Supplemental Figure Legends

Supplemental Figure 1. CAFs exhibit increased LC3 puncta per cell compared to NF.
(A) Representative TEM images of a NF (5000X) or CAF (3000X) cell.
(B) p62/β-tubulin density of NF and CAF patient samples (n=4/each). Error bars represent SEM.
(C) Expanded representative view (20X magnification) of NF compared to CAF with and without CQ (80 μM for 2 hours), LC3 (green), hoescht nuclear (blue).

Supplemental Figure 2. CAF autophagy inhibition significantly decreases HNSCC *in vitro* progression.
(A) Representative immunoblot as validation of CQ autophagy inhibition throughout CM collection.
(B) Representative immunoblot of CAFs grown in complete media (10% FBS DMEM) or after 24 h of serum free media (mimicking conditioned media collection). CQ (20 μM for 6 h) was applied at the end of the treatment period. No significant differences between complete media and conditioned media LC3-II levels demonstrates no increase in autophagy.
(C) 5 min CQ treatment (20 μM) on CAFs did not significantly alter LC3-II conversion as assessed by immunoblot.
(D) 5 min CQ treatment (20 μM) of CAFs prior to CM collection had no difference in HNSCC (OSC19) migration. All error bars represent SEM.
(E) Proliferation, migration and invasion of HNSCC (HN5) with CAF-CM with and without CQ pre-treatment (Pre-Tx). Graph depicts two independent experiments in triplicate repeats.
(F) Representative immunoblot demonstrate BECN siRNA (siBECN) inhibits LC3-II conversion compared to control siRNA (siCon); CQ (20 μM for 6 h) was applied to inhibit autophagic flux
(G) Representative immunoblot demonstrates ATG7 siRNA (siATG7) inhibits LC3-II conversion compared to control siRNA (siCon); CQ (20 μM for 6 h) was applied to inhibit autophagic flux.
(H) siATG7 CAF-CM significantly reduced HNSCC (HN5) migration and invasion relative to siCon siRNA CAF-CM.

Supplemental Figure 3. IL-6 and IL-8 induce fibroblast autophagy.
(A) Expanded view (10X) of NF treated with VC (water), IL-6 (10 ng/mL), or IL-8 (80 ng/mL) for 24 h, CQ (80 μM for 2 h) used to inhibit autophagic flux.
(B) representative images of NF alone or co-cultured in 1:1 ratio with HNSCC (HN5) for 24 h with either VC (water) or neutralizing antibody to IL-6 (anti-IL-6) or IL-8 (anti-IL-8); CQ (80 μM for 2 h) used to inhibit autophagic flux. LC3 (green), cytokeratin 14 (red), or hoescht (blue). Graph depicts LC3 puncta per cell of at least 20 fibroblast cells (as

determined by cytokeratin 14 exclusion) per treatment group with error bars representing SEM.

Supplemental Figure 4. bFGF treatment increases autophagy regulated secreted factors

(A) expanded view (10X) of NF compared to NF + HNSCC (HN5) in 1:1 ratio for 24 hours in SFM with and without CQ (80 μM for last 2 hours), LC3 (green), cytokeratin 14 (red), hoescht nuclear (blue).
(B) expanded view (10X) of NF with and without bFGF (100ng/mL) and or CQ (80 μM for last 2 hours), LC3 (green), hoescht nuclear (blue).
(C) expanded view (20X) of NF alone or co-cultured with either control siRNA (siCon) or bFGF siRNA (sibFGF) transfected HNSCC (HN5) for 24 h in 1:1 ratio, and CQ (80 μM for last 2 h); LC3 (green), cytokeratin 14 (red), hoescht nuclear (blue).
(D) NF treated with bFGF (100 ng/mL) increased secretion of (A) IL-6 or (B) IL-8 in conditioned media as determined by ELISA. Graphs depict 2 replicate experiments using 2 NF lines, and are normalized to protein concentration in conditioned media.
(E) PCR microarray of NF compared to NF sorted from co-culture with CFSE labeled HNSCC (HN5) for 72 h. Heat map represents fold change (red high, green low), and table describes values, of co-cultured NFs relative to NF alone.
(F) Summary of HNSCC mediated autophagy induction
(G)Representative gel image of PCR products from NFs or NFs after sorting from co-culture with CFSE labeled HNSCC for 48 h with and without FGFR inhibitor AZD4547 (2 μM). Graph depicts densitometric analyses of mTOR or SOX2 PCR product analyses relative to β-actin and normalized to NF alone; co-cultured NFs were sorted from CFSE labeled HNSCC (HN5) co-culture after 72 h with and without treatment using FGFR inhibitor AZD-4547 (2 μM).
(H) Representative immunoblot of NF treated with HNSCC-conditioned media (CM), with and without FGFR inhibitor AZD4547 (2 μM) for 24 h, and CQ (20 μM for 6 h) of phospho-STAT3 and LC3.

Supplemental Figure 5. Autophagy inhibition reduces HNSCC in combination therapy, and does not affect CAF proliferation.

(A) CQ significantly reduces HNSCC (HN5) proliferation.
(B) Combination of CQ (IC_{50}) and radiation (3 Gy) significantly reduces HNSCC (HN5) proliferation over 72 hours.
(C) SAR405 significantly reduces HNSCC (HN5) proliferation over 72 hours.
(D) CAF proliferation is not effected by SAR405 inhibition over 72 hour period.
(E) SAR405 (1μM) potentiates the effects of cisplatin (4 μM) to inhibit HNSCC (HN5) proliferation over 72 hour. All graphs depict three independent experiments in triplicate, error bars represent SEM.

Supplemental Figure 6. Examples of Electron Microscopy Autophagosomes. Autophagosomes (identified by arrowheads) were counted by blinded observer following these characteristics: 1) double membrane structure (Can be observed by arrow), 2) cytoplasmic cargo enclosed, 3) vesicular architecture to differentiate from Golgi or ER, and 4) clear distinction from mitochondria (asterisk). Images representative of two HNSCC tumor cells at 1200x magnification. Autophagosome inlet is at 12000X magnification.