Figure S6

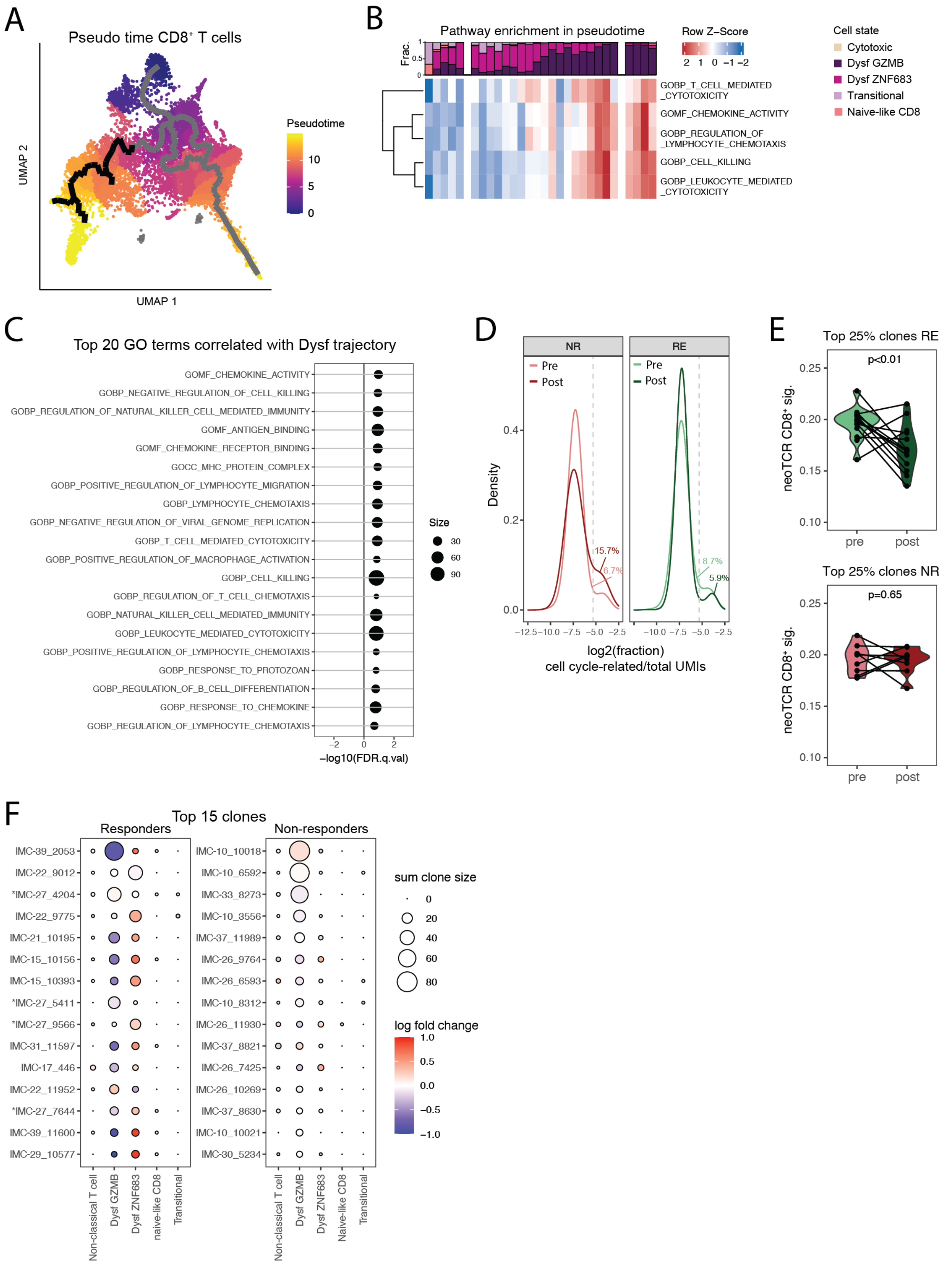

Figure S6. Dual ICB-induced changes in dysfunctional CD8⁺ T cells of responding patients towards a less dysfunctional state

A) Pseudo time colored scaling plotted on top of the CD8$^+$ T cell trajectory, in which the start of the trajectory is located at the naïve-like CD8$^+$ T cell compartment. Trajectory between the dysfunctional CD8$^+$ T cell subsets is shown in black, the remainder of the trajectory between CD8$^+$ T cell states is depicted in grey. Note that the trajectory represents transcriptional relatedness between cell pools, and hence does not necessarily reflect a direct differentiation path between cell pools. B) Single cell gene set enrichment on the dysfunctional CD8$^+$ T cell trajectory of five significantly correlated GO term gene sets. Cells are divided over 30 bins and average gene set scores are calculated per bin. Top bar plot shows the fraction of cell states in each of the bins, colored by cell state. C) Top 20 GO terms enriched in the dysfunctional CD8$^+$ T cell trajectory, using gene set enrichment on the genes in the trajectory that correlated with the dysfunctional CD8$^+$ T cell trajectory. Size of the data points reflects the gene set size. D) Expression of a cell cycle gene set[26] across the entire dysfunctional CD8$^+$ T cell compartment in pre- and on-treatment biopsies of responders and non-responders, calculated as fraction of cell-cycle related UMIs among total UMIs and shown as density. Cells with a cell cycle score above the dashed line are marked as proliferating. E) Expression of the neoTCR CD8$^+$ signature in the top 25% clones per patient with the highest neoTCR CD8$^+$ signature score[12] in dysfunctional CD8$^+$ T cells, in pre- and on-treatment biopsies of responding and non-responding patients. F) Fold change between pre- and on-treatment samples in the fraction of CD8-dysf$_{GZMB}$ T cells, CD8-dysf$_{ZNF683}$ T cells, non-classical T cells, naïve-like CD8 T cells and transitional CD8$^+$ T cells within individual T cell clones that were detected > 2 times in pre- and on-treatment biopsies. Size of data points corresponds to total size of the T cell clone.