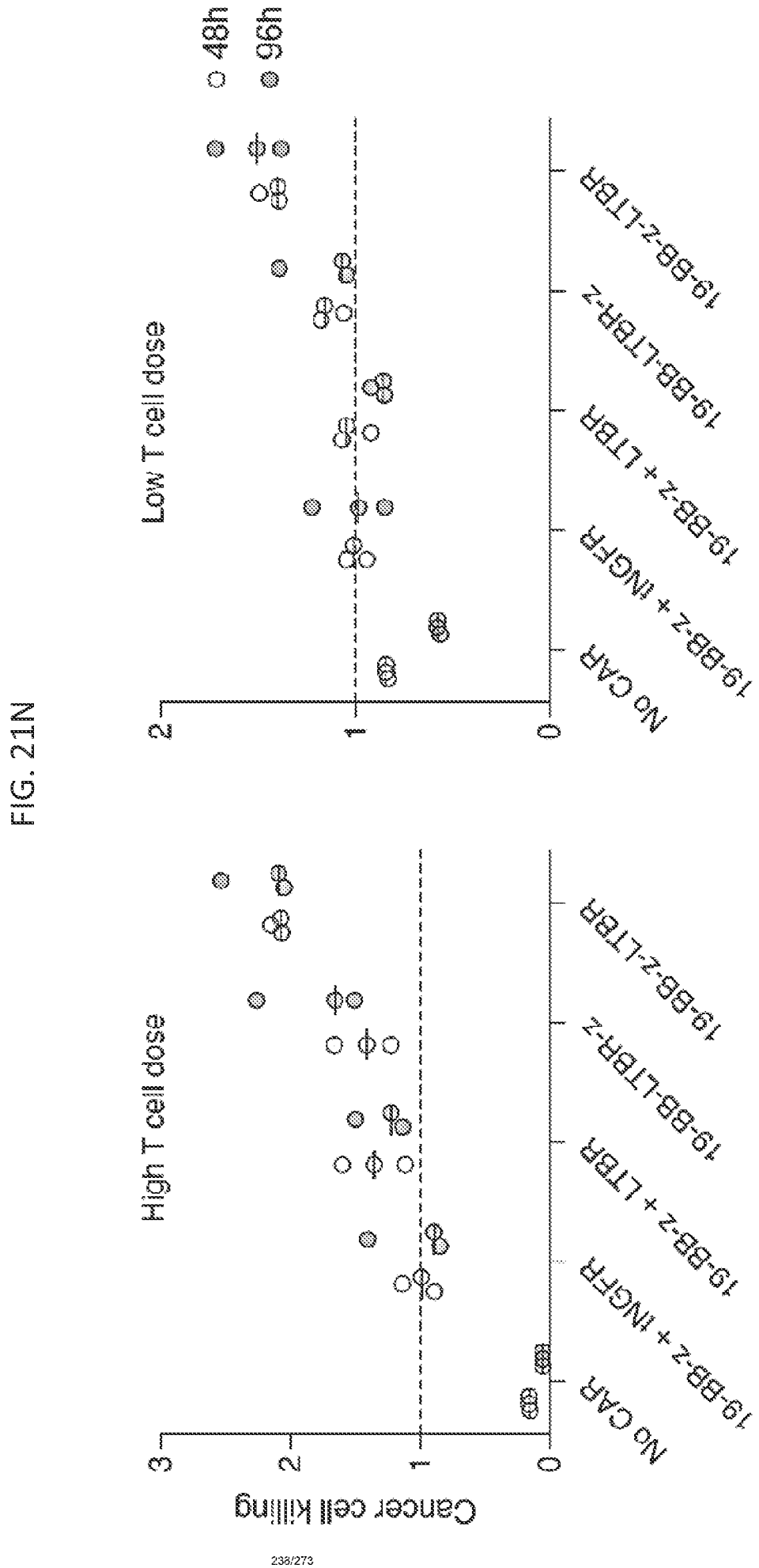

48h
96h
Low T cell dose
High T cell dose
Cancer cell killing
0
1
2
3
No CAR
19-BB-Z + iNGFR
19-BB-Z + LTBR
19-BB-LTBR-Z
19-BB-Z-LTBR

FIG. 21N

FIG. 22A

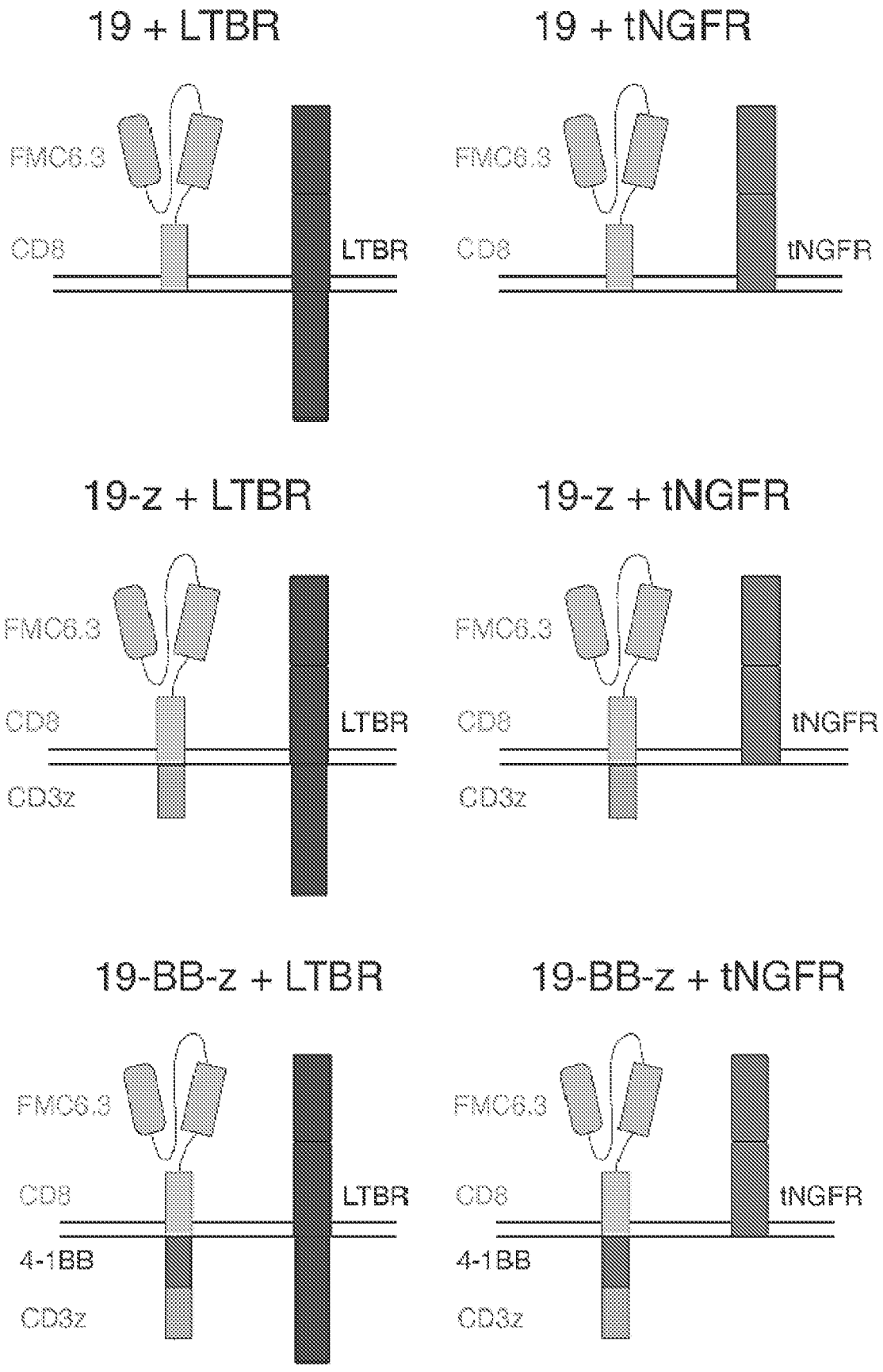

19 + LTBR
FMC6.3
CD8
LTBR
19 + tNGFR
FMC6.3
CD8
tNGFR
19-z + LTBR
FMC6.3
CD8
CD3z
LTBR
19-z + tNGFR
FMC6.3
CD8
CD3z
tNGFR
19-BB-z + LTBR
FMC6.3
CD8
4-1BB
CD3z
LTBR
19-BB-z + tNGFR
FMC6.3
CD8
4-1BB
CD3z
tNGFR

FIG. 22B

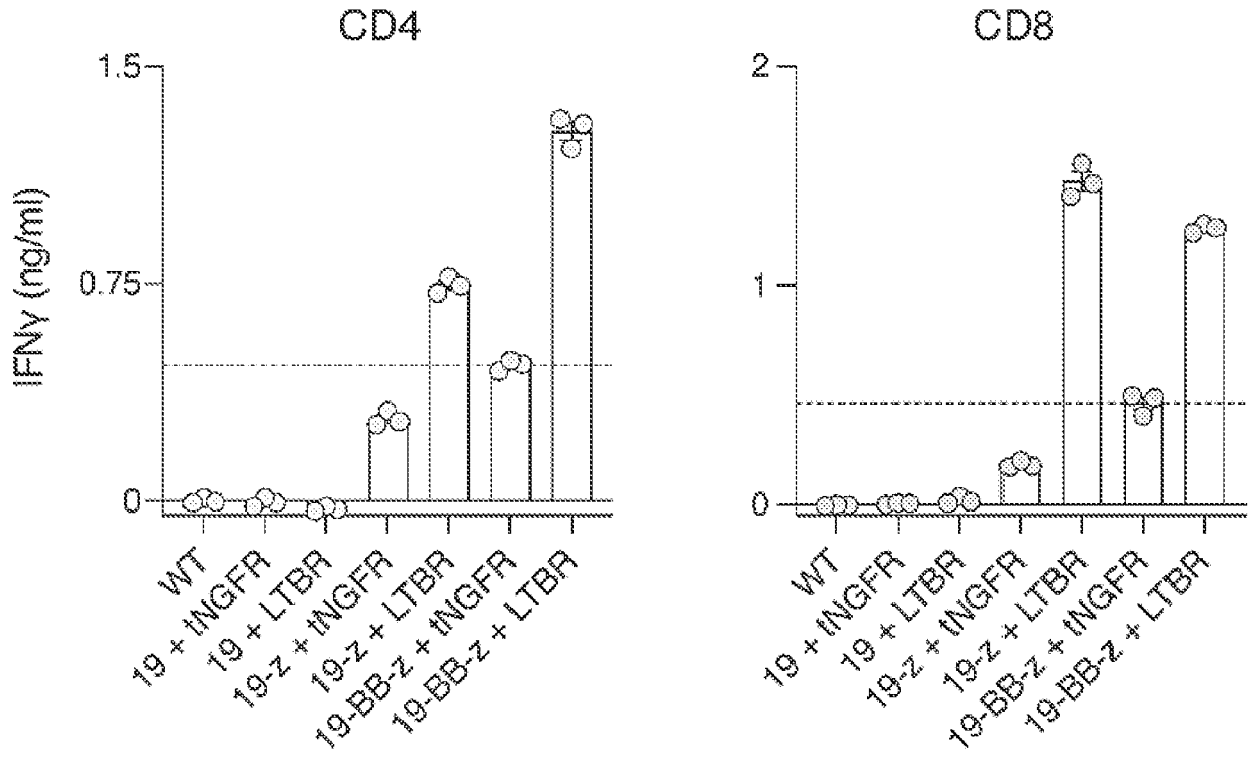
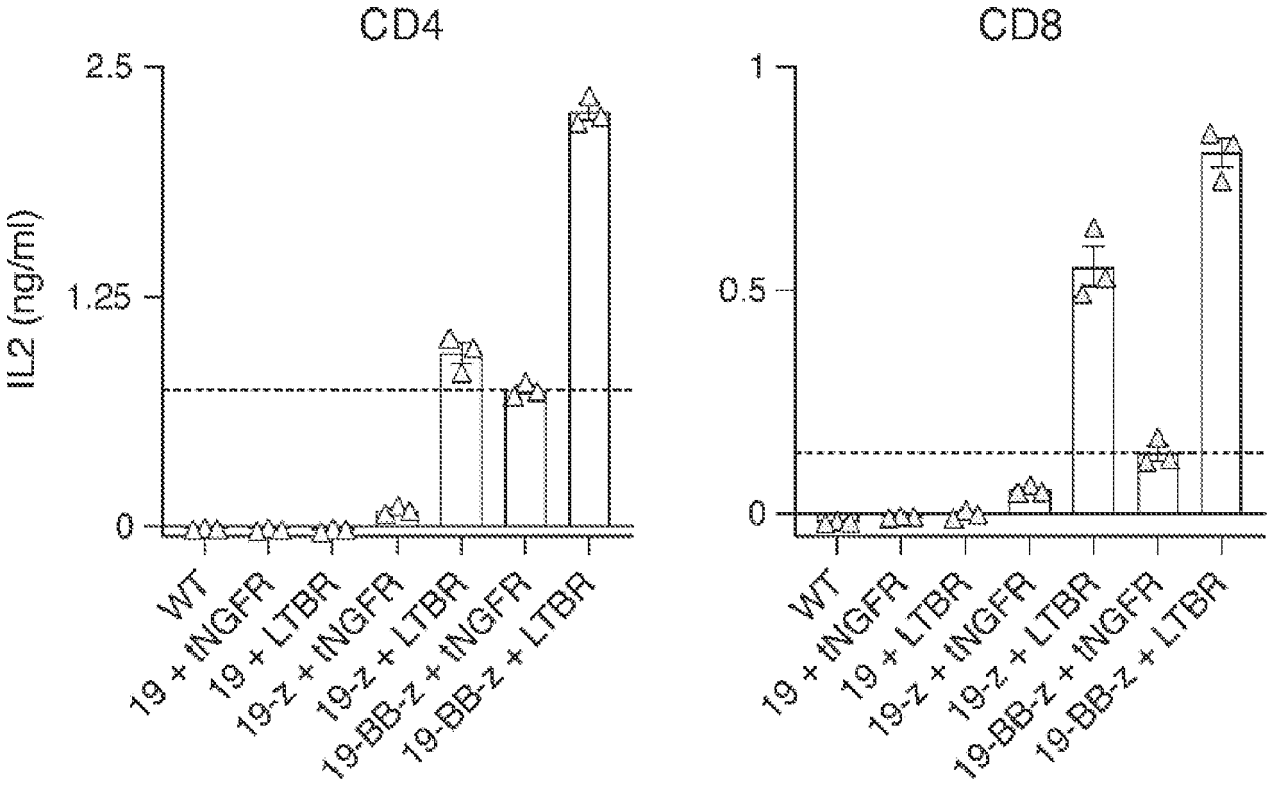


FIG. 22C



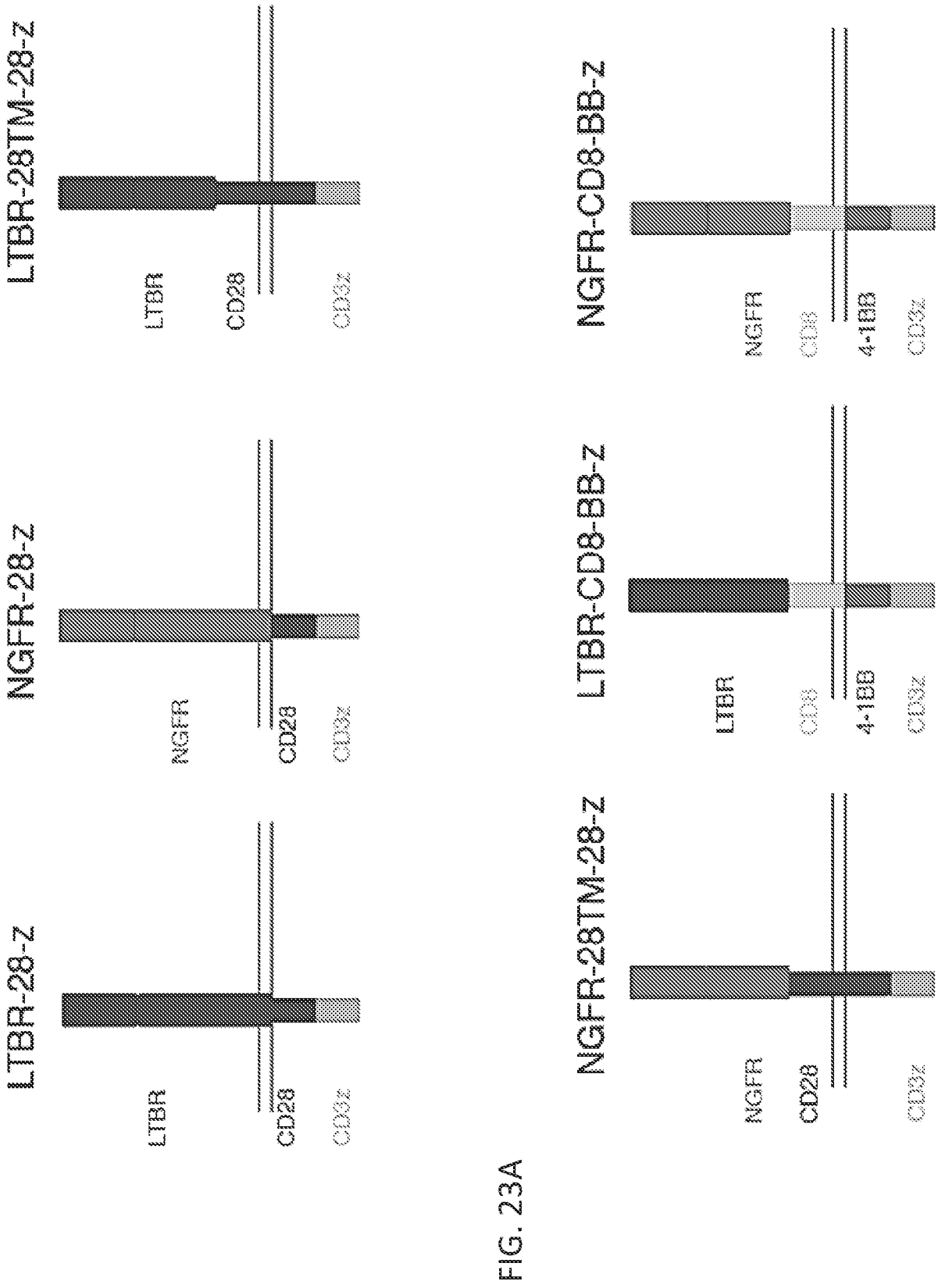

LTBR-28-z
LTBR
CD28
CD3ζ
NGFR-28-z
NGFR
CD28
CD3ζ
LTBR-28TM-28-z
LTBR
CD28
CD3ζ
NGFR-28TM-28-z
NGFR
CD28
CD3ζ
LTBR-CD8-BB-z
LTBR
CD8
4-1BB
CD3ζ
NGFR-CD8-BB-z
NGFR
CD8
4-1BB
CD3ζ

