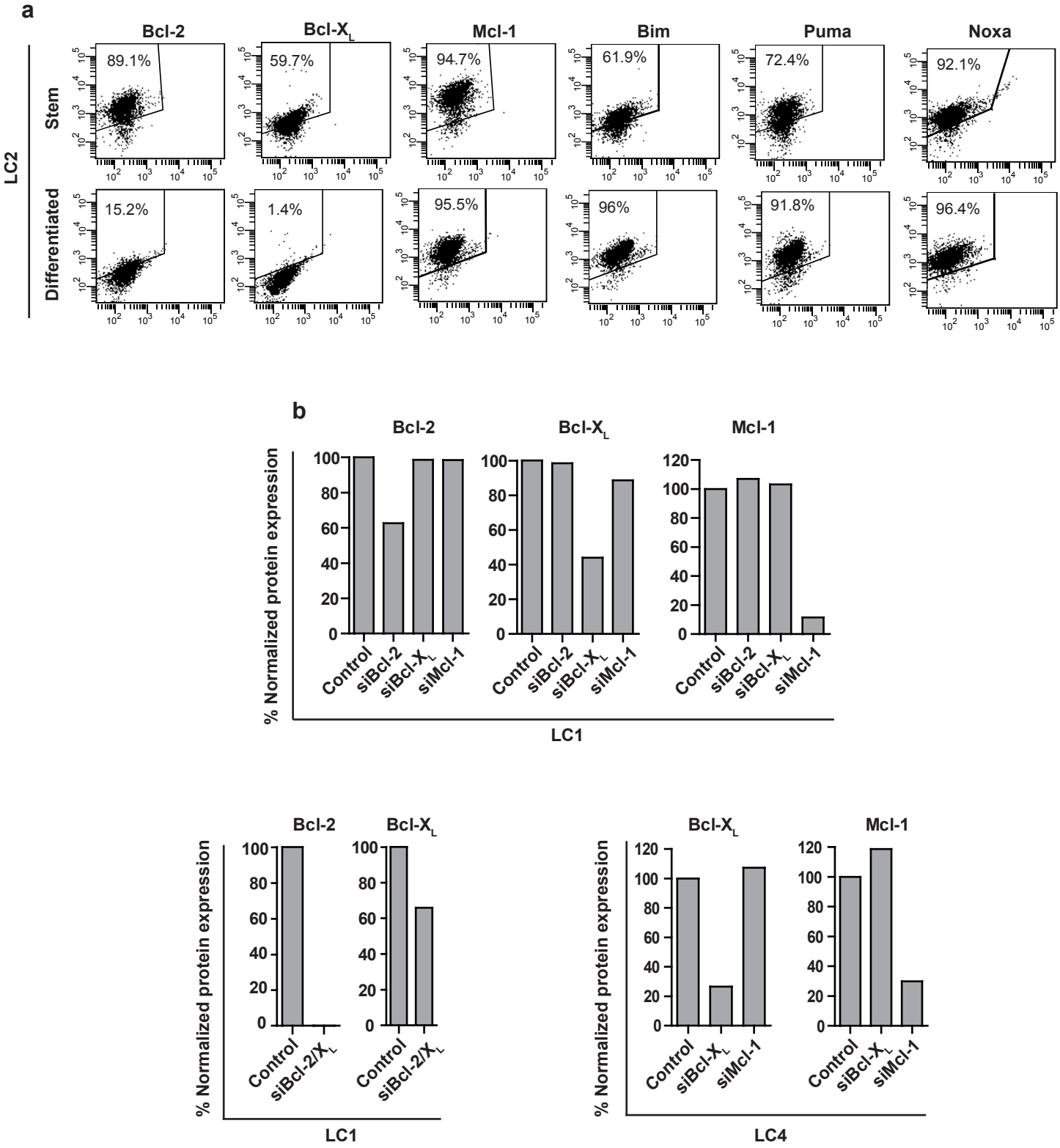
LCSC Line	PATIENT (sex/age)	TUMOR SUBTYPE	TNM (stage/grading)
LC1	M/63	LCNEC	pT2pN2pMx (III A)/G3
LC2	M/70	SCC	pT2pN2pMX (III A)/G2
LC3	M/66	AC	pT2pN2pMx (IIIA)/G2
LC4	M/75	SCC	pT3pN0pMx (IIB)/G3

