Supporting Information

Utilizing the protein corona around silica nanoparticles for dual drug loading and release

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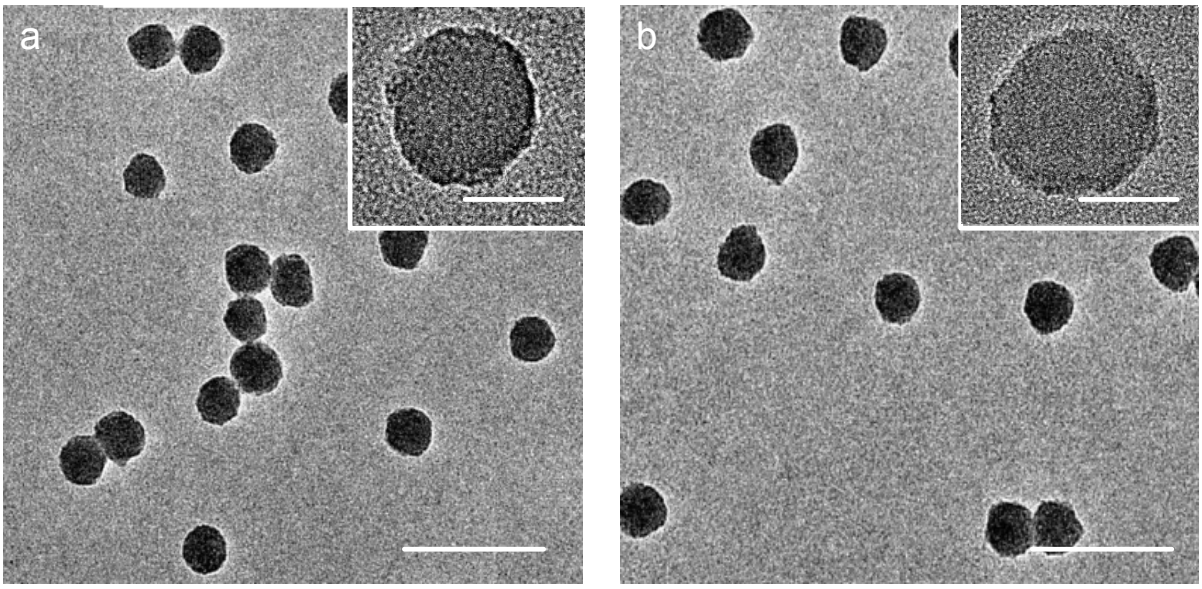

Figure S1. TEM micrographs of SNP (a) and FSNP (b), the insets are images showing the single particles. Scale bars are 100 and 20 nm in images and insets, respectively.