FIG. 23A

FIG. 23B

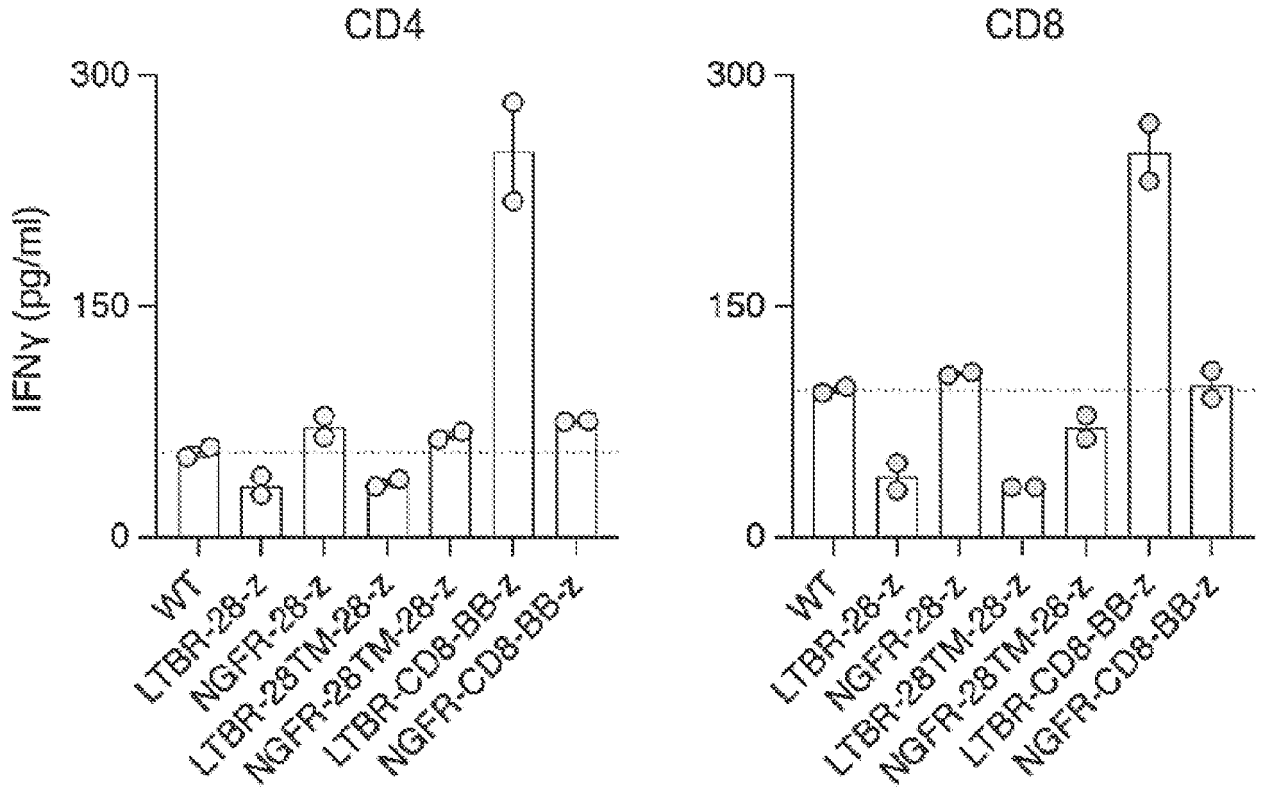


FIG. 23C

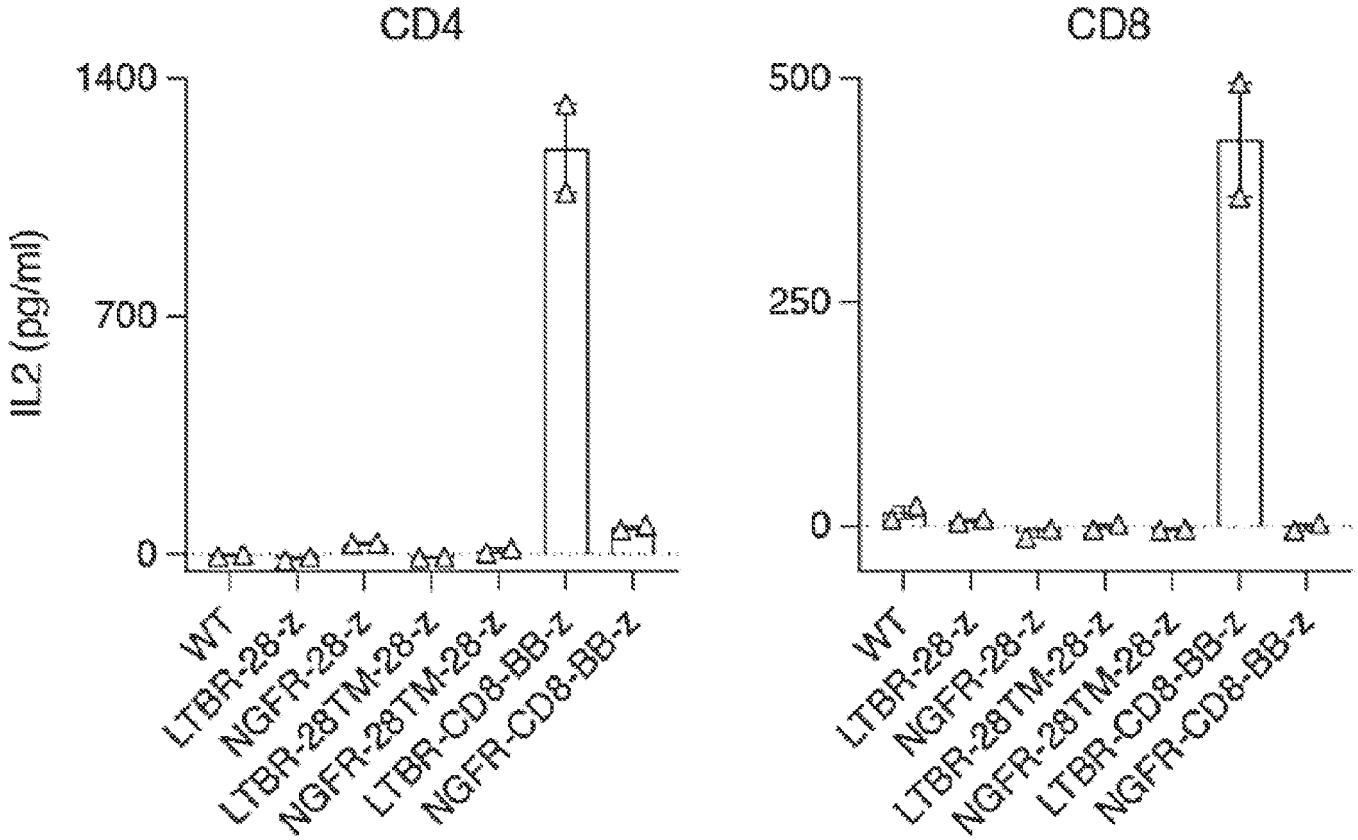


FIG. 24A

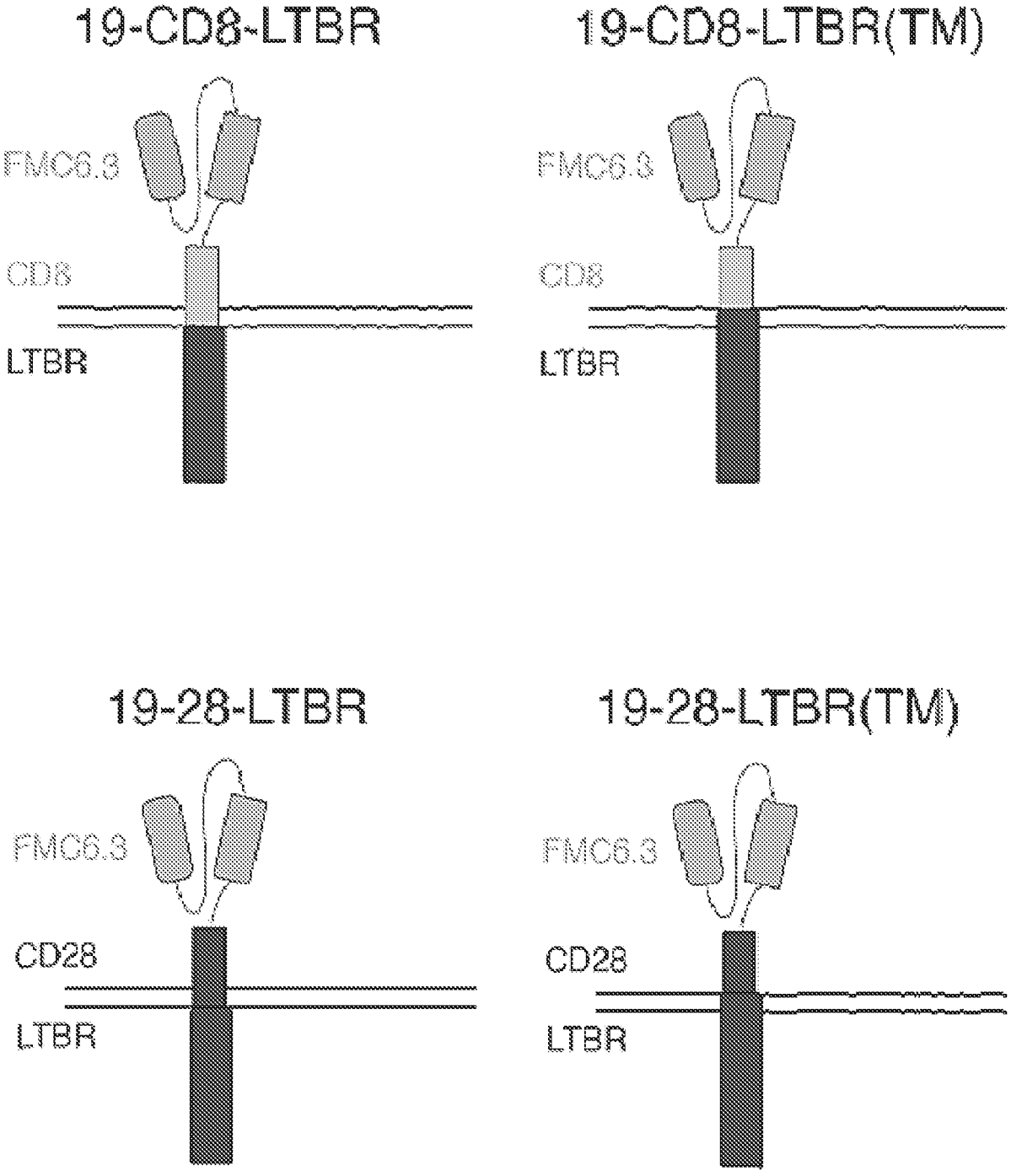
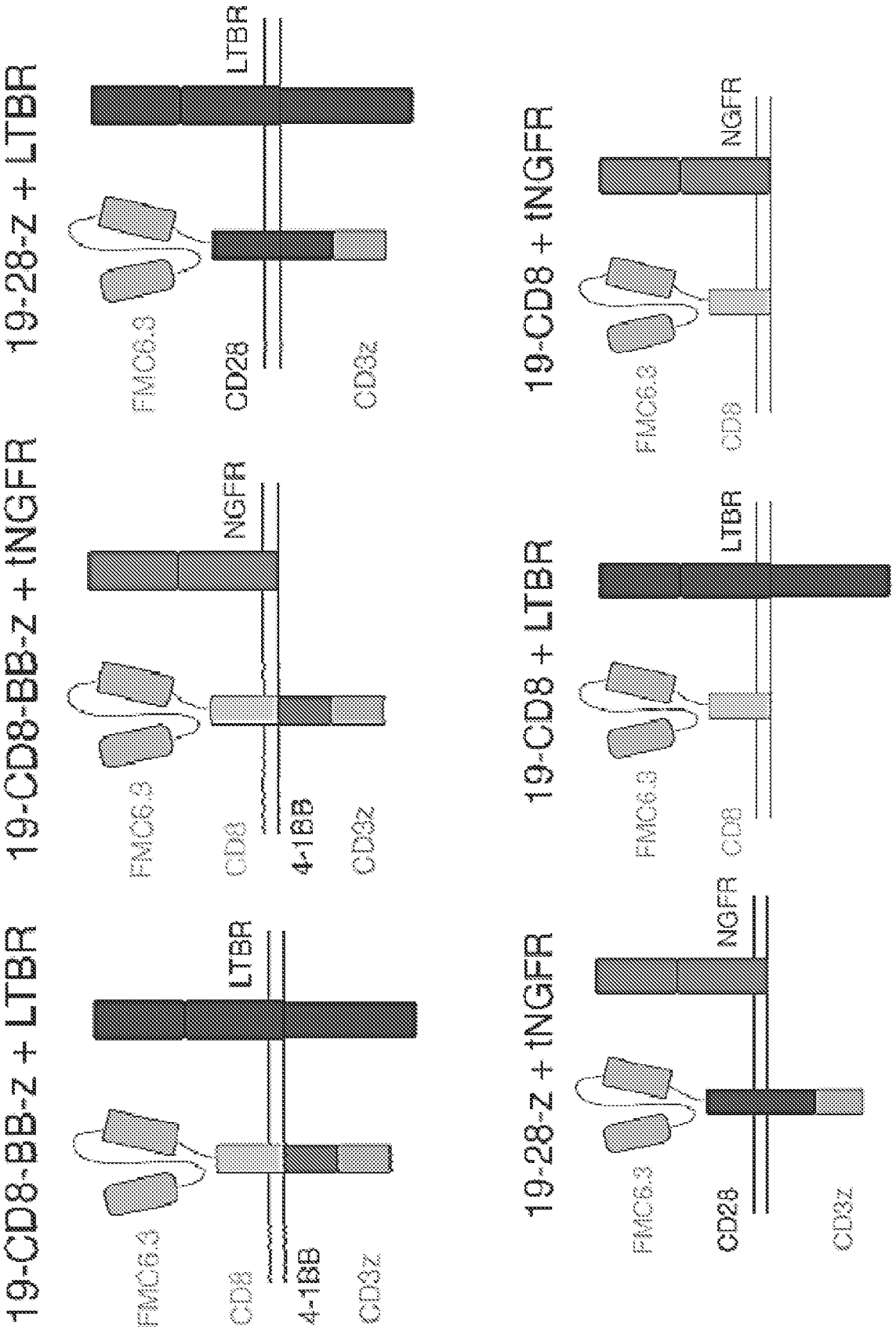

19-CD8-LTBR
FMC6.3
CD8
LTBR
19-CD8-LTBR(TM)
FMC6.3
CD8
LTBR
19-28-LTBR
FMC6.3
CD28
LTBR
19-28-LTBR(TM)
FMC6.3
CD28
LTBR

FIG. 24B


19-CD8-BB-z + LTBR
FMC63
CD8
4-1BB
CD3z
LTBR
19-CD8-BB-z + tNGFR
FMC63
CD8
4-1BB
CD3z
NGFR
19-28-z + LTBR
FMC63
CD28
CD3z
LTBR
19-28-z + tNGFR
FMC63
CD28
CD3z
NGFR
19-CD8 + LTBR
FMC63
CD8
LTBR
19-CD8 + tNGFR
FMC63
CD8
NGFR

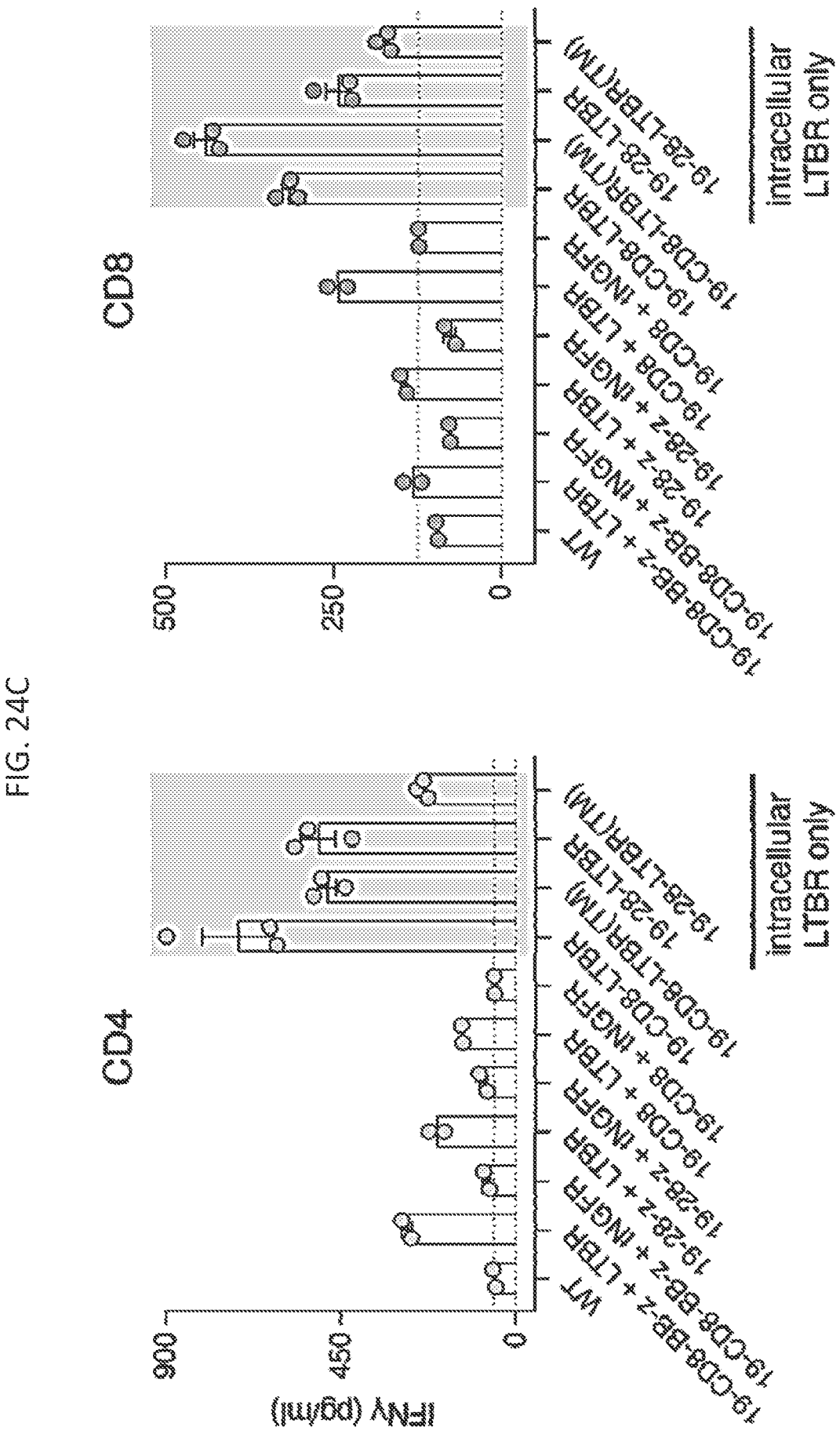

CD4
CD8
IFNγ (pg/ml)
900
450
0
500
250
0
intracellular
LTBR only
WT
19-CD8-BB-z + LTBR
19-28-z + iNGFR
19-CD8 + iNGFR
19-28-z + LTBR
19-CD8 + LTBR
19-CD8-LTBR(TM)
19-28-LTBR