Mutation	LCSC line			
	LC1	LC2	LC3	LC4
KRAS exon 1	WT	WT	WT	WT
KRAS exon 2	**WT**	**WT**	**WT**	**WT**
EGFR exon 18	WT	WT	WT	WT
EGFR exon 19	**WT**	**WT**	**WT**	**WT**
EGFR exon 21	WT	WT	WT	WT
p53 exon 5	WT	WT	WT	WT
p53 exon 6	**mut**	**mut**	WT	**WT**
p53 exon 7	WT	WT	**mut**	WT
p53 exon 8	**WT**	**WT**	**WT**	**WT**

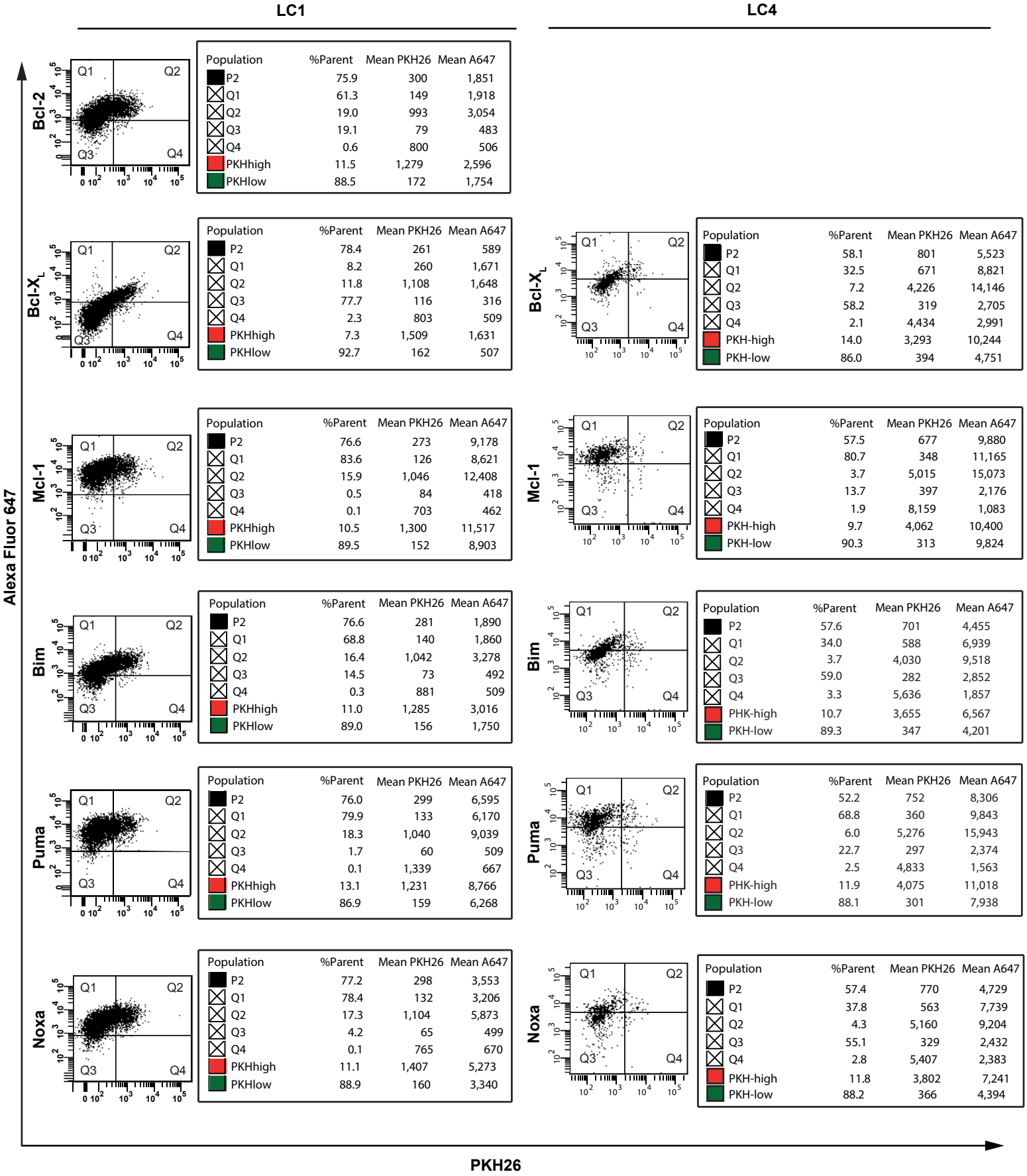
Supplementary Figure 1: Characteristics of patients and tumors used to derived LCSC lines. LCNEC, large cell neuroendocrine carcinoma; AC, adenocarcinoma; SCC, squamous cell carcinoma. WT, wild type; mut, mutated.

