Supplementary Information

Transformation Cycle of Magnetosomes in Human Stem Cells: from Degradation to Biosynthesis of Magnetic Nanoparticles Anew

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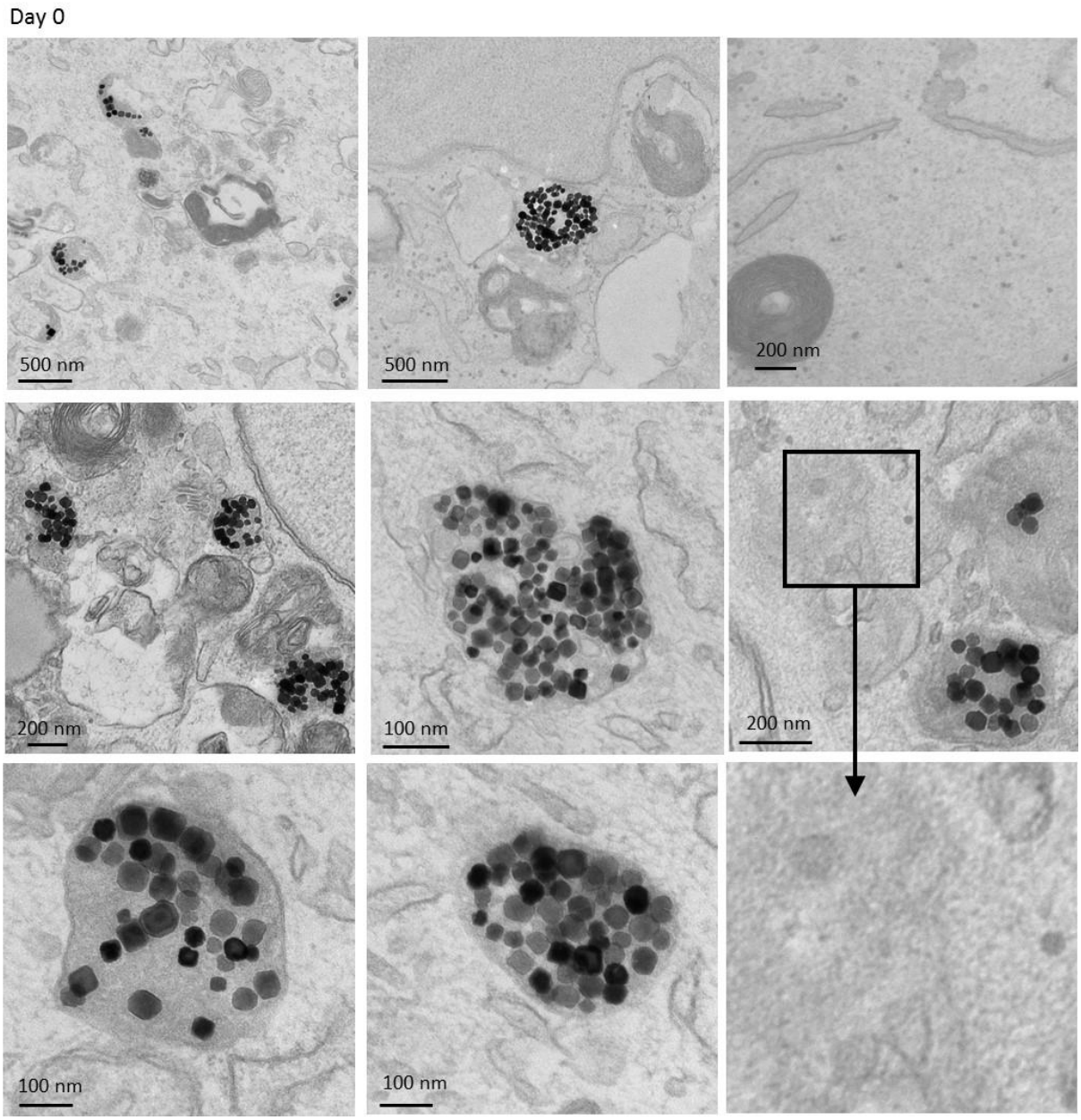

Figure S1: TEM images of the cells upon magnetosomes internalization are observed at day 0. The magnetosomes are internalized in the endosomes of the cells and no nano-structures are observed in the cytoplasm (zoomed box).

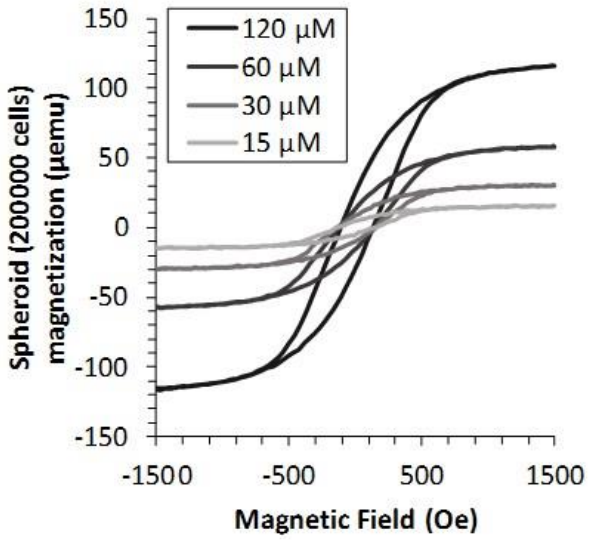

Figure S2: Vibrating sample magnetometry analysis of the magnetosomes internalized into human stem cells (2 hours upon internalization). The hysteresis loop displays a magnetic behavior typical of a ferromagnetic (open hysteresis) material.