FIG. 24C

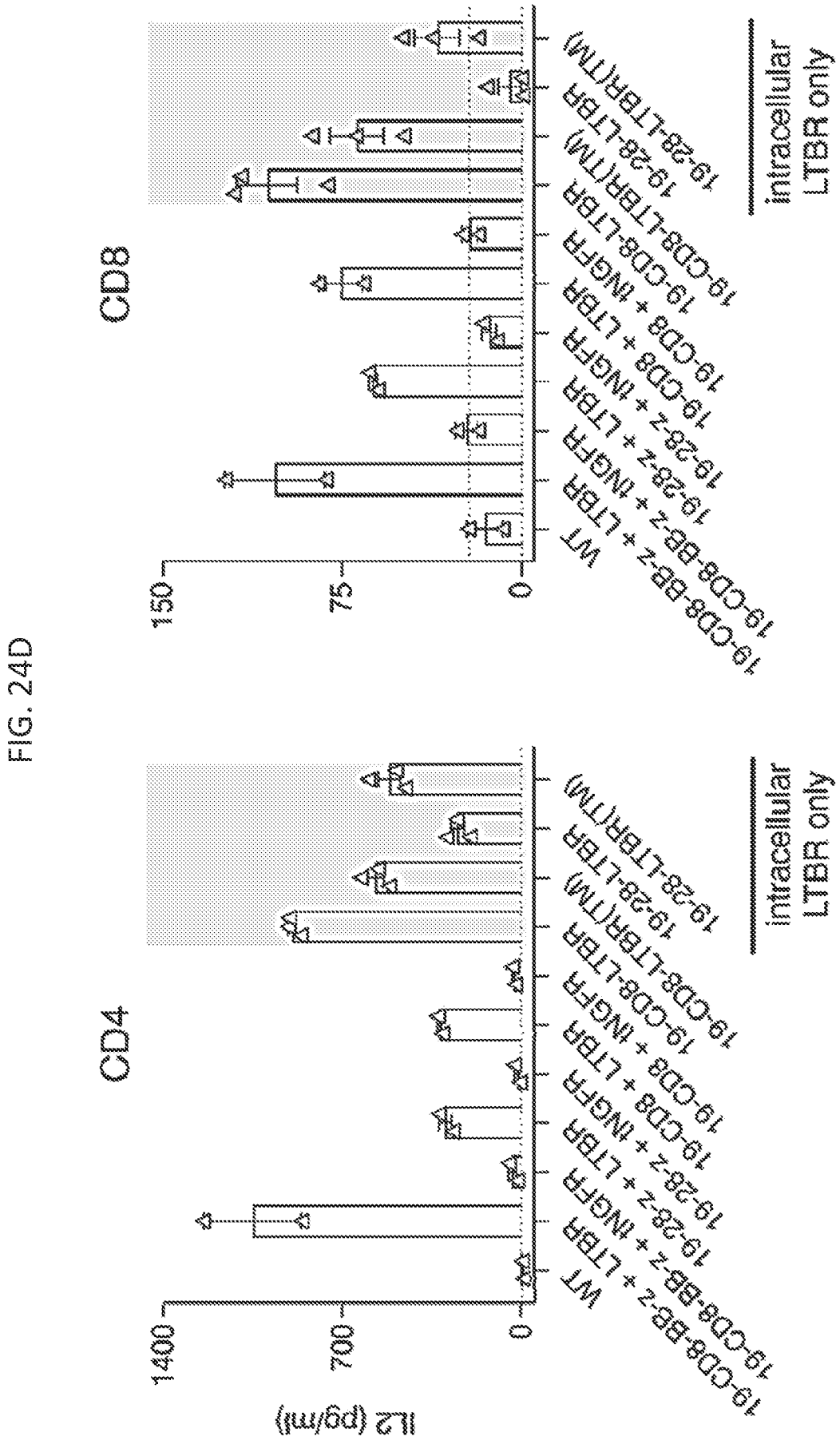

CD4
CD8
IL2 (pg/ml)
1400
700
0
150
75
0
intracellular
LTBR only
WT
19-CD8-BB-z + LTBR
19-28-z + iNGFR
19-28-z + LTBR
19-CD8 + iNGFR
19-CD8 + LTBR
19-CD8-BB-z + iNGFR
19-CD8-BB-z + LTBR
19-28-LTBR
19-28-LTBR(TM)

FIG. 24D

FIG. 24E

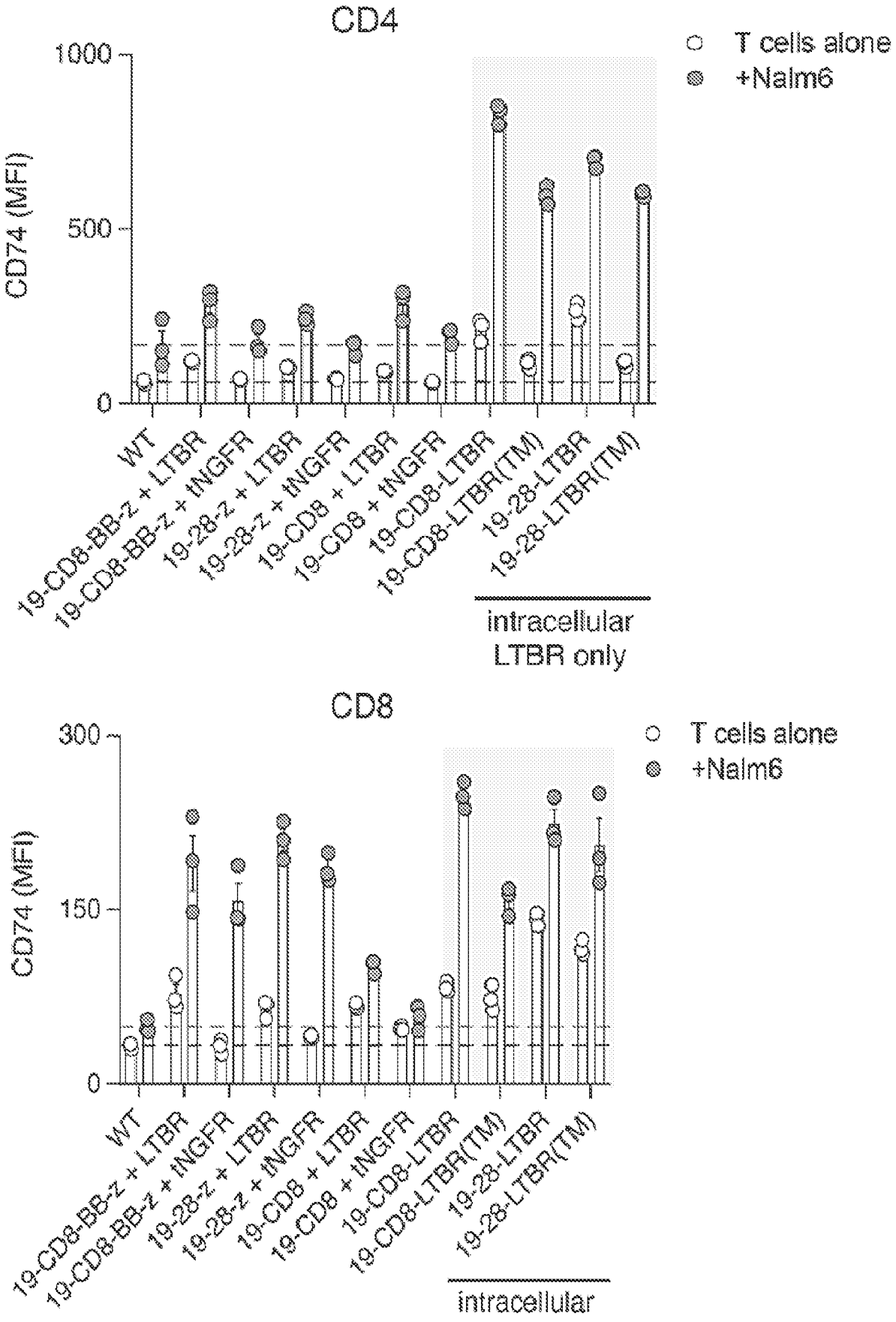

CD4
T cells alone
+Nalm6
CD74 (MFI)
1000
500
0
WT
19-CD8-BB-z + LTBR
19-CD8-BB-z + tNGFR
19-28-z + LTBR
19-28-z + tNGFR
19-CD8 + LTBR
19-CD8 + tNGFR
19-CD8-LTBR
19-CD8-LTBR(TM)
19-28-LTBR
19-28-LTBR(TM)
intracellular
LTBR only
CD8
T cells alone
+Nalm6
CD74 (MFI)
300
150
0
WT
19-CD8-BB-z + LTBR
19-CD8-BB-z + tNGFR
19-28-z + LTBR
19-28-z + tNGFR
19-CD8 + LTBR
19-CD8 + tNGFR
19-CD8-LTBR
19-CD8-LTBR(TM)
19-28-LTBR
19-28-LTBR(TM)
intracellular

FIG. 25A

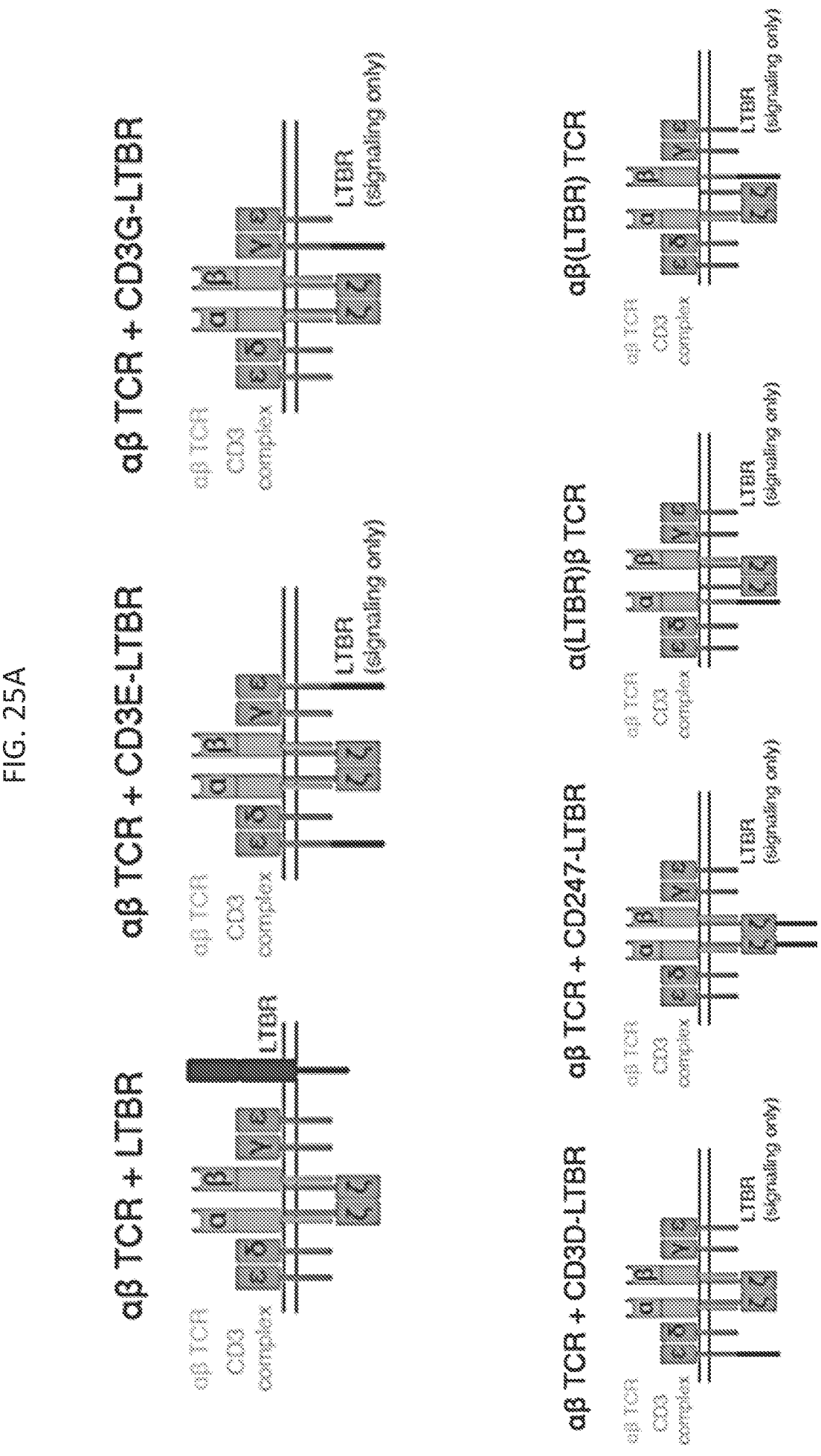

αβ TCR + LTBR
αβ TCR + CD3E-LTBR
αβ TCR + CD3G-LTBR
αβ TCR + CD3D-LTBR
αβ TCR + CD247-LTBR
α(LTBR)β TCR
αβ(LTBR) TCR
αβ TCR
CD3 complex
LTBR
LTBR (signaling only)

FIG. 25B

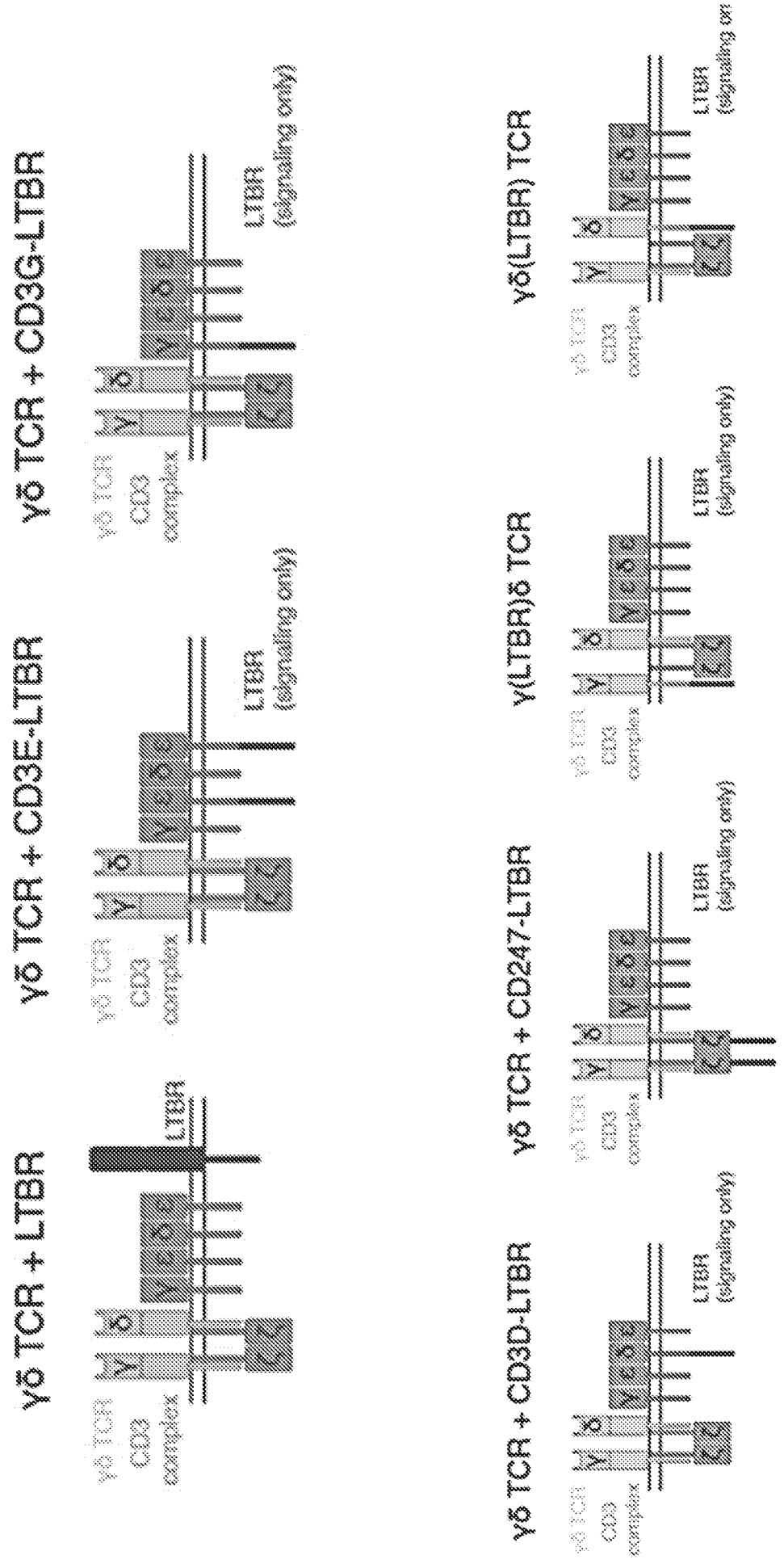

γδ TCR + LTBR
γδ TCR + CD3E-LTBR
γδ TCR + CD3G-LTBR
γδ TCR + CD3D-LTBR
γδ TCR + CD247-LTBR
γ(LTBR)δ TCR
γδ(LTBR) TCR
γδ TCR
CD3 complex
LTBR (signaling only)

FIG. 25C

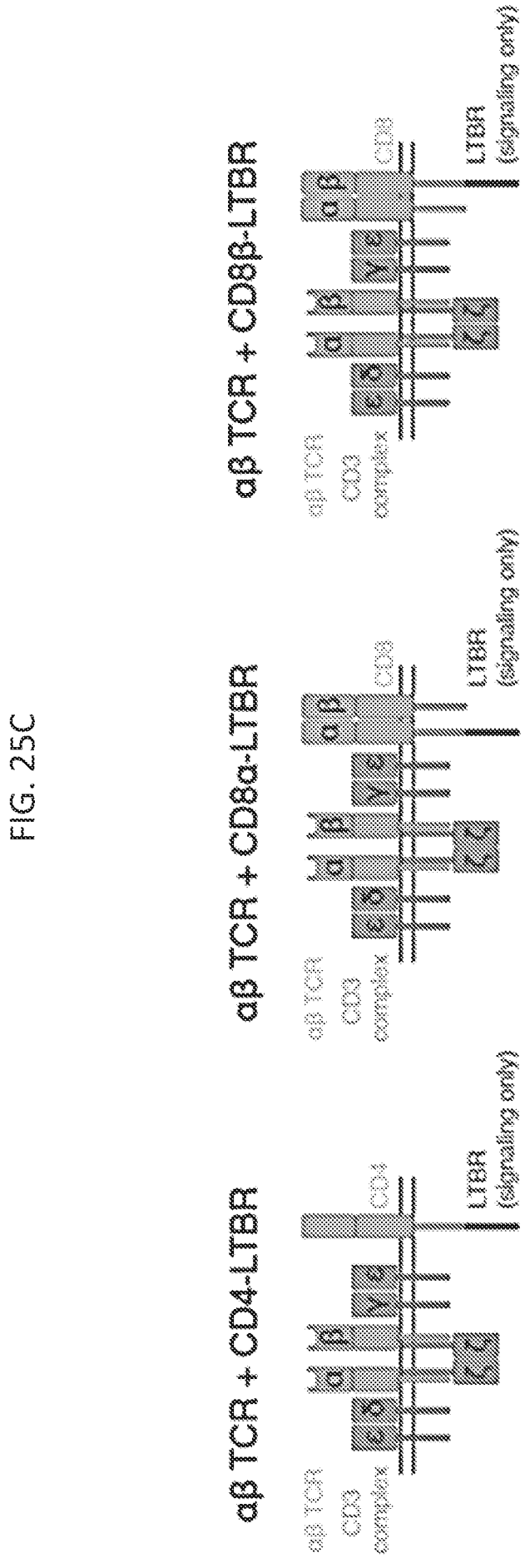

αβ TCR + CD4-LTBR
αβ TCR + CD8α-LTBR
αβ TCR + CD8β-LTBR
αβ TCR
CD3 complex
CD4
CD8
LTBR (signaling only)

