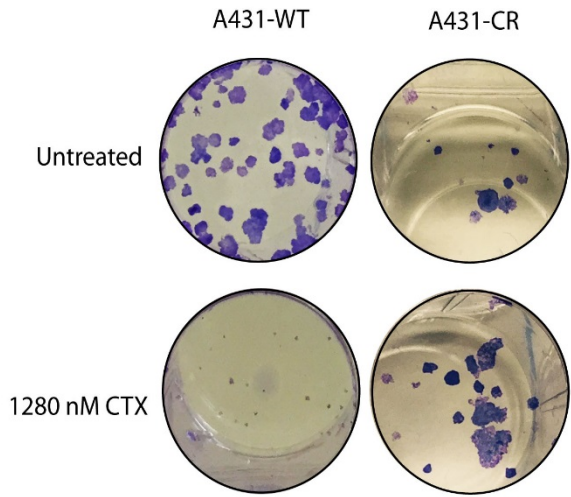
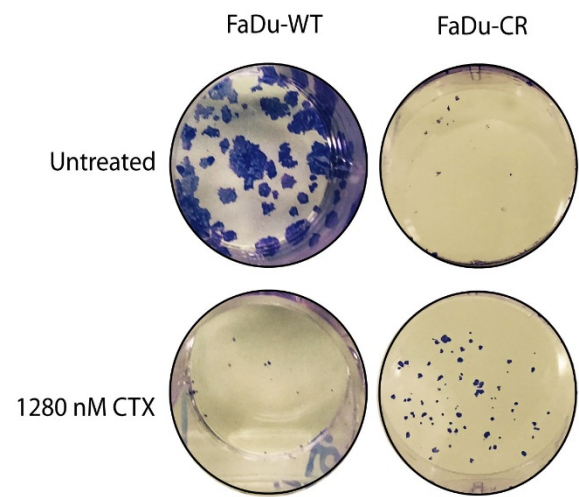
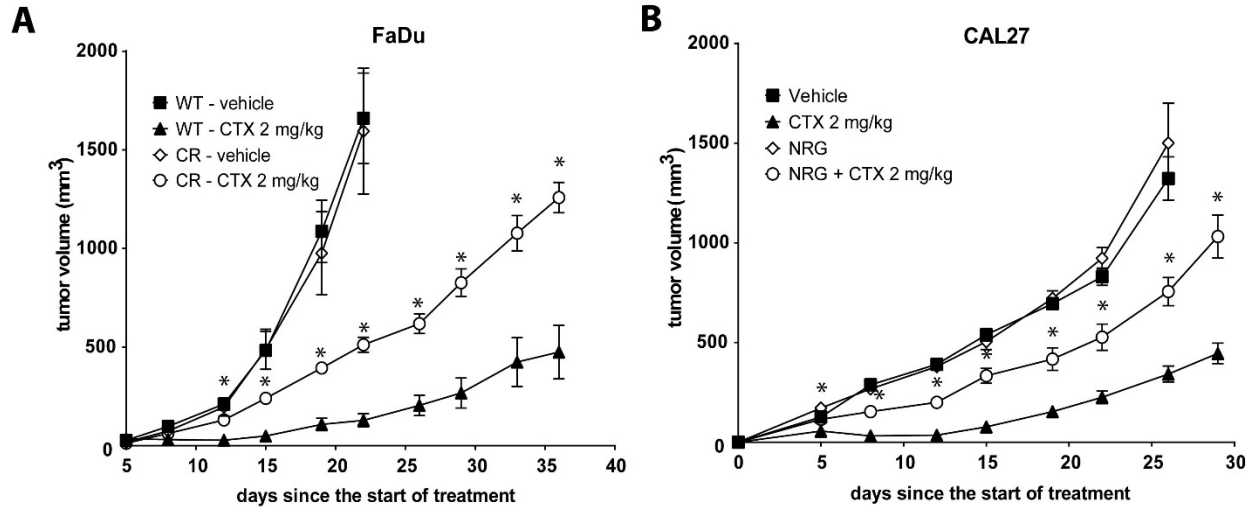


A**B**

SUPPLEMENTARY FIGURE S1.

Supplementary Figure 1. Clonogenic survival of A431 and FaDu clones. (A.) Representative images from the A431 clone populations obtained in the selection process to generate the cetuximab-resistant cell lines are shown. (B.) Representative images from the FaDu clone populations obtained in the selection process to generate the CTX-resistant cell lines are shown.



SUPPLEMENTARY FIGURE S2.

Supplementary Figure 2. *In vivo* models used to explore the therapeutic effects of CDX-3379 in the presence or absence of cetuximab (CTX), neuregulin (NRG) and/or radiotherapy (RT). (A.) Mice bearing tumors derived from FaDu-WT or FaDu-CR cells received vehicle or 2 mg/kg CTX twice a week I.P. until sacrifice. Values are the means \pm SE of eight tumors per group. An * indicates a significant difference ($p \leq 0.05$) compared to the CTX group treatment from the FaDu-WT mice. (B.) Mice bearing tumors derived from CAL27 cells encapsulated in matrigel in the presence or absence of 1 mg per tumor of NRG received a single I.P. injection of vehicle or 2 mg/kg CTX. Values are the means \pm SE of eight tumors per group. An * indicates a significant difference ($p \leq 0.05$) compared to the CTX group treatment from the CAL27 with no NRG mice.

Supplementary Table 1. List of antibodies used in the study.

Antibodies	dilution	source	identifier
rabbit anti-EGFR	1:1,000	Santa Cruz biotechnology, Inc. (Santa Cruz, CA)	sc-03
rabbit anti-pEGFR-Y1068	1:1,000	Cell Signaling (Danvers, MA, USA)	#3777
rabbit anti-pEGFR-Y845	1:1,000	Cell Signaling (Danvers, MA, USA)	#6963
rabbit anti-ErbB2	1:1,000	Cell Signaling (Danvers, MA, USA)	#4290
rabbit anti-pErbB2-Y1221/1222	1:500	Cell Signaling (Danvers, MA, USA)	#2243
rabbit anti-ErbB3	1:1,000	Cell Signaling (Danvers, MA, USA)	#4754
rabbit anti-pErbB3-Y1289	1:1,000	Cell Signaling (Danvers, MA, USA)	#4791
rabbit anti-neuregulin	1:1,000	Cell Signaling (Danvers, MA, USA)	#2573
rabbit anti-AKT	1:1,000	Cell Signaling (Danvers, MA, USA)	#9272
rabbit anti-pAKT-S473	1:1,000	Cell Signaling (Danvers, MA, USA)	#4060
rabbit anti-ERK1/2	1:1,000	Cell Signaling (Danvers, MA, USA)	#4695
rabbit anti-pERK1/2	1:1,000	Cell Signaling (Danvers, MA, USA)	#4370
anti-GADPH	1:1,0000	Proteintech (Rosemont, IL, USA)	HRP-60004