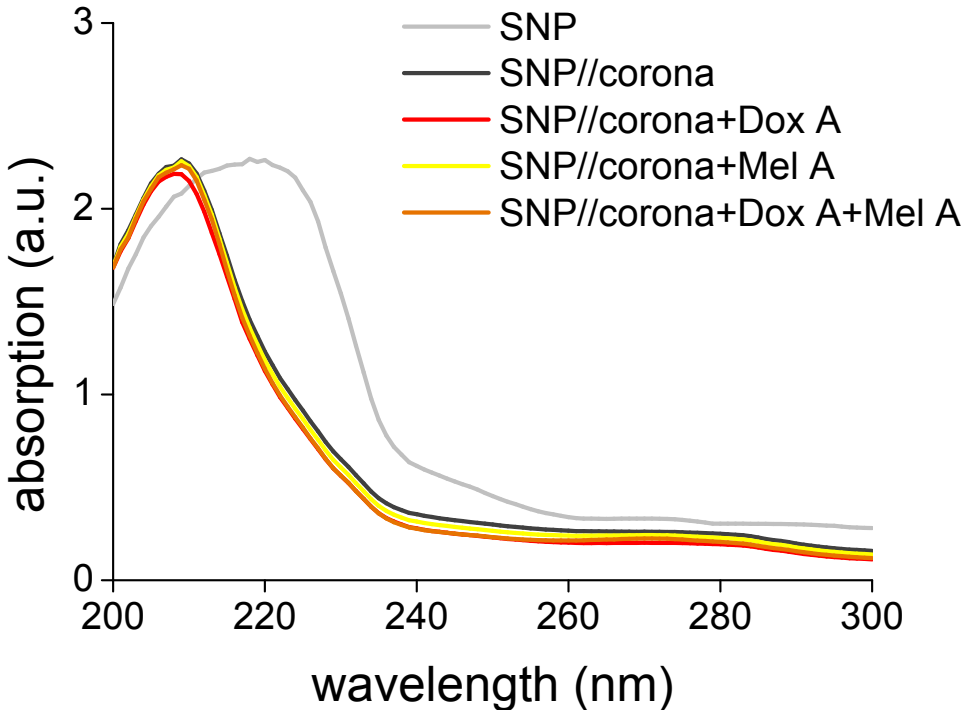

Figure S2. UV-Vis spectra of SNP (light gray), SNP//corona (dark gray), SNP//corona+Dox A (red), SNP//corona+Mel A (yellow) and SNP//corona+Dox A+Mel A (orange) measured in DMEM.