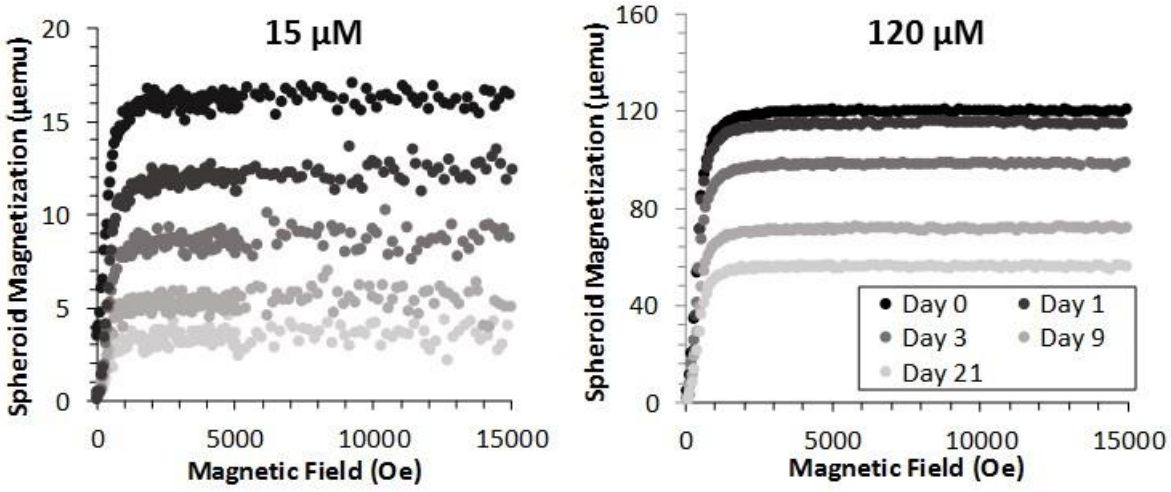

Figure S3: Magnetization curves obtained by vibrating sample magnetometry (VSM) display a progressive decrease in magnetization saturation over time for the cells incubated with either [Fe]=15 µM or 120 µM of magnetosomes solutions.

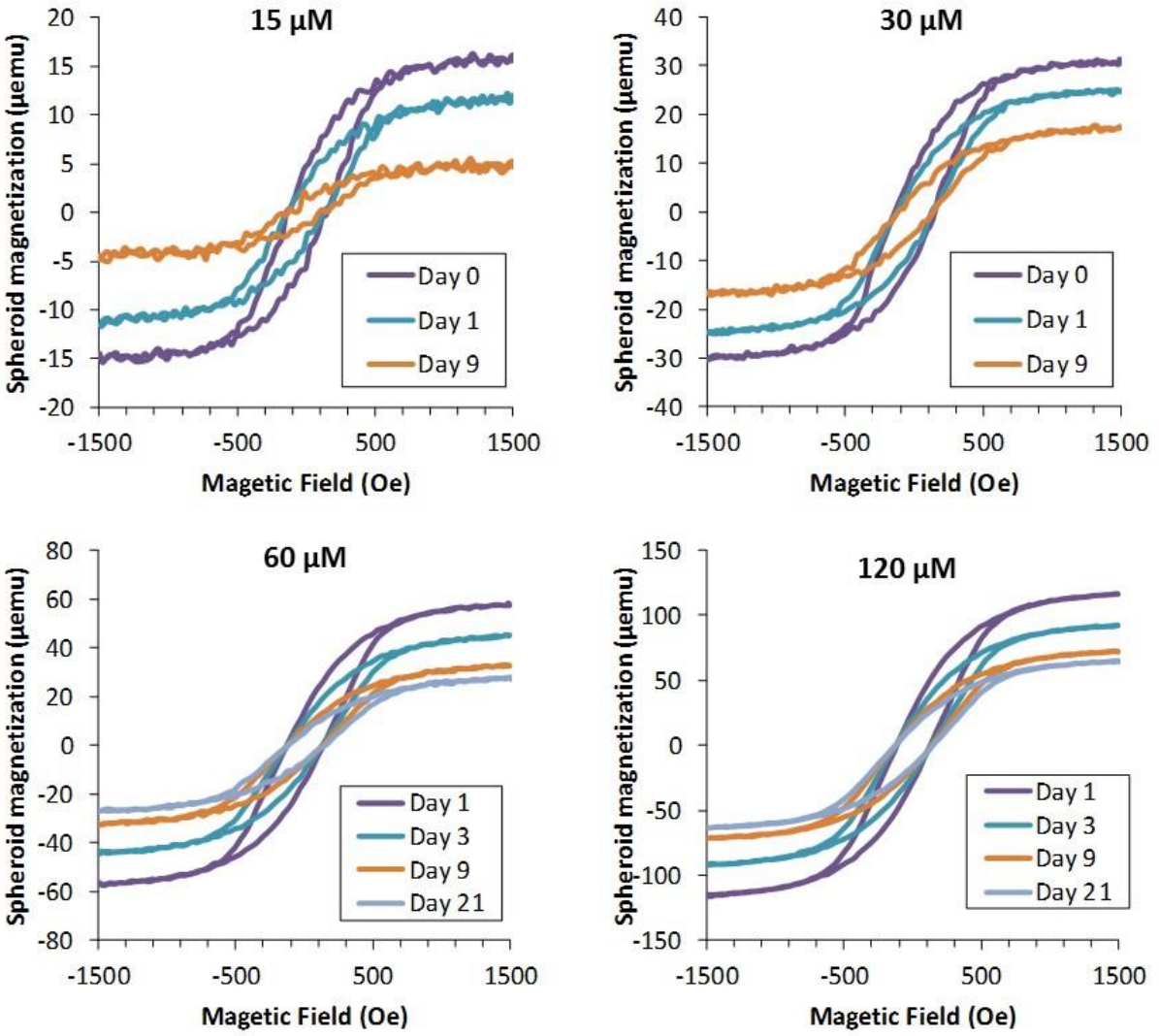

Figure S4: Analysis of the magnetization curves over time shows that the hysteresis loops remain open even after 21 days of culture. Only the intact magnetosomes thus contribute to the signal, and no other magnetic structures are observed.

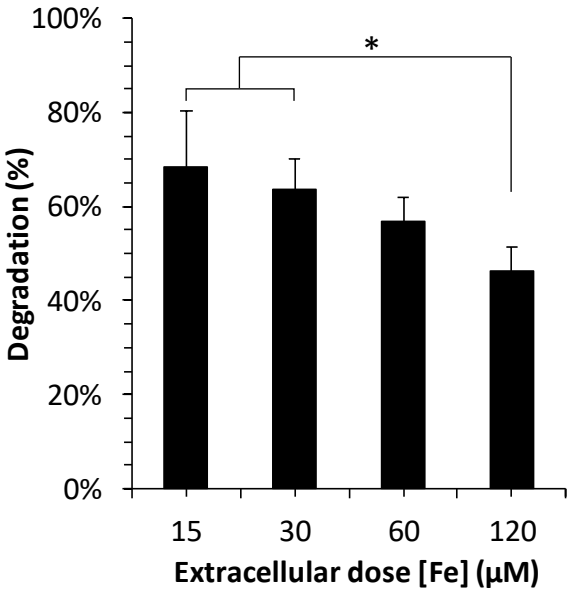

Figure S5: Degradation rate (percent of degraded magnetosomes respective to their initial content) for increasing incubation concentrations.

