

Supplementary Figures

Radiation Promotes Inflammation-Driven Targeting of Chemoradiotherapy Enhancing Nanoparticles

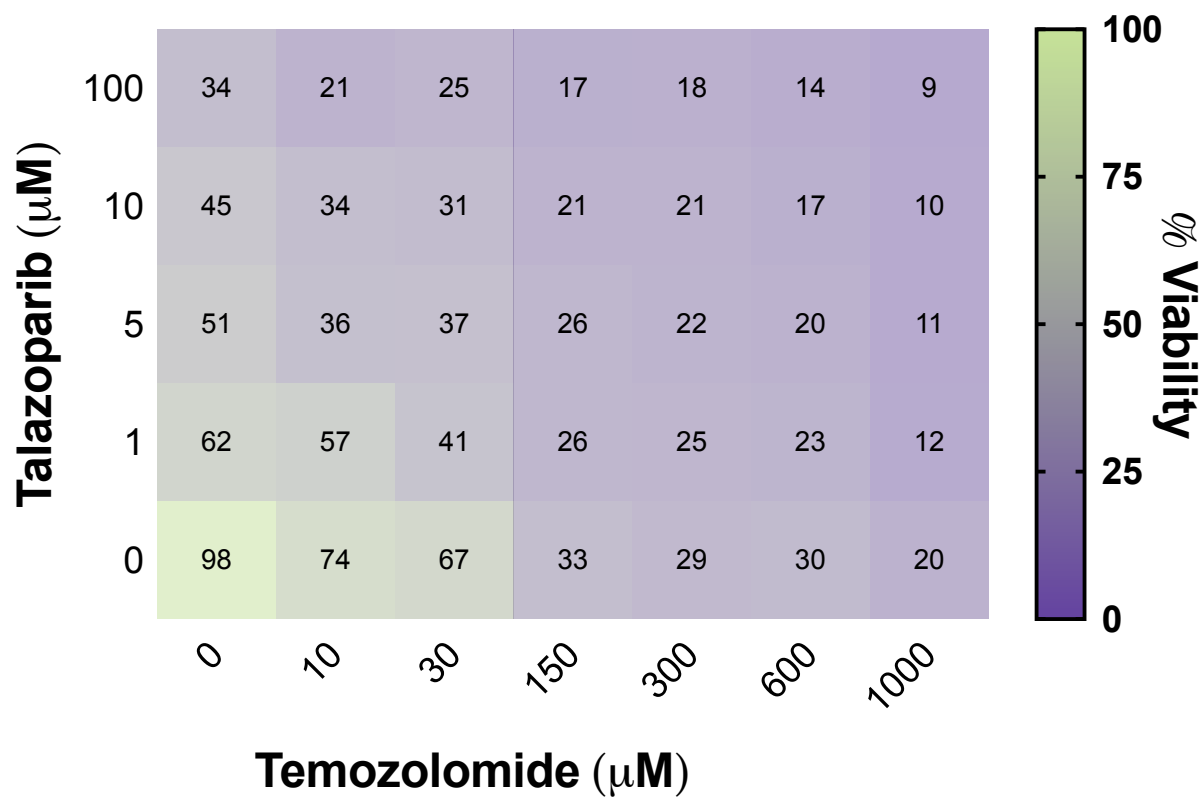
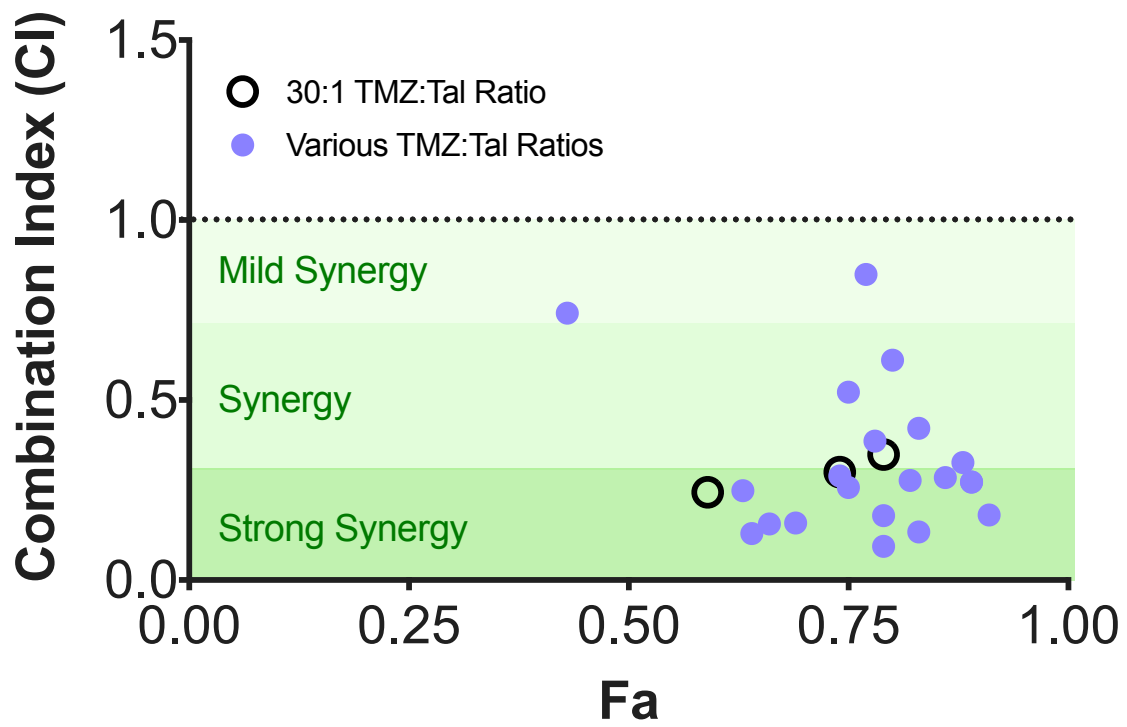
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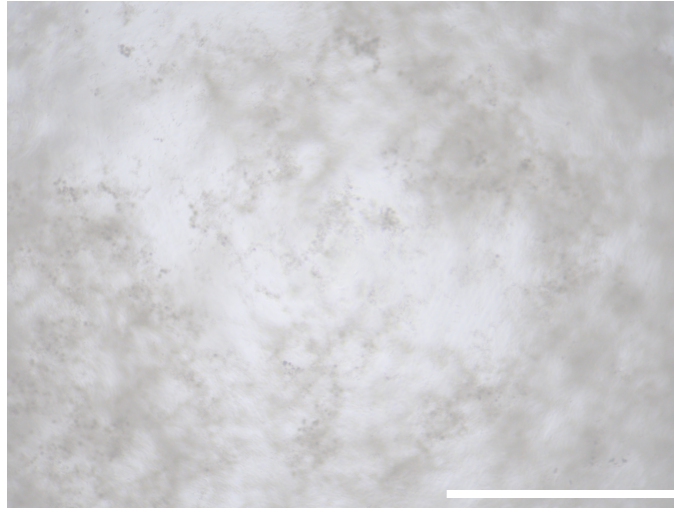
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A**B**

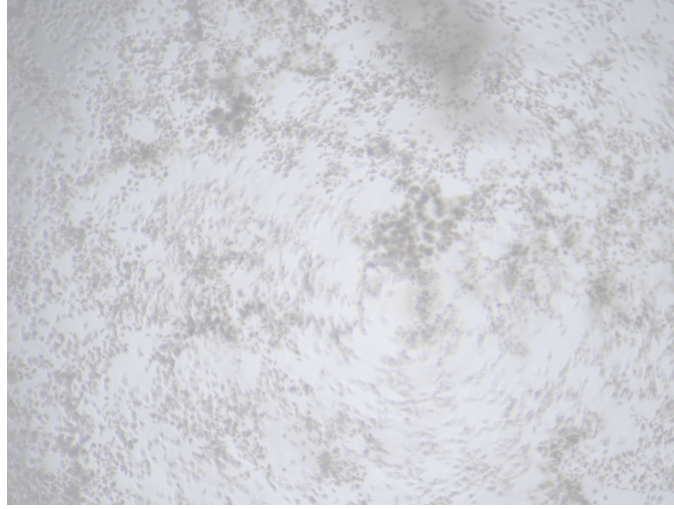
Supplemental Figure 1. A. *In vitro* viability of various TMZ:Tal ratios across a range of combinations. **B.** Combination index values for various TMZ:Tal ratios (purple circles) and several 30:1 TMZ:Tal ratios (black outline circles) where strong synergy is represented by a CI < 0.3, synergy is represented by 0.3 < CI < 0.7, and mild synergy is represented by CI > 0.7.

