SUPPLEMENTARY MATERIAL

Theranostic Mesoporous Silica Nanoparticles Biodegrade after Pro-Survival Drug Delivery and Ultrasound/Magnetic Resonance Imaging of Stem Cells

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Supplementary Video SV1. Confocal Microscopy of MSN-labeled MSCs. Cells were labeled with fluorescently tagged MSNs for 4 hours at 250 µg/mL. After washing, we collected a z-stack of images and combined these into an .avi file. Here the total width of frame is 1 mm and the total distance scanned in the z direction is 50 µm.

Supplementary Video SV2. Implantation of MSN-labeled MSCs into the Left Ventricle Wall of Nude Mice. This is a short axis view of the murine heart during implantation of MSN-labeled MSCs. The area of injection is highlighted and real-time imaging is possible.

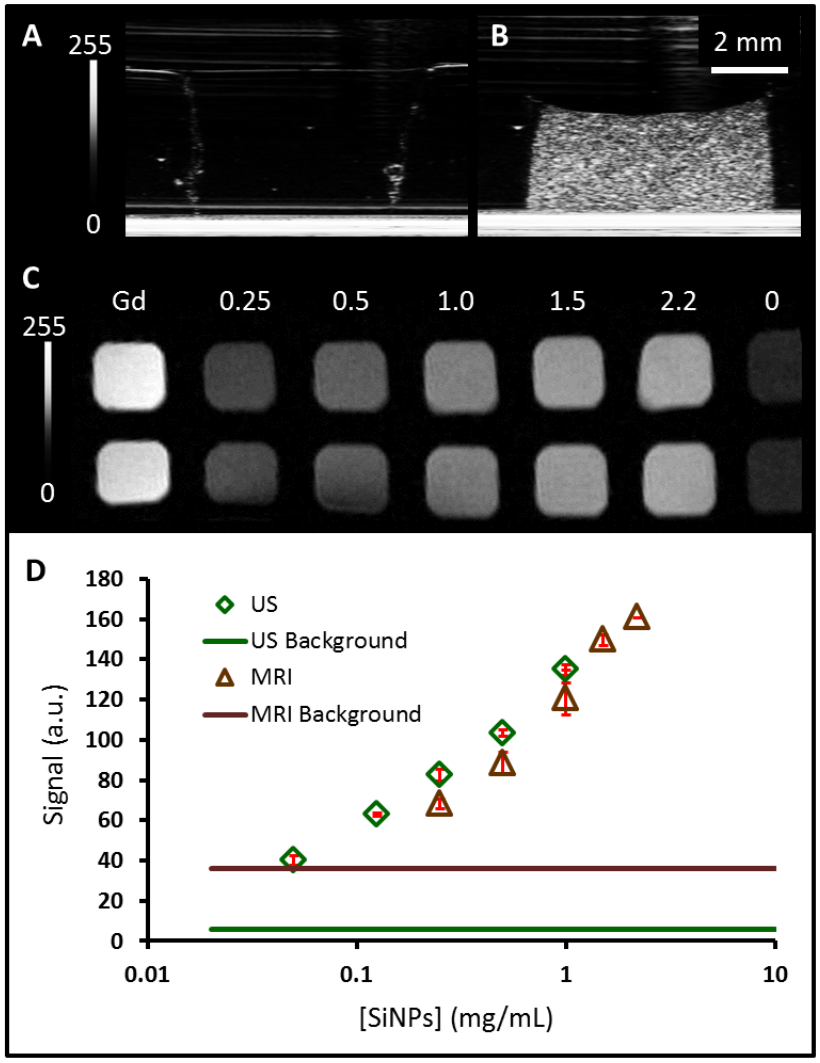

Figure S1. Ultrasound and MRI Signal of the MSNs. Ultrasound image of agarose gel without (**A**) and with (**B**) MSNs. **C**) T1-weighted MRI of MSNs including water and 5 ppm Gd^{3+} controls. Values in C are mg/mL of MSNs and correspond to the values on the abscissa of D. **D**) Dose response curve for the two modalities indicate that the limited of detection 3 standard deviations above background is 1.2 µg/mL via ultrasound and 15.6 µg/mL via MRI.

