Supporting Information

Interaction of Mesoporous Silica Nanoparticles with Human Red Blood Cell Membranes: Size and Surface Effects

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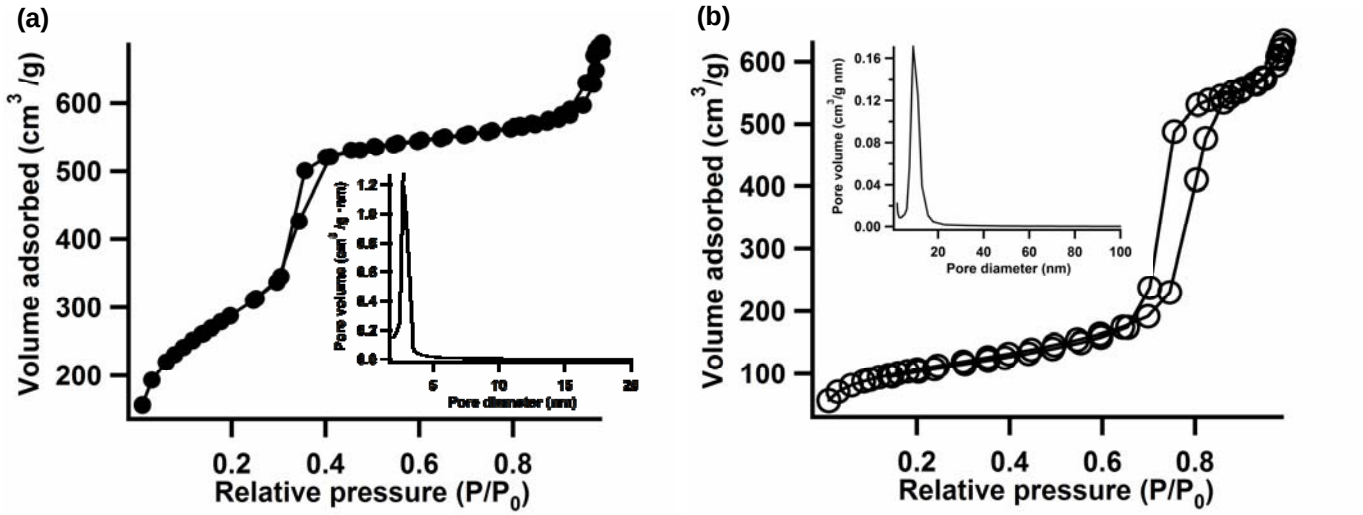


Figure S1. Linear plot of the nitrogen sorption isotherms and pore size distributions of **(a)** *s*-MSN and **(b)** *l*-MSN. Surface areas of *s*-MSN and *l*-MSN were calculated to be 1051.6 ± 2.2 m^2 g^{-1} and 387.0 ± 1.3 m^2 g^{-1}, respectively.