Tal in PBS

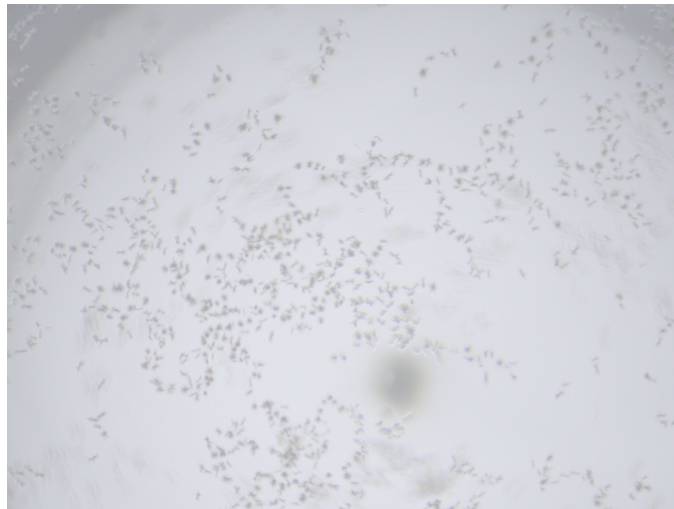
2000 μM



1000 μM



500 μM

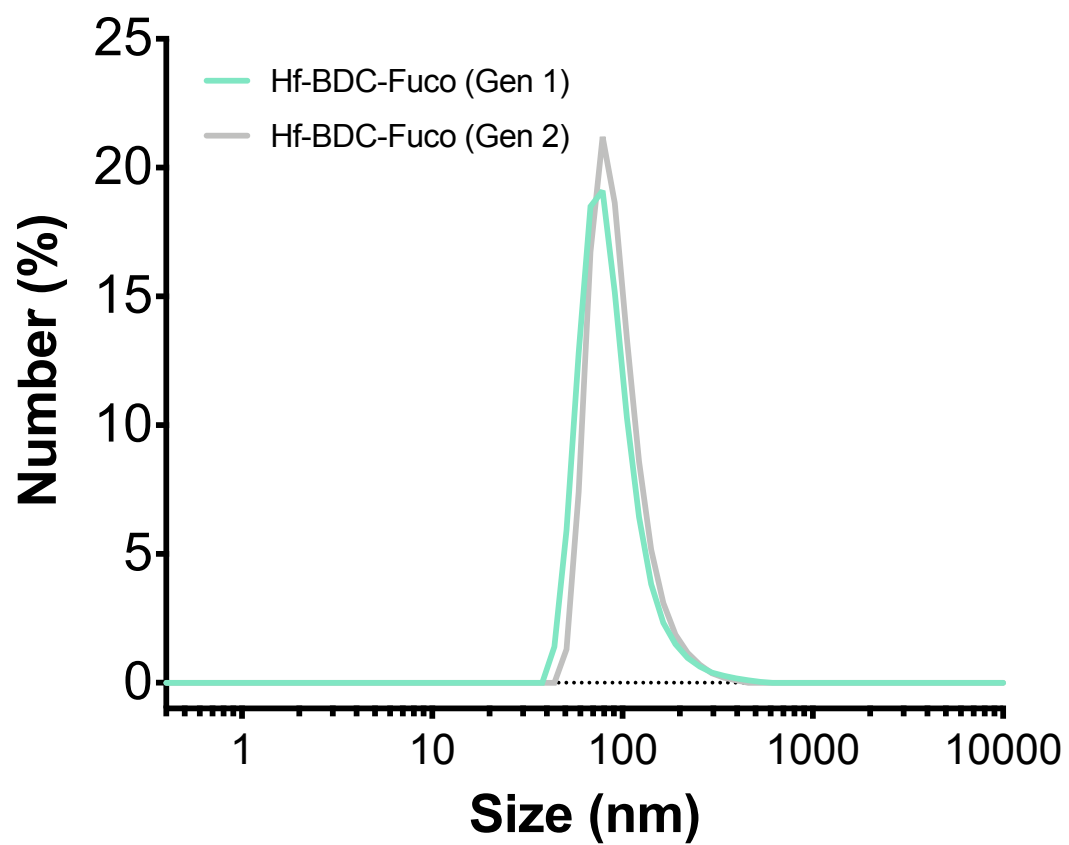
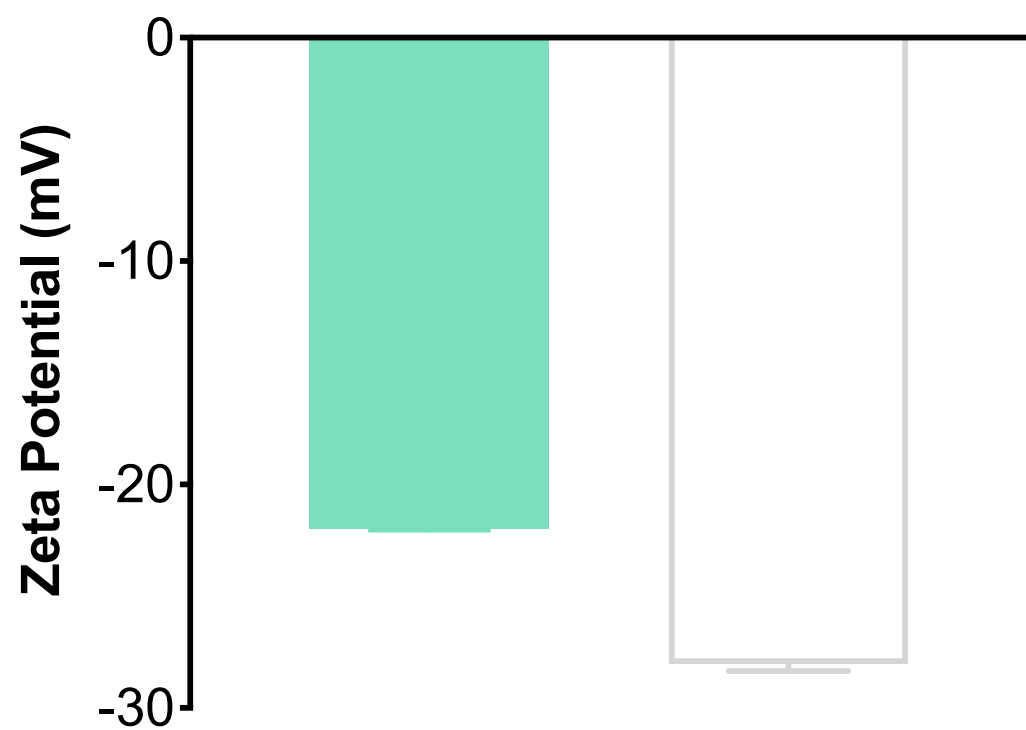
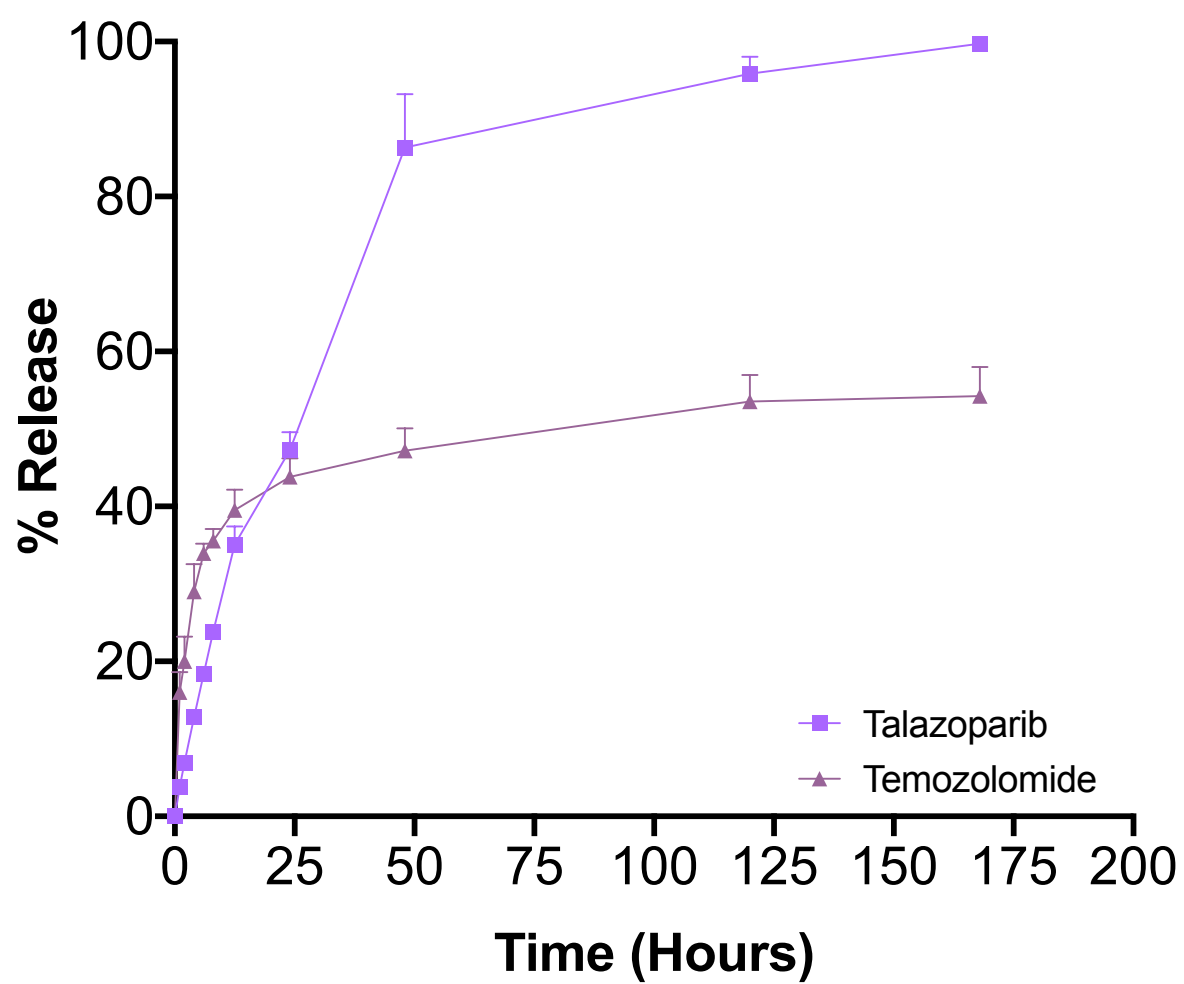