FIG. 26A

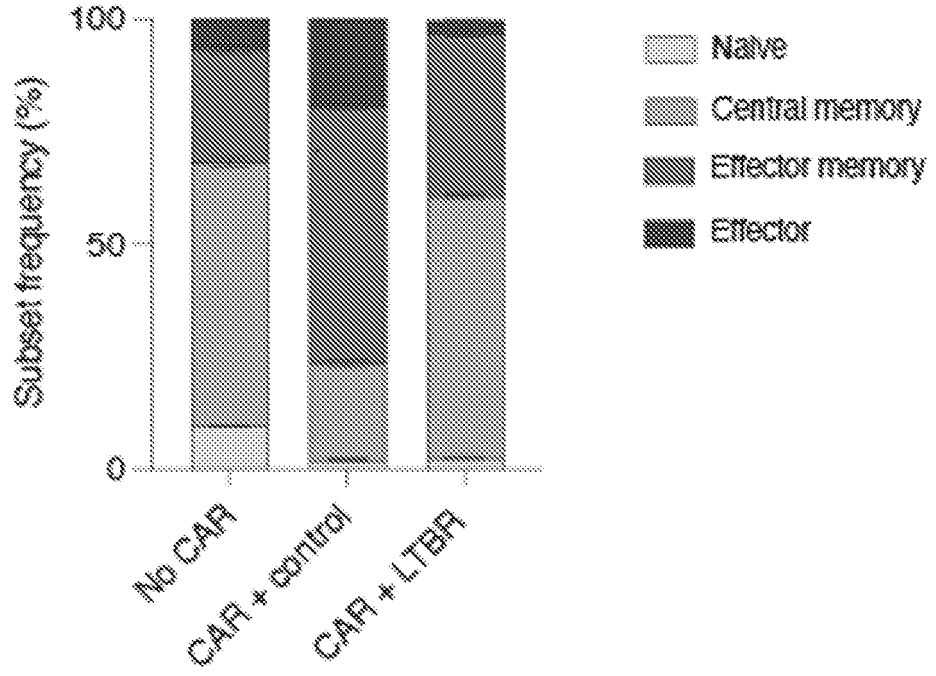


FIG. 26B

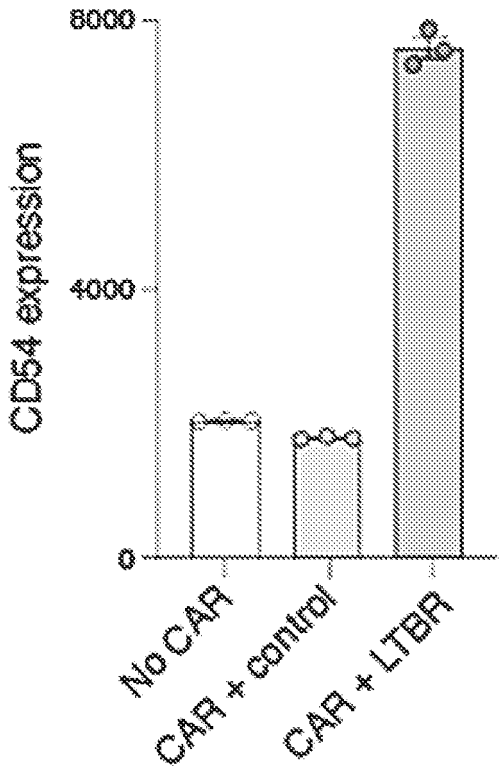


FIG. 26C

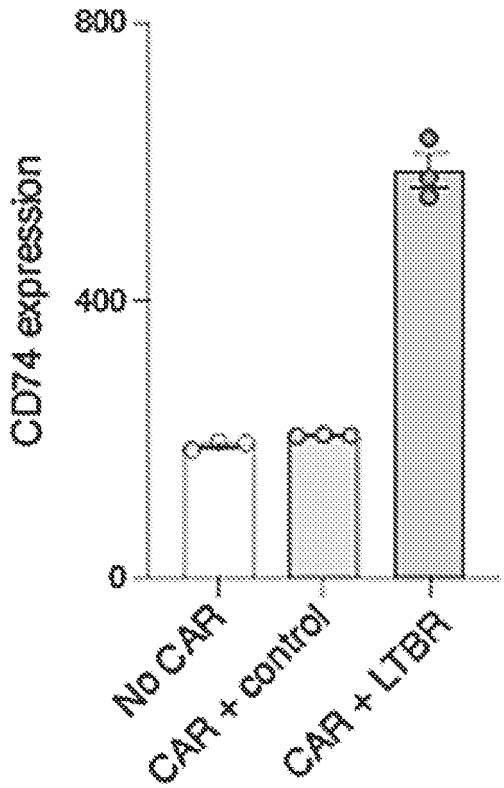


FIG. 26D

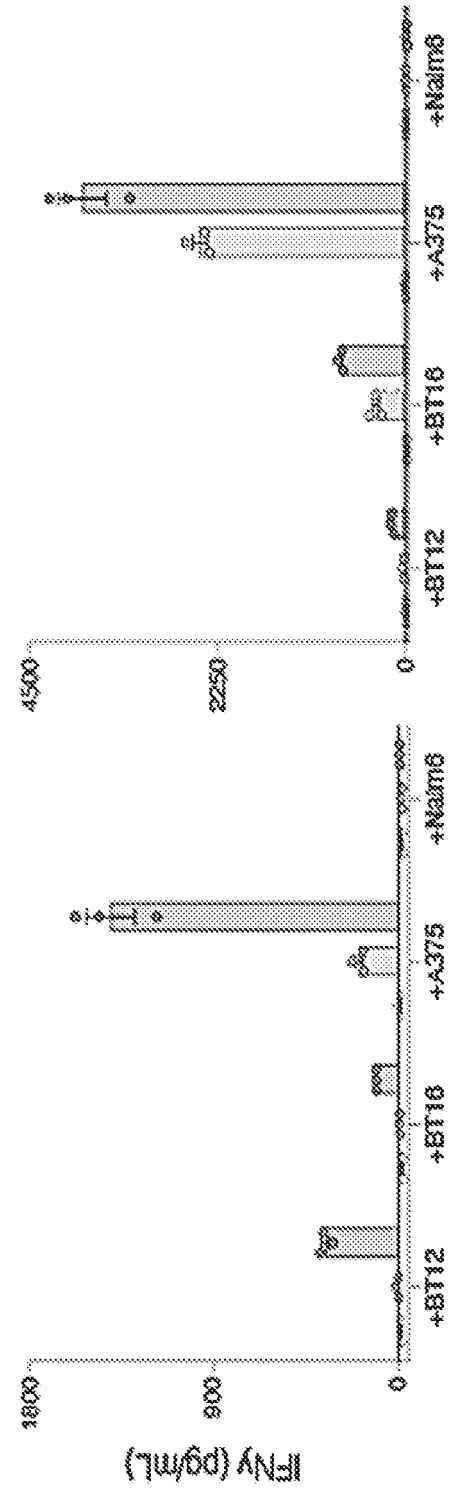


FIG. 26E

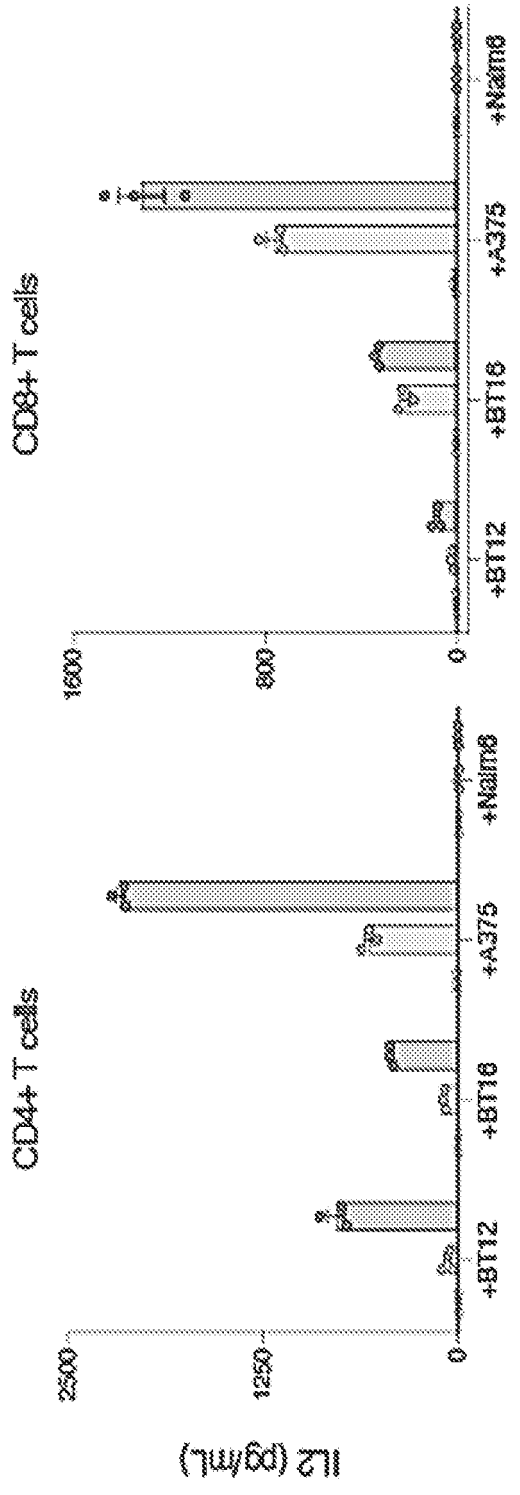


FIG. 26F

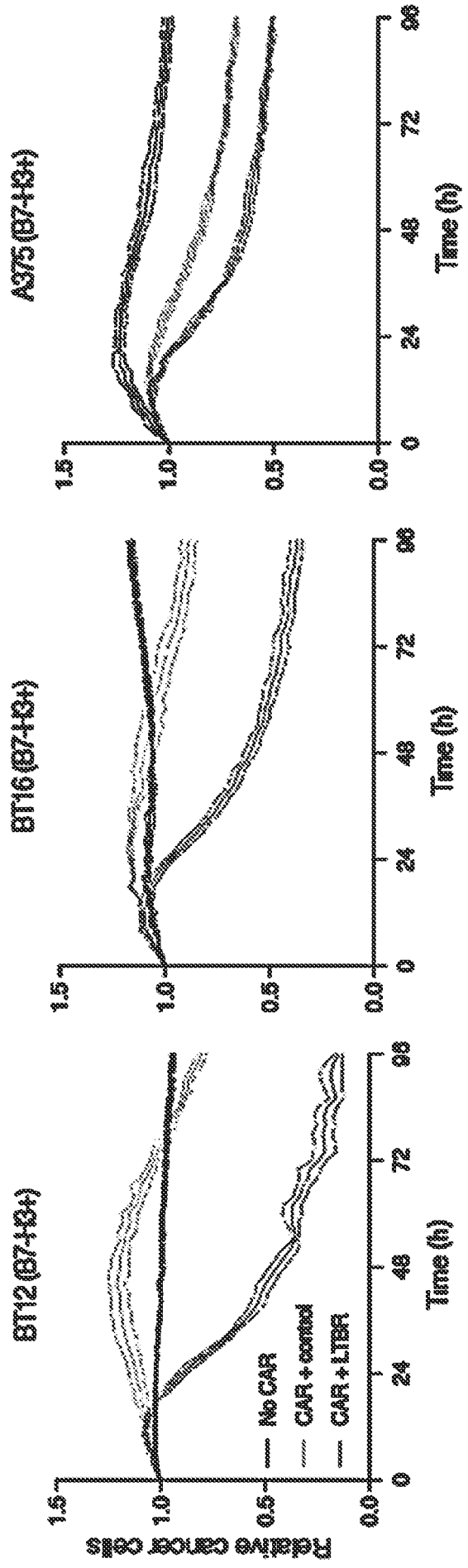


FIG. 26G

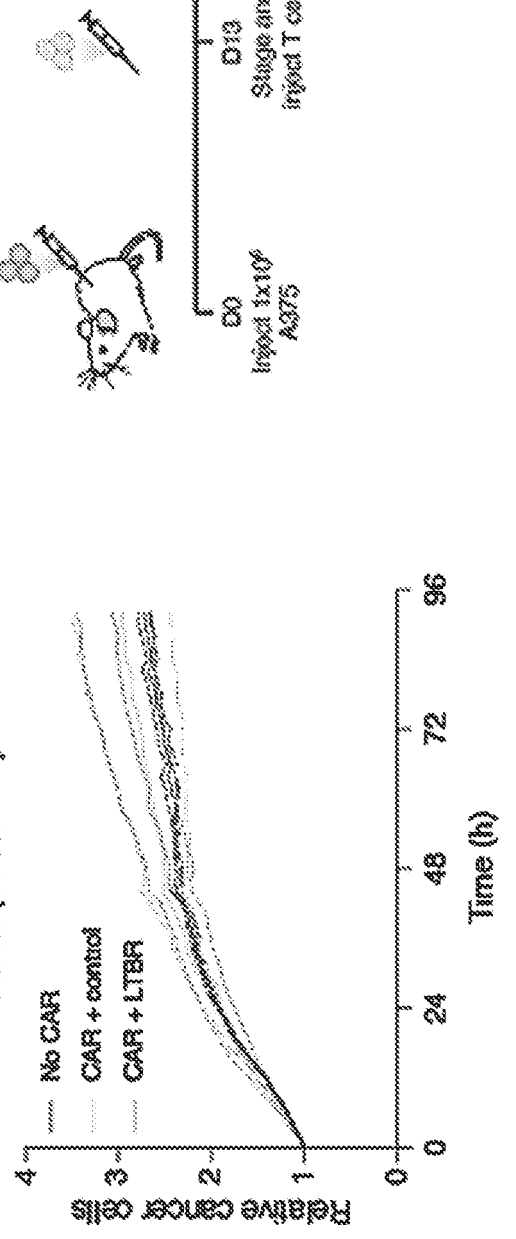


FIG. 26H

FIG. 26J

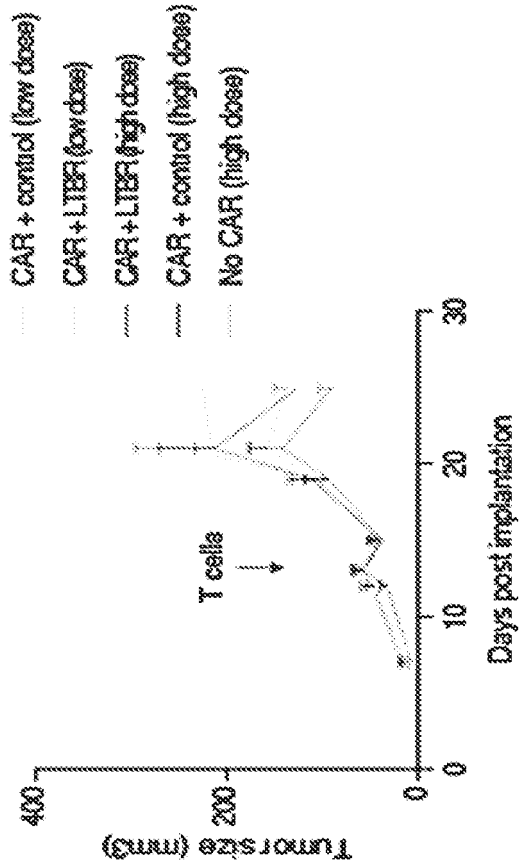


FIG. 26I

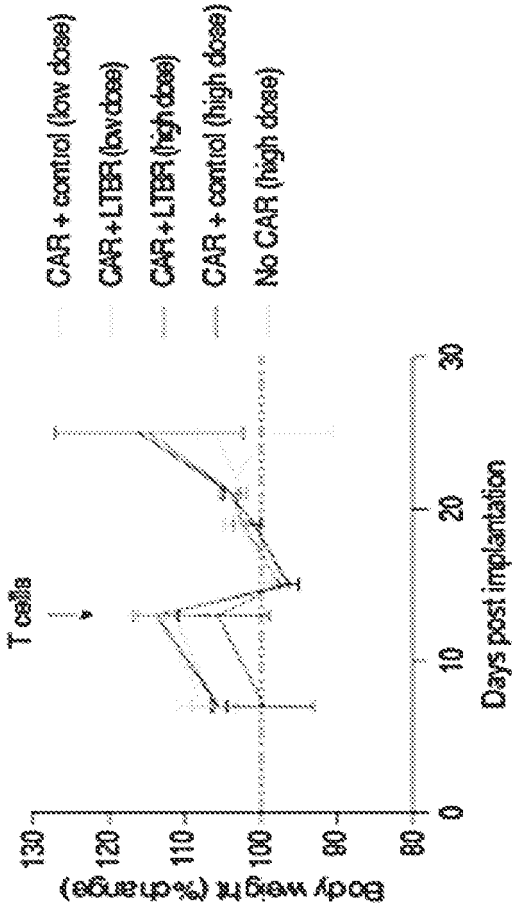


FIG. 26K