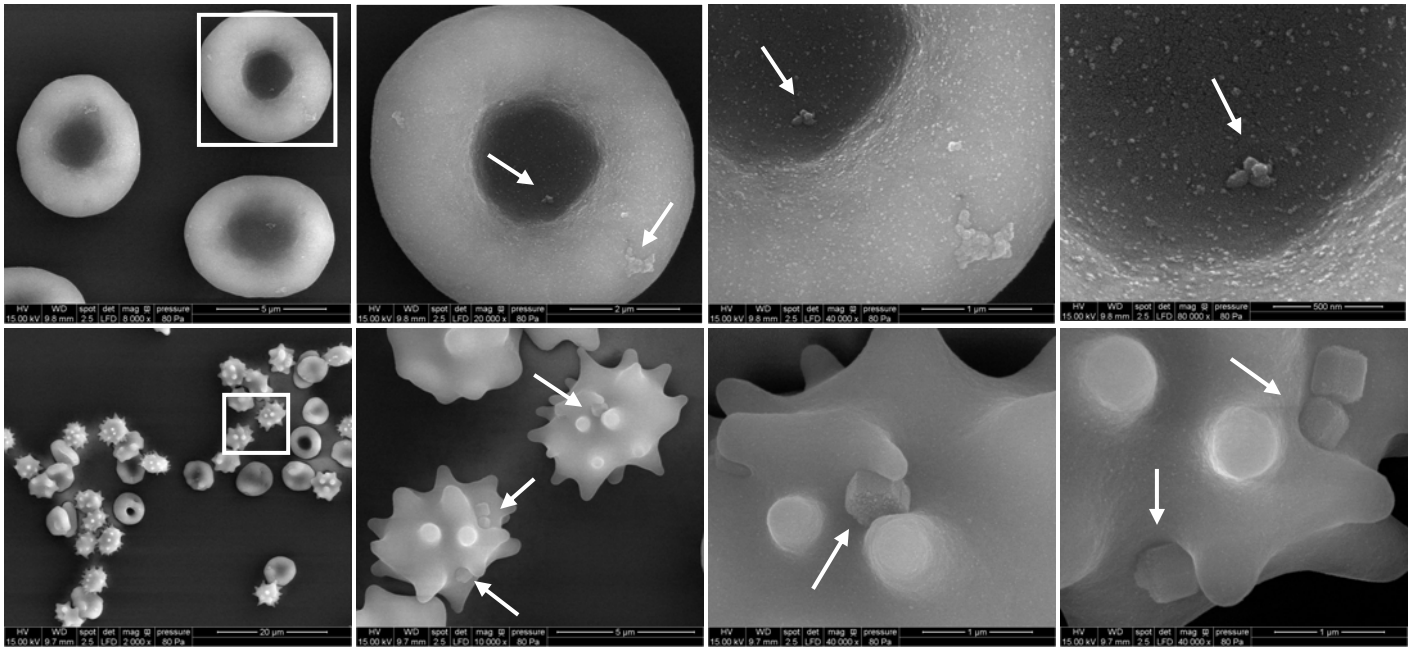


Figure S2. Scanning electron micrographs (SEM) of RBCs (5% hematocrit) incubated with 100 µg mL^{-1} *s*-MSN (top) and *l*-MSN (bottom). Images increase in magnification from left to right with features highlighted with white squares or arrows, indicating the location of particles attached on RBC membrane.

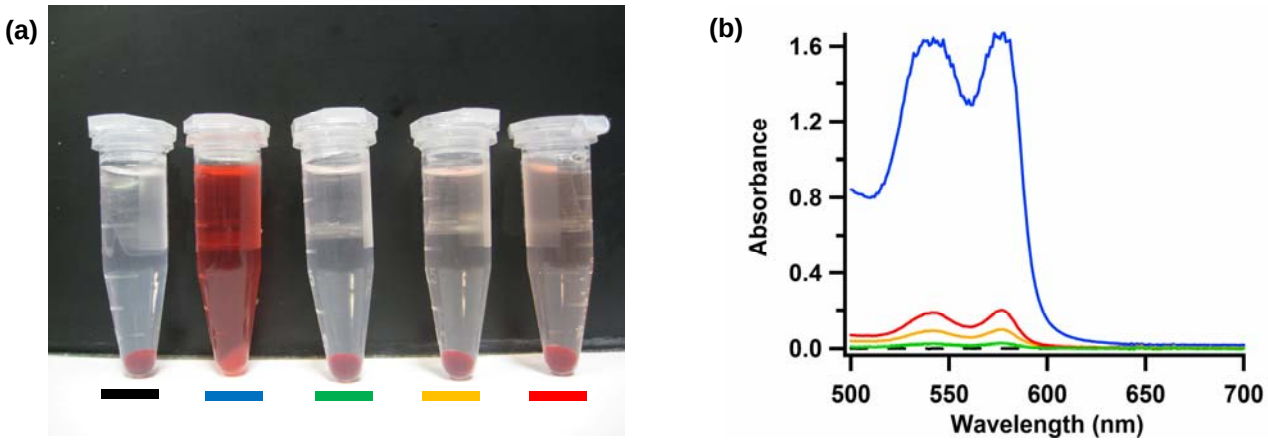


Figure S3. Hemolysis assay for *l*-MSN using water as a positive control (blue lines) and PBS as a negative control (dashed black lines). The materials were suspended at 20 (green), 50 (yellow) and 100 (red) µg mL^{-1}. The mixtures were centrifuged to detect the presence of hemoglobin (red) in the supernatant visually **(a)** and by absorption at 541 nm **(b)**.