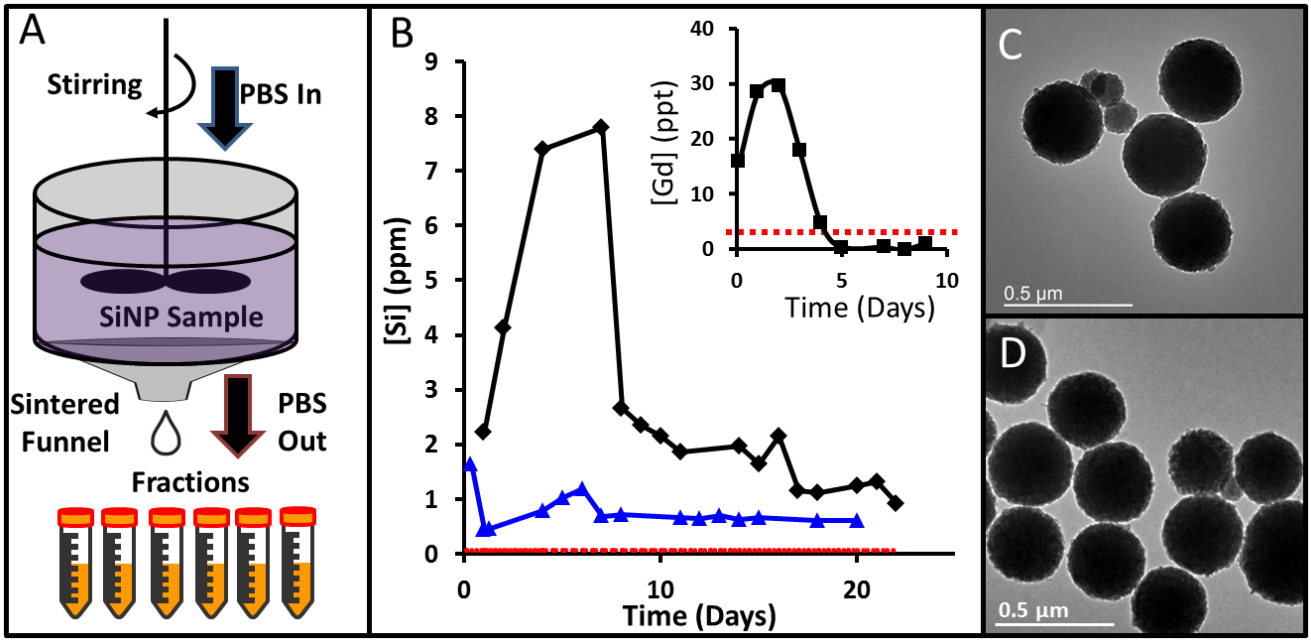

Figure S2. Biodegradation of the MSNs. A) Biodegradation was monitored by adding PBS constantly over a well-stirred solution of MSNs. **B)** Fractions were collected periodically and analyzed for gadolinium and silicon by ICP, which peaked at 48 hours (Gd; inset) and 7 days into the study (Si). The red dashed lines panel B indicate the background levels of Si and Gd present in the dissolution buffer. The blue curve is B is for Stöber nanoparticles. Panels C and D show Stöber nanoparticles before (**C**) and after (**D**) 24 days of dissolution. No change in morphology is seen in comparison to **Figure 2**.

