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Supplementary Material

Differential membrane binding of α/β-peptide foldamers: implications for cellular delivery and mitochondrial targeting

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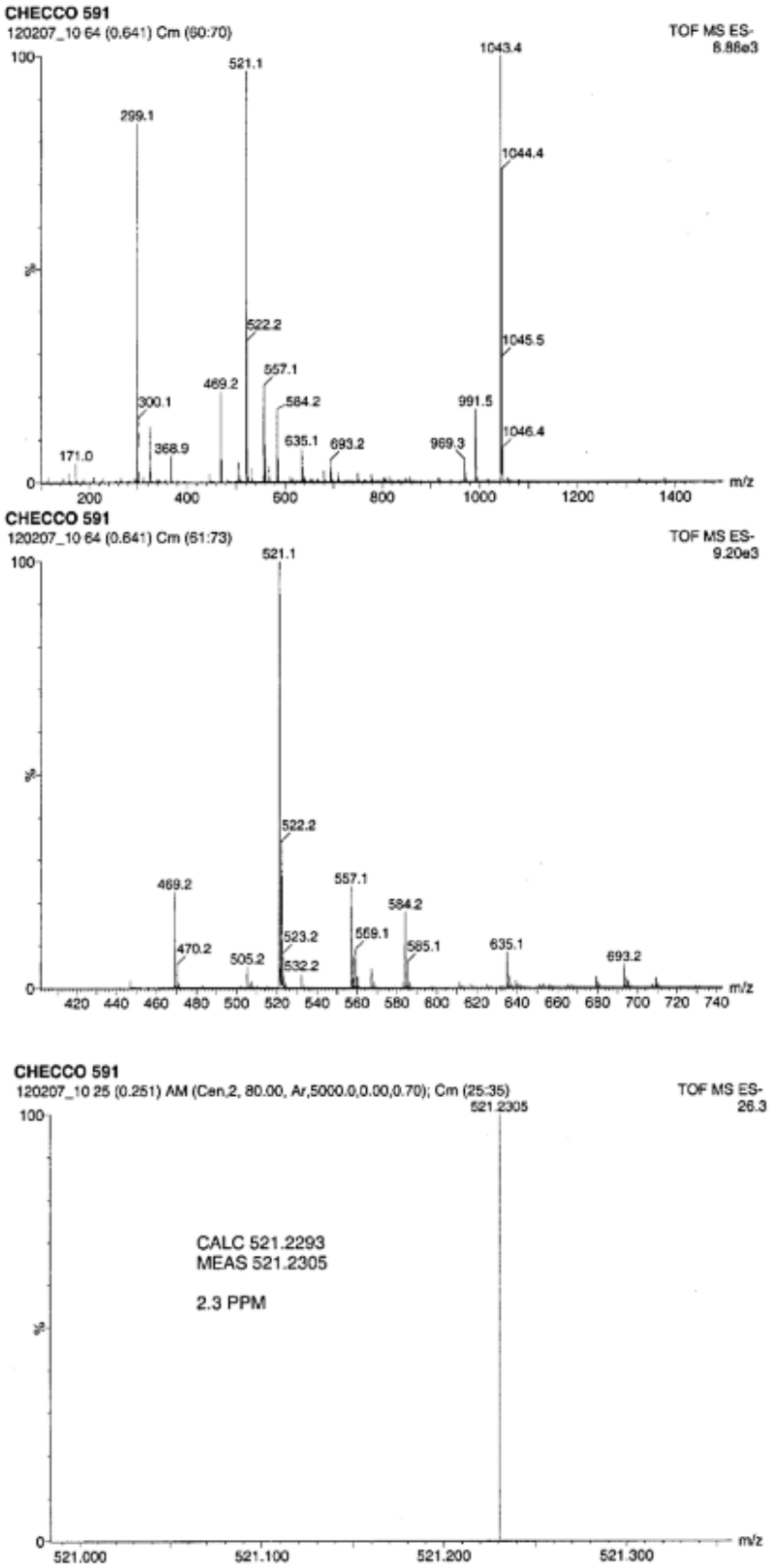

Figure S1 ESI-MS data for Fmoc-J5-OH, calc. $[M-H]^-$ = 521.2.