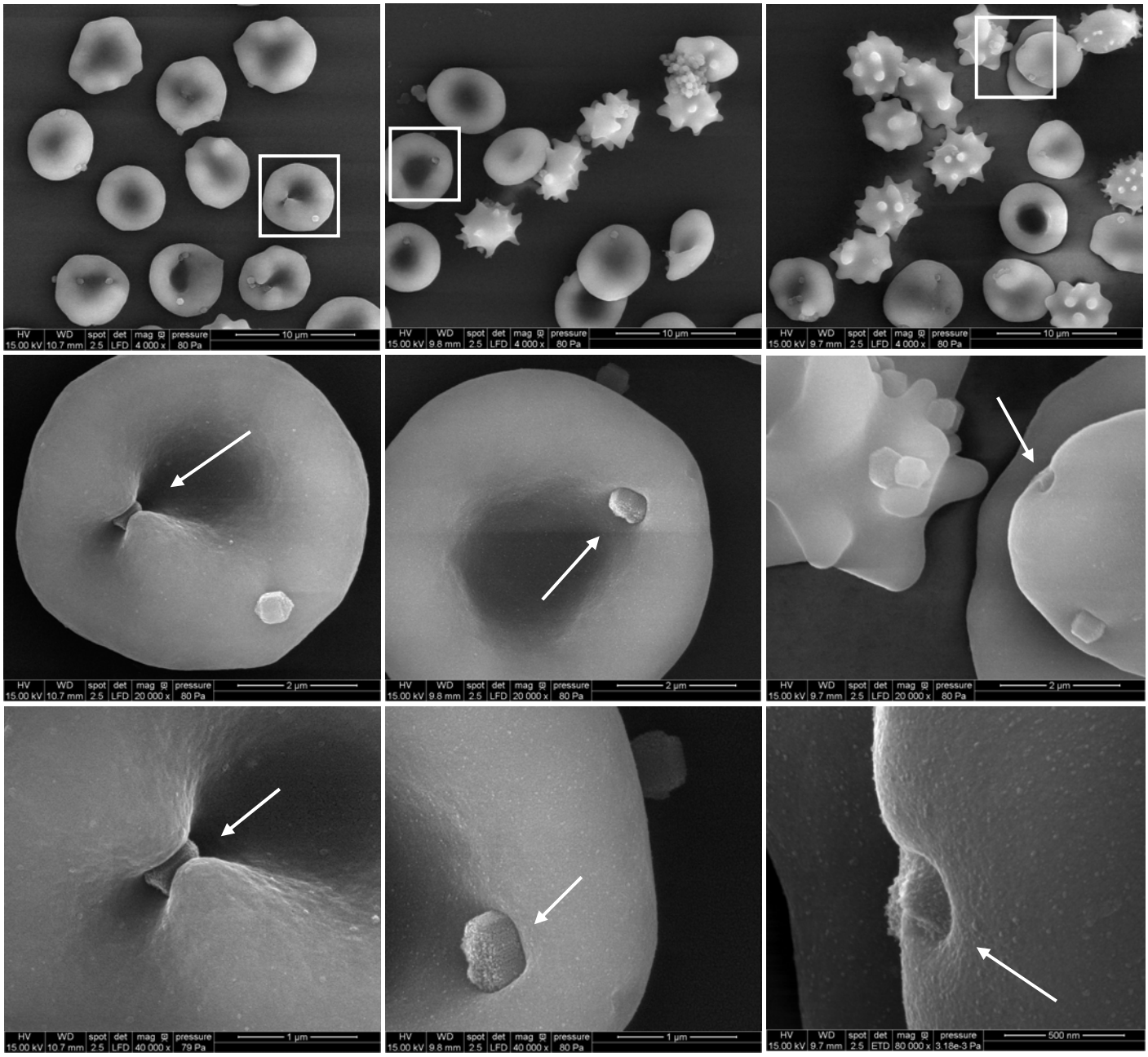


Figure S4. Scanning electron micrographs (SEM) of RBCs (5% hematocrit) incubated with 20 μg mL^{-1} (left), 50 μg mL^{-1}(middle), and 100 μg mL^{-1} of *l*-MSN (right). Percent of spiculated RBCs were observed to be < 10%, ~50% and ~90% from left to right. Images increase in magnification from top to bottom with features highlighted with white squares or arrows, indicating the location of particles attached on RBC membrane.