250 μM

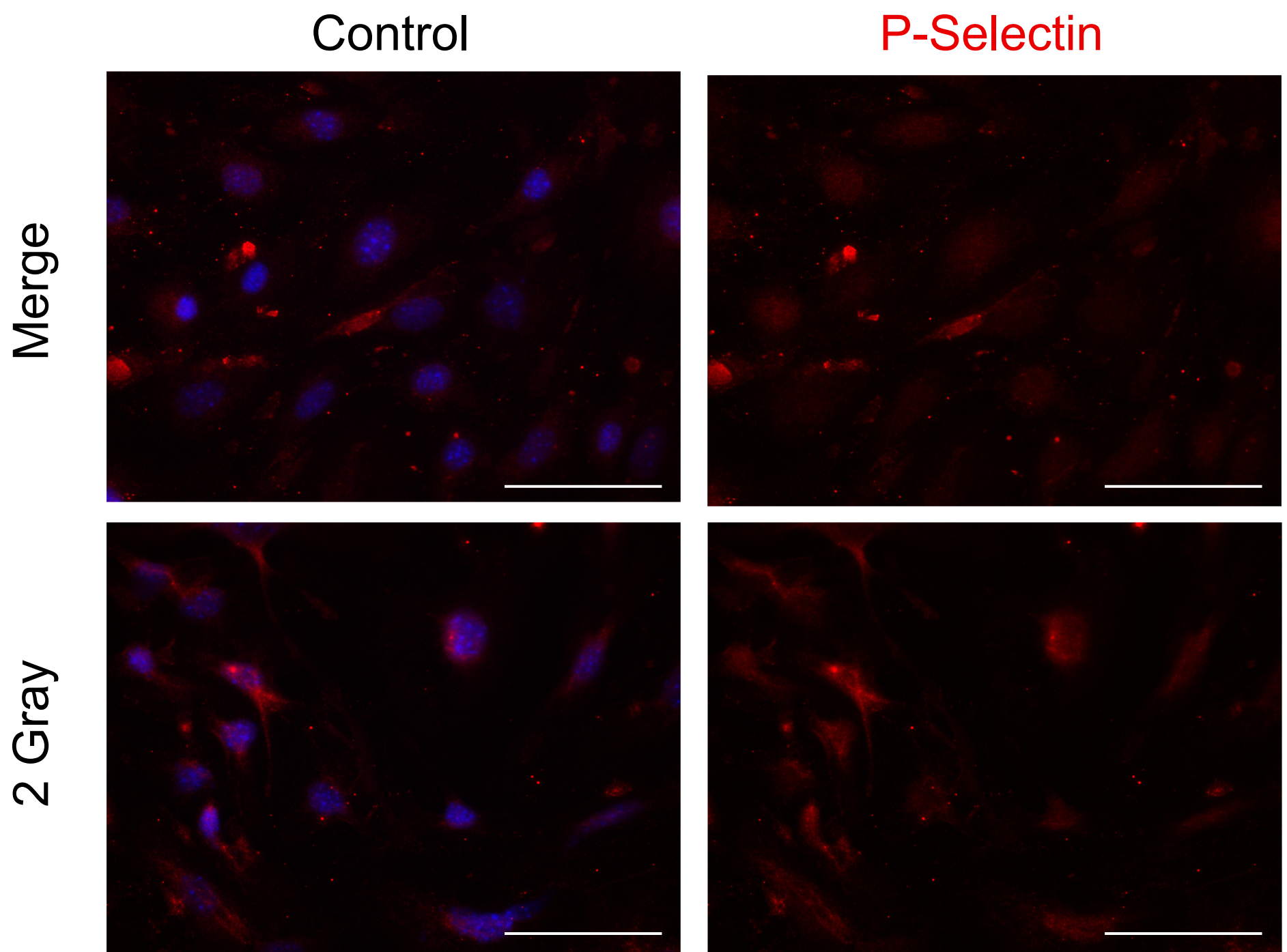


125 μM

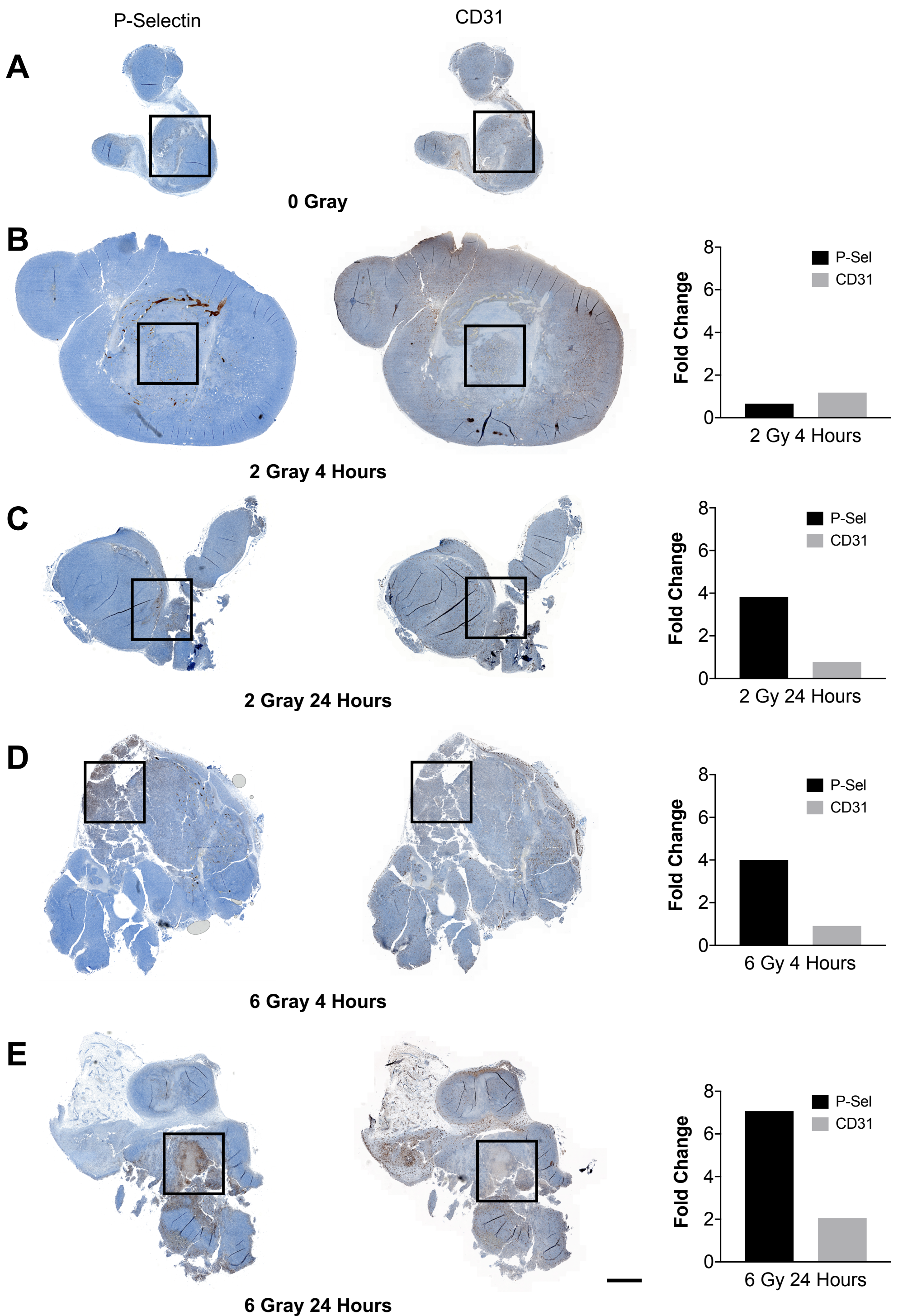


A**B****C**

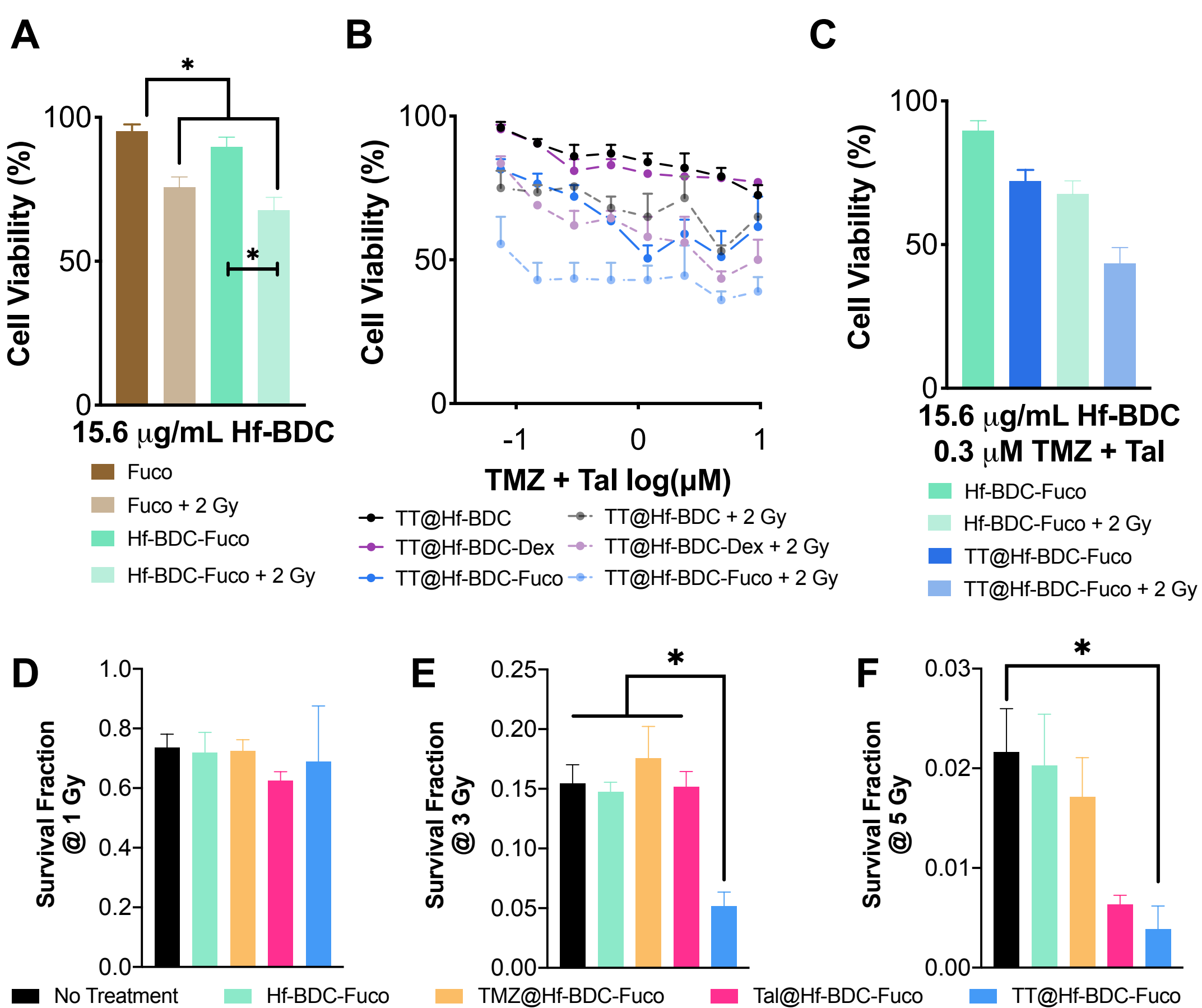
Supplemental Figure 3. A. Size by number and **B.** ζ potential as measured by DLS comparing the two slightly different coating methods. **C.