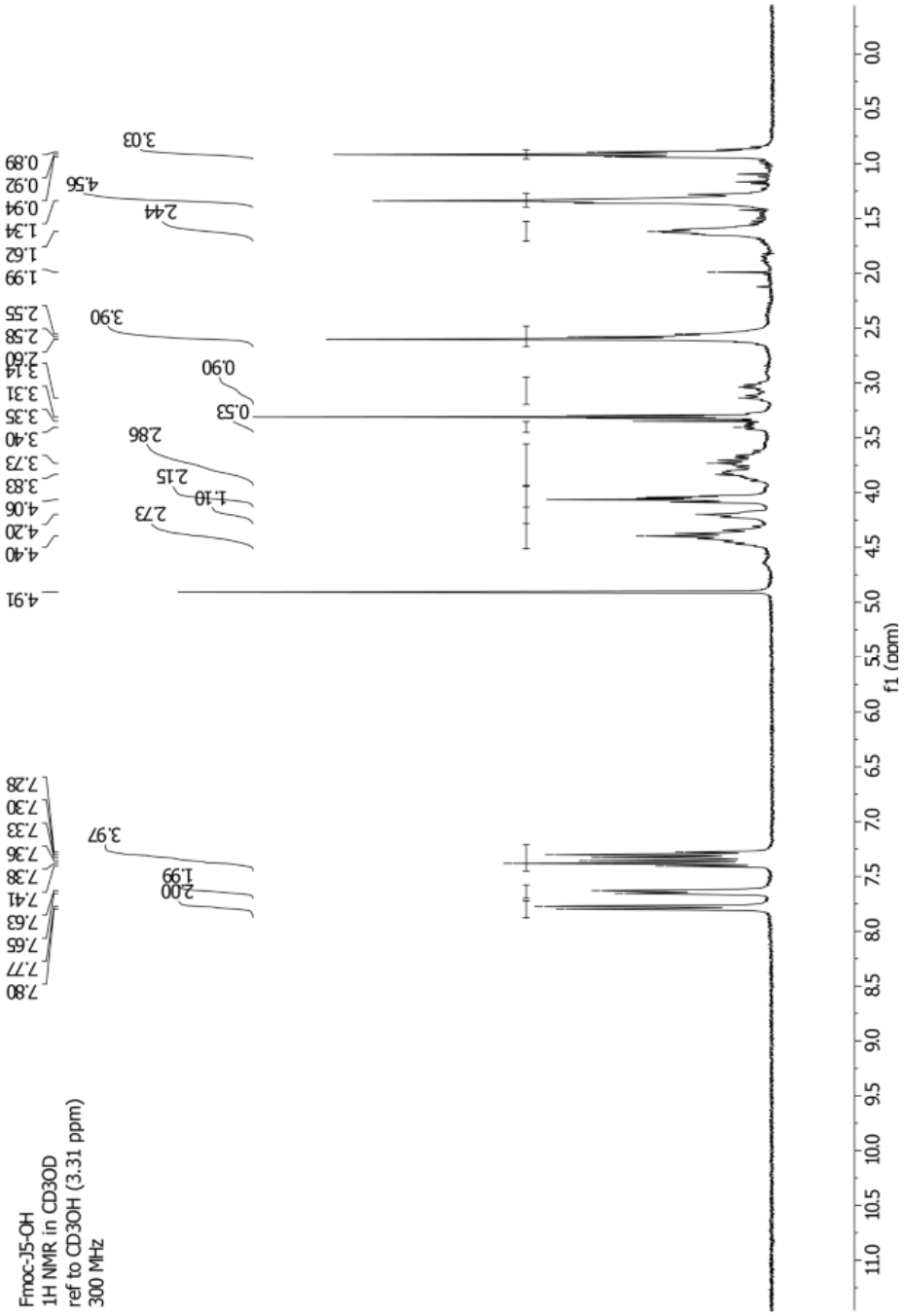

Figure S2 ^{1}H-NMR data for Fmoc-J5-OH.