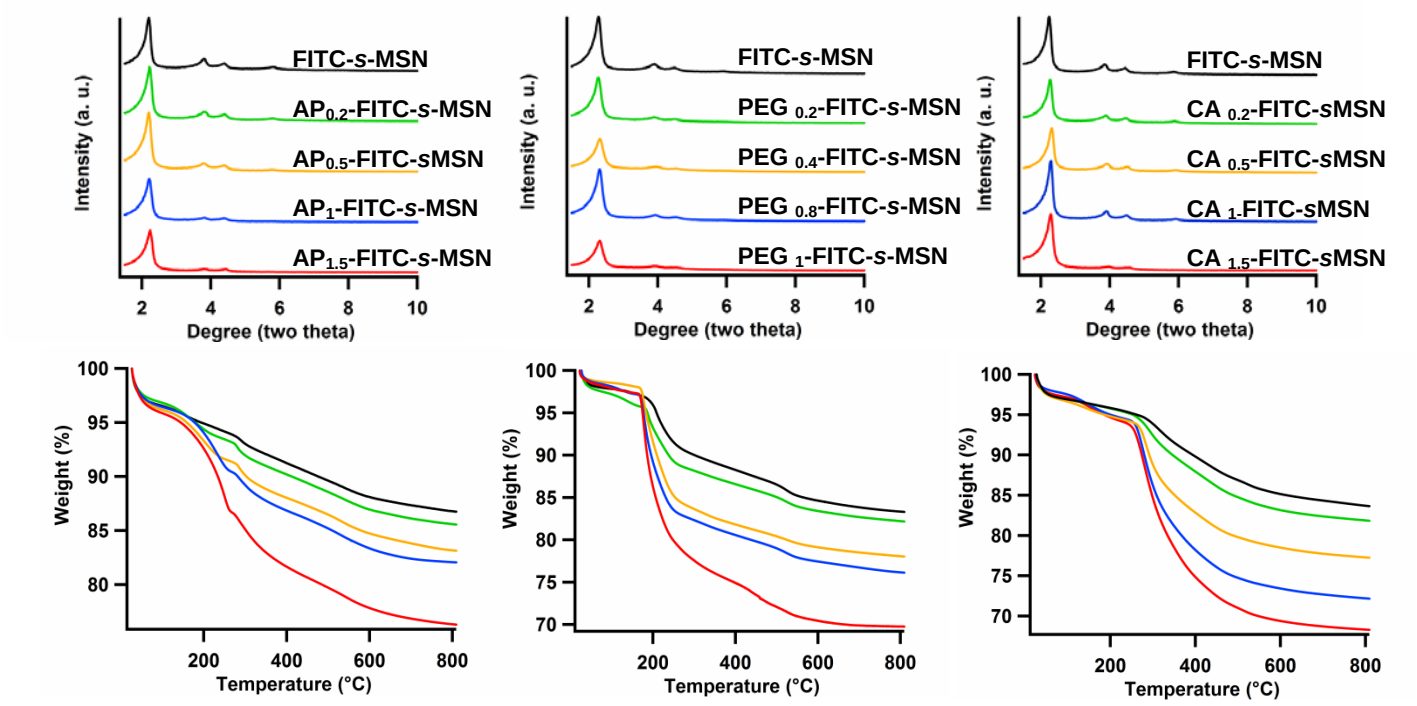


Figure S5. X-ray diffraction patterns (top) and thermogravimetric analysis (bottom) of FITC-*s*-MSN, AP_x-FITC-*s*-MSN (left), PEG_x-FITC-*s*-MSN (middle) and CA_x-FITC-*s*-MSN (right) (*x*: amount of organic groups introduced in mmol g^{-1}).

