Supporting Information

Modified Bovine Milk Exosomes for Doxorubicin Delivery to Triple-Negative Breast Cancer Cells

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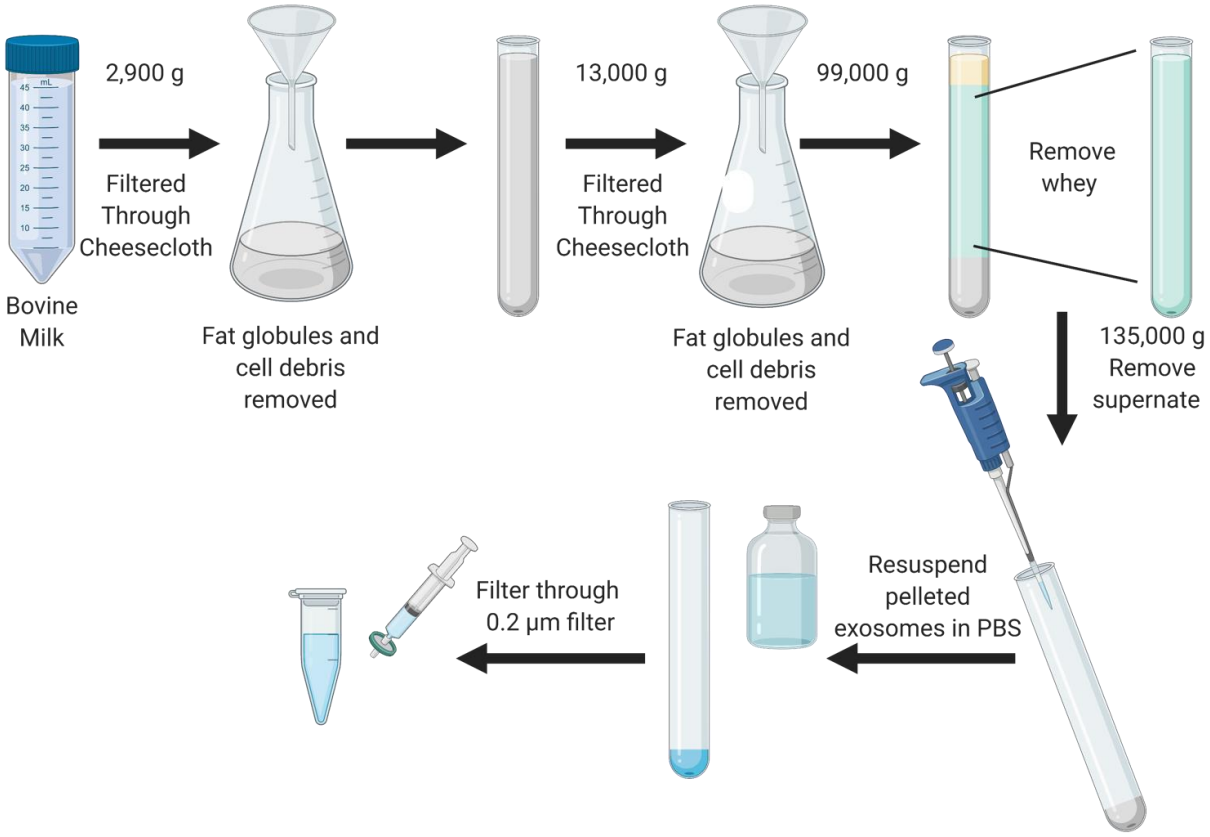

Figure S1. Schematic of isolation of bovine milk exosomes.