** Release profile of TMZ and Tal from gen 1 TT@Hf-BDC-Fuco nMOF.



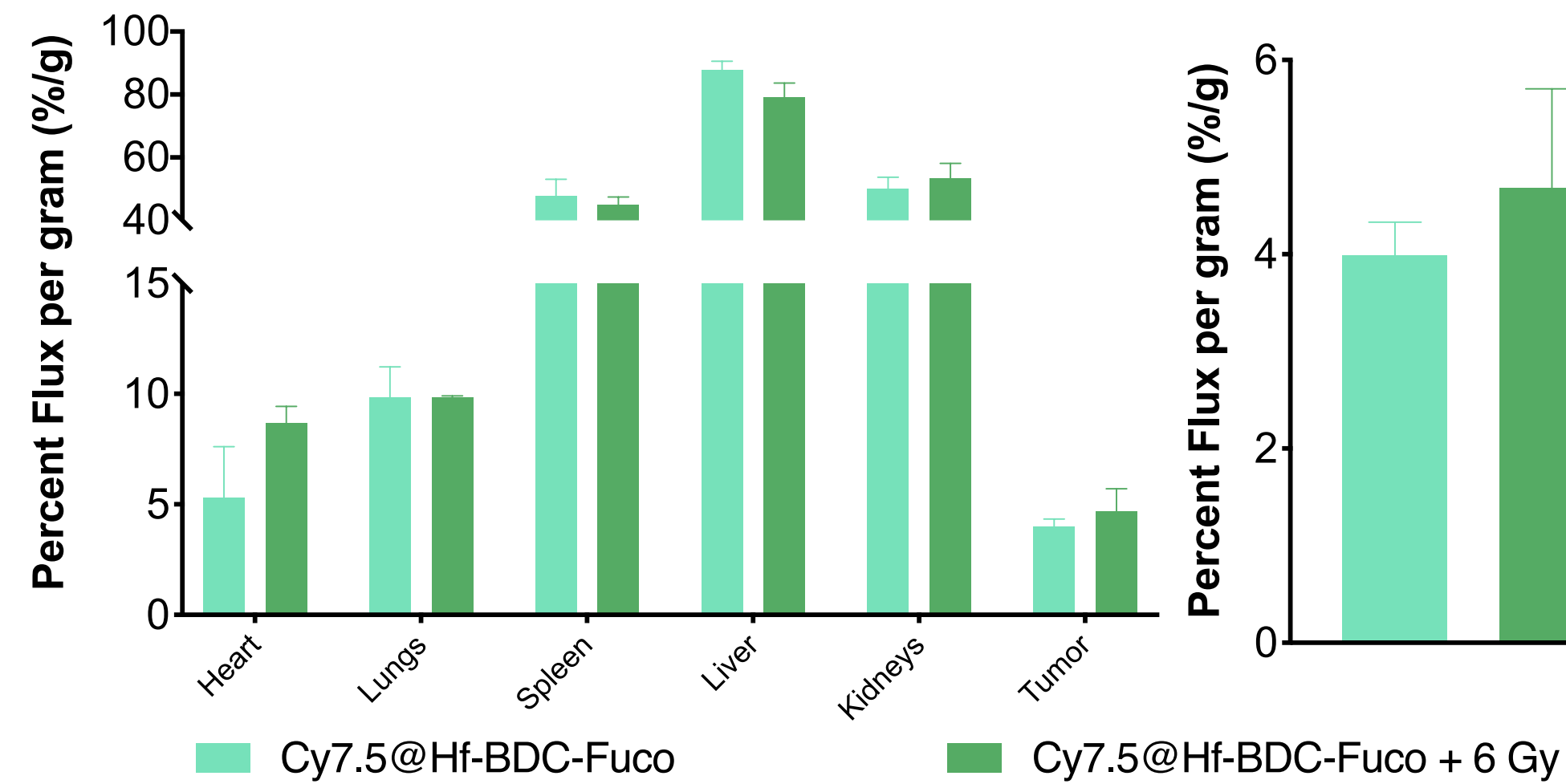
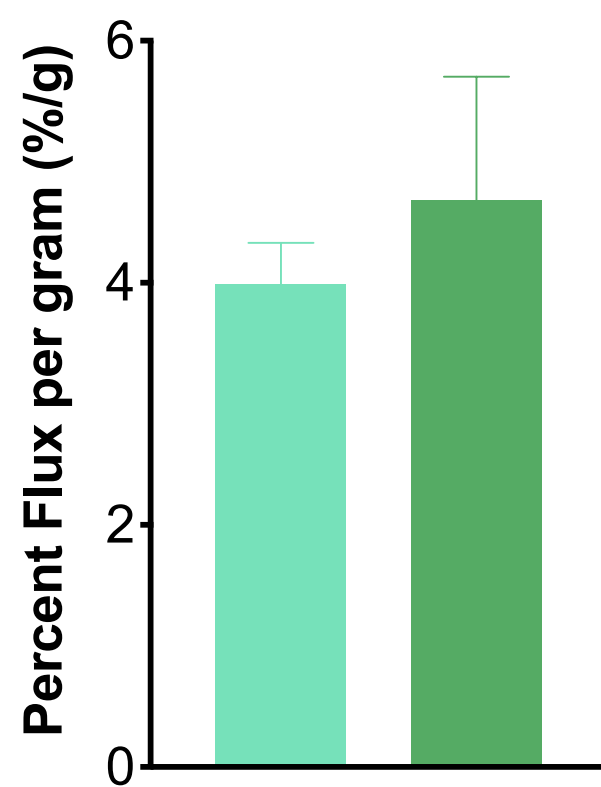
Supplemental Figure 4. Representative images of P-selectin expression in bEnd.3 endothelial cells with and without a radiation dose of 2 gray. Scale bars represent 200 μm .