Table S1. Characteristics of FITC-*s*-MSN, AP_x-FITC-*s*-MSN, PEG_x-FITC-*s*-MSN and CA_x-FITC-*s*-MSN (*x*: amount of organic groups introduced in mmol g^{-1}).

Materials	Surface groups (mmol g^{-1})	Zeta potential (mV)	Surface area (m^2 g^{-1})	Pore size (nm)
FITC-*s*-MSN	0.02	-27.9	1043.4 ± 4.2	3.0
$AP_{0.2}$-FITC--sMSN	0.1-0.2	-22.9	948.3 ± 7.9	2.8
$AP_{0.5}$-FITC-*s*-MSN	0.4-0.6	-10.9	878.7 ± 11.7	2.8
AP_1-FITC-*s*-MSN	0.6-0.8	+3.2	796.8 ± 1.6	2.8
$AP_{1.5}$-FITC-*s*-MSN	1.2-1.6	+6.87	689.0 ± 29.0	2.7
FITC-*s*-MSN	0.03	-29.3	1036.4 ± 11.2	2.6
$PEG_{0.2}$-FITC-*s*-MSN	0.03-0.04	-26.1	985.6 ± 9.0	2.6
$PEG_{0.4}$-FITC-*s*-MSN	0.1-0.2	-22.3	839.6 ± 9.3	2.4
$PEG_{0.8}$-FITC-*s*-MSN	0.2-0.3	-20.7	770.8 ± 1.6	2.4
PEG_1-FITC-*s*-MSN	0.4-0.5	-13.1	628.9 ± 2.6	2.4
FITC-*s*-MSN	0.03	-28.6	1107.8 ± 8.6	2.7
$CA_{0.2}$-FITC-*s*-MSN	0.07-0.1	-34.3	967.4 ± 2.9	2.5
$CA_{0.5}$-FITC-*s*-MSN	0.3-0.4	-36.1	913.6 ± 19.2	2.4
CA_1-FITC-*s*-MSN	0.5-0.7	-39.2	863.0 ± 9.2	2.4
$CA_{1.5}$-FITC-*s*-MSN	0.7-1	-42.7	779.2 ± 5.0	2.5