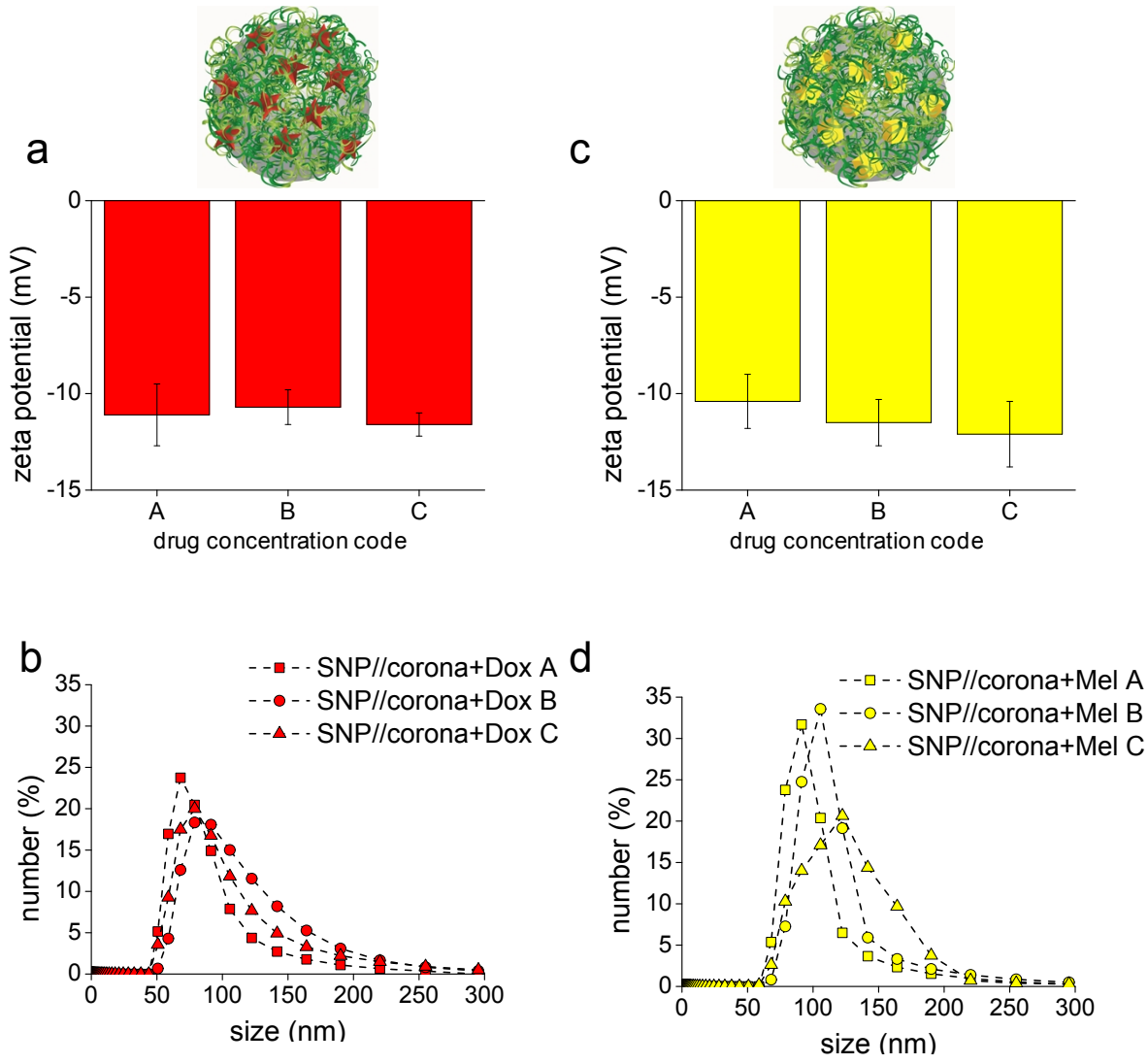

Figure S3. Zeta potential values and size distribution obtained by DLS for SNP and FSNP without or with corona (a, b) and for drug loaded SNP//corona with concentration code A (c, d). Zeta potential data were obtained from triplicate measurements. As defined in Table 1, for SNP//corona+Dox A 0.0431 µmol Dox, for SNP//corona+Dox B 0.862 µmol Dox, for SNP//corona+Dox C 0.1293 µmol Dox, for SNP//corona+Mel A 1.6669 µmol Mel, for SNP//corona+Mel B 3.3338 µmol Mel and for SNP//corona+Mel C 5.007 µmol Mel were applied for loading the particle corona with drugs.