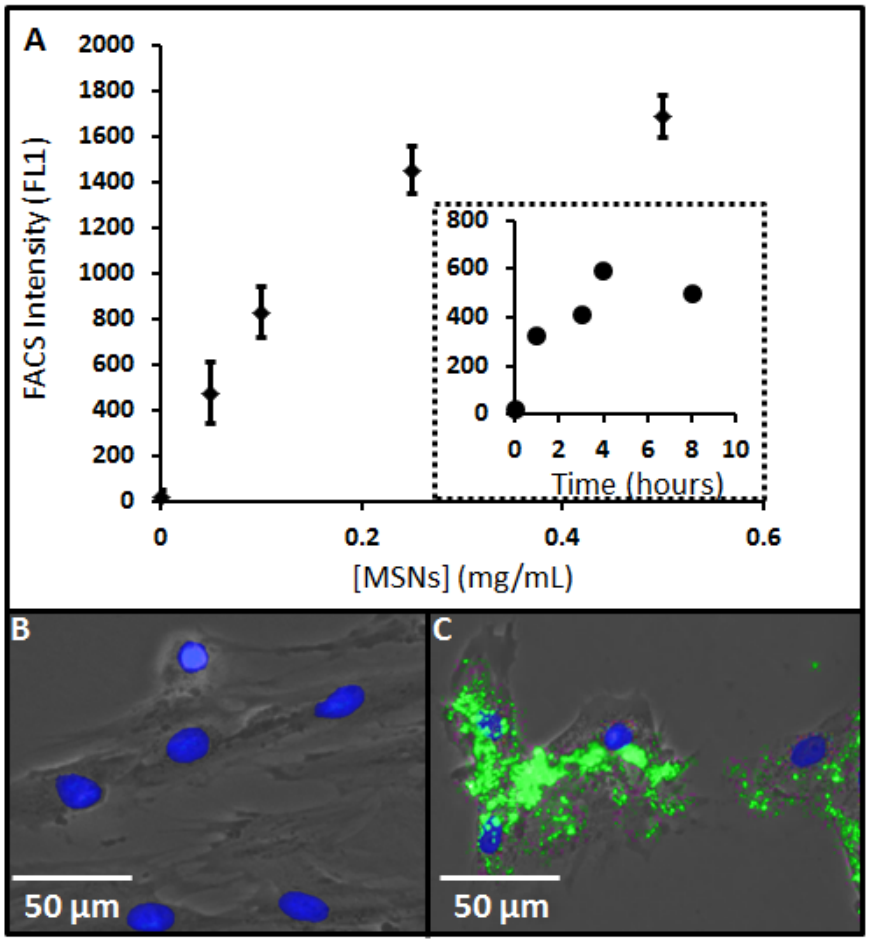

Figure S3. MSN-labeled MSCs. **A)** Increasing concentrations of MSNs to 0.5 mg/mL were added to adherent MSCs, incubated for four hours, stained with Eth-DIII and analyzed with flow cytometry. Increasing signal in the cell gate is plotted on the left axis and shows little additional increase above 0.25 mg/mL. Inset in panel A shows a similar experiment holding concentration constant at 0.1 mg/mL and the time variable from 1 to 8 hours. Maximum signal is seen at 4 hours. Bottom panels are MSCs without **(B)** and with **(C)** MSN labeling and show nucleus in blue and MSNs in green.