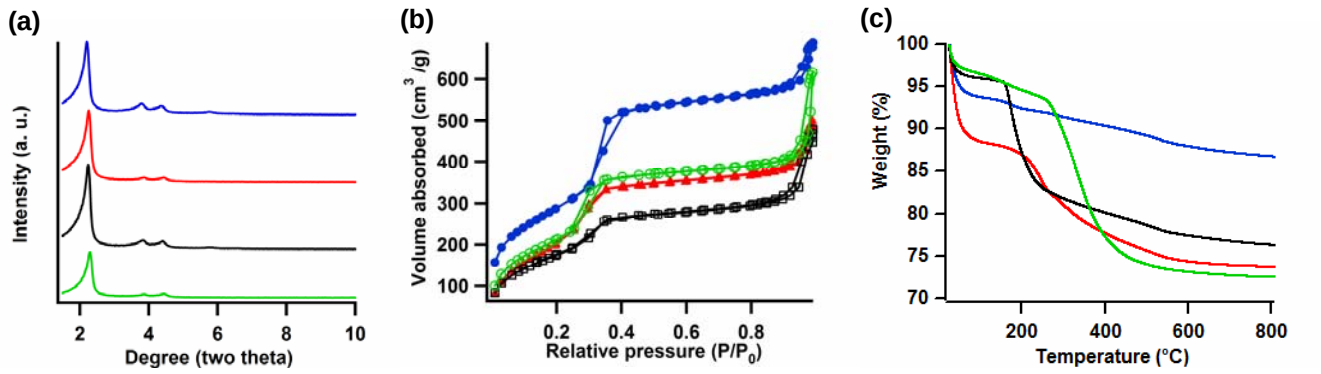
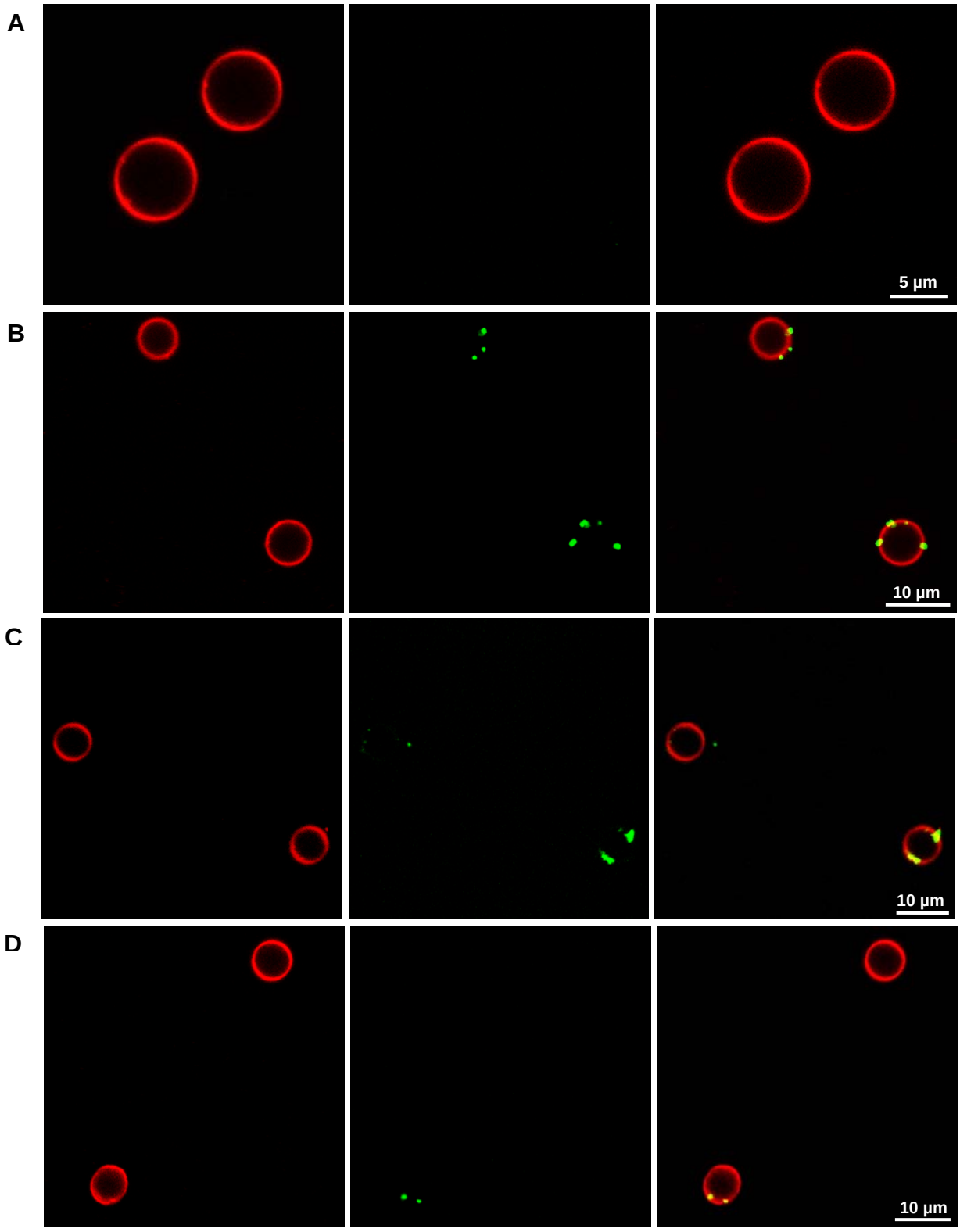


Figure S6. (a) X-ray diffraction (XRD) patterns, **(b)** linear plot of the nitrogen sorption isotherms and **(c)** thermogravimetric analysis (TGA) of *s*-MSN (blue), $AP_{1.5}$-*s*-MSN (red), PEG_1-*s*-MSN (black) and $CA_{1.5}$-*s*-MSN (green).

Table S2. Characteristics of *s*-MSN, $AP_{1.5}$-*s*-MSN, PEG_1-*s*-MSN, $CA_{1.5}$-*s*-MSN and *l*-MSN.

