Figure S7

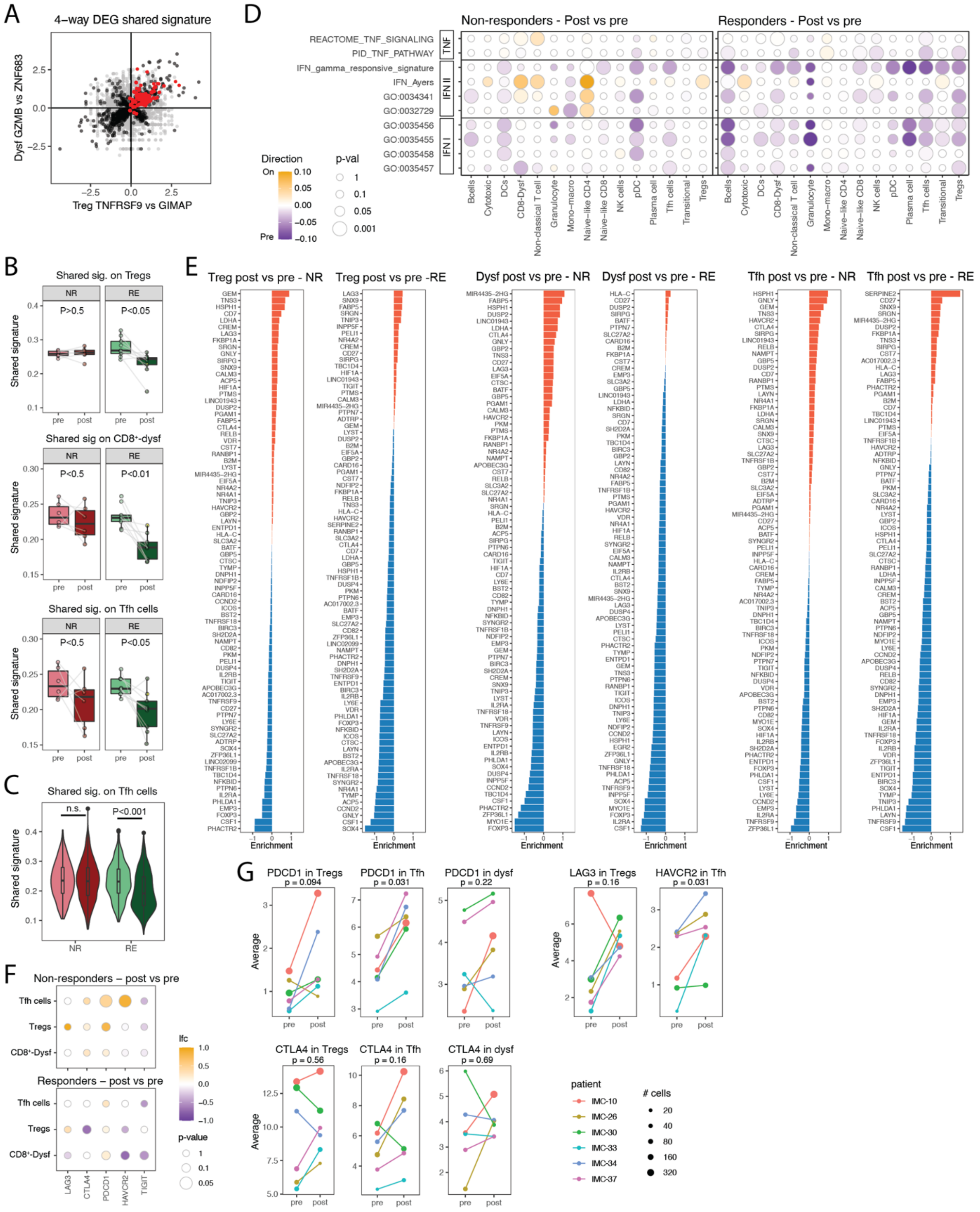

Figure S7. Gene expression changes associated with response and resistance to ICB across cell states

A) Two-way differential gene expression between the Treg$_{GIMAP}$ and Treg$_{TNFRSF9}$ subsets and CD8- dysf$_{GZMB}$ and CD8-dysf$_{ZNF683}$ subsets, shown as log fold change in both directions. Significantly different genes are marked in black. Genes included in the shared signature are highlighted in red. B) Average enrichment per patient of the shared signature on the Treg, $CD8^+$ dysfunctional T cell and TH cell subsets in pre- and on-treatment biopsies of responding and non-responding patients. Each dot represents the biopsy of one patient, IMC-04 and patients for which matched data was lacking were excluded from analysis (IMC-38 and IMC-12), data points from IMC-27 are marked in purple. Boxes show the median and 25th and 75th percentiles. Whiskers depict 1.5 × IQR and data points represent individual patients. A Paired Wilcoxon signed ranks test was performed. C) Enrichment Iof the shared signature in TH cell subsets in pre- and on-treatment biopsies of responding and non-responding patients. A two-tailed Mann–Whitney U test was performed between the different patient groups. D) Fold change of the average single cell gene set enrichment on each cell state for on- and pre-treatment samples. The tested gene sets and signatures consist out of GO terms, REACTOME_TNF_PATHWAY, PID_TNF_pathway, a responsive IFN gamma-responsive gene signature, and IFN and antigen presentation pathways. A two-tailed Mann–Whitney U test was performed on the pre- versus ontreatment comparison. E) Differential expression of the shared signature across dysfunctional $CD8^+$ T cells, Tregs and TH cells from pre- and on-treatment biopsies of responding patients. Genes depicted in blue are more strongly expressed pre-treatment, genes depicted in red are more strongly expressed on-treatment. F) Fold change of the expression of inhibitory receptors across Treg, $CD8^+$ dysfunctional T cell and TH cell subsets in pre- and on-treatment samples of responders (top) and non-responders (bottom). A two-tailed Mann–Whitney U test was performed on the pre- versus on-treatment comparison. G) Expression of inhibitory receptors across $CD8^+$ dysfunctional T cell, Treg and TH cell subsets in pre- and on-treatment biopsies of non-responding patients. Each dot represents a patient.

A Paired Wilcoxon signed ranks test was performed.