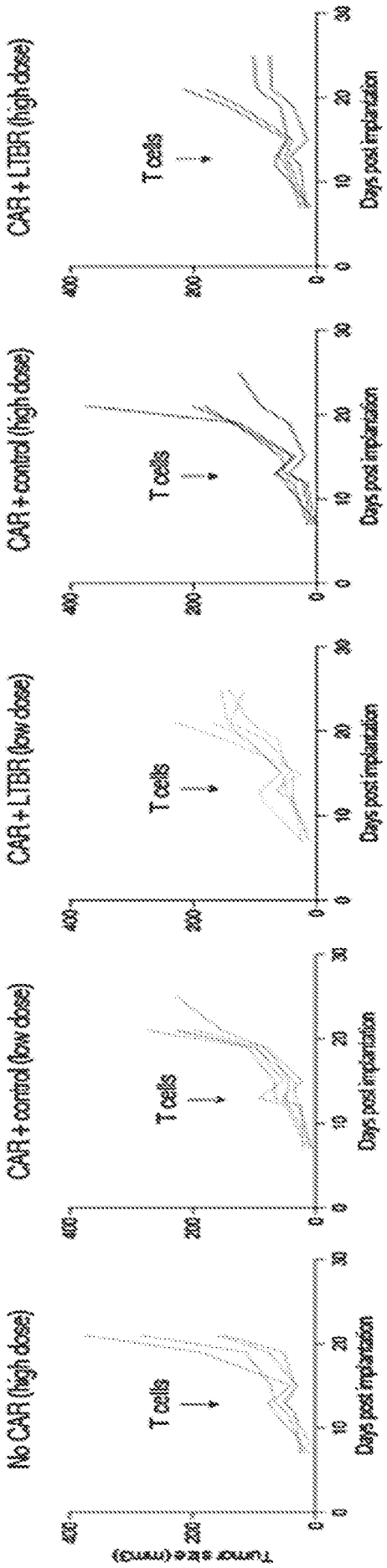


FIG. 27A

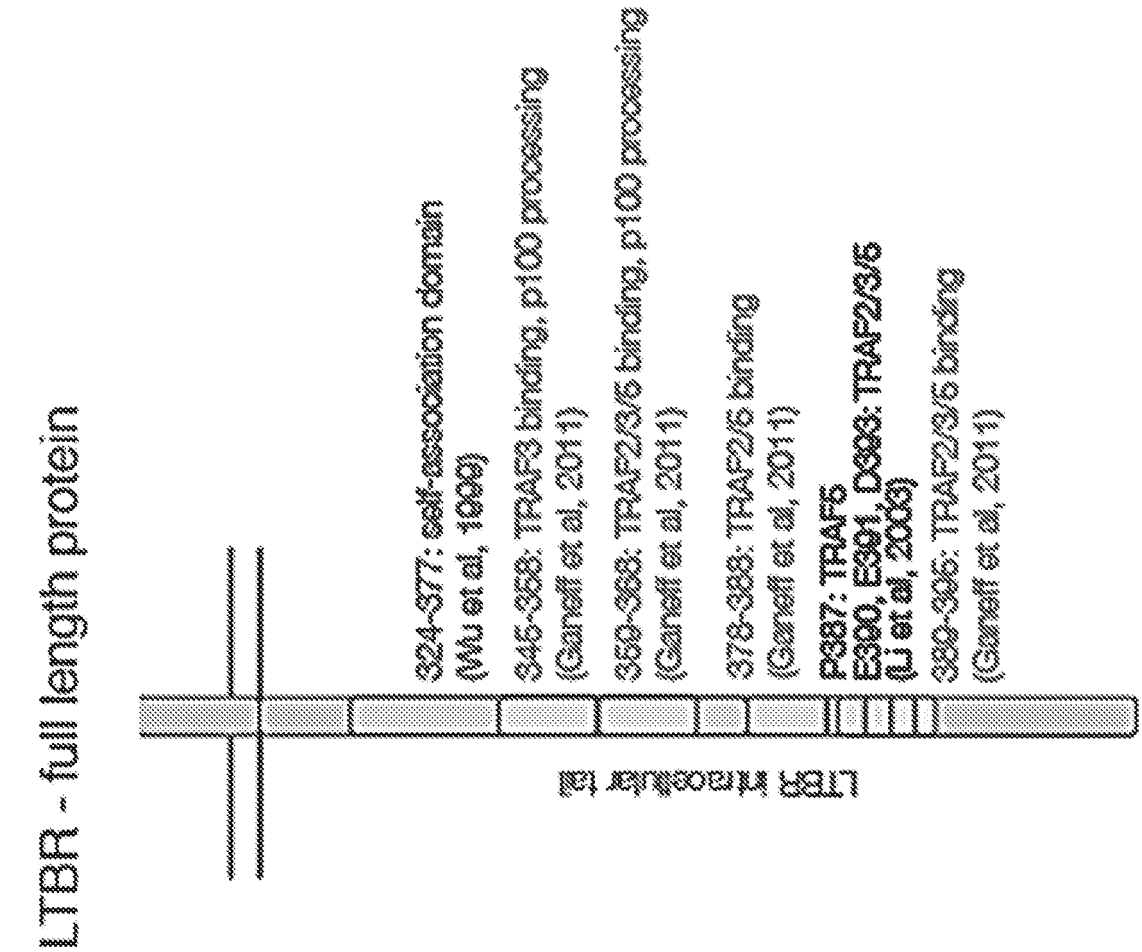


FIG. 27B

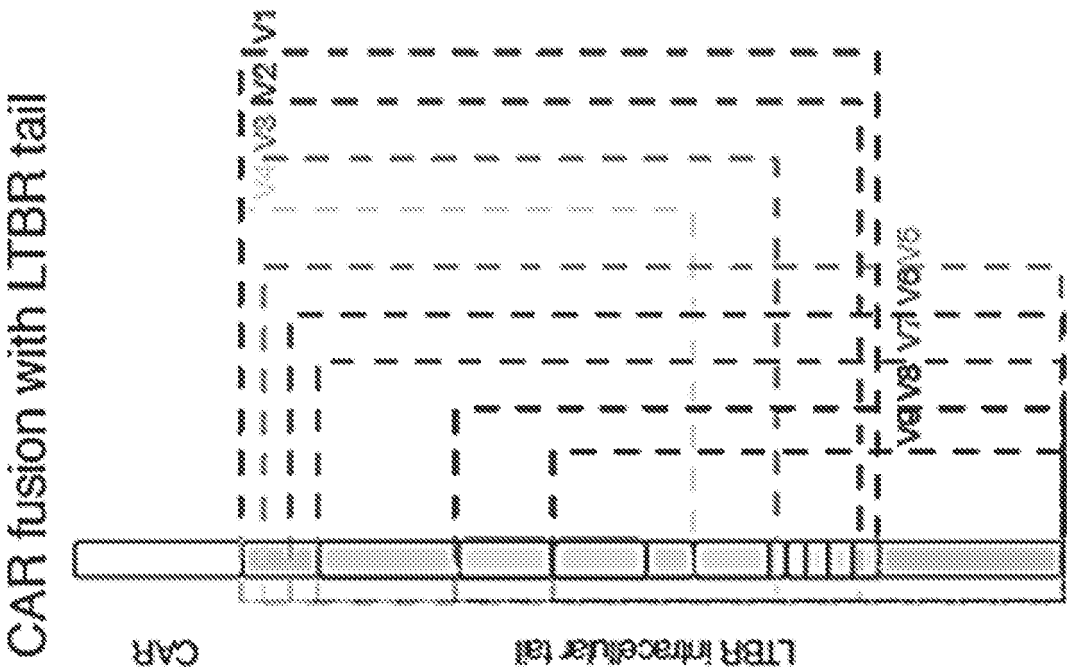


FIG. 27C

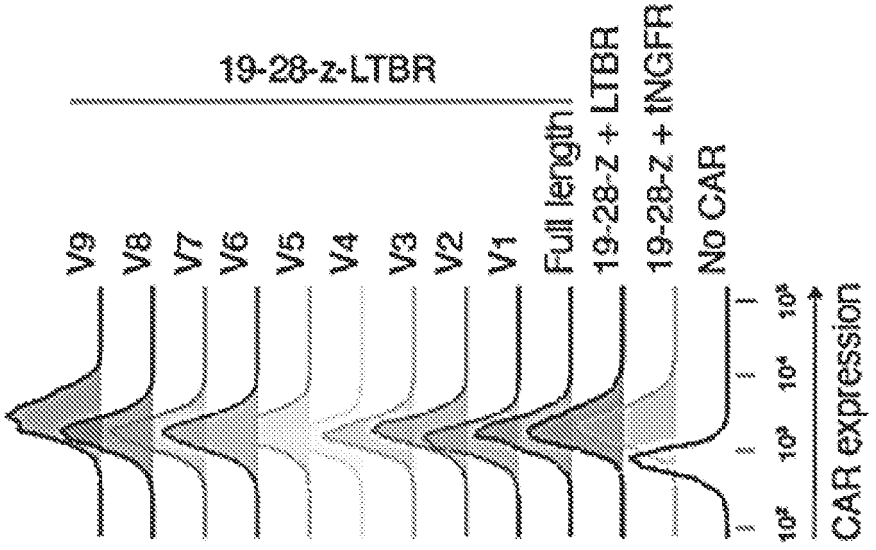


FIG. 27D

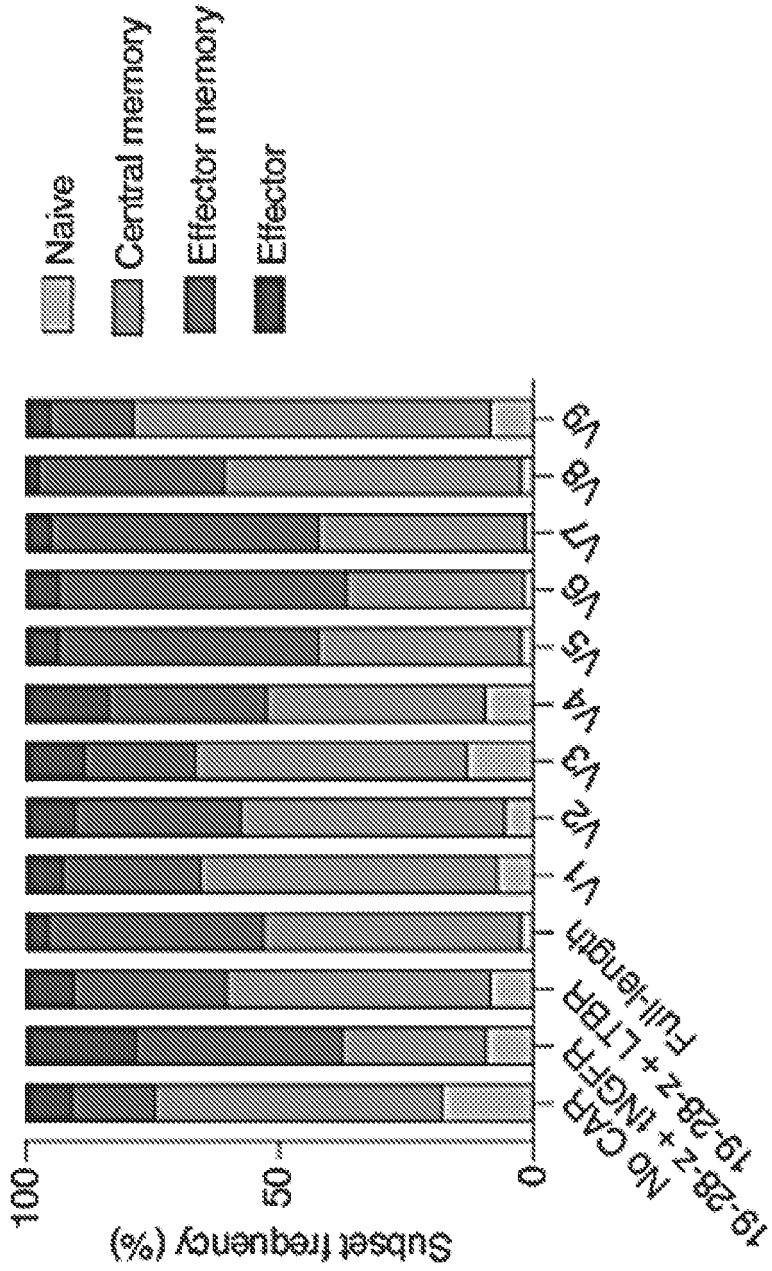


FIG. 27F

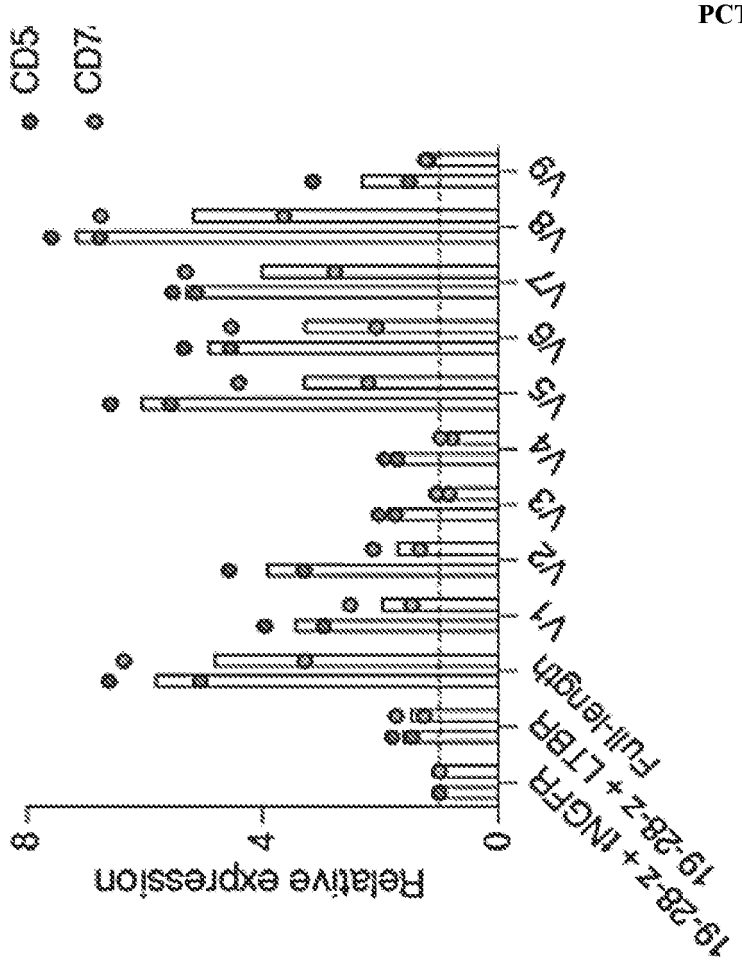


FIG. 27E

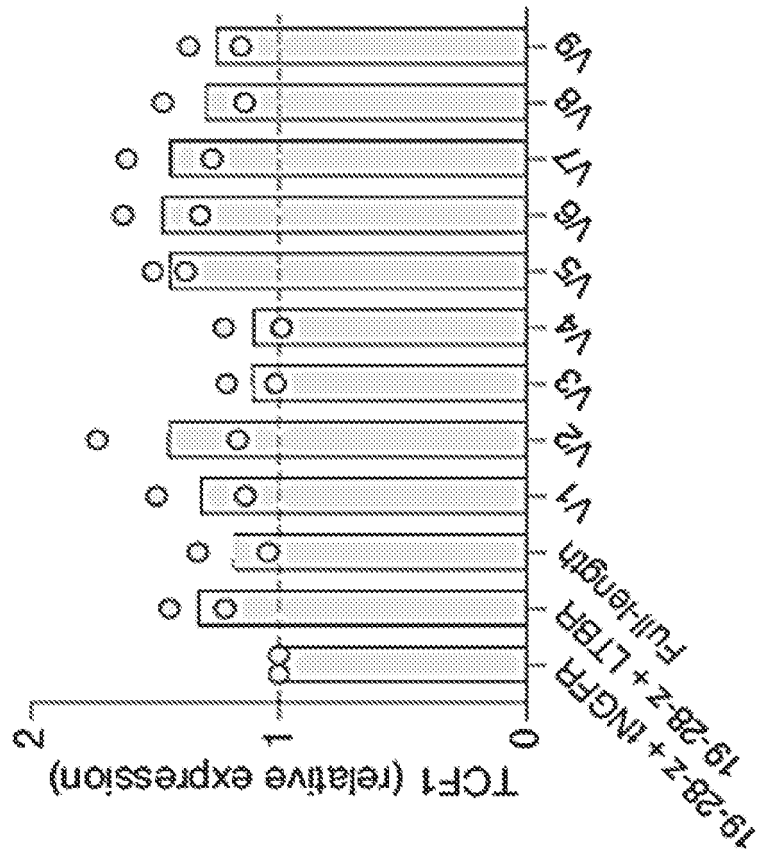


FIG. 27G

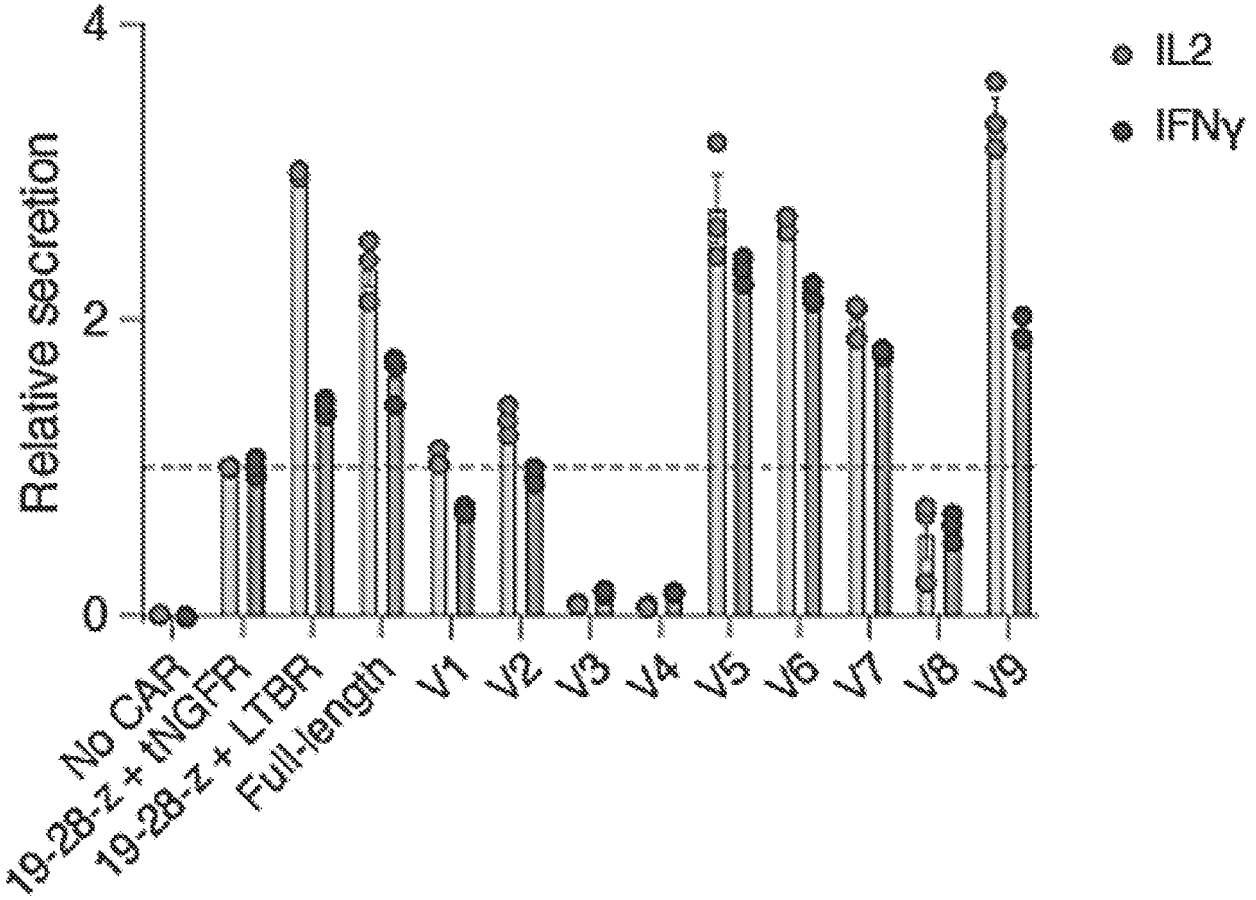

Relative secretion
4
2
0
IL2
IFNγ
No CAR
19-28-z + tNGFR
19-28-z + LTBR
Full-length
V1
V2
V3
V4
V5
V6
V7
V8
V9