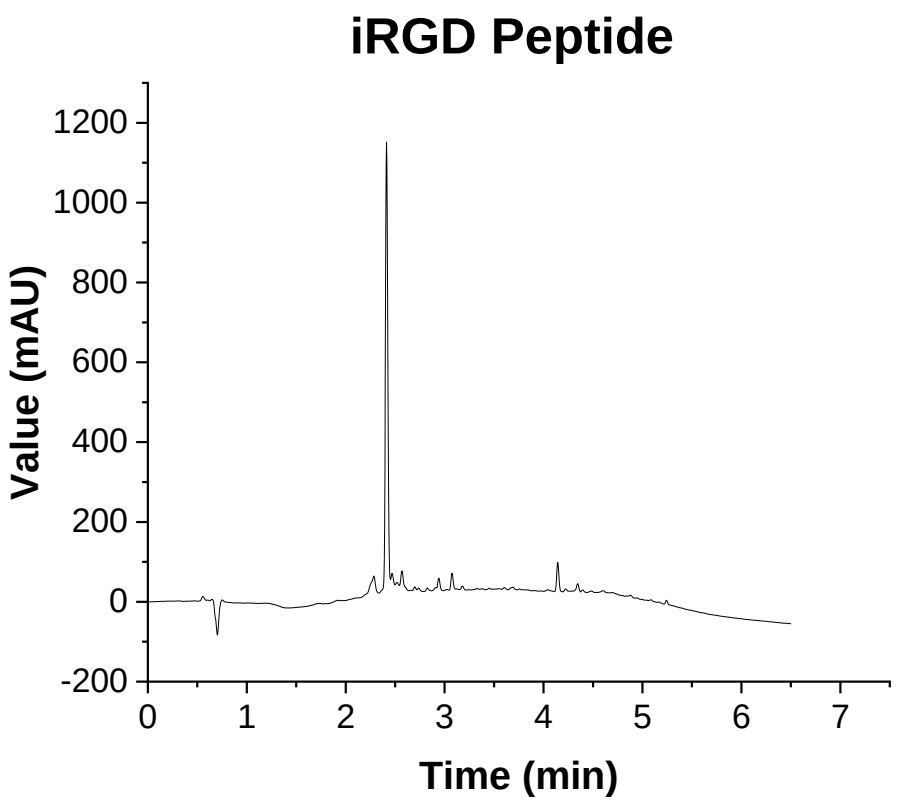

Figure S2. C18 Reverse-phase HPLC chromatogram for the iRGD peptide.