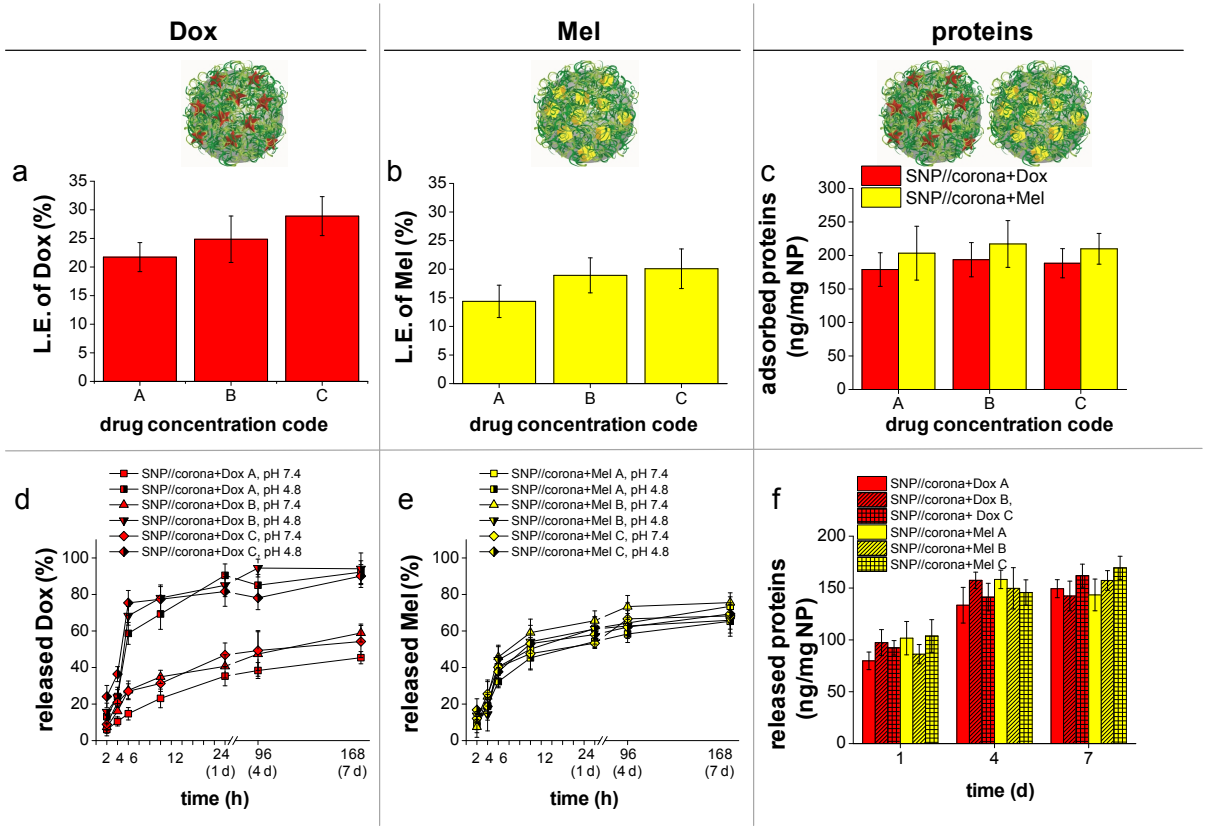

Figure S4. Loading and release of drugs and proteins in and from the corona around SNPs. Loading efficiency (L.E.) of Dox (a) and Mel (b) and adsorbed amount of proteins (c) in the corona around SNPs were determined after 4 h incubation with FCS at 37 °C. Panels d-f show the release of Dox (d), Mel (e) and protein (f) during incubation for up to 7 d. The data of drugs release for each time point investigated (d, e) are given as percentage of the initially amount loaded for each concentration (a, b). The data were obtained from triplicate measurements.

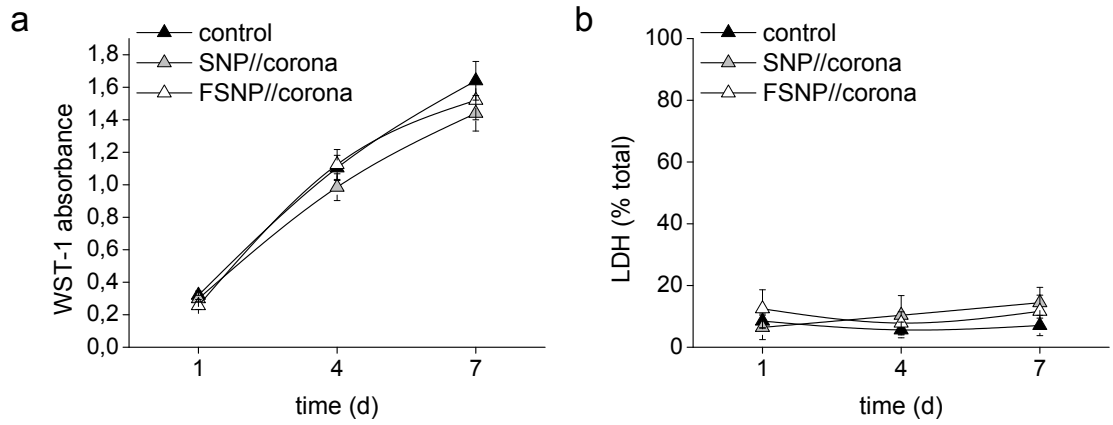

Figure S5. Proliferation (a) and LDH release (b) of MG-63 control cells (without drugs or particles) after exposure to SNP//corona and FSNP//corona for 1, 4 or 7 d, measured with WST-1 assay and LDH assay, respectively. LDH leakage was calculated by dividing the amount of activity in medium (extracellular) by the total activity (medium plus cell lysate) and indicated in percentage. All data are expressed as mean ± SD of values obtained in three independent experiments. No significant difference was observed between the values obtained for SNP//corona or FSNP//corona and control.