FIG. 28A

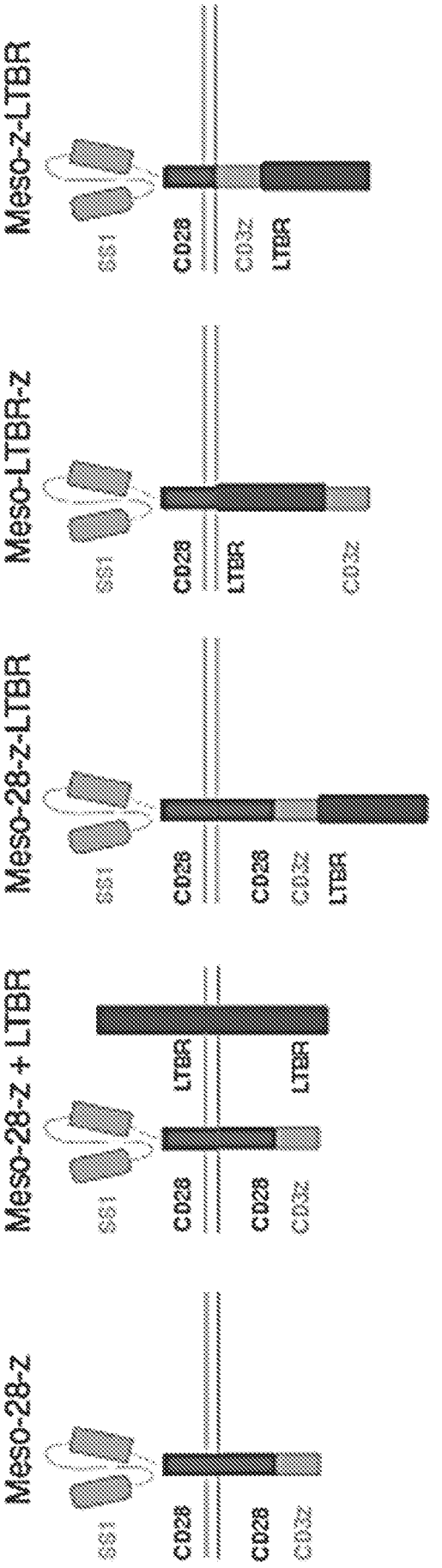


FIG. 28B

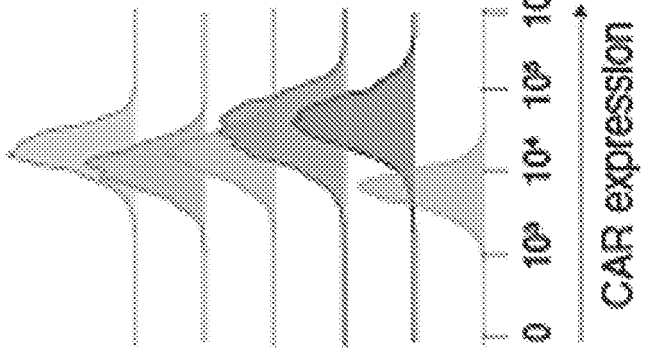


FIG. 28C

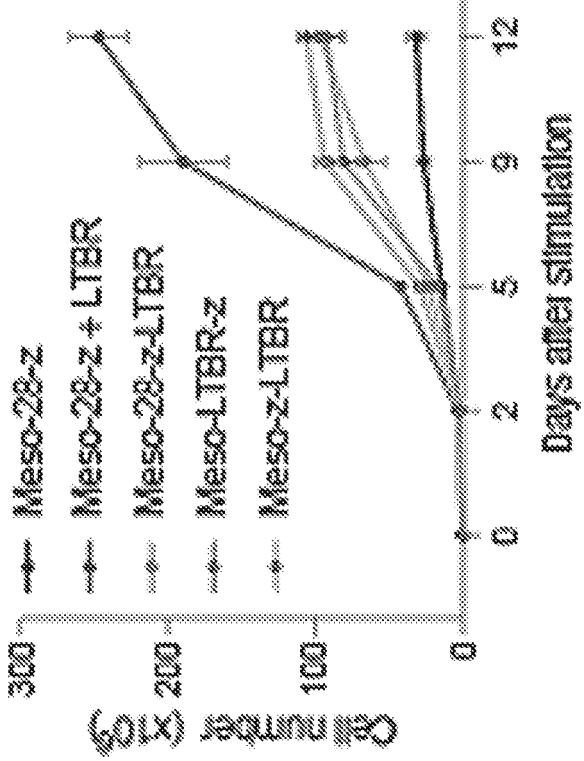


FIG. 28D

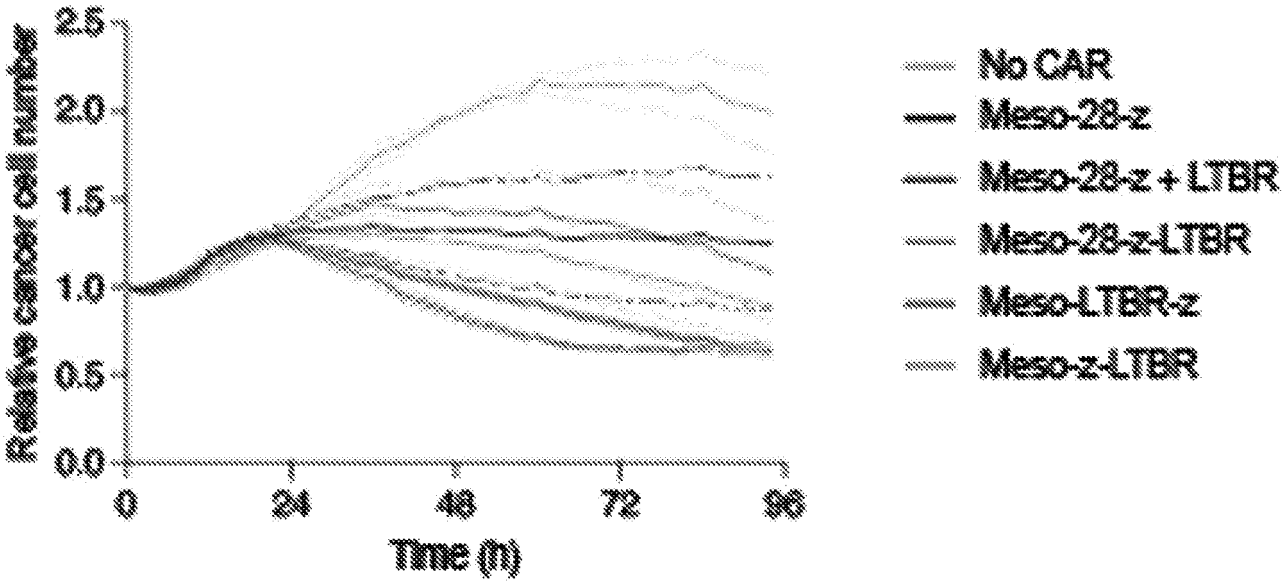


FIG. 28E

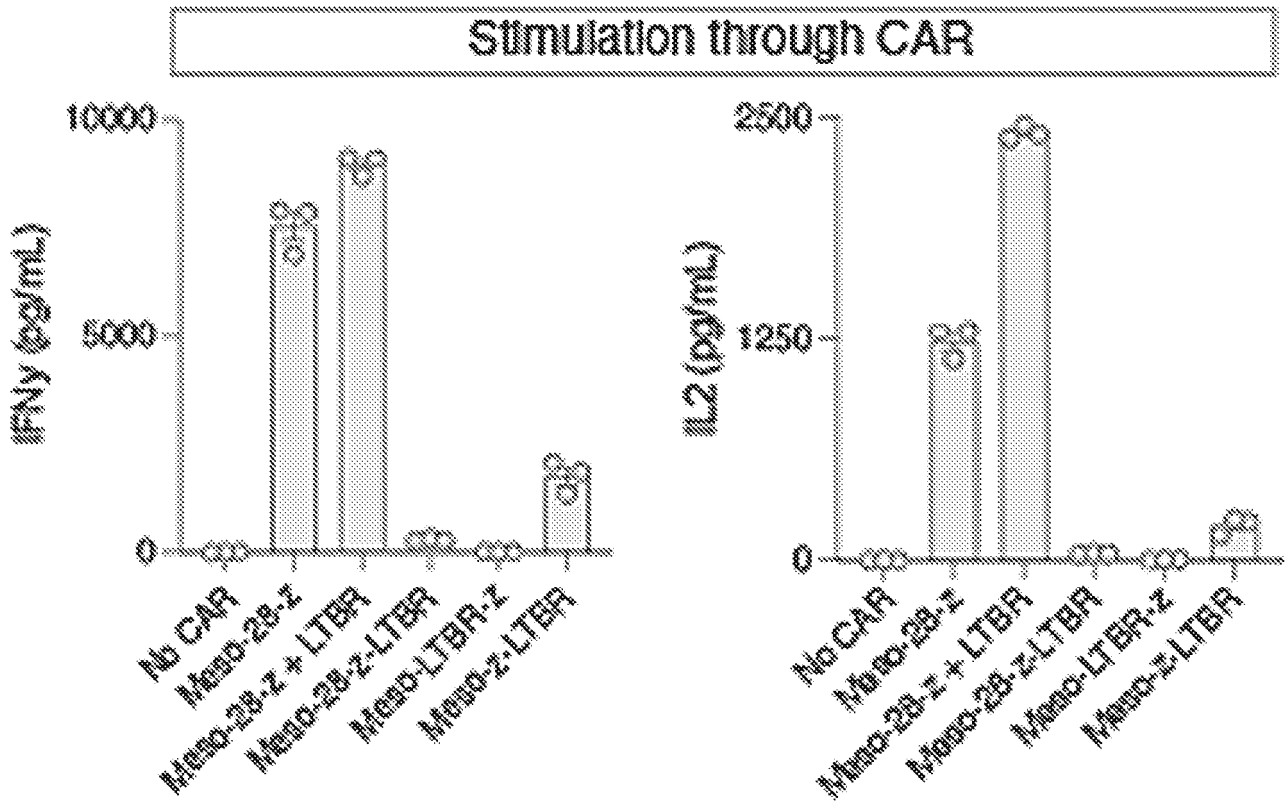


FIG. 28F

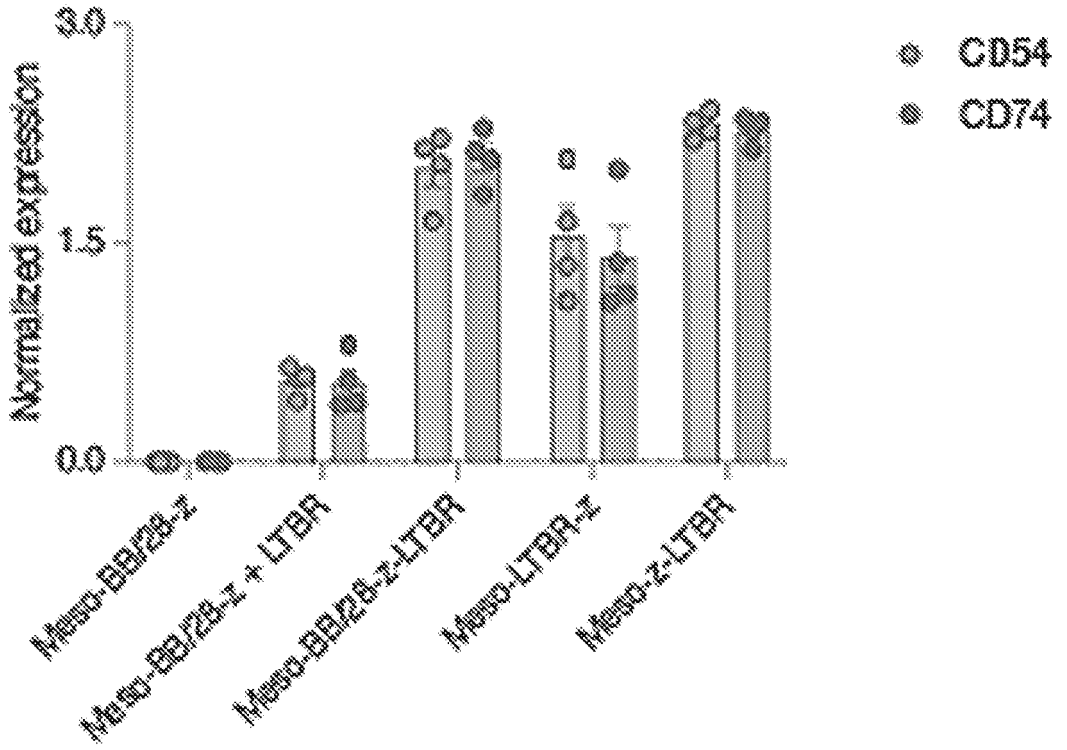


FIG. 28G

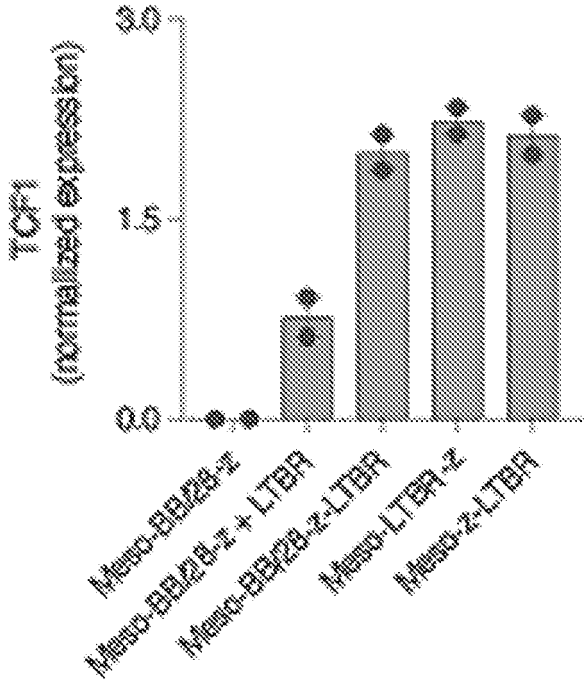


FIG. 28H

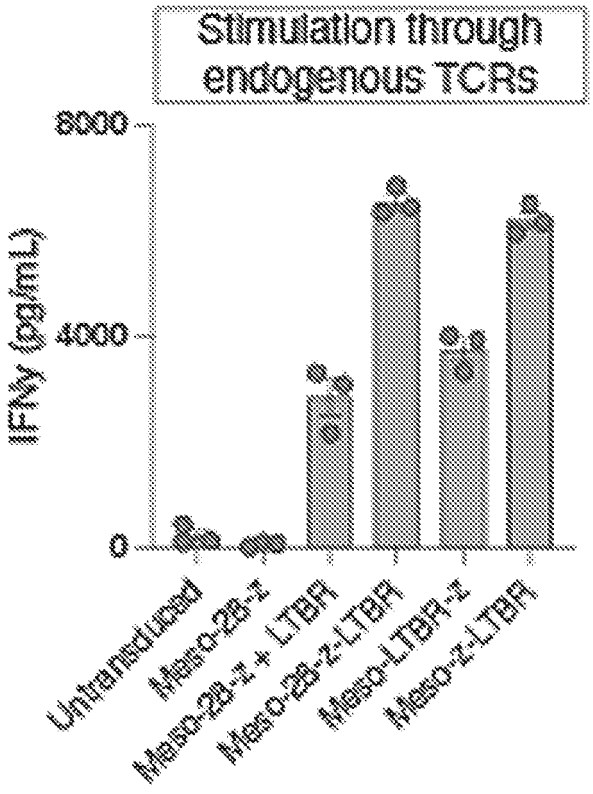


FIG. 28I

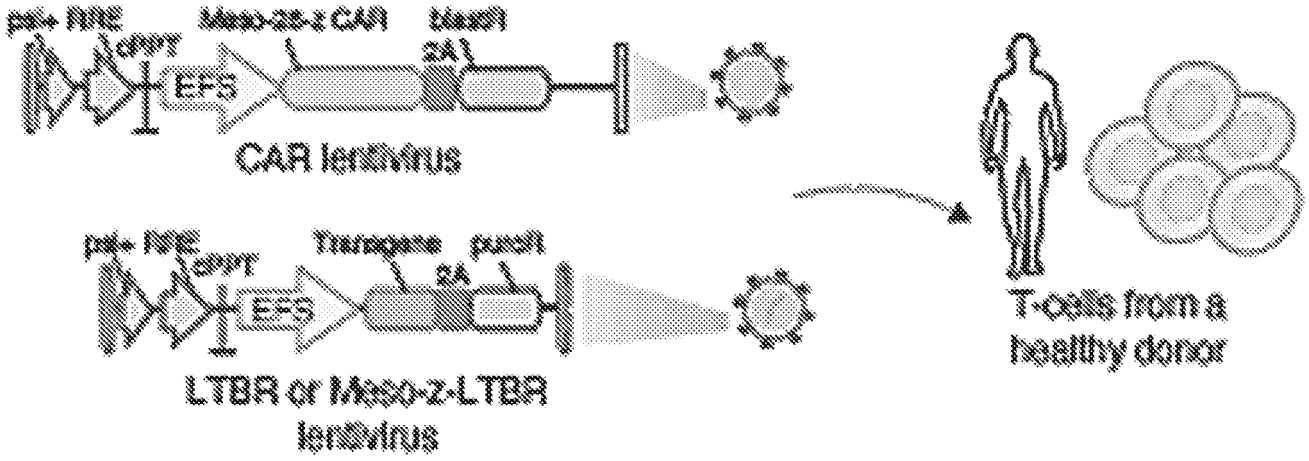


FIG. 28J

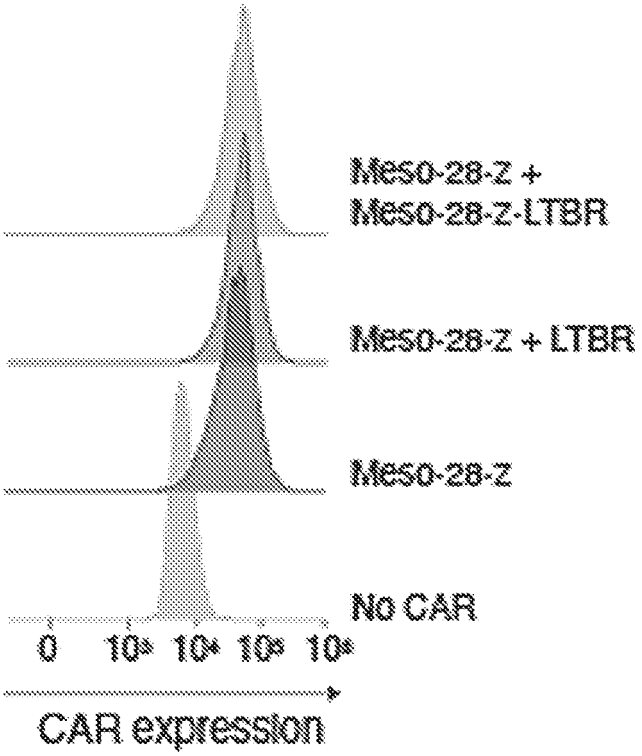


FIG. 28K

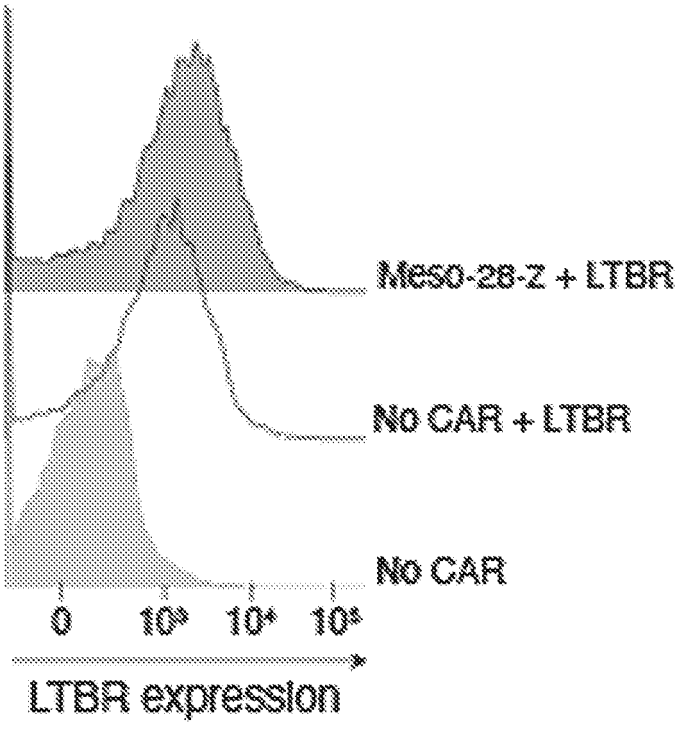


FIG. 28L

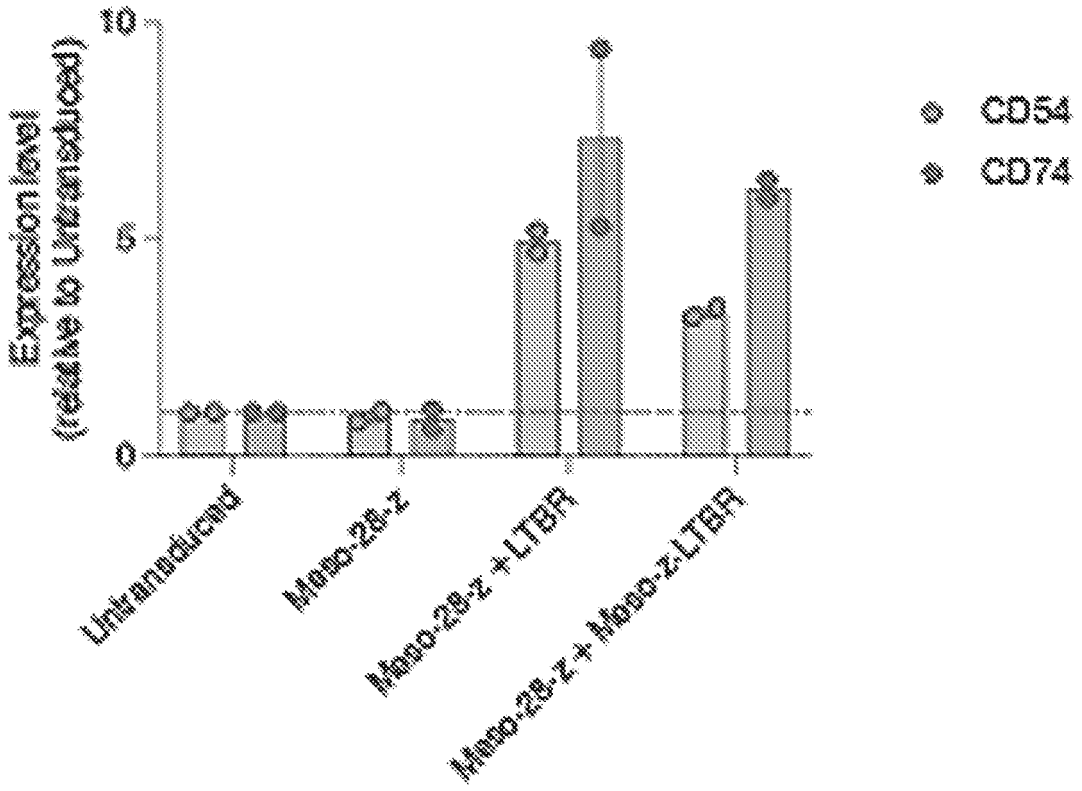


FIG. 28M

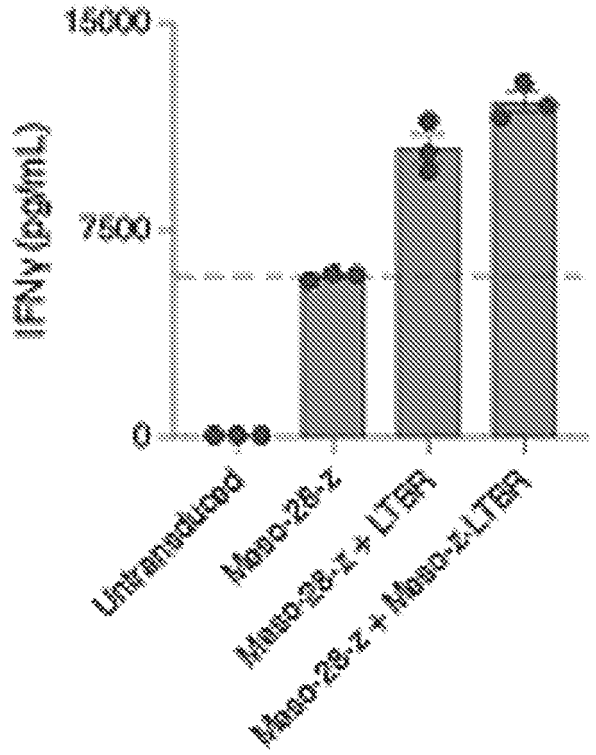


FIG. 28N