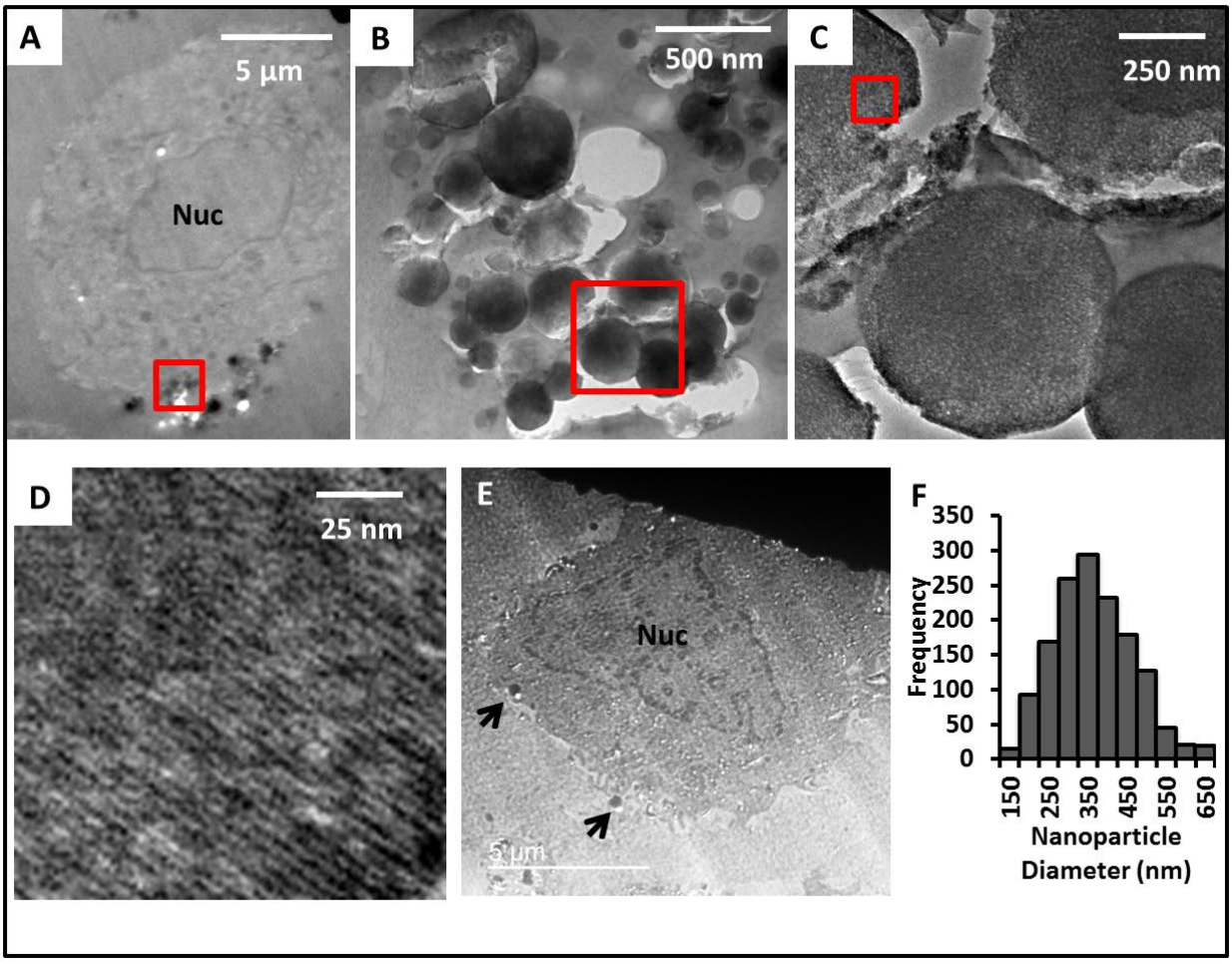

Figure S4. Electron microscopy of MSN-labeled MSCs. MSCs with MSNs were imaged at increasing magnifications. Red squares in each panel indicate the area of higher magnification in the next subsequent panel. **A)** Low magnification image shows MSC including nuclear envelope with dark areas indicating MSNs. Panels **B** and **C** show higher magnification images of the MSNs in the MSCs. Panel **D** is a digital magnification of area in **C** showing that pore lattice is retained even *in vivo*. Panel E is a MSN-labeled MSC grown for one week and then imaged with TEM. Arrows indicate MSNs still present in the MSC. Panel **F** presents *in vivo* sizing data for the MSNs incorporated into the MSCs—the mode size was 350 nm similar to *in vitro* analysis. White areas in **A** are tears in the epoxy due to higher MSN rigidity relative to the rest of the cell.