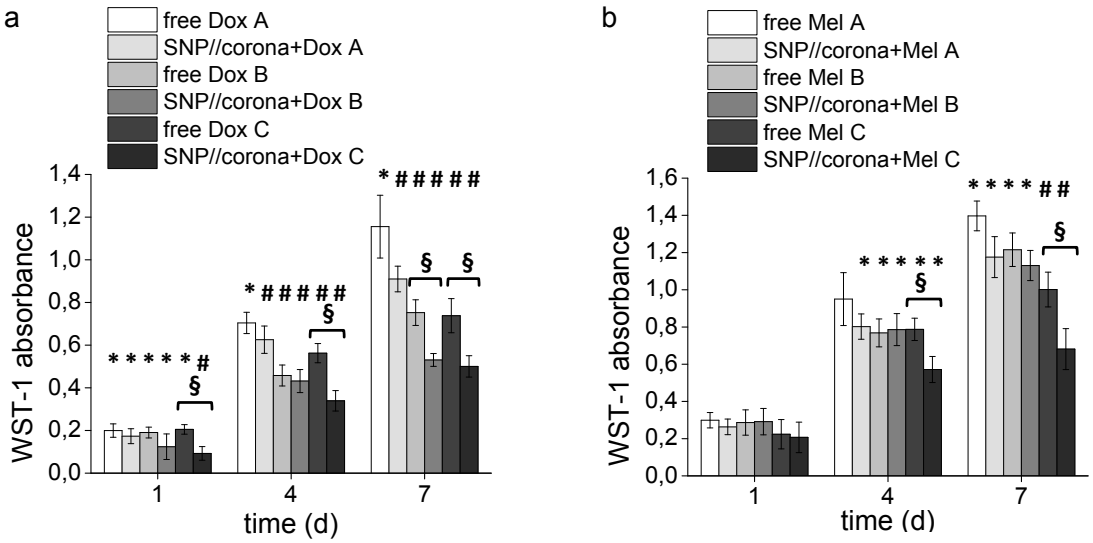

Figure S6. Proliferation of MG-63 measured by the WST-1 assay after exposure to free Dox or SNP//corona+Dox (a) and free Mel or SNP//corona+Mel (b), each at three different concentration codes, for 1, 4 or 7 d. All data are expressed as mean ± SD of values obtained in three independent experiments. Significant differences in comparison to the respective controls are indicated by *p<0.05 and # p<0.01. Differences between data (for incubations with free drugs and NP//corona+drugs) that share a symbol (§) are significant (p<0.05).