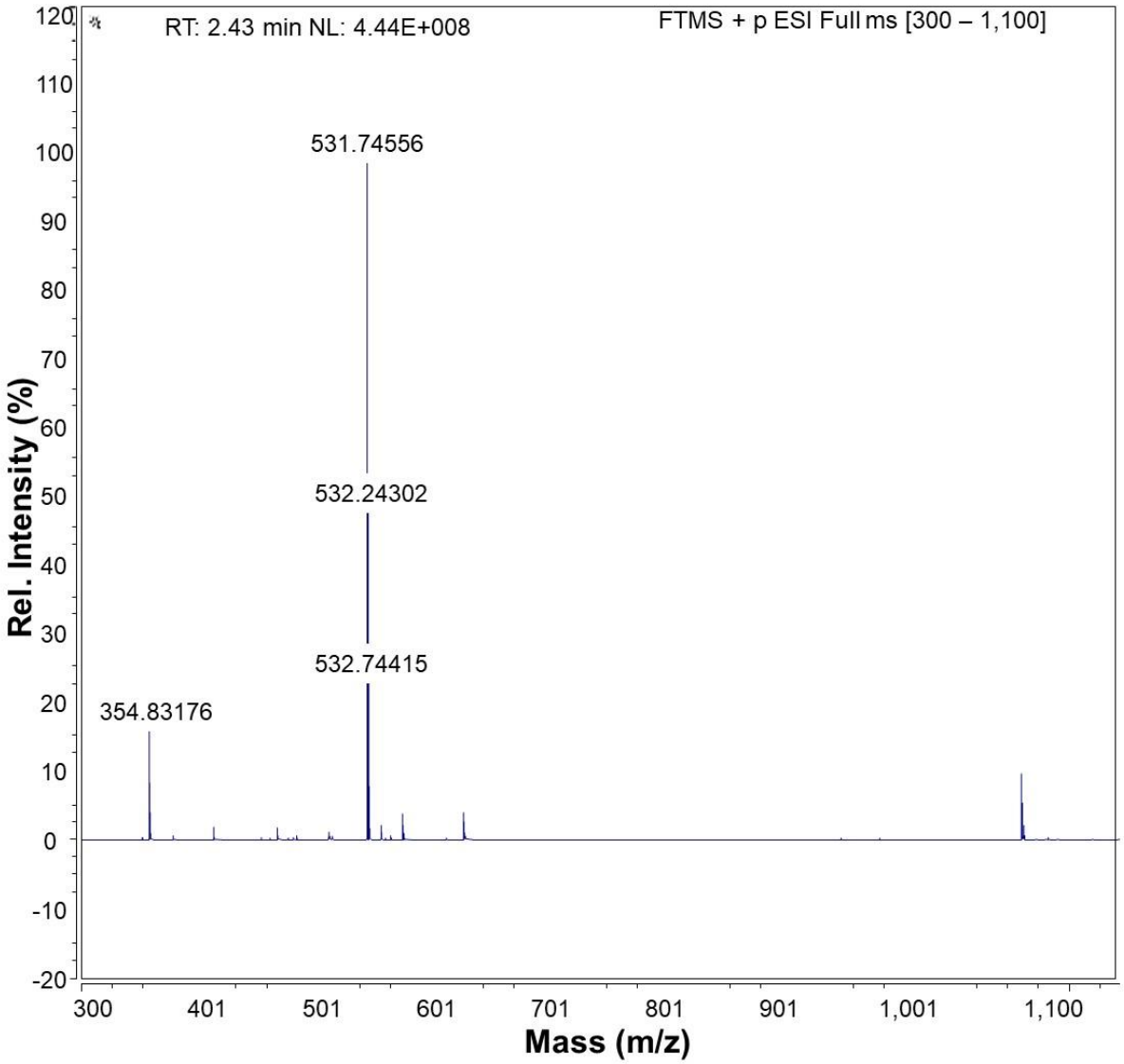

Figure S3. ESI mass Spectrum of iRGD peptide.