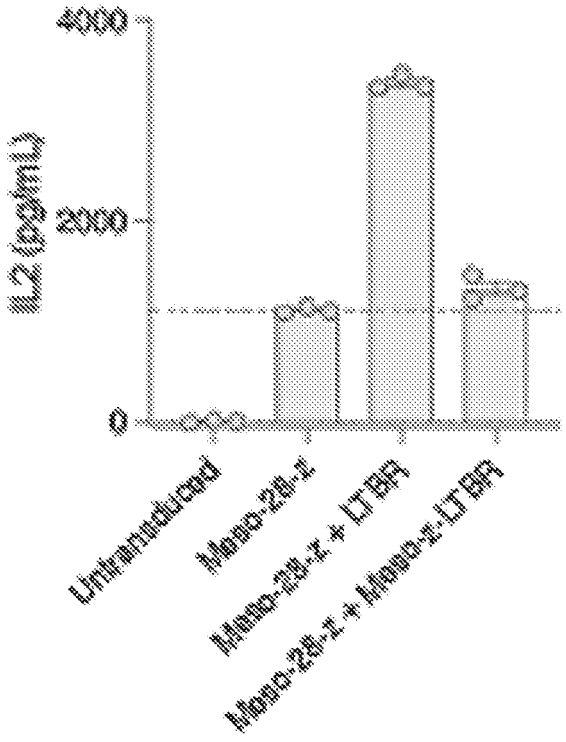


FIG. 29A

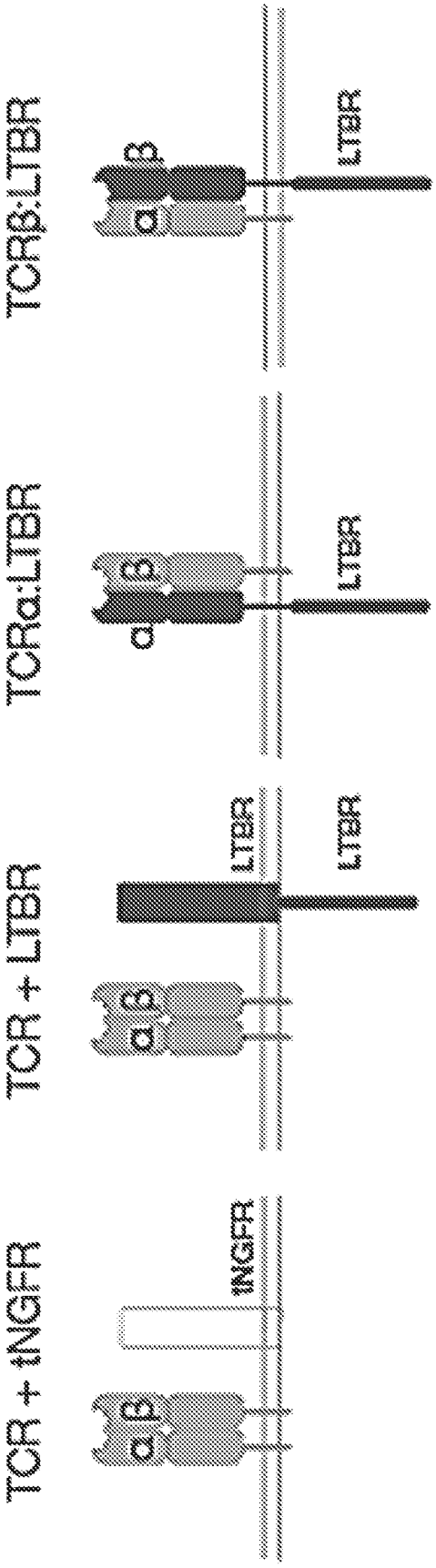


FIG. 29C

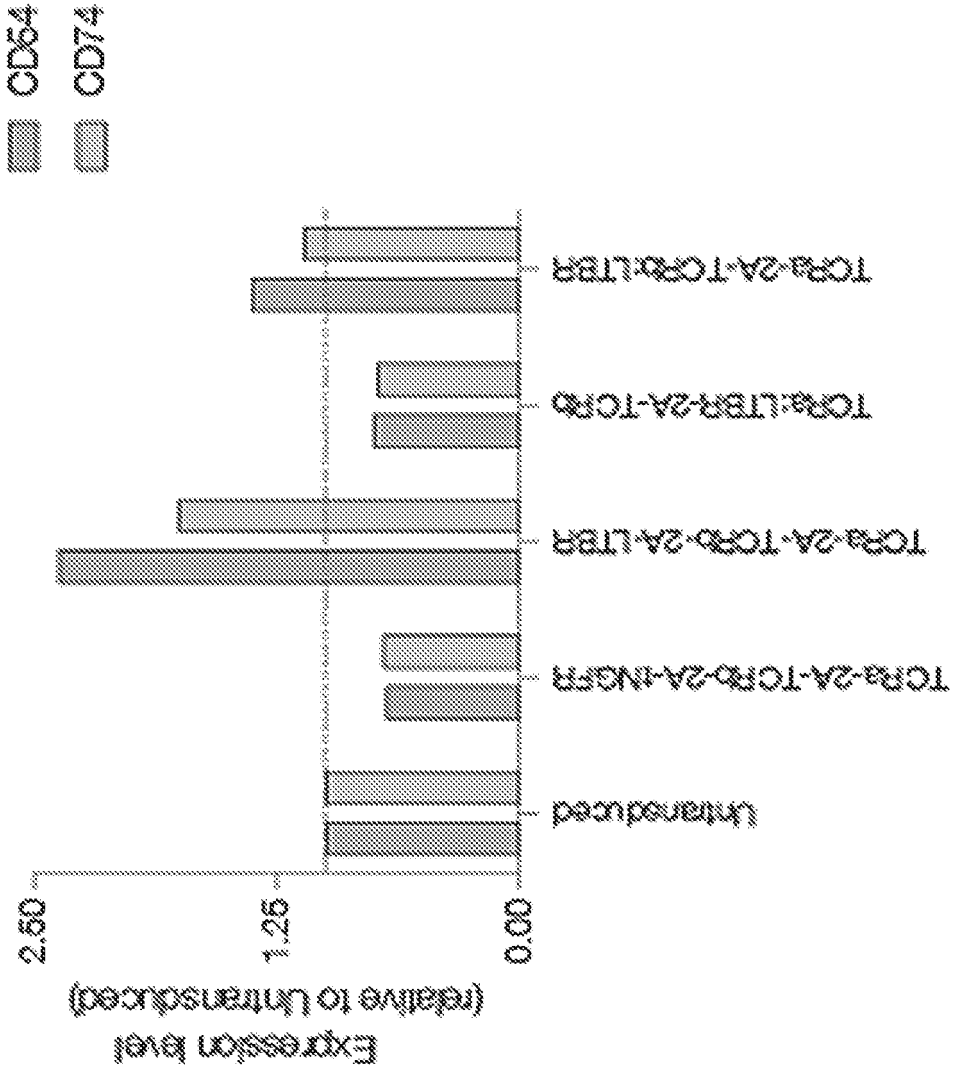


FIG. 29B

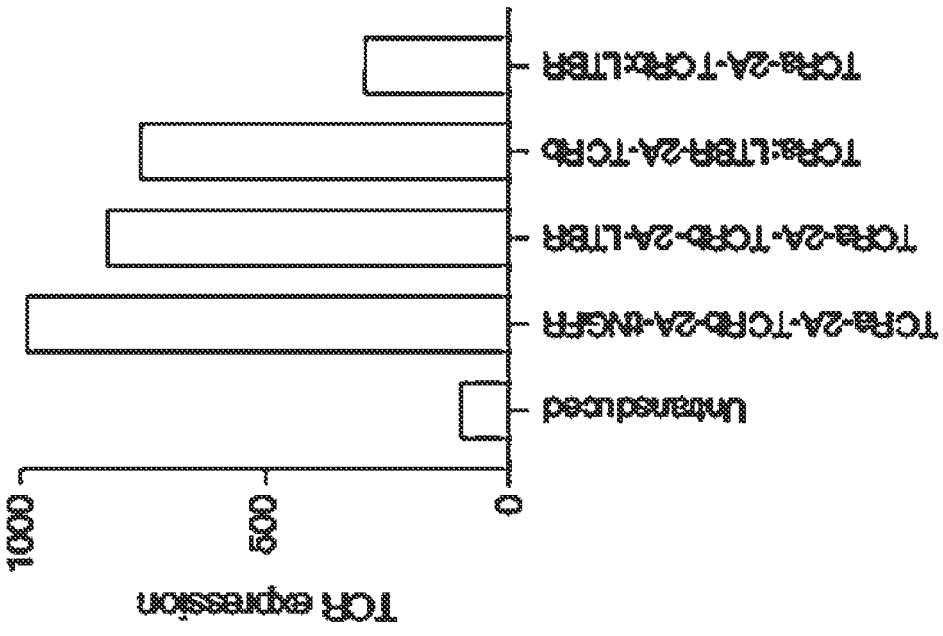


FIG. 29D

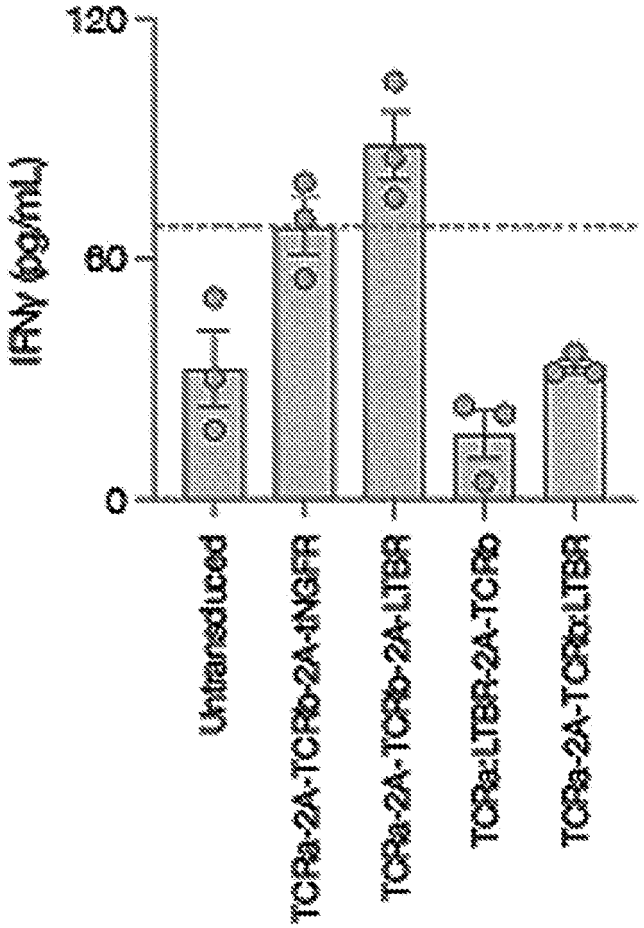


FIG. 29E

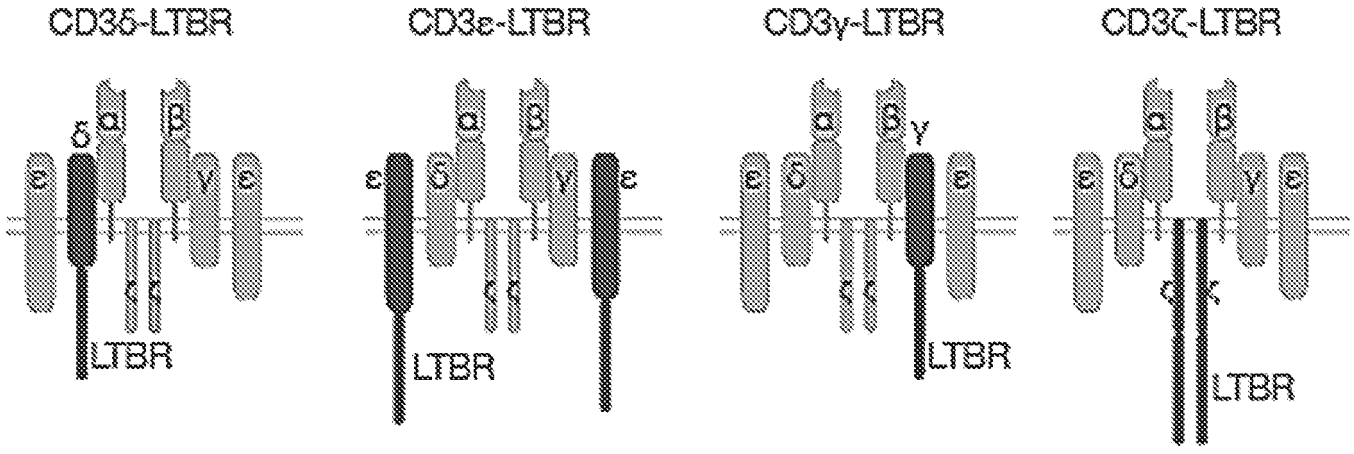


FIG. 29F

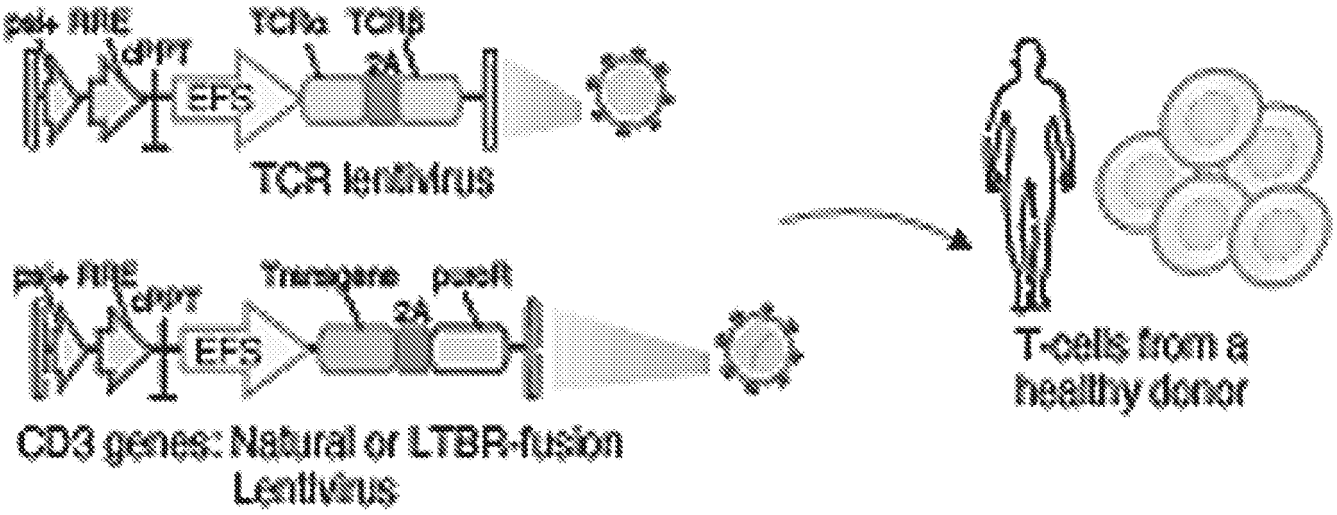


FIG. 29G

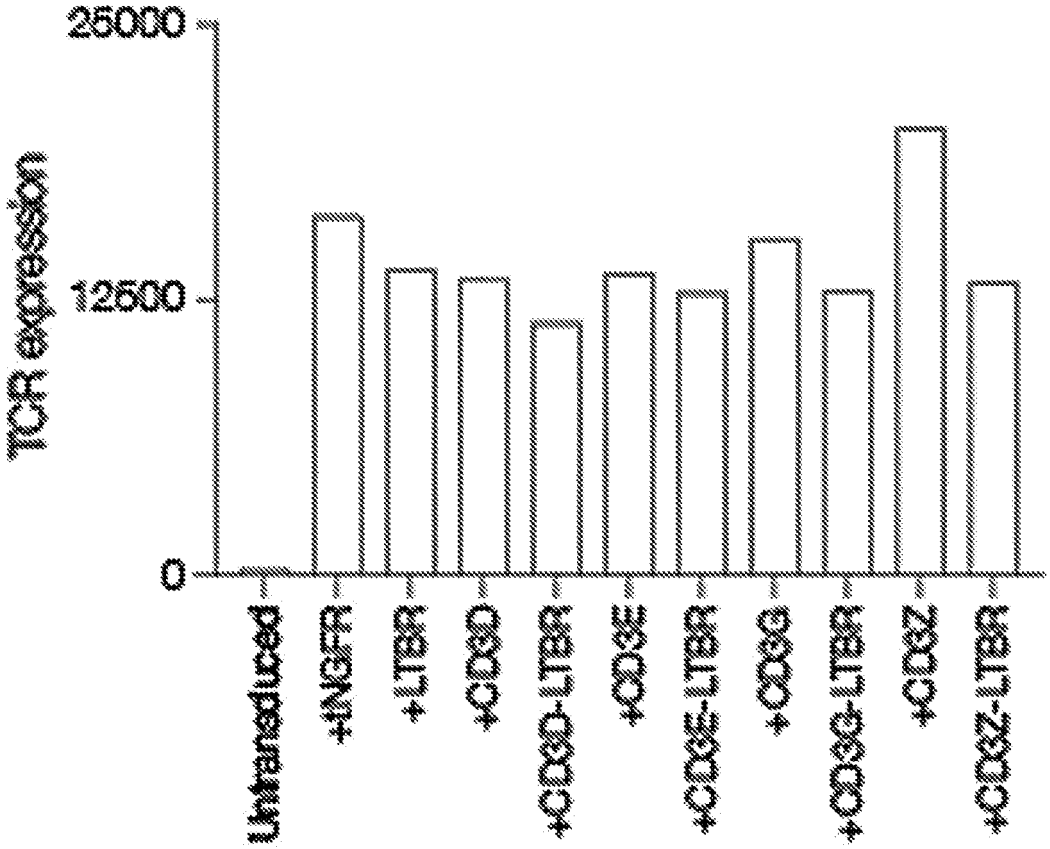


FIG. 29H

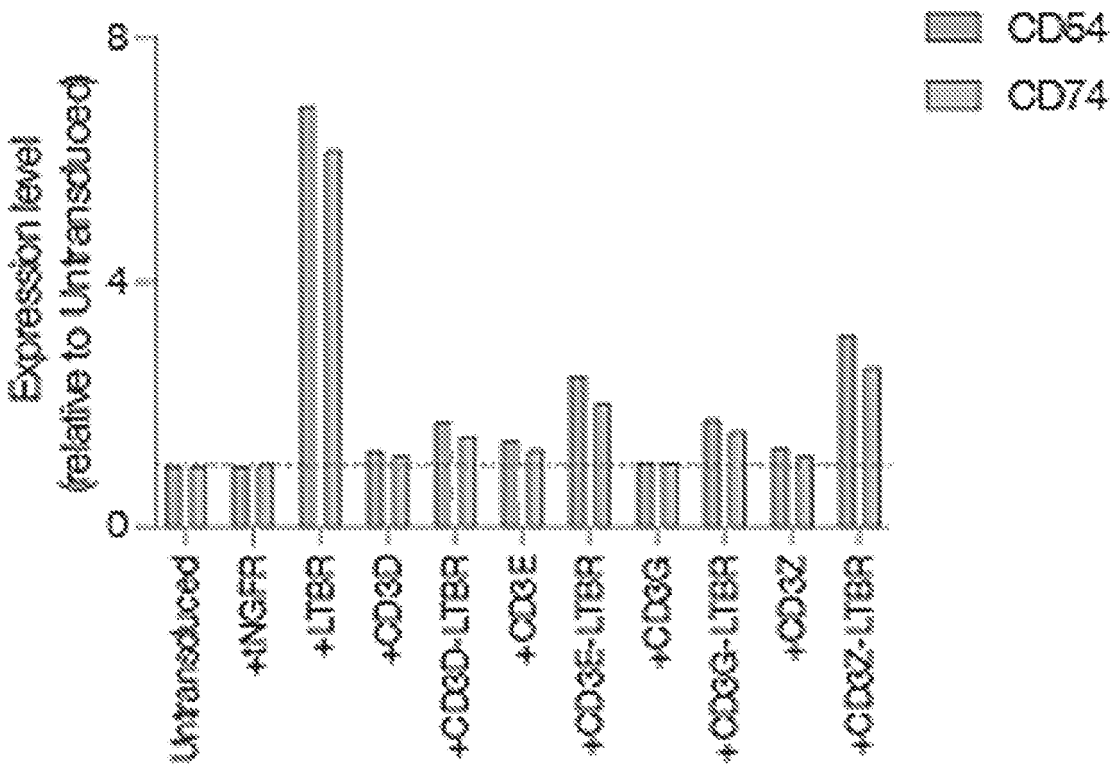


FIG. 29I

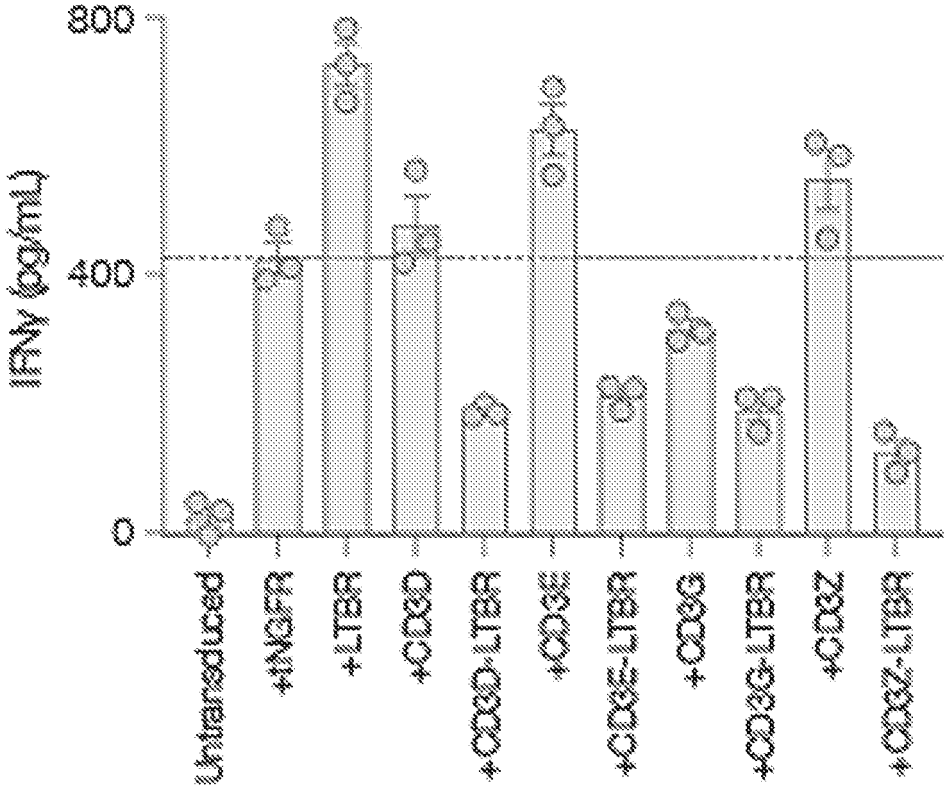


FIG. 30A

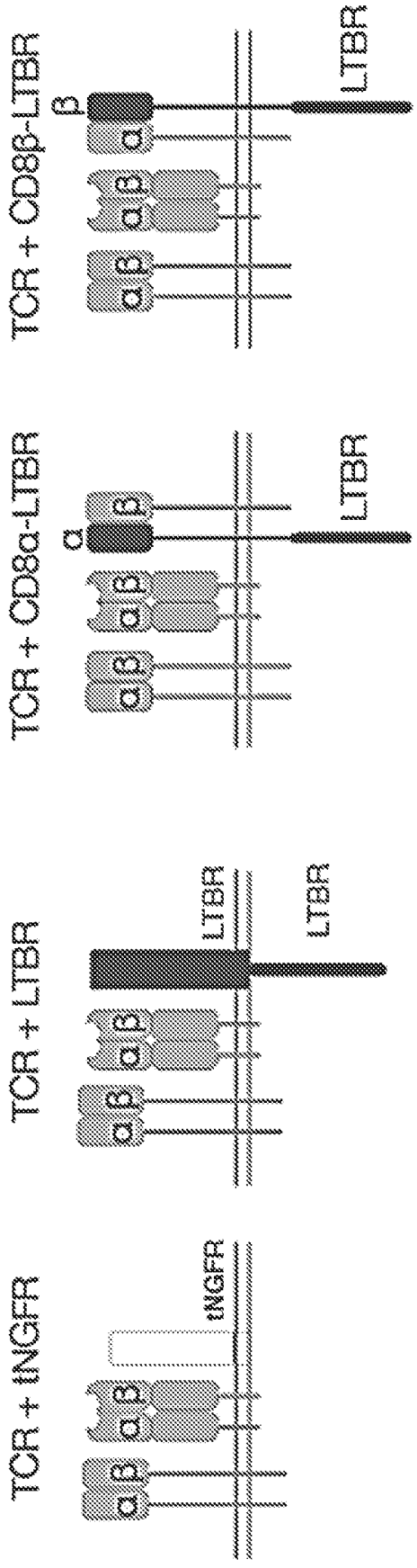


FIG. 30B

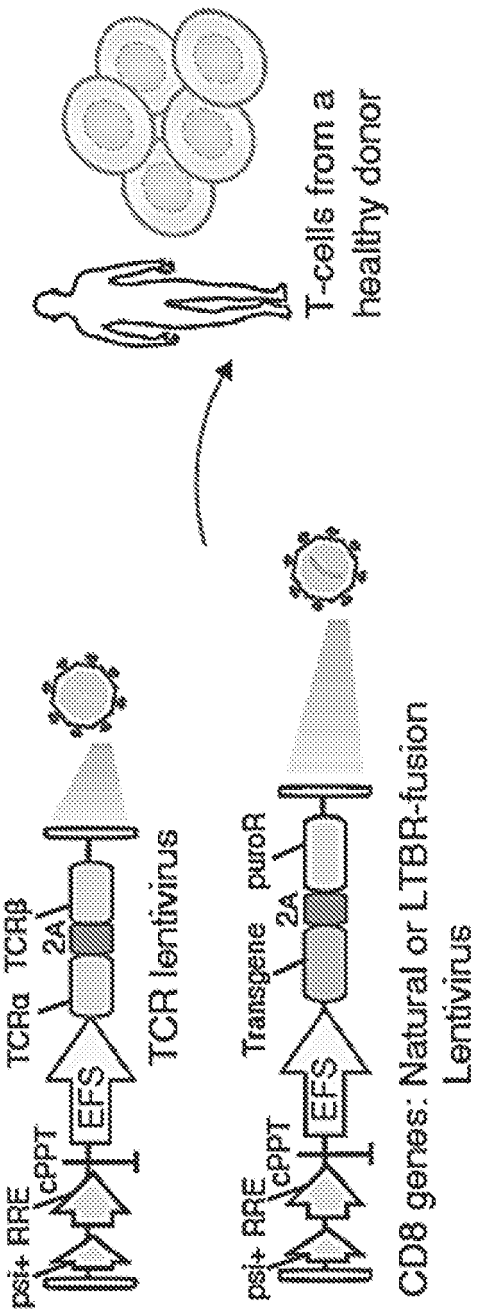


FIG. 30C

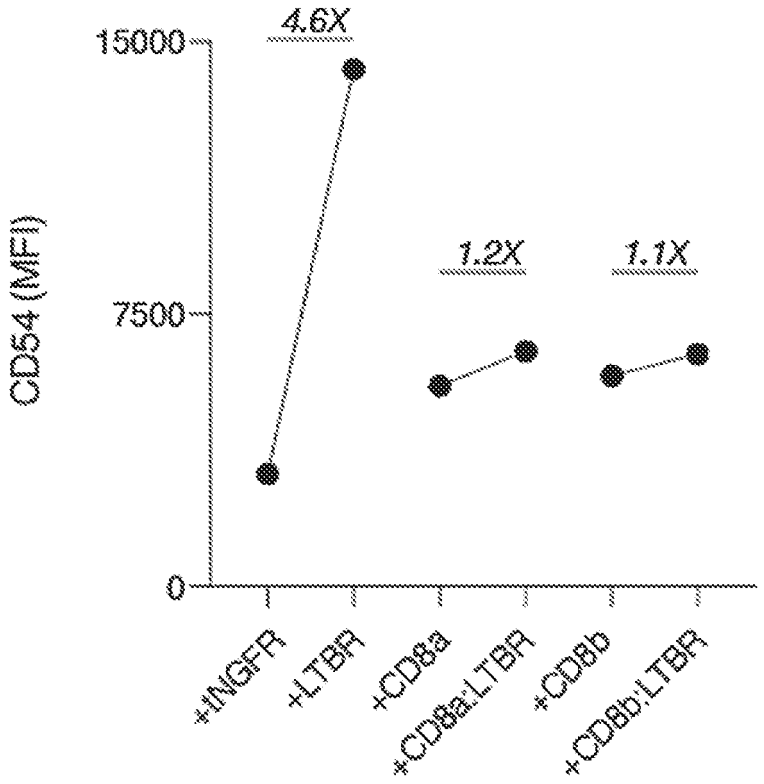


FIG. 30D