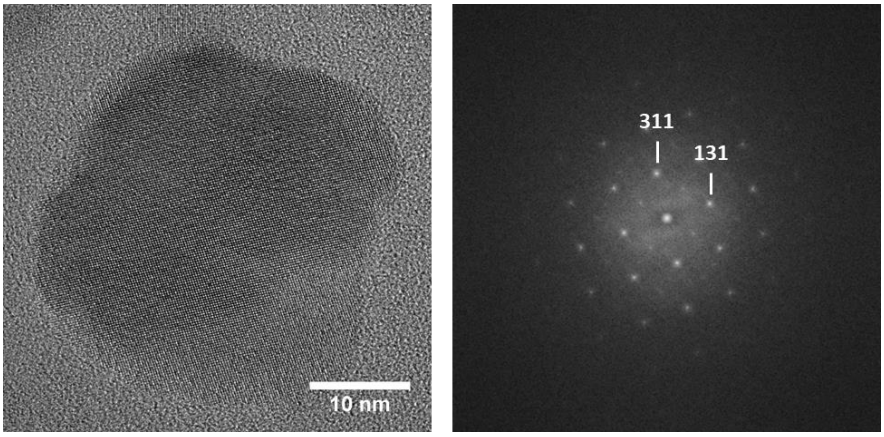

Figure S6: HR-TEM image of a still intact intracellular magnetosome, after 21 days of stem cell maturation.

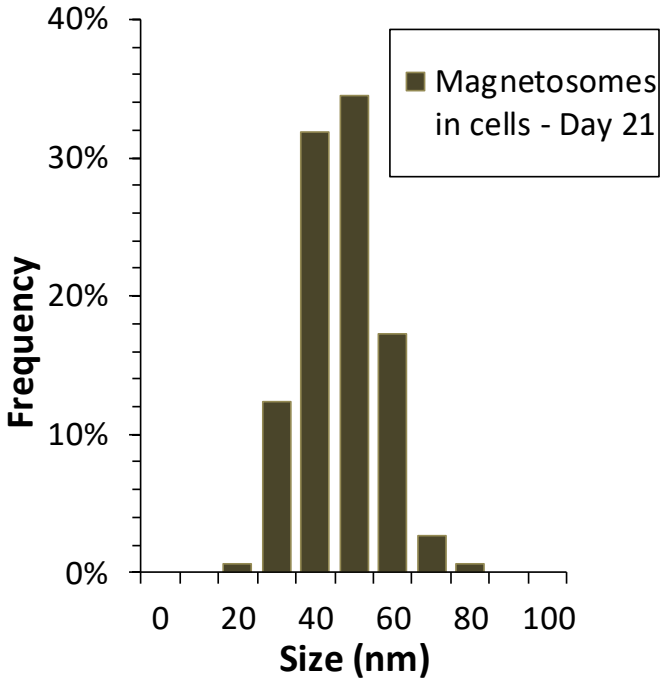

Figure S7: Size distribution of still intact magnetosomes observed after 21 days of stem cells spheroids maturation.

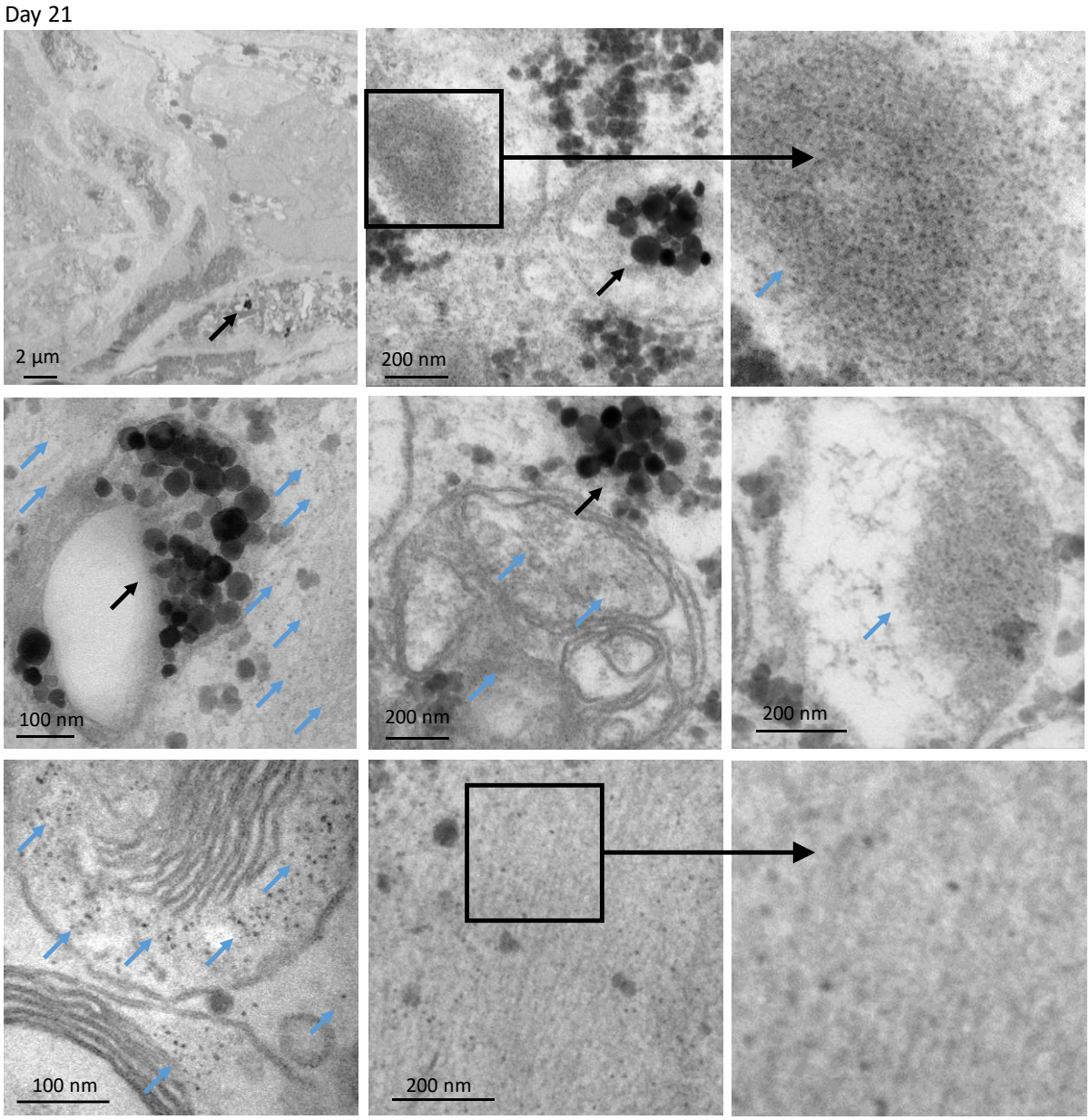

Figure S8: TEM images of the cells at day 21 showing the presence of still intact magnetosomes (black arrows) as well as areas filled with ferritin (blue arrows), both within and outside the endosomes.