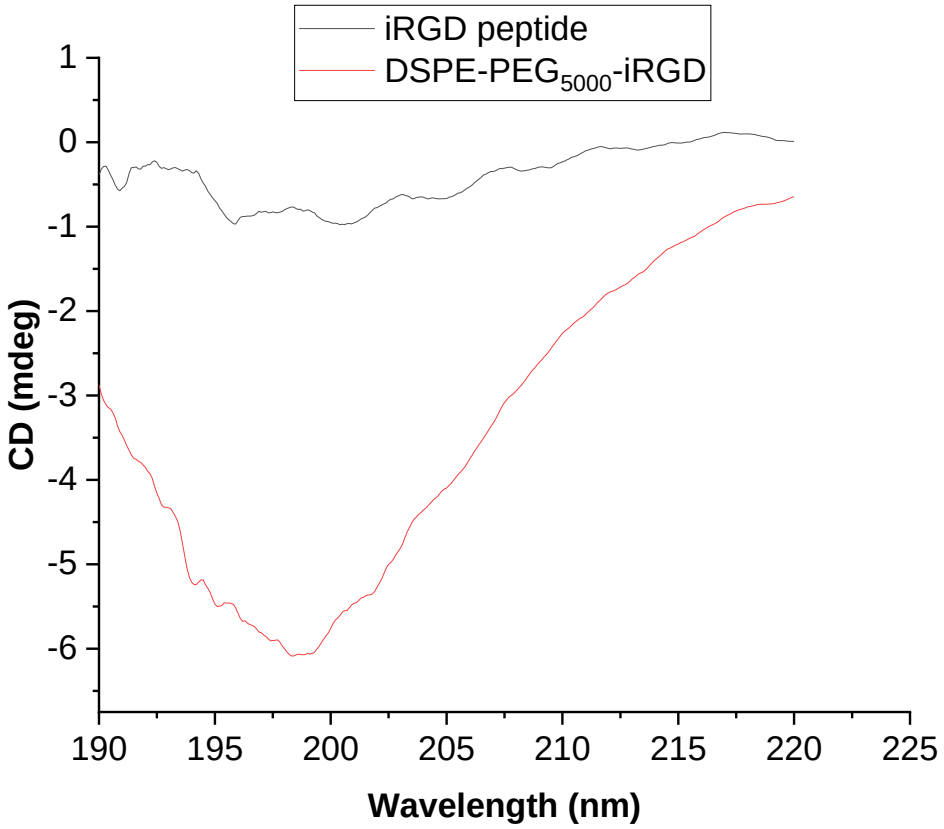

Figure S4. Circular dichroism (CD) spectrum of the synthesized cyclic iRGD peptide and its cognate with DSPE-PEG_{5000} lipid.