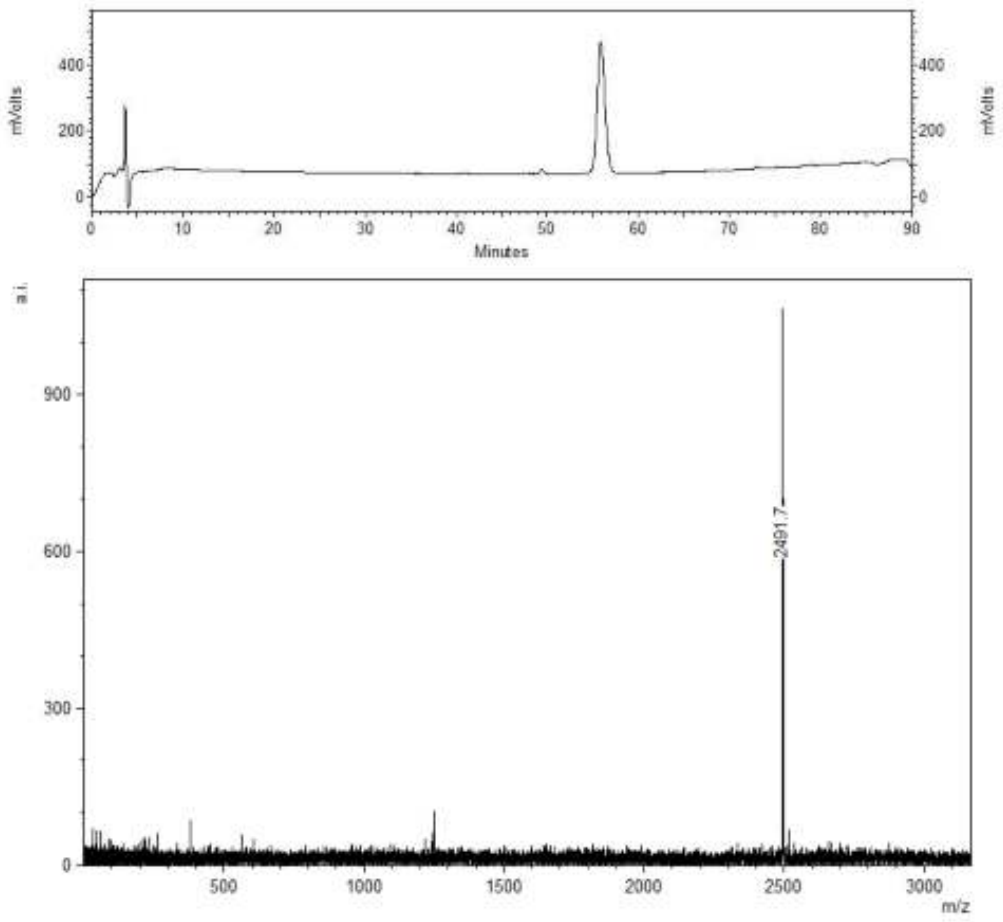

Figure S3 HPLC and MALDI-TOF characterisation of DPI-5-5. (Top panel) HPLC analysis. Solvent A: H_2O with 0.1% TFA, solvent B: acetonitrile with 0.1% TFA, flow rate: 1 mL/min, gradient = 10-90% solvent B over 80 minutes, absorbance measured at 220 nm. (Bottom panel) MALDI-TOF analysis. Calculated monoisotopic $[M+H]^+$ = 2491.4

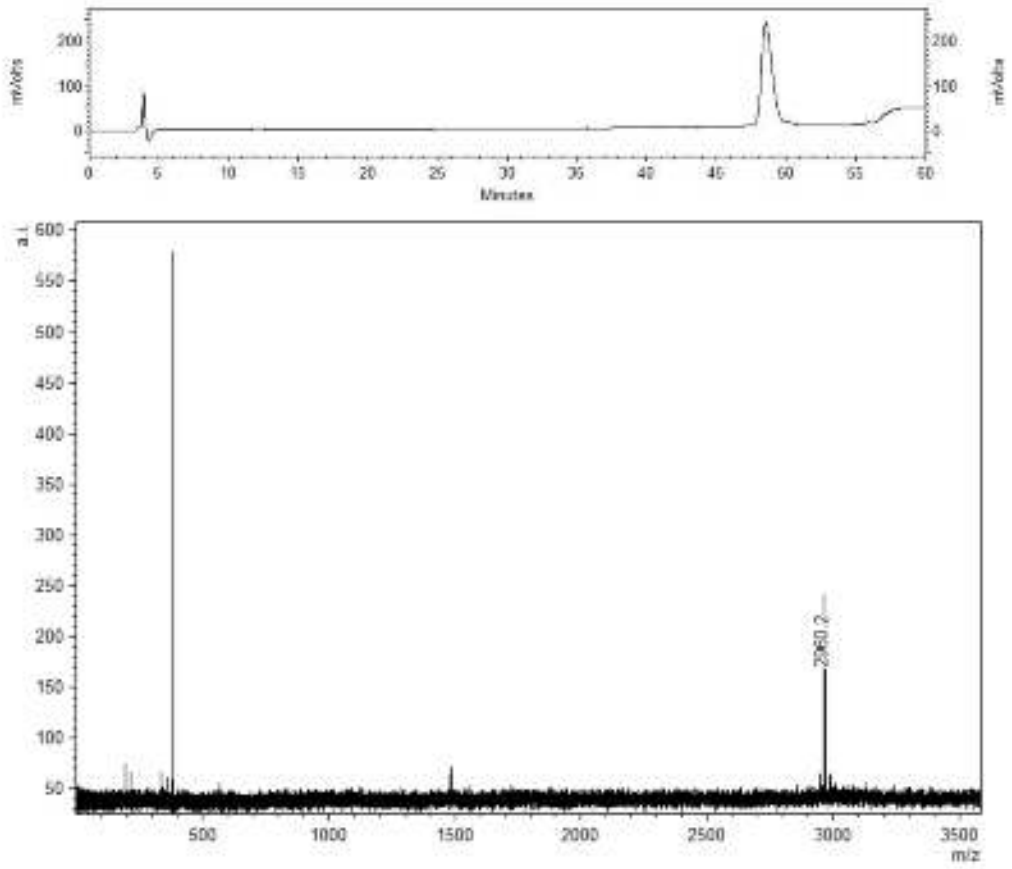

Figure S4: HPLC and MALDI-TOF characterisation of DPI-5-5-RRR. (Top panel) HPLC analysis. Solvent A: H_2O with 0.1% TFA, solvent B: acetonitrile with 0.1% TFA, flow rate: 1 mL/min, gradient = 10-60% solvent B over 50 minutes, absorbance measured at 220 nm. (Bottom panel) MALDI-TOF analysis. Calculated monoisotopic $[M+H]^+$ = 2959.7.