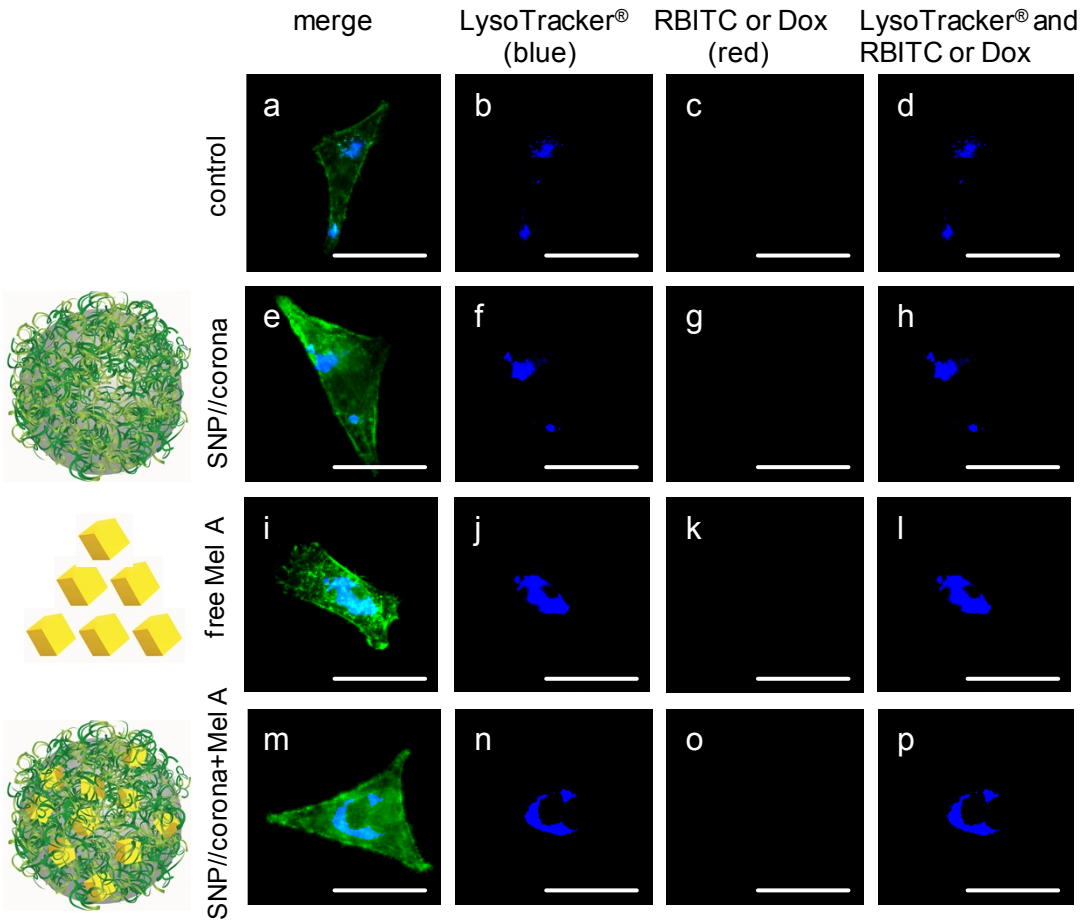

Figure S7. Fluorescence microscopy images of MG-63 cells at day 4, including control (a-d) and exposed to SNP//corona (e-h), free Mel A (i-l) and NP//corona+Mel A (m-p). In the first column on the left the merged micrographs of green (actin cytoskeletons), blue (lysotracker®) and red are represented. The second and third columns show the images in single blue and red channel, respectively. The fourth column indicates the overlay of blue fluorescence of lysotracker® and red. As Mel does not have any fluorescence properties, it is not possible to visualize free Mel or SNP//corona+Mel using fluorescence microscopy. Scale bars: 50 µm.

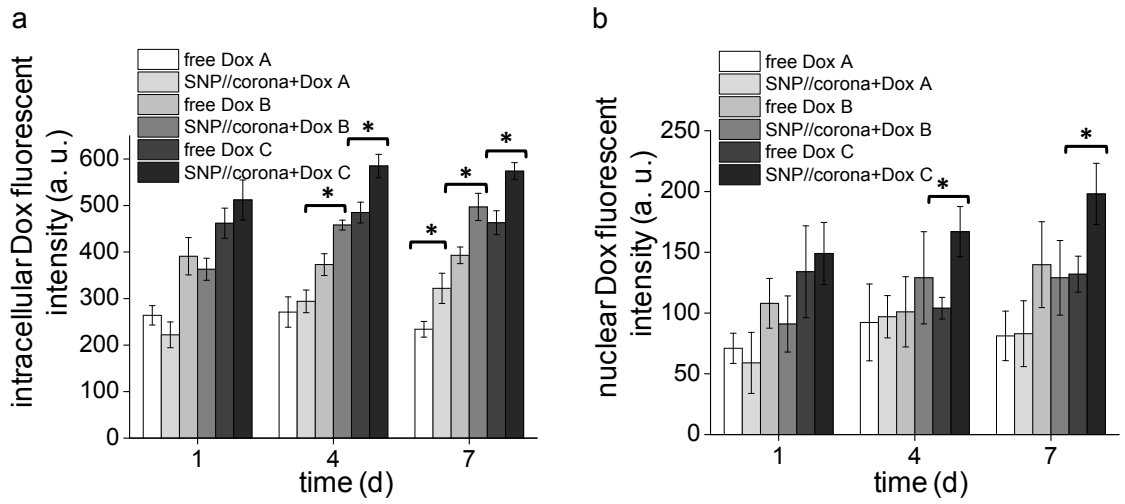

Figure S8. Quantitative comparison of total cellular Dox fluorescence (a) and nuclear Dox fluorescence (b) signal intensity in MG-63 cells that had been incubated for 1, 4 or 7 d with free Dox or SNP//corona+Dox, each at three different concentration codes. The data on intracellular Dox fluorescence represent means ± SD of values obtained in three independent experiments. To quantify nuclear Dox internalization for each sampling point, red fluorescence signal of 20 nuclei were analysed by the Carl Zeiss Zen software. In panels (a, b) asterisks (*) indicate significant difference (p<0.05) between the values obtained for SNP//corona+Dox compared to the free Dox applied at the respective concentrations.