Materials	**Surface groups (mmol g^{-1})**	**Zeta potential (mV)**	**Surface area (m^2 g^{-1})**	**Pore size (nm)**	**Hydrodynamic particle size (nm)**
s-MSN		-22.2	1051.6 ± 2.2	3.1	122
$AP_{1.5}$-*s*-MSN	1.1-1.5	+5.79	780.3 ± 9.0	2.4	142
PEG_1-*s*-MSN	0.3-0.4	-11.6	650.5 ± 2.9	2.7	122
$CA_{1.5}$-*s*-MSN	0.6-0.9	-43.1	792.9 ± 4.4	2.9	142
l-MSN		-16.5	387.0 ± 1.3	9.0	531


A
5 µm
B
10 µm
C
10 µm
D
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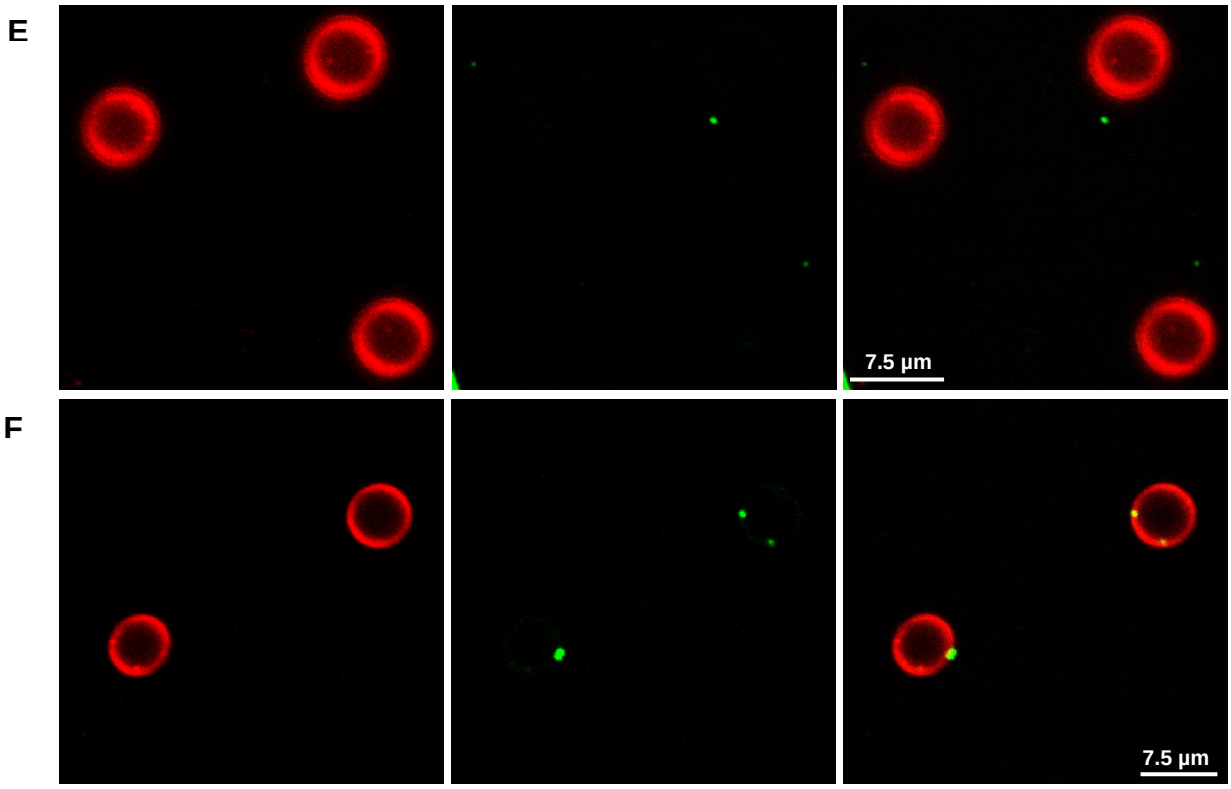

Figure S7. Confocal fluorescence micrographs of (**A**) RBCs (5×10^6 cells mL^{-1}) incubated with 20 µg mL^{-1} of (**B**) FITC-*l*-MSN, (**C**) FITC-*s*-MSN, (**D**) $AP_{1.5}$-FITC-*s*-MSN, (**E**) PEG_1-FITC-*s*-MSN and (**F**) $CA_{1.5}$-FITC-*s*-MSN. The channels from left to right correspond to red blood cells stained with PKH26 red fluorescence dye, FITC-MSNs and the merged images.