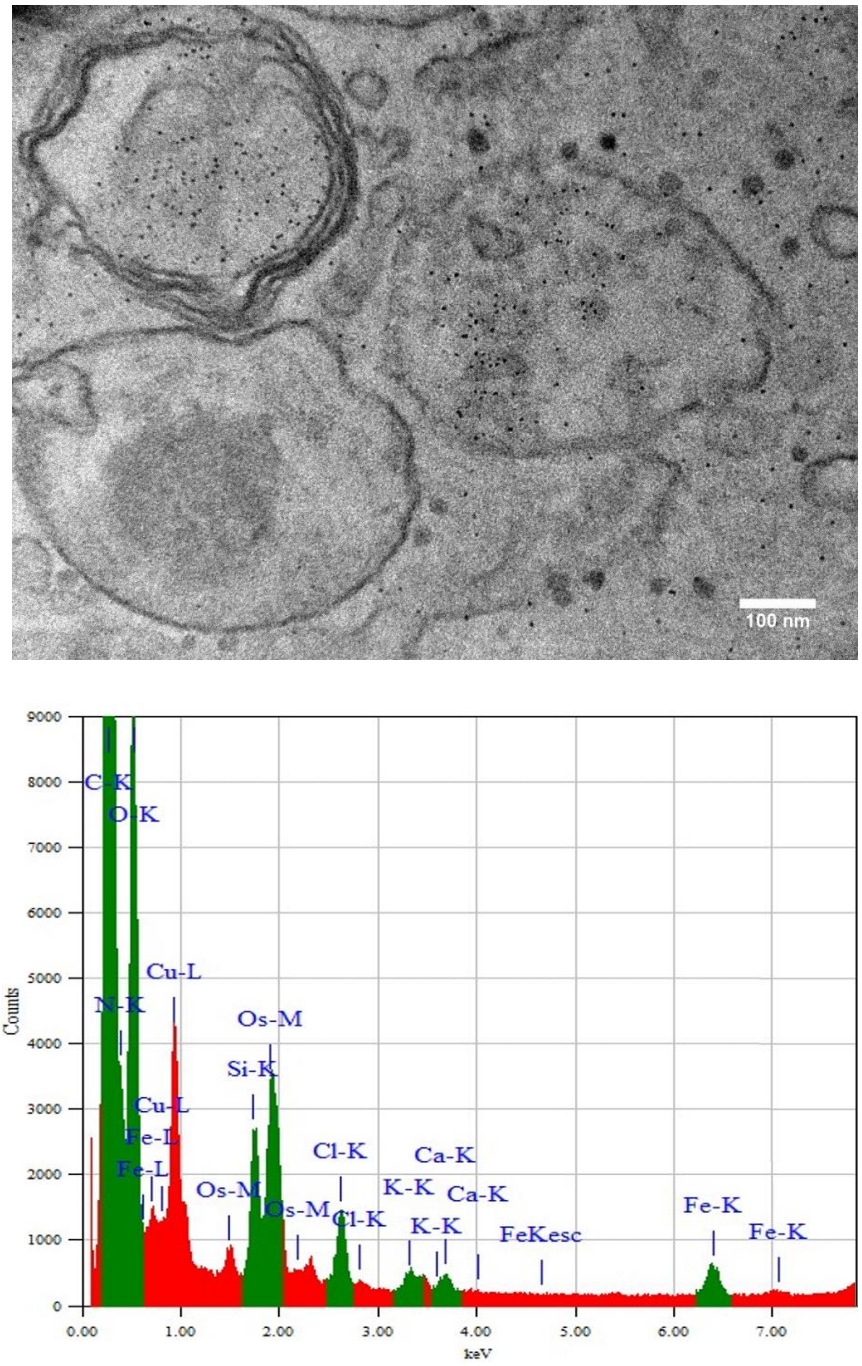

Figure S9: Energy-dispersive X-ray spectroscopy (EDS) spectrum of the zone presented above (TEM image) performed by 200 kV FE (Field Emission) analytical electron microscope JEM-2100F (JEOL). It shows a significant peak of iron (bottom graph), suggesting that the iron released from the magnetosome degradation has been stored in the relatively monodisperse 5-7 nm deposits, probably formed by the ferritin protein.

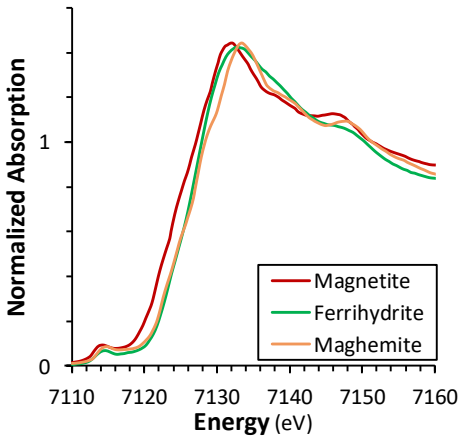

Figure S10: XANES absorption reference spectra at the Fe K-edge for magnetite, maghemite and ferrihydrite.

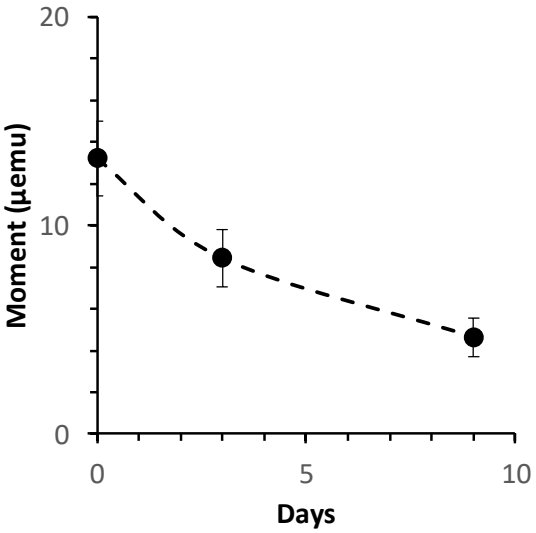

Figure S11: Decrease of the cellular magnetism over time for human endothelial cells (HUVEC) in 2D culture.