Figure 1 Supplementary, Zeuner et al.



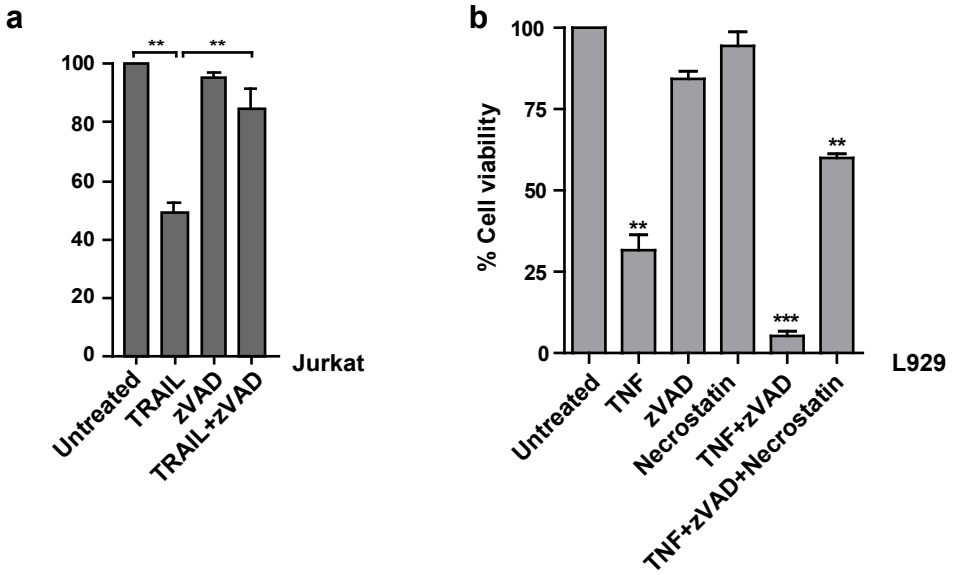
Supplementary Figure 2: (**a**) Flow cytometry analysis of pro- and anti-apoptotic proteins in LCSC (Stem; line LC2) and their differentiated progeny (Differentiated). (**b**) Quantification of western blots shown in Figure 2c for Bcl-2, Bcl-X_L and Mcl-1 on LCSC LC1(upper panel and lower left) and LC4 (lower right) treated with small interfering RNA (si) against the single transcripts (siBcl-2, siBcl-X_L, siMcl-1) or in combination (siBcl-2/X_L). Bands were quantified with a ChemiDoc XRS and the ImageLab software.

Figure 2 Supplementary, Zeuner et al.