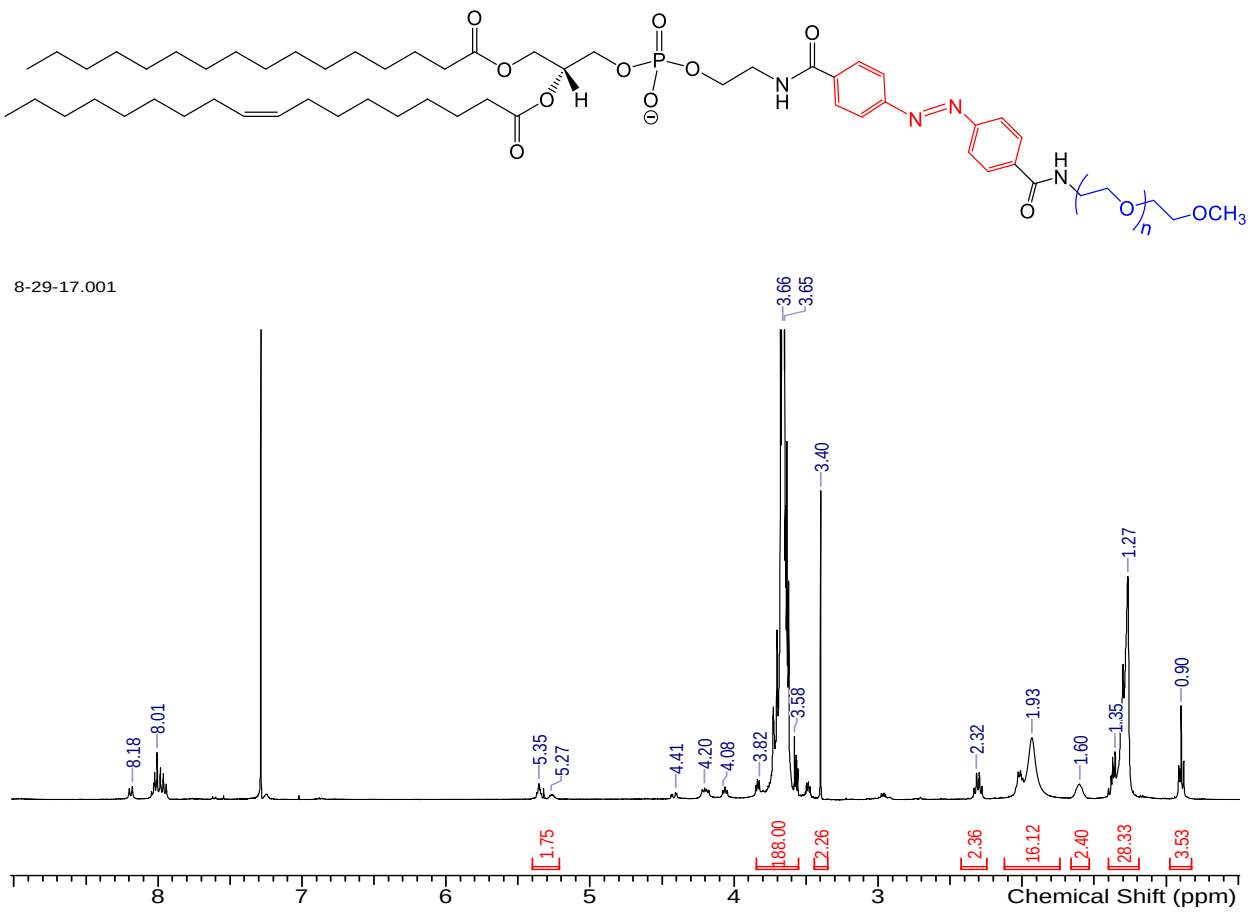

Figure S5. ^{1}H NMR (400 MHz, chloroform-d) spectrum of hypoxia-responsive lipid PEG-Azobenzene-POPE. ppm: 7.55-8.23(CH=CH- CH, m, 8 H), 5.35-5.27(CH2-CH=CH-CH2, m, 2 H), 4-4.5 (-CH-CH2-O, m, 4 H), 3.66 ((CH2-CH2-O), t, 4 H), 3.40 ((CH3-O), s, 3 H), 2.32 ((CH2-C=O), m, 4 H), 2.16 (CH2-CH=CH- CH2, m, 4 H), 1.26 ((- CH2-CH2), m, 44 H), 0.9 ((CH3- CH2), t, 6 H).

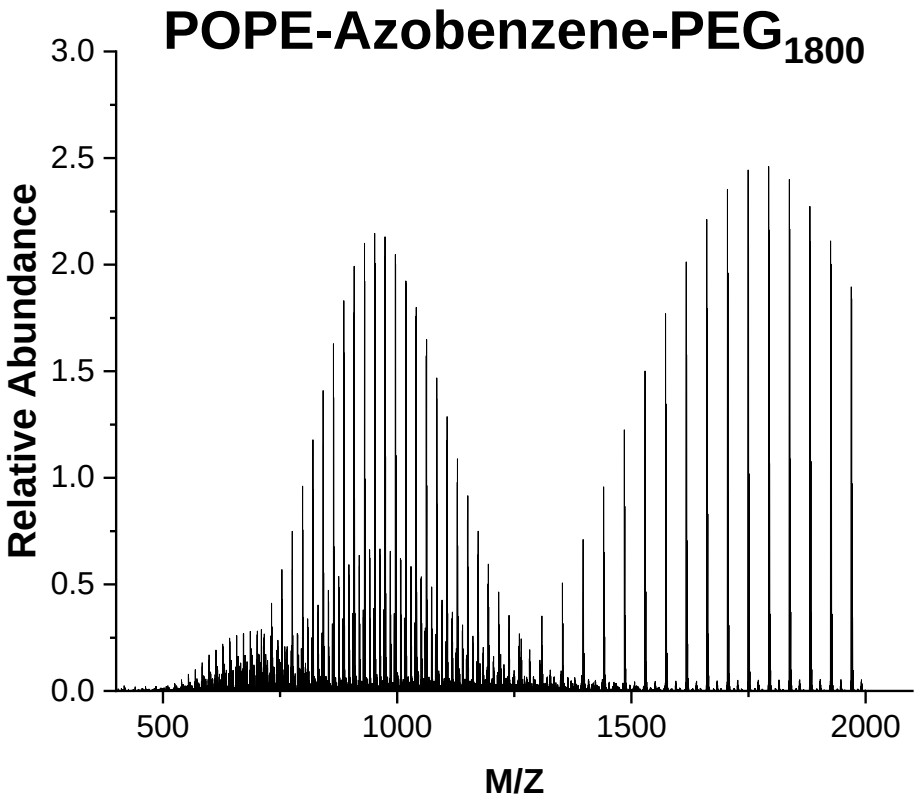

Figure S6. TOF ESI mass spectrum of hypoxia responsive lipid.