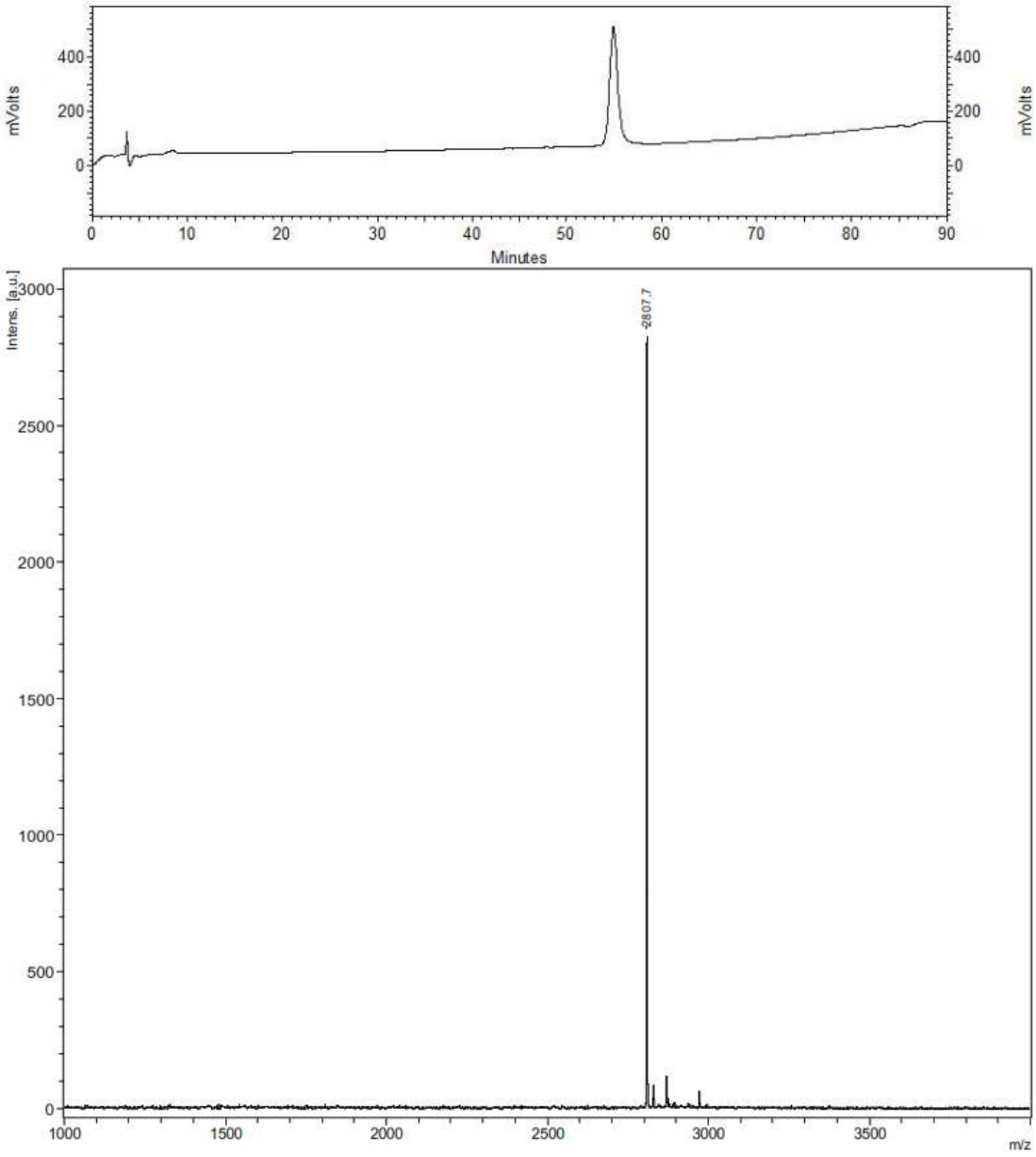

Figure S5: HPLC and MALDI-TOF characterisation of Flu-DPI-5-5. (Top panel) HPLC analysis. Solvent A: H_2O with 0.1% TFA, solvent B: acetonitrile with 0.1% TFA, flow rate: 1 mL/min, gradient = 10-90% solvent B over 80 minutes, absorbance measured at 220 nm. (Bottom panel) MALDI-TOF analysis. Calculated monoisotopic $[M+H]^+$ = 2807.4.