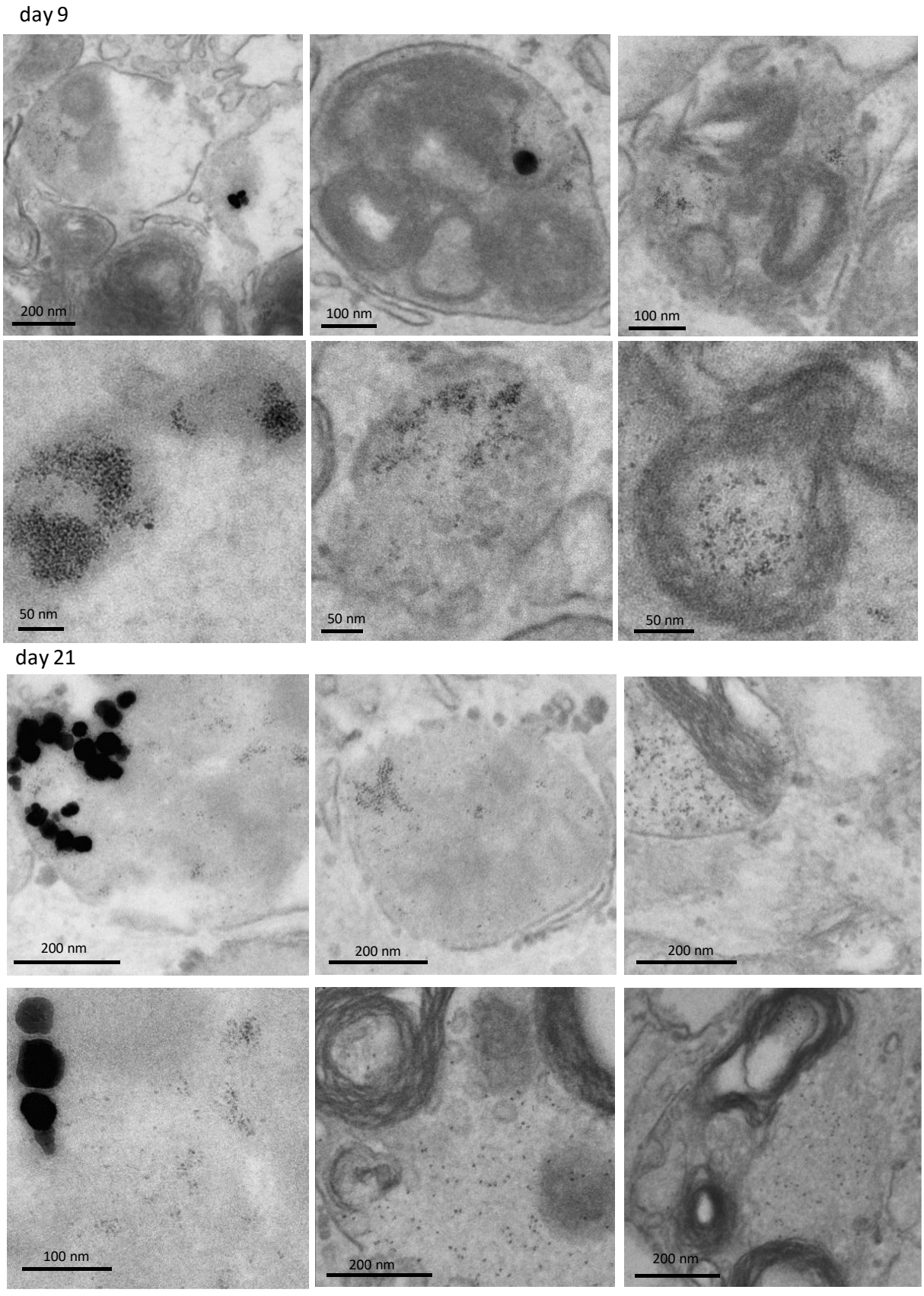

Figure S12: TEM images of remaining magnetosomes and newly synthesized nanoparticles, always found in endosomes, 9 days (top images) and 21 days (bottom images) after magnetosomes internalization.

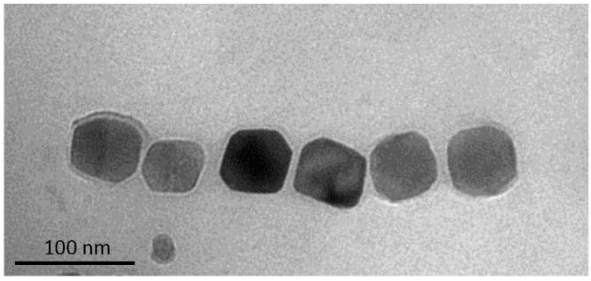

Figure S13: TEM image of magnetosomes before incubation with the cells. Purified magnetosomes were deposited on a TEM grid, their observation shows the presence of a membrane surrounding each magnetosome.