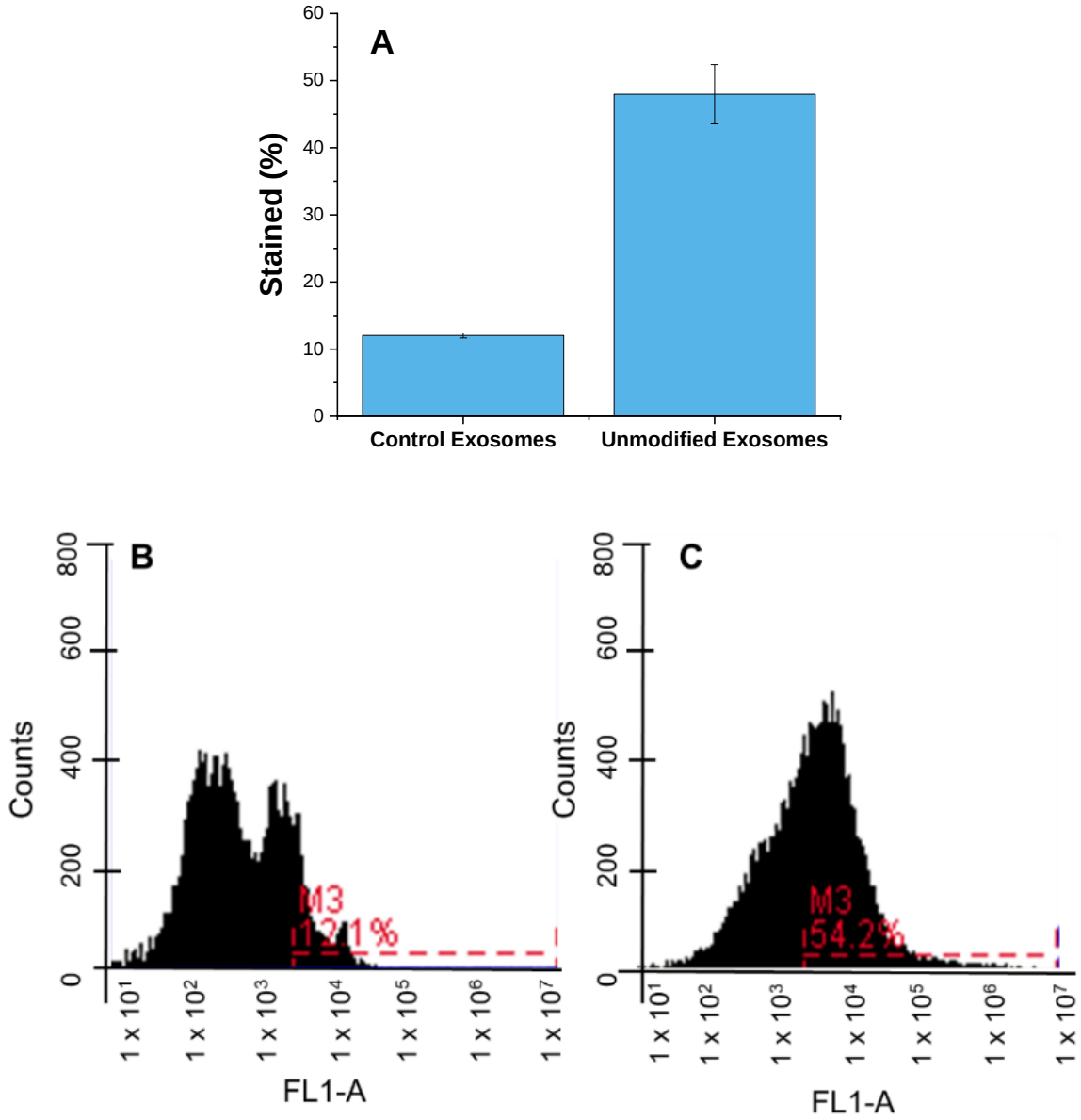

Figure S7. Flow Cytometry for CD63 of bovine milk exosomes. (**A**) Bar graph representing the difference in stained and unstained raw bovine milk exosomes. Control, unstained exosomes represent exosomes not exposed to the antibody; unmodified exosomes are exposed to the antibody but no further chemical modifications, N = 3, p <0.001. Flow Cytometry plot of (**B**) raw unstained exosomes and (**C**) raw stained. 