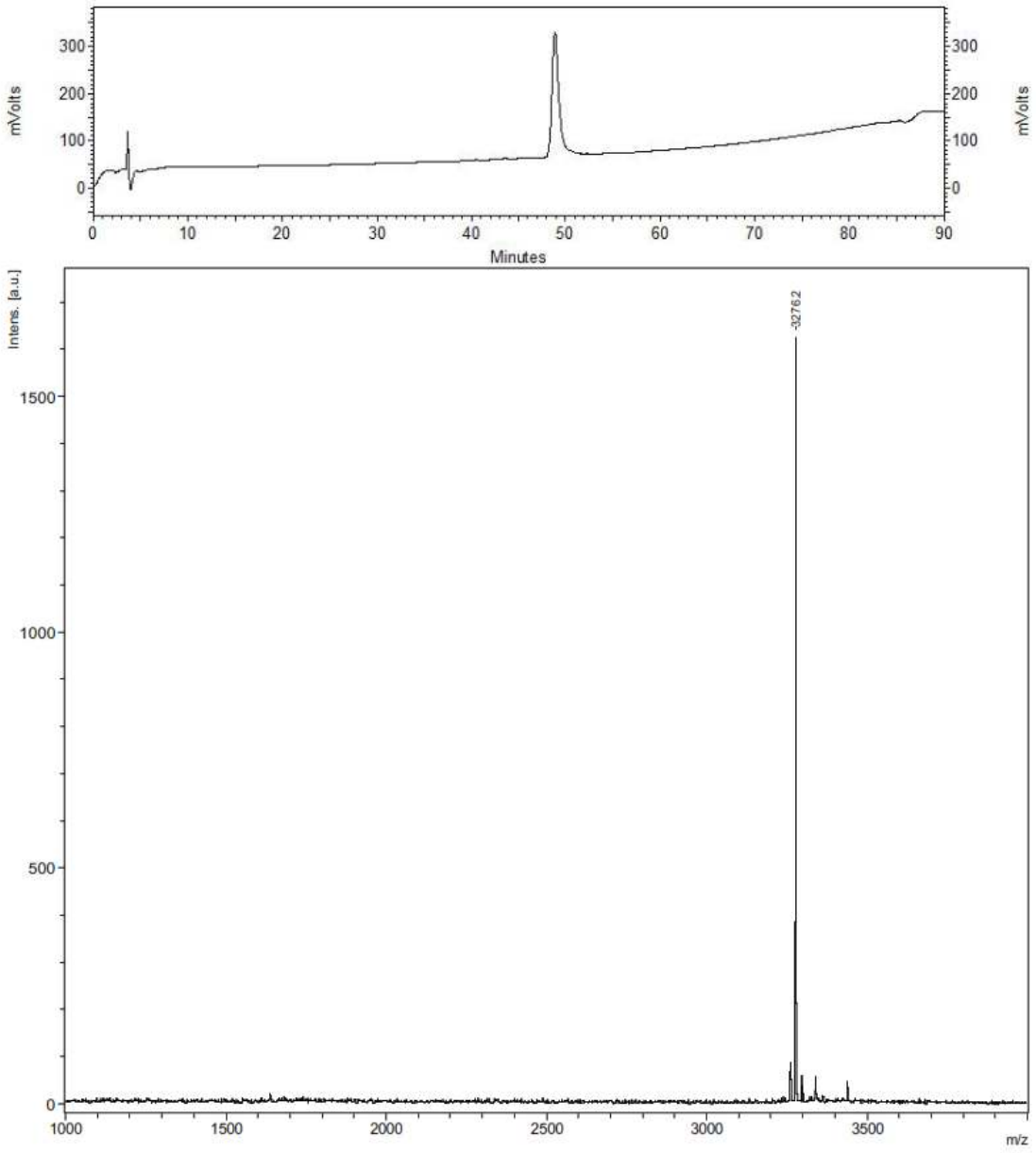

Figure S6: HPLC and MALDI-TOF characterisation of Flu-DPI-5-5-RRR. (Top panel) HPLC analysis. Solvent A: H_2O with 0.1% TFA, solvent B: acetonitrile with 0.1% TFA, flow rate: 1 mL/min, gradient = 10-90% solvent B over 80 minutes, absorbance measured at 220 nm. (Bottom panel) MALDI-TOF analysis. Calculated monoisotopic $[M+H]^+$ = 3275.7.

