

Supplementary FIGURES

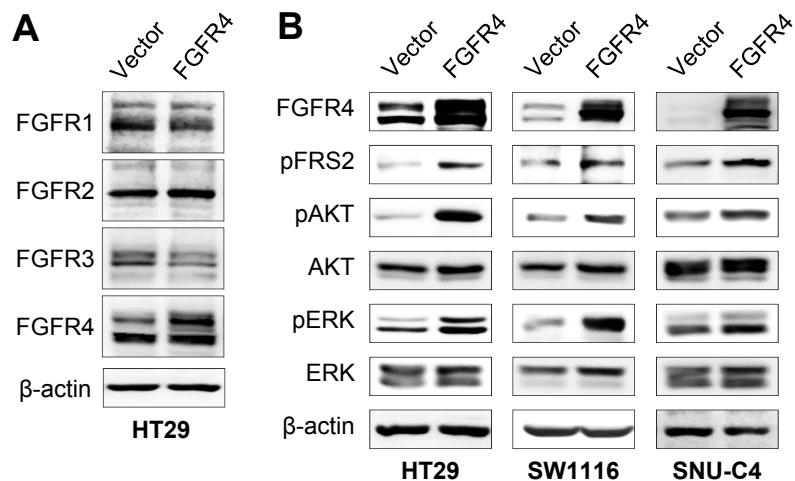


FIGURE S1

FGFR4 activates the PI3K/AKT and RAS/RAF/ERK pathways in colon cancer cells. **A**, The expression of FGFR family members in stable FGFR4-transfected HT29 cells was measured by western blotting. **B**, Activation of FGFR specific substrate FRS2 and downstream signaling pathways, including PI3K/AKT and RAS/RAF/ERK pathway, was measured in FGFR4-transfected cells by western blotting. β -actin was used as a loading control.

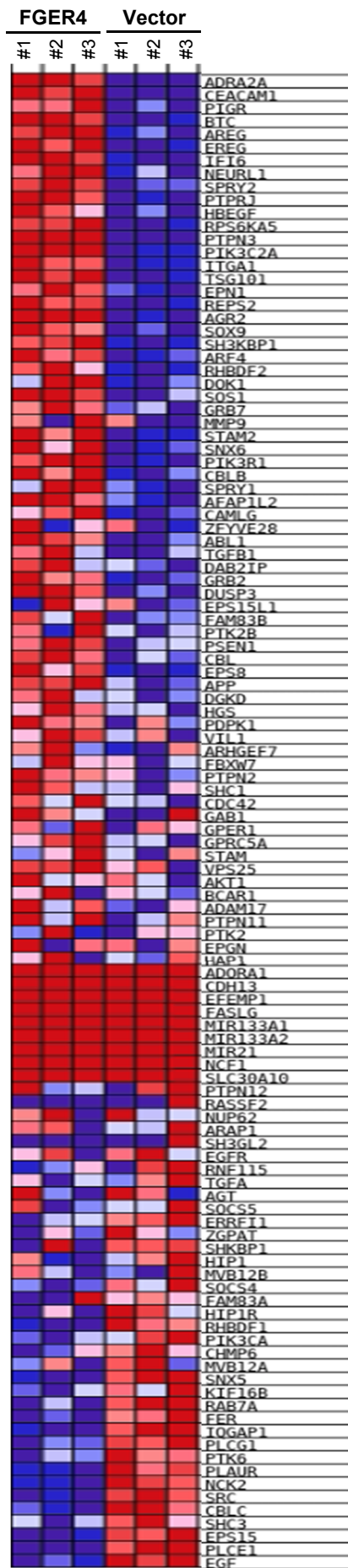


FIGURE S2

Heat map from GSEA analysis of genes related to epidermal growth factor receptor signaling pathway genes altered by FGFR4 expression.