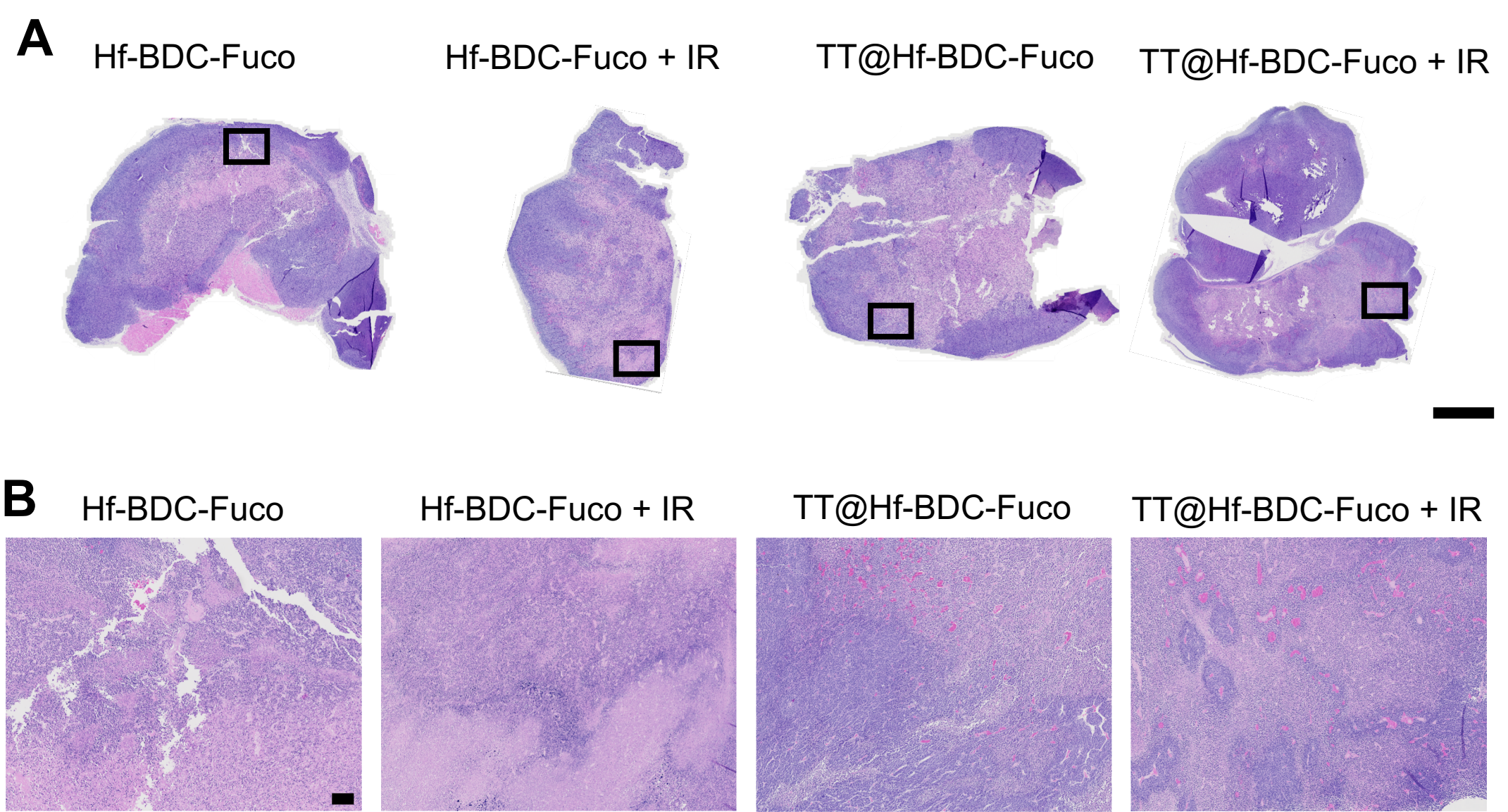
Supplemental Figure 5. Representative tumor tissue slice for P-selectin (left) and CD31 (middle) expression in tumors after various IR treatments. Fold change in expression of P-selectin or CD31 over 0 Gy control (right). **A.** Control tissue no IR. **B.** Tissue harvested 4 hours after a dose of 2 Gy. **C.** Tissue harvested 24 hours after a dose of 2 Gy. **D.** Tissue harvested 4 hours after a dose of 6 Gy. **E.** Tissue harvested 24 hours after a dose of 6 Gy. Boxes represent zoomed images from figure 3C. Scale bar represents 2000 μ m for all tissues.