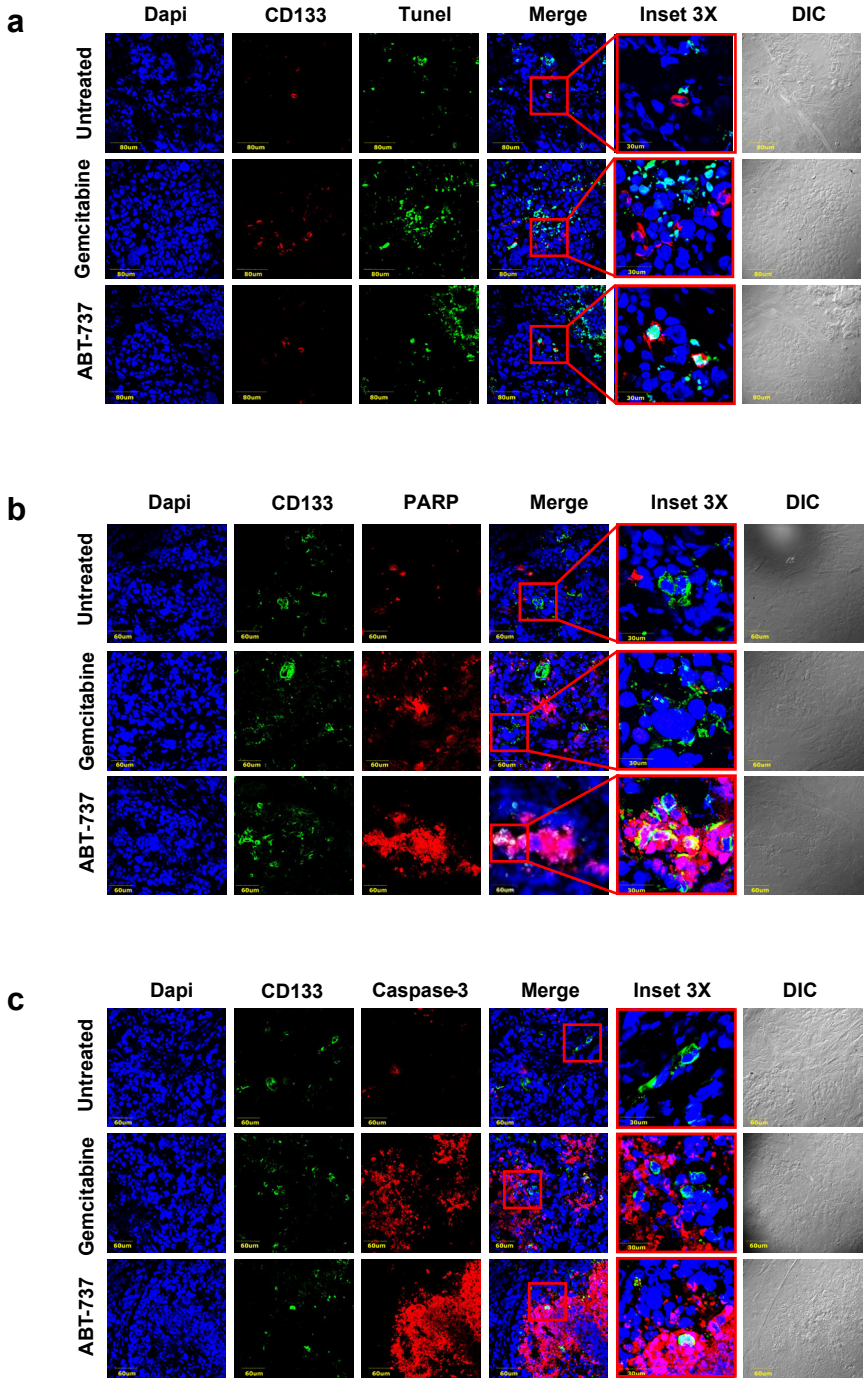
Supplementary Figure 3: Flow cytometry analysis of pro- and anti-apoptotic proteins in LCSC (lines LC1 and LC4). Cells were cultured for ten days after PKH staining, fixed, permeabilized, stained with antibodies against the indicated proteins and subsequently incubated with Alexa Fluor 647 (A647) secondary antibodies. P2 refers to the percentage of live single cells gated according to physical parameters (forward scatter/side scatter) and to doublet exclusion (side scatter width/side scatter area).

Figure 3 Supplementary, Zeuner et al.



Supplementary Figure 4: **a**) Inhibition of TRAIL-induced apoptosis in Jurkat leukemia cells. Cells were pretreated with 40 μM zVAD for 1 hour and then treated with 200 μg/ml leucine-zipper TRAIL (TRAIL) for 48 hours. **P≤0.01 (n=3). **b**) Inhibition of necroptosis by necrostatin in L929 cells. L929 mouse fibrosarcoma cells were treated for 24 hours with 100 ng/ml tumor necrosis factor (TNF) and/or 25 μM necrostatin in the presence or in the absence of 40 μM zVAD and cell viability was assessed as described in Materials and Methods. Bars represent mean±S.D.; **P≤0.01 and ***P≤0.001 (n=3).

Figure 4 Supplementary, Zeuner et al.



Supplementary Figure 5: Effects of ABT-737 on LCSC in tumor xenografts. Mice bearing LCSC-derived tumor xenografts were treated with vehicle (Control), gemcitabine or ABT-737 as described in Materials and Methods. After 48 hours, tumors were removed, embedded in OCT and frozen. Tumor sections were stained with CD133 and either TUNEL (**a**) or antibodies against cleaved poly-ADP-ribose polymerase (PARP) (**b**) or cleaved caspase-3 (**c**). 60x magnification, bar 80 µm (a) or 60 µm (b and c). Inset 3x zoom (3X). DIC, differential interference contrast.

Figure 5 Supplementary, Zeuner et al.