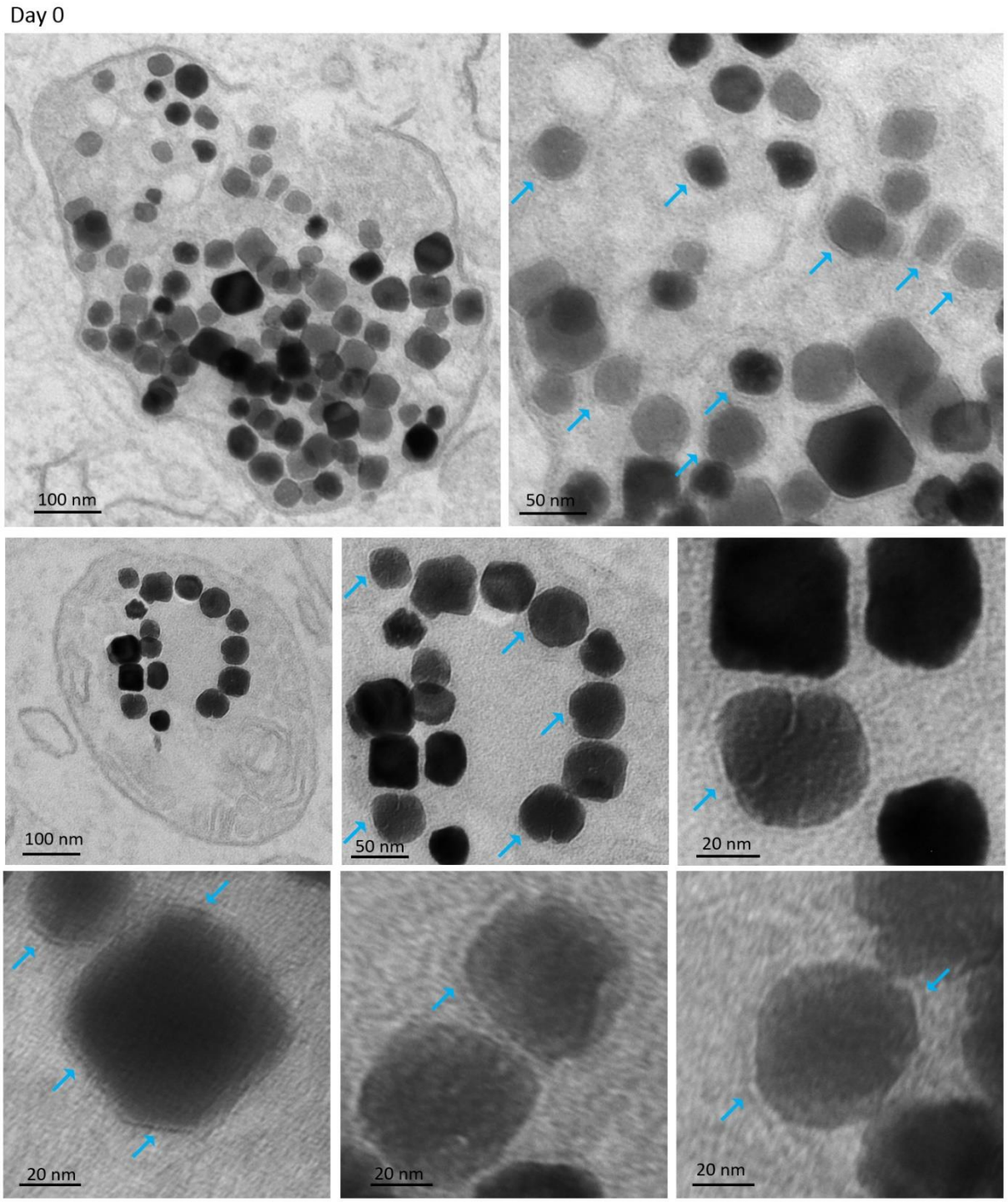

Figure S14: TEM observations of magnetosomes upon uranyl acetate staining on samples fixed the day of their incorporation within stem cells (day 0). Blue arrows indicate the presence of a membrane surrounding the particles. This membrane was observed around almost all magnetosomes, they are not all indicated with an arrow for means of clarity.

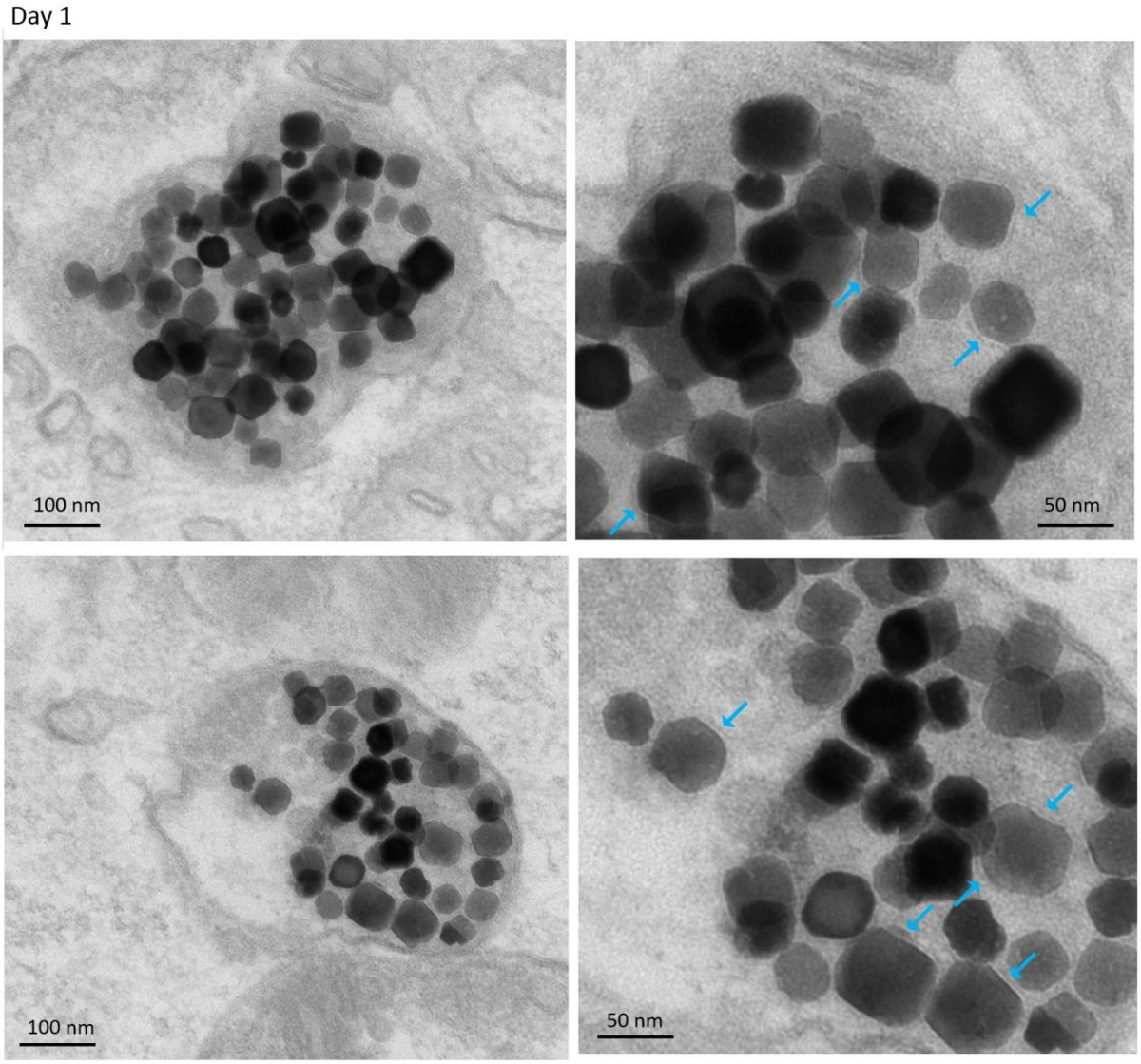

Figure S15: TEM observations of samples fixed one day after magnetosomes' incorporation within stem cells (day 1). Blue arrows on the close up image (right) indicate the presence of a membrane surrounding the particles. Most magnetosomes still appear with a membrane, yet, for some, the presence of the membrane becomes less obvious.