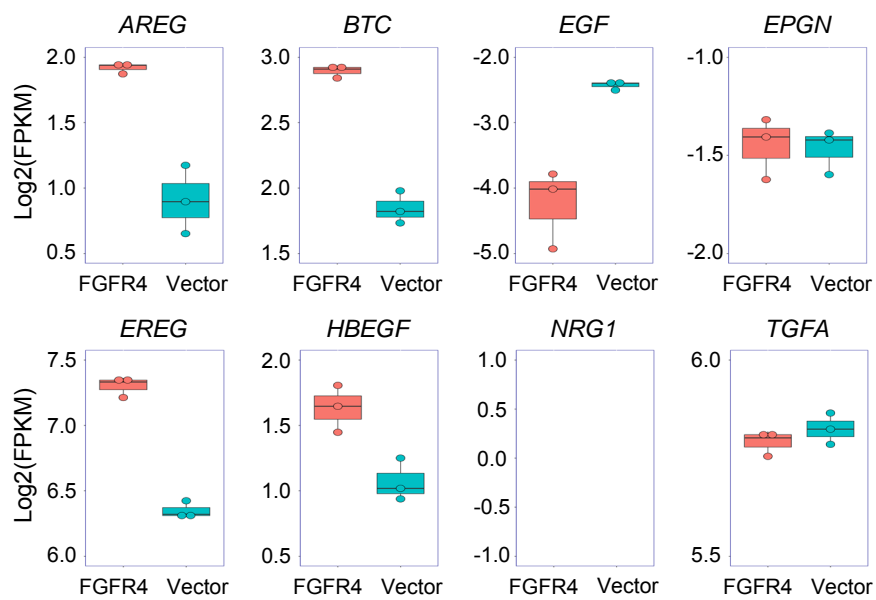


FIGURE S3

RNA-seq analysis of FGFR4-transfected and vector control HT29 cells. Box plot showing expression value (log₂ FPKM) of ErbB family ligands in RNA-seq experiment.

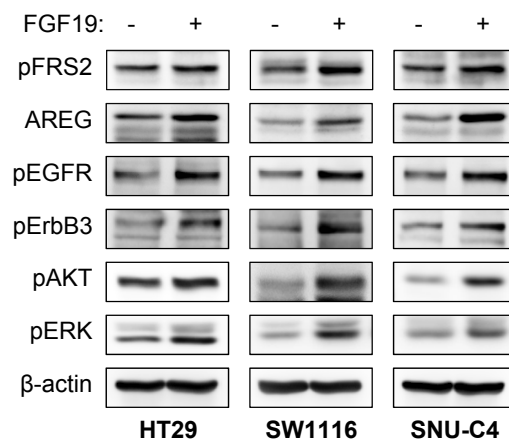


FIGURE S4

FGFR4 activation promotes EGFR signaling. Colon cancer cells were starved with serum free medium for 12 hours and then treated with 200 ng/ml FGFR4 specific ligand FGF19. After 24 hours incubation, cell lysates were prepared and subjected to western blotting with antibodies to the indicated proteins. β -actin was used as a loading control.