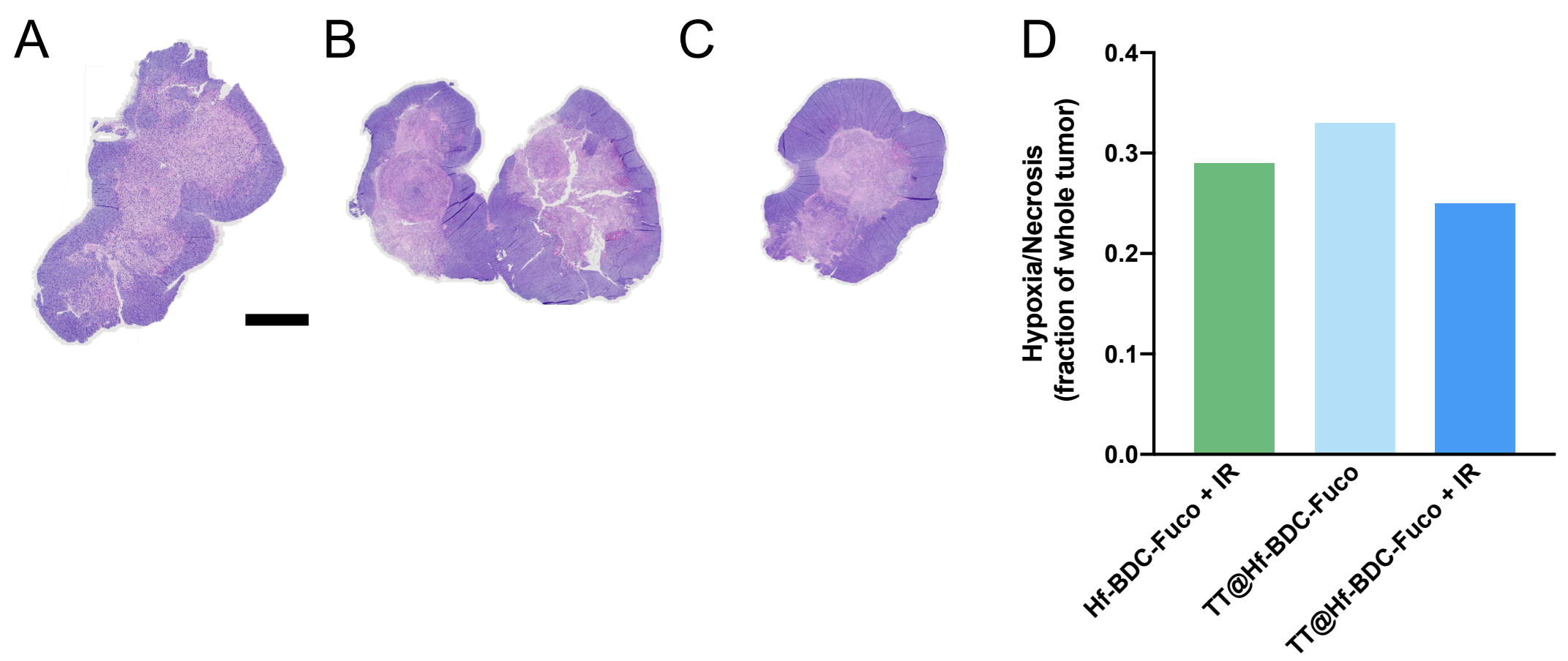
Supplemental Figure 6. **A.** Comparison of +/- IR fuco vs Hf-BDC-fuco at concentration used for drug-loaded viability. Asterisks (*) represent statistically significant difference ($p < 0.05$) analyzed by one-way ANOVA with multiple comparisons. **B.** TT concentration that does provide any significant benefit. **C.** TT concentration that does not provide any significant benefit. **D.** Comparison of +/- IR Hf-BDC-Fuco and TT@Hf-BDC-Fuco. Clonogenic assay survival fraction values at **E.** one, **F.** three and, **G.** five gray demonstrates significantly decreased survival with TT-@Hf-BDC-Fuco at three and five gray radiation. Asterisks (*) represent statistically significant difference ($p < 0.05$) analyzed by one-way ANOVA with multiple comparisons.