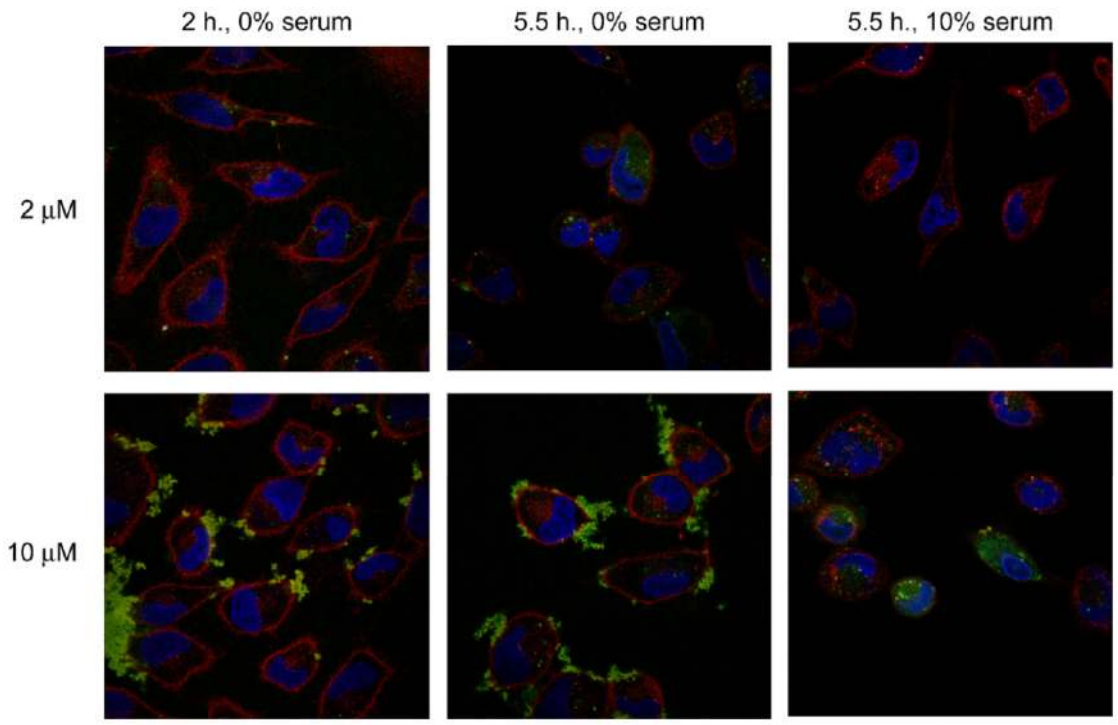

Figure S7 Analysis of HeLa cellular uptake of Flu-DPI-5-5 by live-cell confocal microscopy. Images show channels for green (fluorescein, α/β-peptide), red (WGA488, outer membrane stain), and blue (Hoescht 33342, nuclear stain).

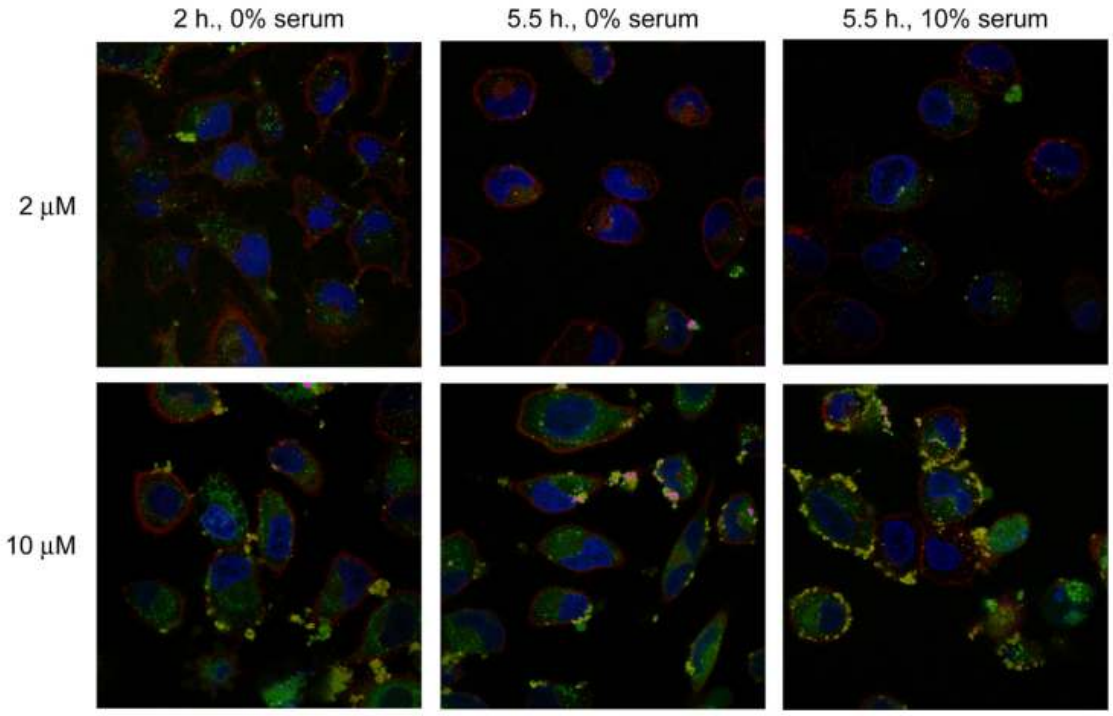

Figure S8 Analysis of HeLa cellular uptake of Flu-DPI-5-5-RRR by live-cell confocal microscopy. Images show channels for green (fluorescein, α/β-peptide), red (WGA488, outer membrane stain), and blue (Hoescht 33342, nuclear stain).