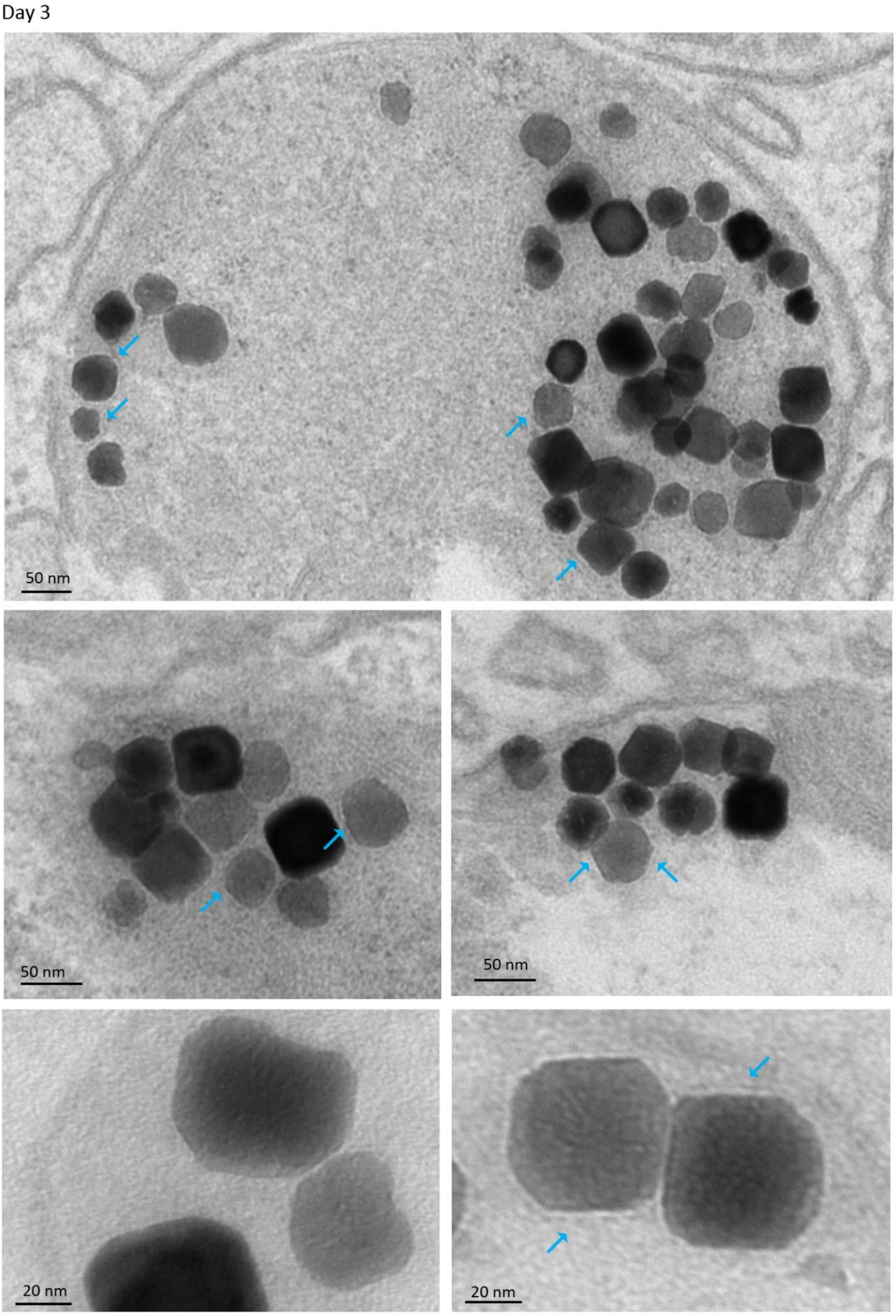

Figure S16: TEM observations of samples fixed three days after magnetosomes' incorporation within stem cells (day 3). Blue arrows indicate the presence of a membrane

surrounding the particles, present in less magnetosomes than for the earlier times (day 0 and day 1).