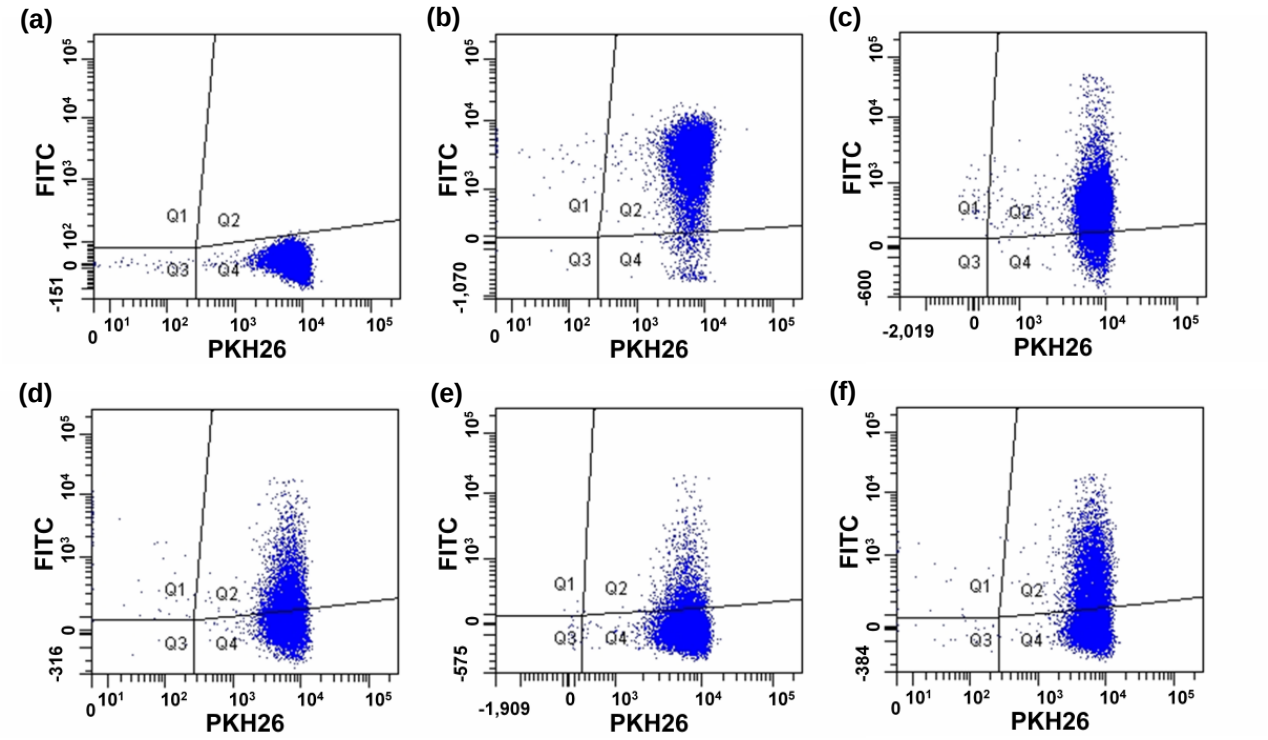

Figure S8. Dot plot from the flow cytometry analysis of **(a)** PKH26 labeled RBC incubated with **(b)** FITC-*l*-MSN, **(c)** FITC-*s*-MSN, **(d)** $AP_{1.5}$-FITC-*s*-MSN, **(e)** PEG_1-FITC-*s*MSN and **(f)** $CA_{1.5}$-FITC-*s*-MSN. The axes correspond to the intensity of red fluorescence due to PKH26 labeling (horizontal axis) and green fluorescence due to the attachment of FITC-MSNs onto PKH26-RBCs (vertical axis). The plot was gated to show PKH26 labeled RBCs in area Q4 and FITC-fluorescent PKH26-RBCs in area Q2.