SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure S1.

Schematic representation of conditioned medium assay (CMA).

Supplementary Figure S2.

Measurements of additional receptor ligands from conditioned media. Picograms/ml of EGF, HB-EGF, NRG1 and HGF in media conditioned by sensitive and resistant LIM1215, OXCO-2, and DiFi cells for 72 hours with and without cetuximab (CTX). Error bars represent the mean ± SD of three independent experiments.

Supplementary Figure S3.

Alternative comparative presentation of results presented in Figure 3 C-F. (A and B), secretion of TGFα and amphiregulin (AR) by LIM1215 and DiFi sensitive and resistant cells during a 72 hour time course with and without cetuximab (CTX). Ligand levels were normalized to number of cells at each time point expressed as pg/10^6 cells. Error bars represent the mean ± SD of two independent experiments. S: sensitive, R: resistant, CTX: CTX treated. * $p \leq 0.05$, between cell populations in the same column (Student's *t* test, two tailed).

Supplementary Figure S4.

LIM1215 knocked-in with a *KRAS* G12R mutation are also capable of paracrine protection of sensitive wild type (wt) cells and secrete higher levels of TGFα. (A), conditioned medium assay (CMA) performed by transfer of conditioned media with cetuximab (CTX) from knock-in (KI) cells or sensitive (S) cells (1:1 - fresh:CM) on top of sensitive cell population. Cell viability is normalized to sensitive wt cells incubated with CM from sensitive cells with CTX (2 µg/ml). Error bars represent the mean ± SD of three independent experiments. (B and C), levels of TGFα, AR, EGF, HB-EGF, NRG1 and HGF in media conditioned by LIM1215 sensitive and *KRAS* mutant knock-in (KI-KRAS) cells with and without CTX (2 µg/ml). Error bars represent the mean ± SD of three independent experiments. * $p \leq 0.05$, ** $p < 0.01$ compared to untreated sensitive cells (Student's *t* test, two tailed).