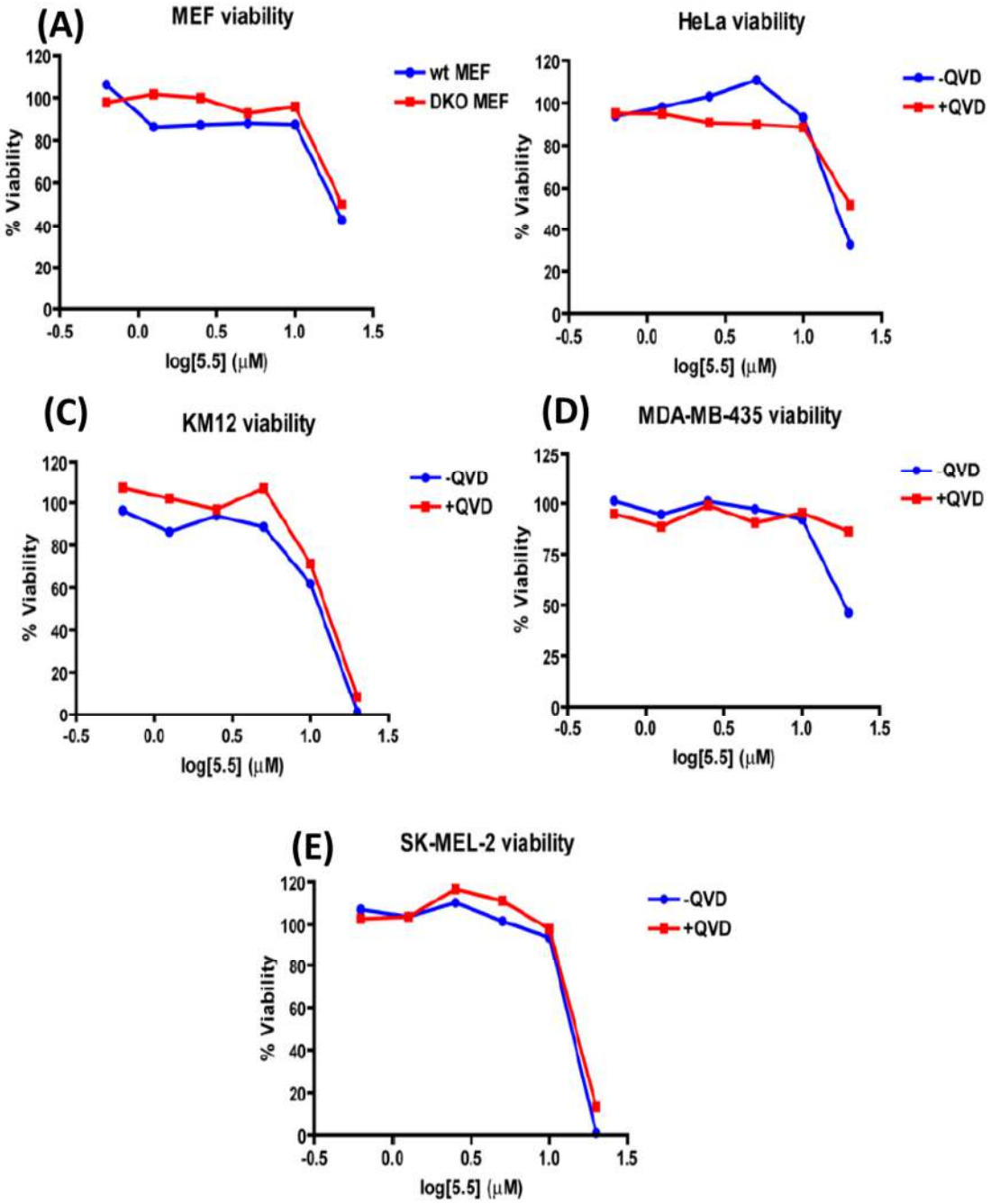

Figure S9: Viability of (A) wild-type (wt, blue) or *bax*$^{-/-}$/*bak*$^{-/-}$ double knock-out (DKO) MEFs cells; (B) HeLa cells; (C) KM12 cells; (D) MDA-MB-435 cells AND (E) SK-MEL-2 cells (relative to DMSO control) when treated with various concentrations of DPI-5-5 (abbreviated 5.5) in the absence (blue) or presence (red) of caspase inhibitor Q-VD-OPh (QVD), as determined by CellTiter-Glo assay. Cells were treated with the indicated α/β-peptide for 24 hours. Each data point represents a single well on a plate.