20,000 hits were recorded. N = 3, p <0.001, indicating a significant difference between the two groups.

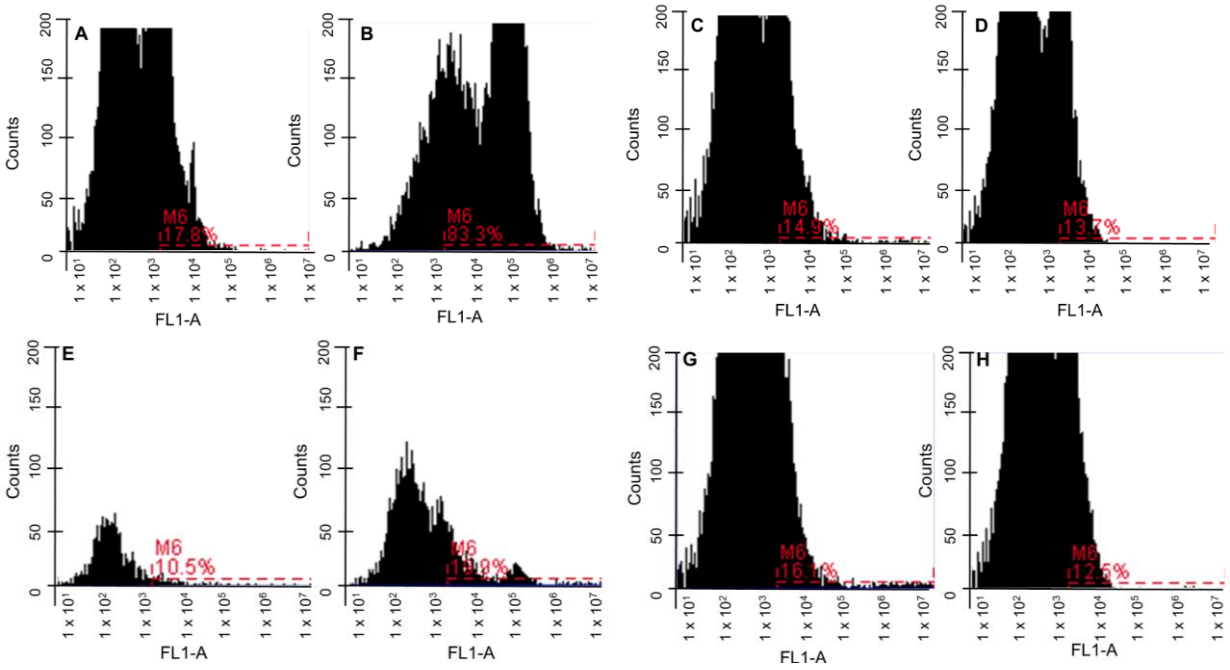

Figure S8. Flow cytometry of NRP-1. (**A**) MDA-MB-231 cells in normoxia; (**B**) MDA-MB-231 cells in hypoxia; (**C**) MDA-MB-468 cells in normoxia; (**D**) MDA-MB-468 cells in hypoxia; (**E**) HCC 1806 cells in normoxia; (**F**) HCC 1806 cells in hypoxia; (**G**) HCC 1937 cells in normoxia; (**H**) HCC 1937 cells in hypoxia.