A**B**

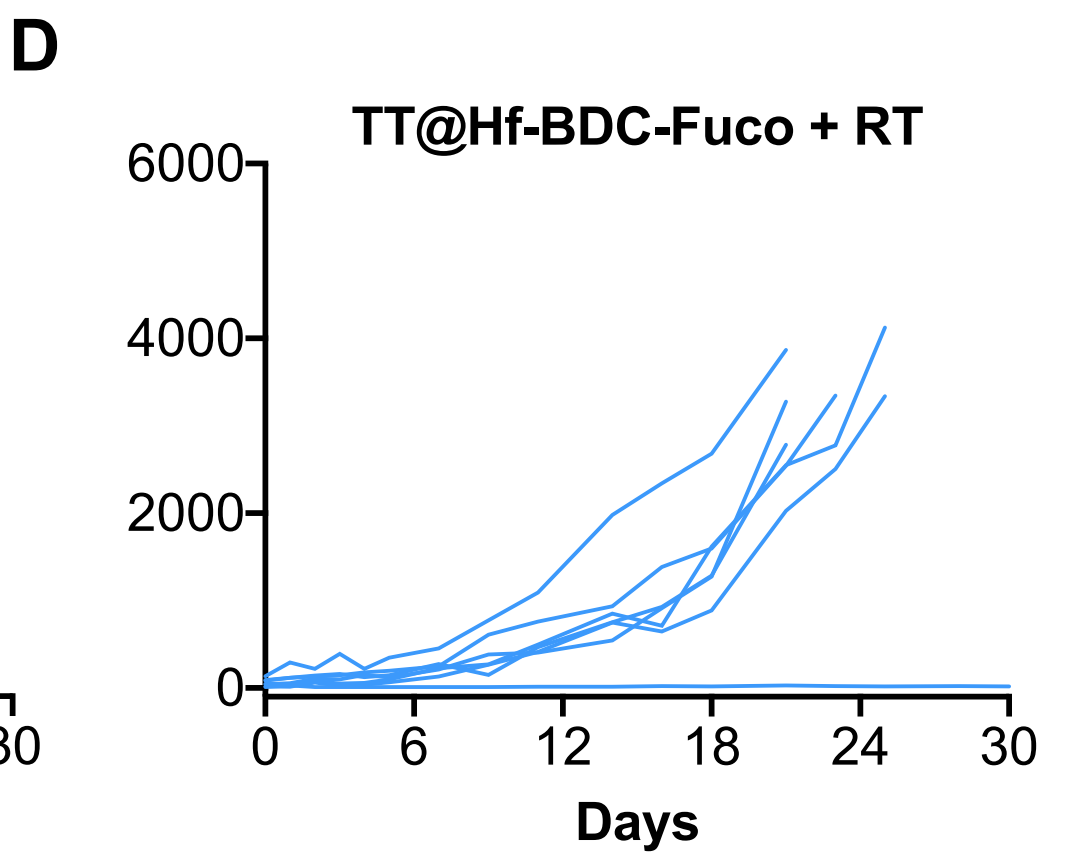
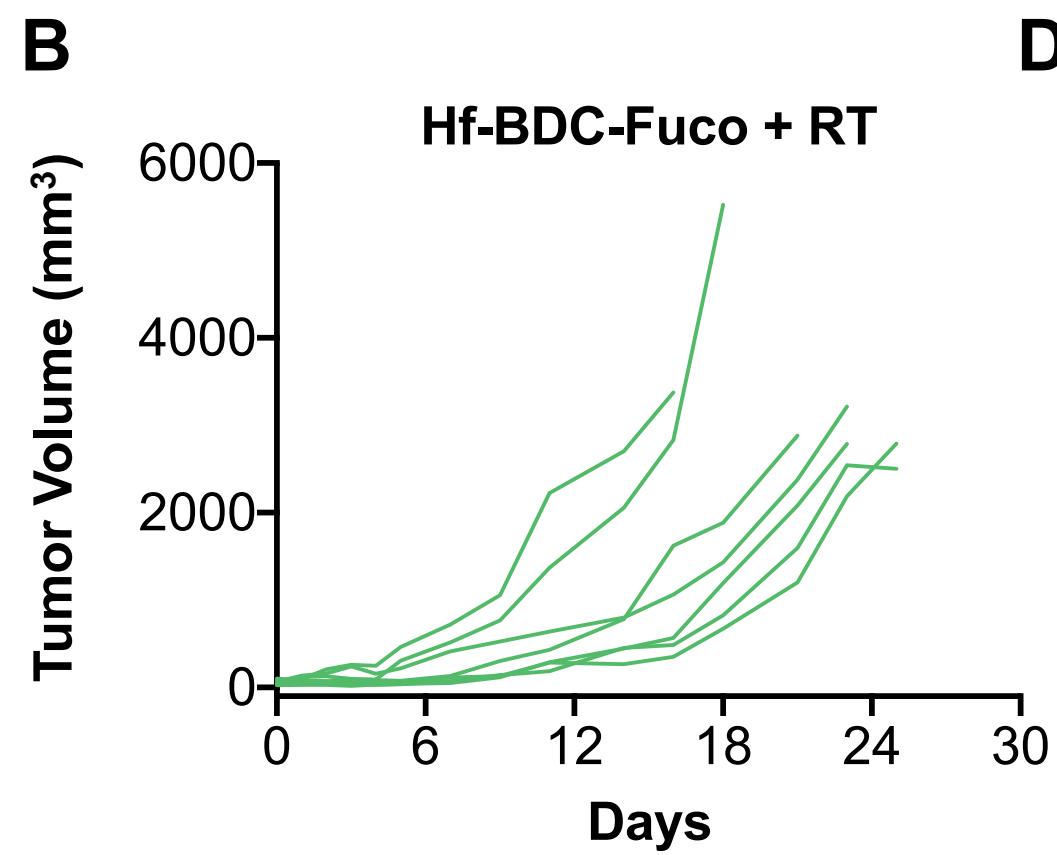
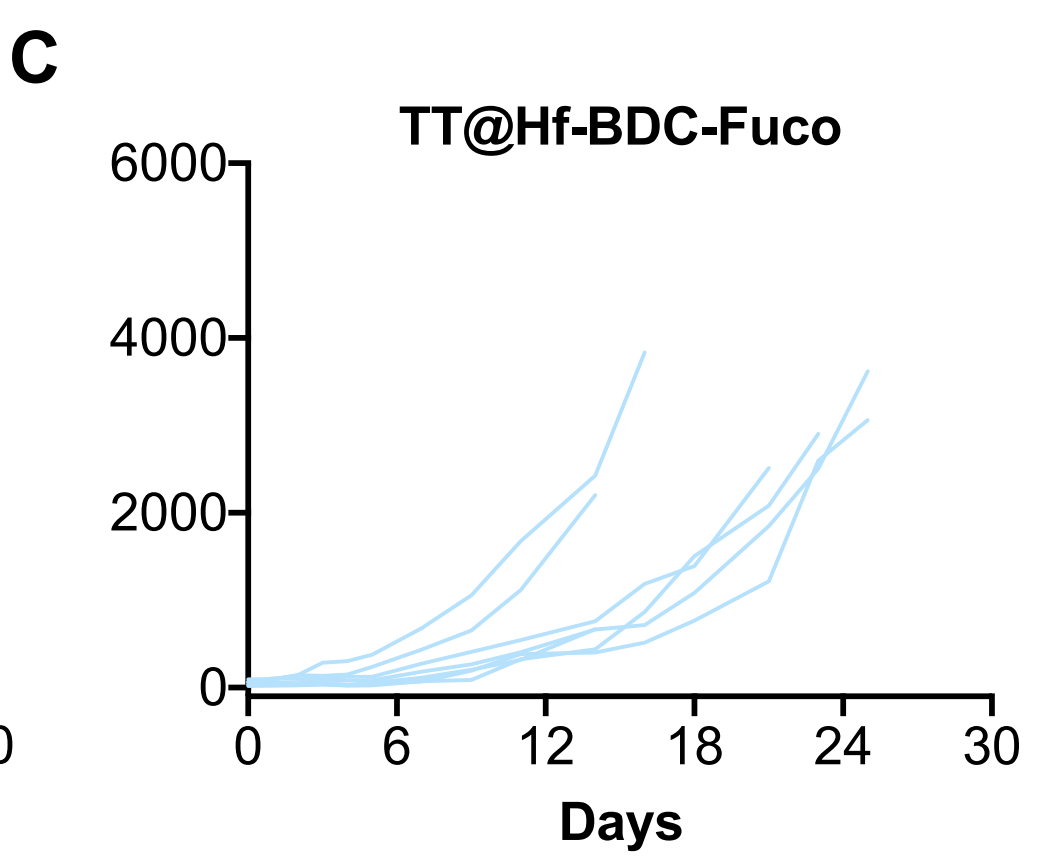
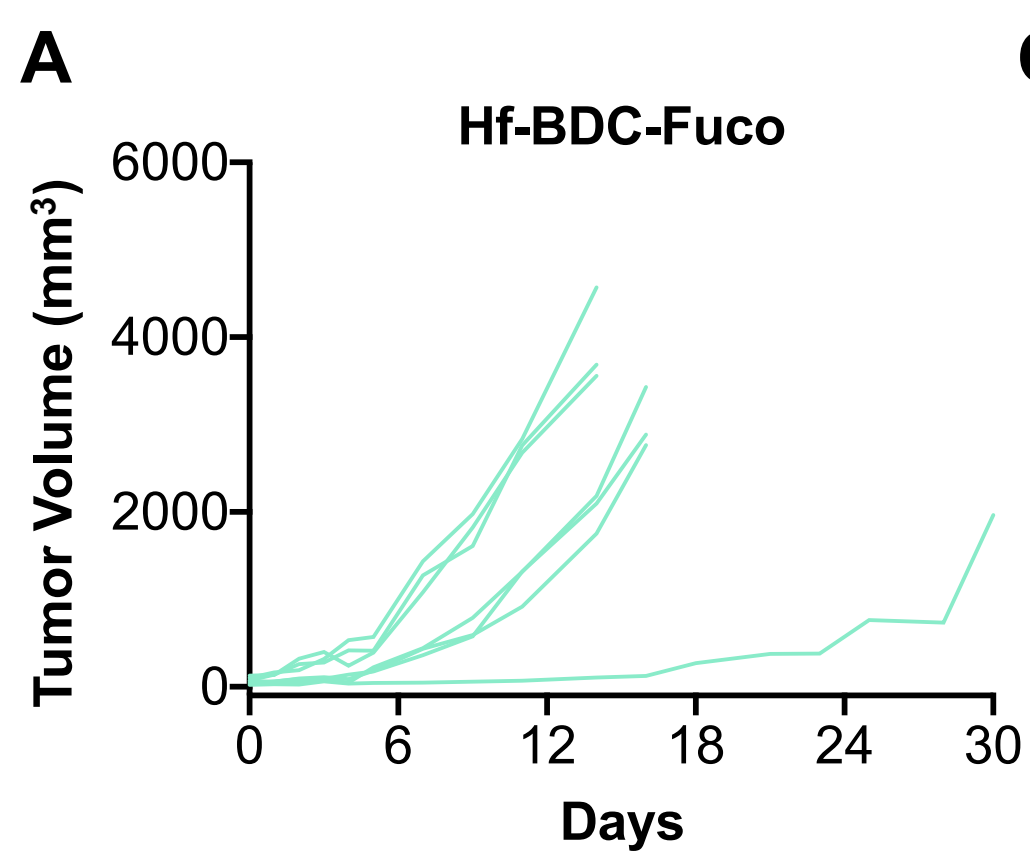
Supplementary Figure 7. A. Whole-organ biodistribution as quantified by IVIS imaging for mice treated with (6 gy) or without radiation and administered P-selectin targeting Hf-BDC-Fuco nMOFs. **B.** Tumor-only biodistribution.



