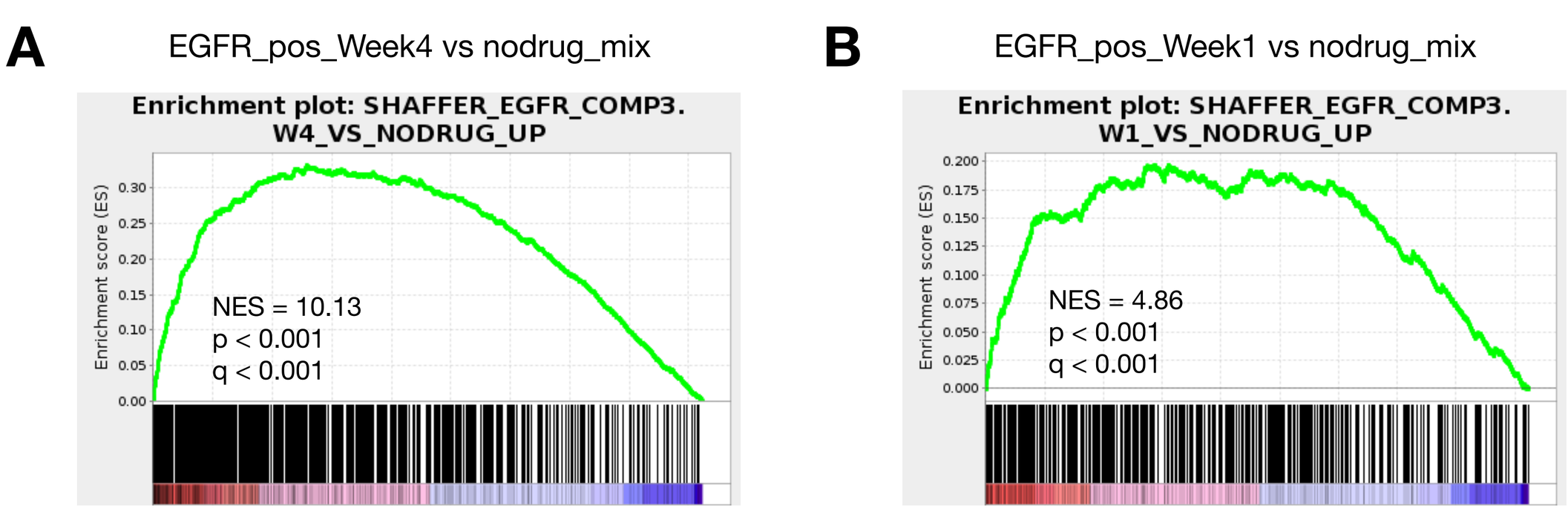

Supplemental Fig. S12 | High concordance between the gene signatures identified by SAKE and Shaffer et al. Differential expression analysis was performed using DESeq2 on bulk RNA-Seq published by Shaffer et al. Cells were either untreated, sort for EGFR positive staining after BRAFi treatment for 1week and 4week. Genes identified as differentially expressed (DE) between EGFR positive and untreated cells, with an adjusted p-value less than 0.05 and absolute log2FoldChange greater than 1, were used for gene set enrichment analysis (GSEA) on our 451Lu 10x data sets. GSEA was performed using a pre-ranked list. Genes up-regulated after BRAFi treatment were shown in **A)** 4 weeks and **B)** 1 weeks. The degree of enrichment positively correlated with the time of the drug treatment, suggesting the required time for the cells to response and transition into resistance state. Genes down-regulated after BRAFi treatment were shown in **C)** 4 weeks and **D)** 1 weeks. The significant GSEA results demonstrates the potential common mechanisms of developing resistance after BRAFi treatment in melanoma cells.