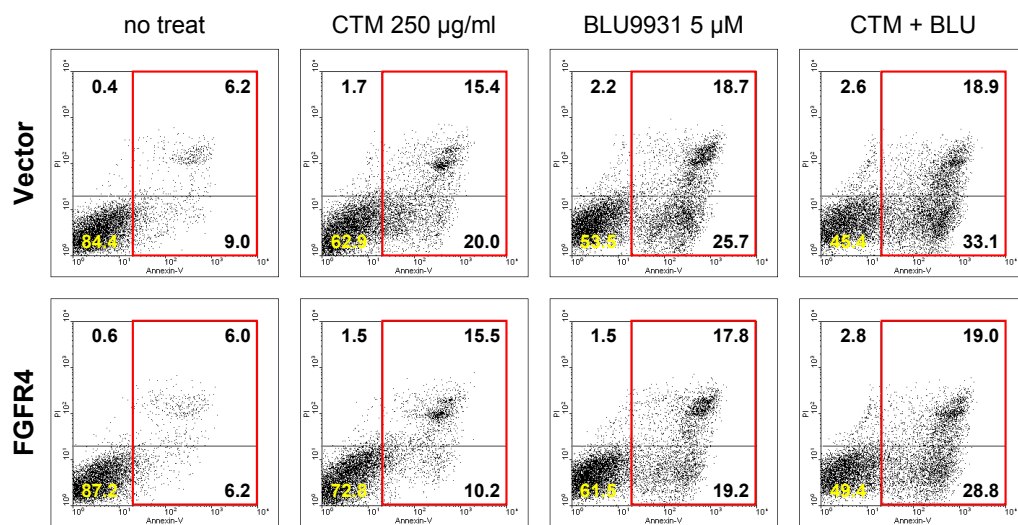


FIGURE S5

FGFR4 induces response of SNU-C4 cells to cetuximab and BLU9931. FGFR4-transfected and vector control SNU-C4 cells were treated with 250 µg/ml cetuximab and/or 5 µM BLU9931 for 48 hours. The cells were stained with Annexin V-FITC and propidium iodide (PI) for flow cytometric analysis. The numbers in the quadrants of each plot indicate the percentage of the total cell population. Early and late apoptotic cells are marked with red boxes.

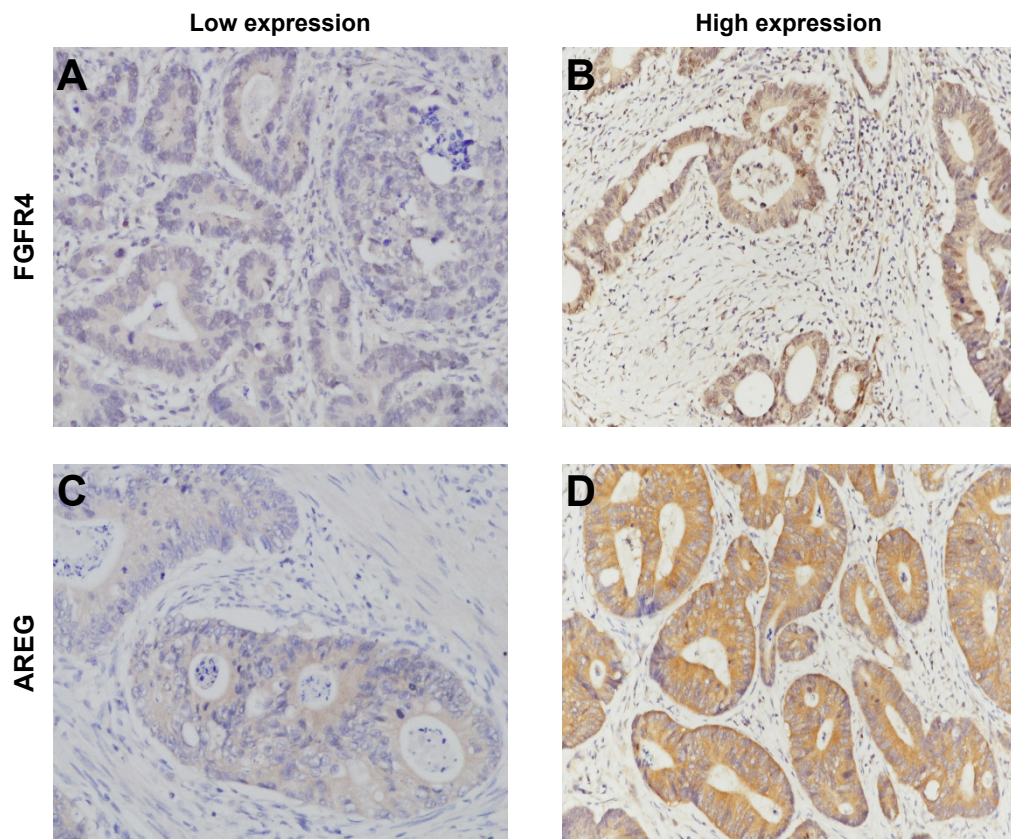


FIGURE S6

FGFR4 and AREG expression in colon cancer. **A**, Low FGFR4, **B**, high FGFR4, **C**, low AREG and **D**, high AREG expressions. Magnification was $\times 200$.