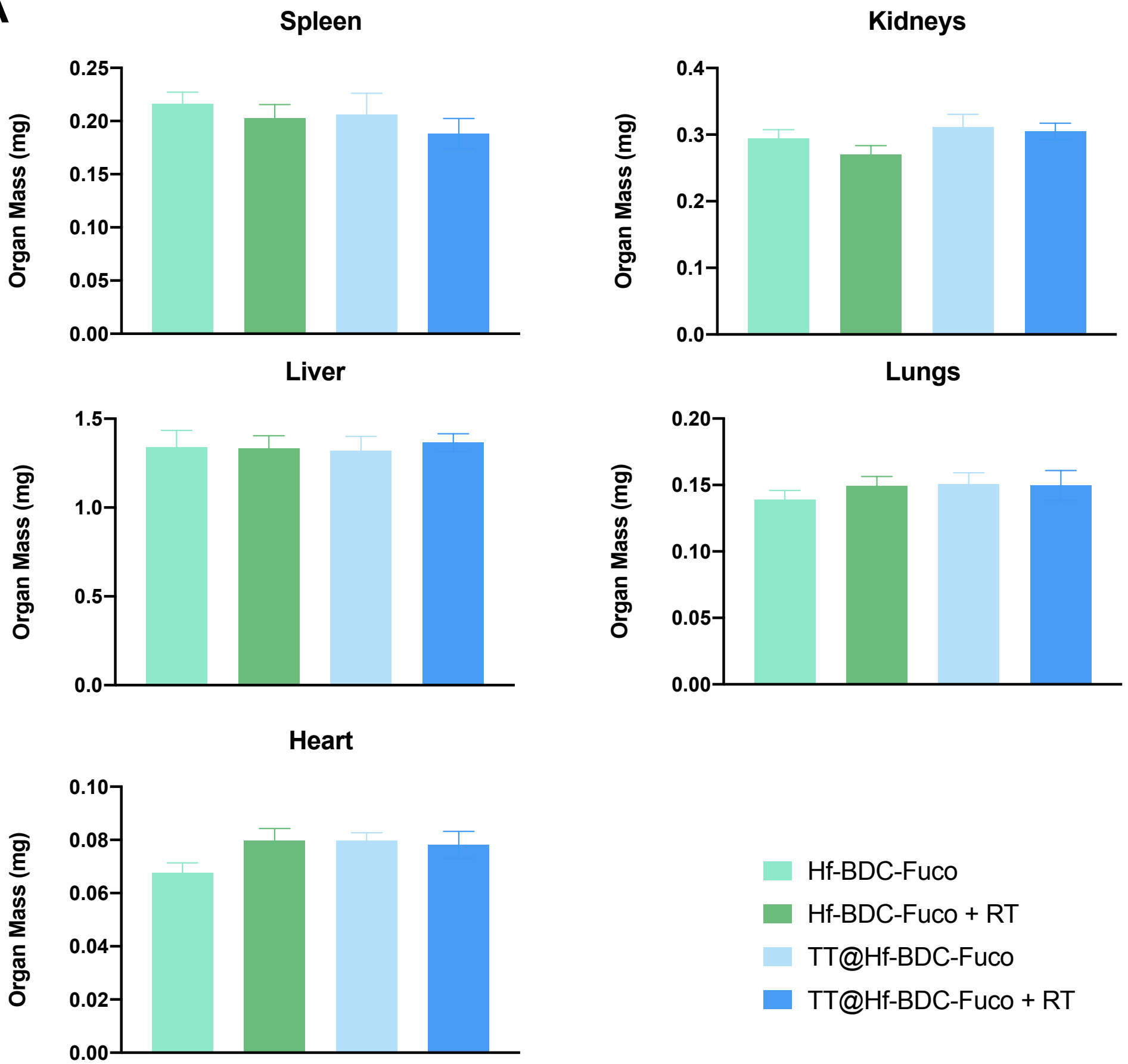
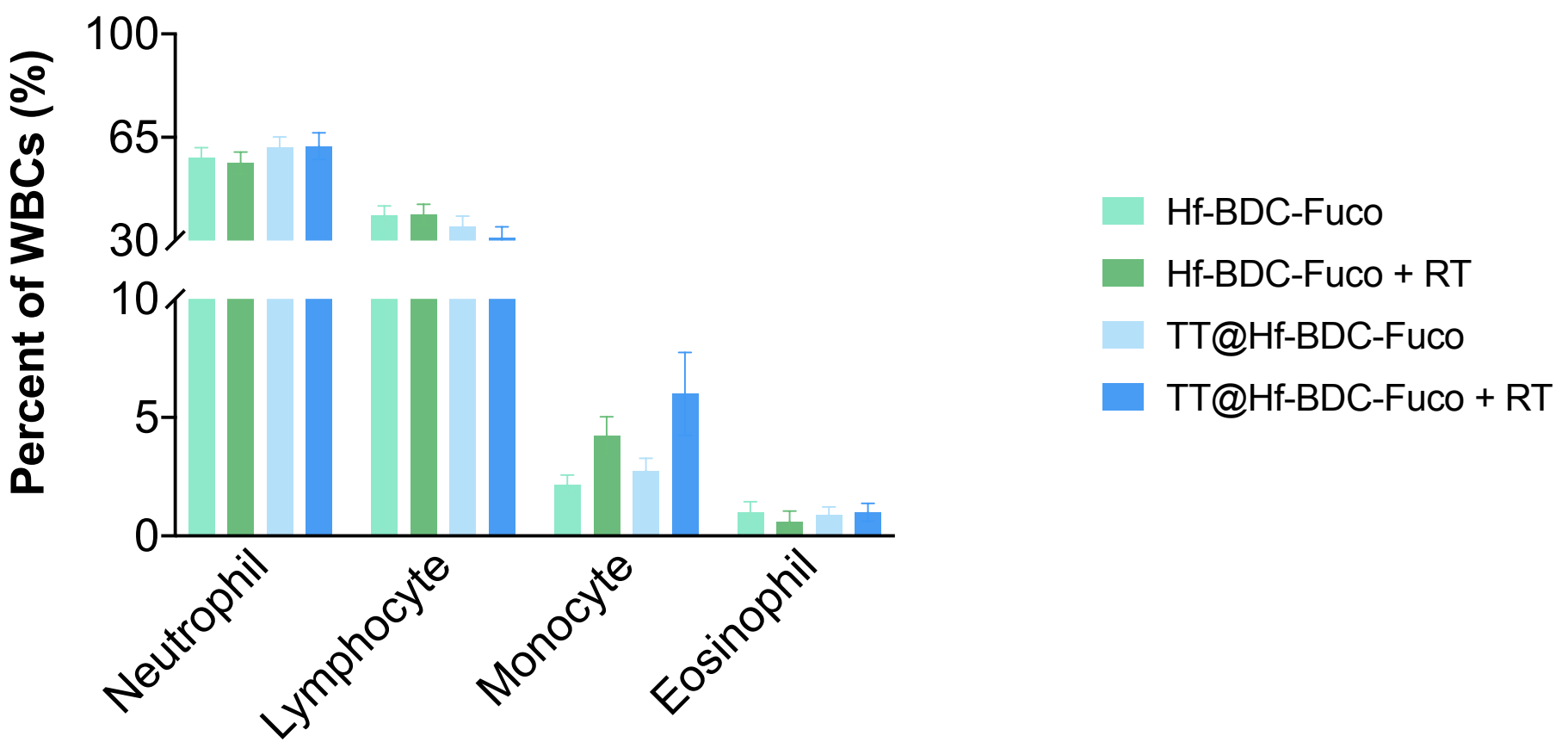
Supplementary Figure 8. H&E stain of **A.** Whole-tumor and **B.** zoomed inset harvested on day 14. Scale bar represents 5000 (A) or 200 (B) μm .



Supplemental Figure 9. H&E stain of **A.** Hf-BDC-Fuco +IR, **B.** TT@Hf-BDC-Fuco, and **C.** TT@Hf-BDC-Fuco + IR tumors harvested on day 21. Scale bars represent 5000 μm . **D.** Quantification of hypoxic/necrotic regions as a fraction of whole tumor slice from figures in A-C



Supplemental Figure 10. Individual tumor curves for each treatment group for mice from multimodality treatment study, used to develop curves in figure 7. **A.** Mice treated with Hf-BDC-Fuco alone. **B.** Mice treated with TT@Hf-BDC-Fuco alone. **C.** Mice treated with Hf-BDC-Fuco and 2 fractions of 2 gray. **D.** Mice treated with TT@Hf-BDC-Fuco and 2 fractions of 2 gray.

A**B**

Supplemental Figure 11. A. Organ weight averages for mice in each treatment group upon sacrifice. **B.** White blood cell (WBC) evaluation showing the percentage of each type of cell as a portion of total white blood cells.

Supplemental Table 1

	IC₅₀ (μM)	Fold Change IC₅₀
Tal	5.1	N/A
TMZ	34.3	N/A
TMZ:Tal (30:1)	10.7 (0.35 Tal, 10.35 TMZ)	Tal: -14.6X TMZ:-3.3X

Supplemental Table 1. IC₅₀ values calculated for the viability curves in figure 1A along with the change in IC₅₀ for both drugs when delivered in combination.

Supplemental Table 2

	<i>Number Average (d.nm)</i>	<i>Polydispersity Index (PDI)</i>	<i>Zeta Potential (ZP)</i>
<i>Hf-BDC</i>	84.1 ± 4.0	0.25 ± 0.01	20.4 ± 1.6
<i>Hf-BDC-Dex</i>	90.3 ± 6.5	0.20 ± 0.004	-24.5 ± 0.4
<i>Hf-BDC-Fuco (Gen 1)</i>	91.0 ± 11.1	0.24 ± 0.03	-20.7 ± 2.3
<i>Hf-BDC-Fuco (Gen 2)</i>	97.5 ± 6.5	0.17 ± 0.01	-28.0 ± 0.6
<i>TT@Hf-BDC-Fuco</i>	100.0 ± 1.2	0.17 ± 0.03	-18.0 ± 0.3

Supplemental Table 2. Table showing z-average (nm), polydispersity index (PDI), and zeta potential (ZP) values for nanoparticles coated using generation 1 or generation 2 methods.

Supplemental Table 3

<i>Conc. Added (μM)</i>		<i>Theoretical Loading (μM)</i>		<i>Encapsulation Efficiency (EE%)</i>		<i>TMZ: Tal Ratio</i>	
TMZ	Tal	TMZ	Tal	TMZ	Tal	TMZ	Tal
500	500	354 ± 36	369 ± 4	71 ± 5	74 ± 1	1	1
7000	400	6289 ± 74	216 ± 39	90 ± 1	54 ± 10	29	1

Supplemental Table 3. Table demonstrating concentrations added, theoretical loading, encapsulation efficiencies, and final TMZ: Tal ratio for sample gen 1 (row 1) or gen 2 (row 2) nMOFs.