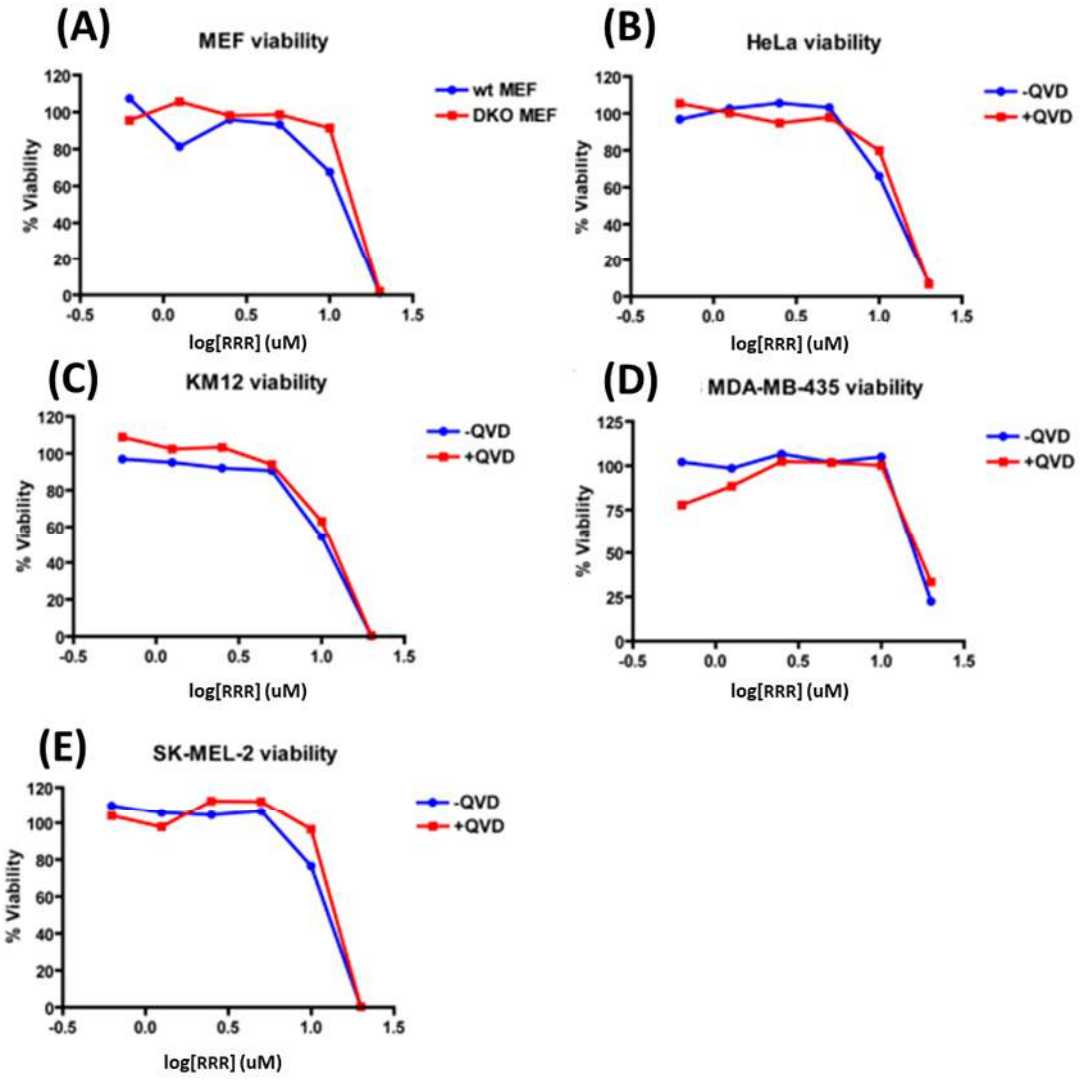

Figure S10: Viability of (A) wild-type (wt, blue) or *bax*$^{-/-}$/*bak*$^{-/-}$ double knock-out (DKO) MEFs cells; (B) HeLa cells; (C) KM12 cells; (D) MDA-MB-435 cells AND (E) SK-MEL-2 cells (relative to DMSO control) when treated with various concentrations of DPI-5-5-RRR (abbreviated RRR) in the absence (blue) or presence (red) of caspase inhibitor Q-VD-OPh (QVD), as determined by CellTiter-Glo assay. Cells were treated with the indicated α/β-peptide for 24 hours. Each data point represents a single well on a plate.