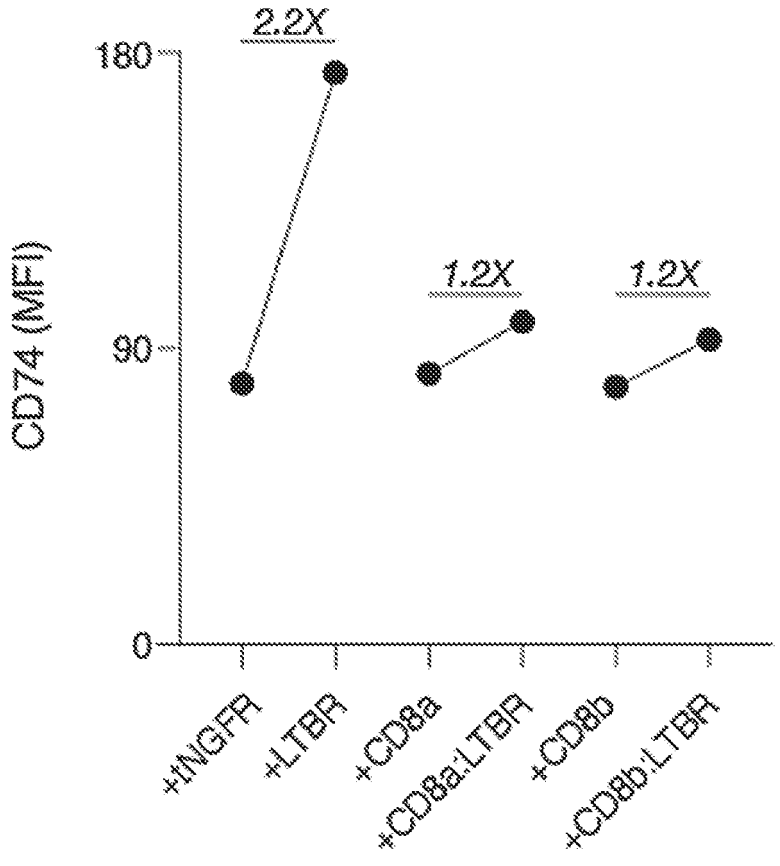


FIG. 30E

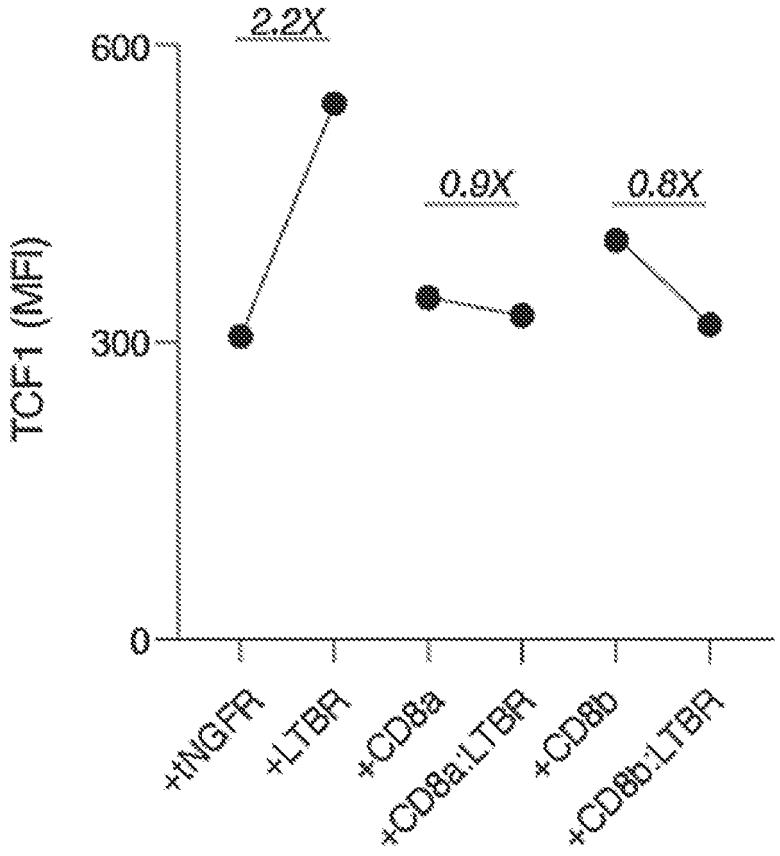

2.2X
0.9X
0.8X
600
300
0
TCF1 (MFI)
+tNGFR
+LTBR
+CD8a
+CD8a:LTBR
+CD8b
+CD8b:LTBR

FIG. 30F

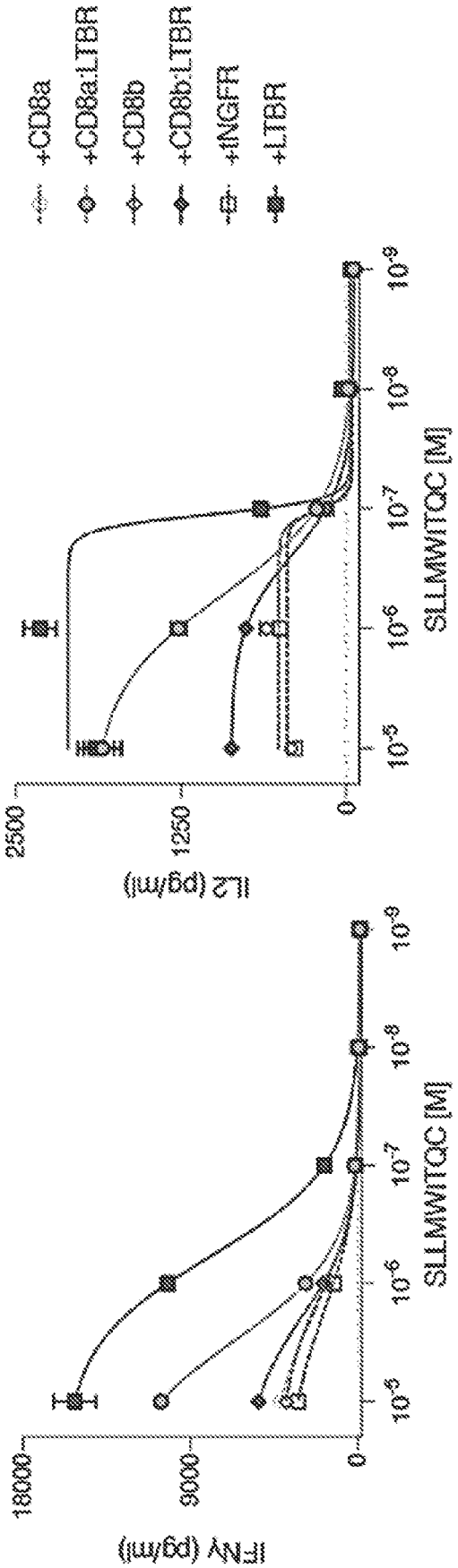
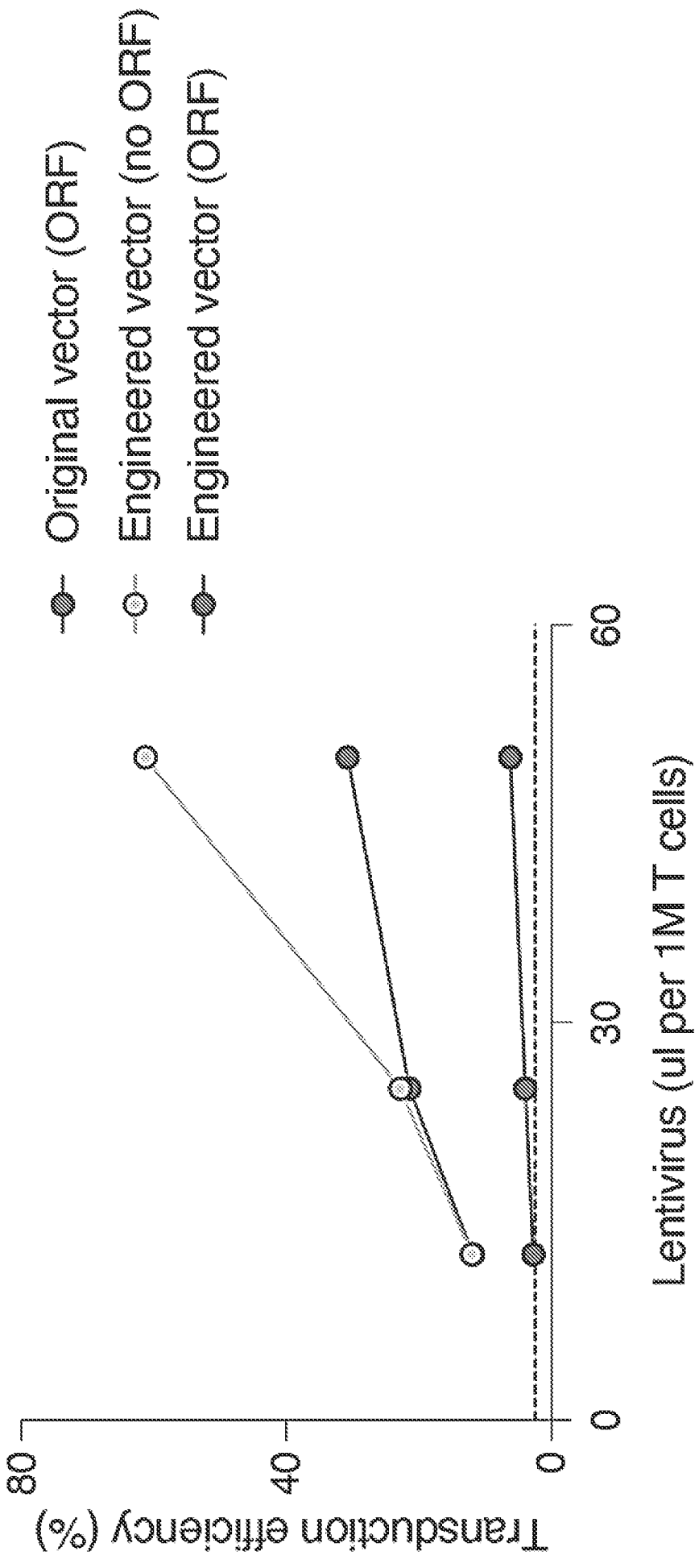


FIG. 30G

Sample / IC_{50} [M]	IFNγ	IL2
+CD8a	$2x10^{-8}$	$1x10^{-7}$
+CD8a:LTBR	$3x10^{-8}$	$5x10^{-7}$
+CD8b	$1x10^{-8}$	$1x10^{-7}$
+CD8b:LTBR	$2x10^{-8}$	$2x10^{-7}$
+tNGFR	$2x10^{-8}$	$1x10^{-7}$
+LTBR	$6x10^{-7}$	$1x10^{-7}$

FIG. 31


Original vector (ORF)
Engineered vector (no ORF)
Engineered vector (ORF)
Transduction efficiency (%)
80
40
0
0
30
60
Lentivirus (ul per 1M T cells)

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