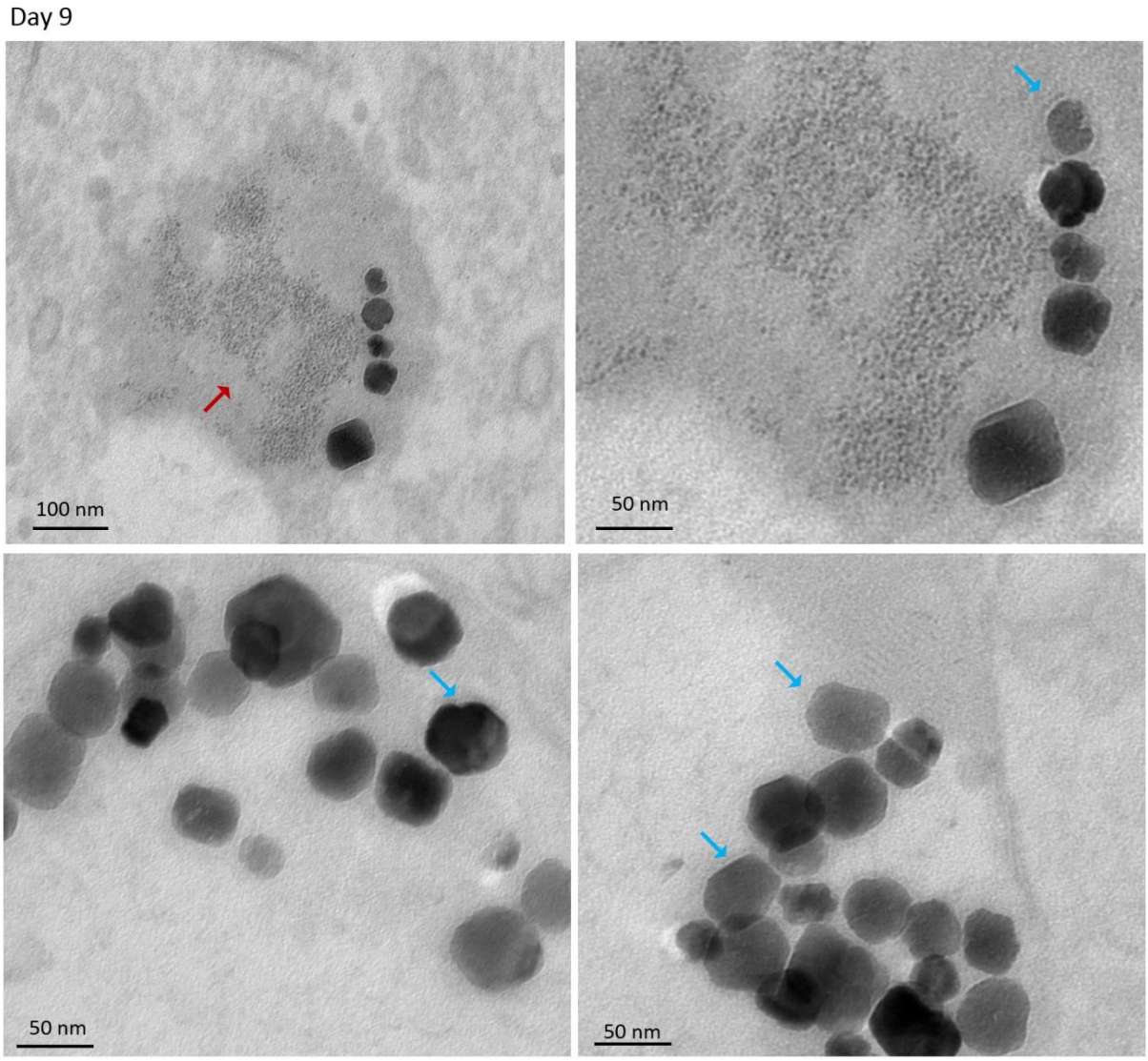

Figure S17: TEM observations of samples fixed nine days after magnetosomes' incorporation within stem cells (day 9). Zones containing magnetosomes still intact were selected (less numerous than at days 0-3). A zone with coexisting intact magnetosomes and biosynthesized nanoparticles anew (red arrow) is shown on the top row. Blue arrows indicate the (rarer) presence of a membrane surrounding the magnetosomes.

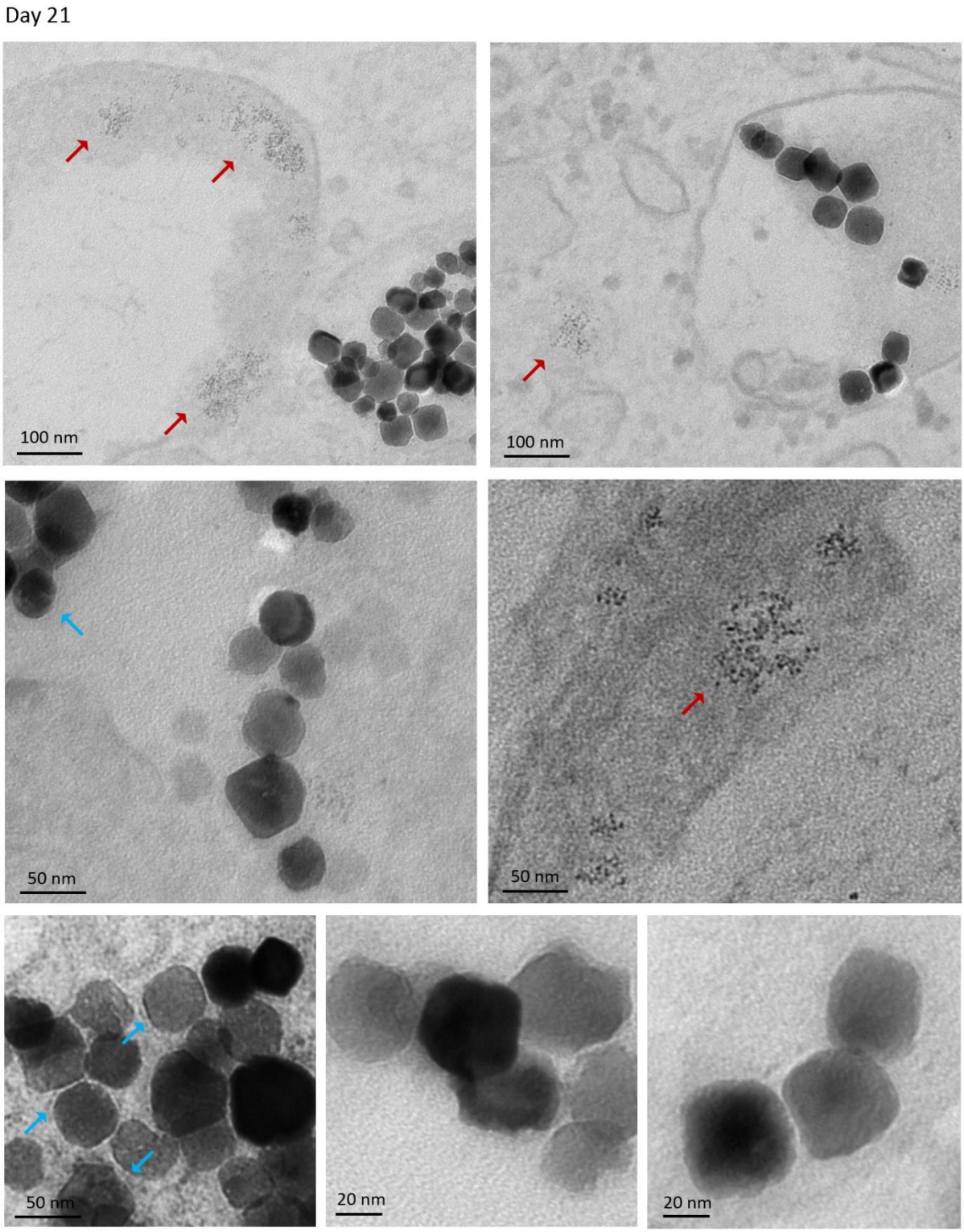

Figure S18: TEM observations of samples fixed three weeks after magnetosomes' incorporation within stem cells (day 21). Rare zones containing still intact magnetosomes were selected. Blue arrows indicate the (much rarer) presence of a membrane surrounding these particles. Newly biosynthesized nanoparticles (red arrows) are indicated with red arrows.

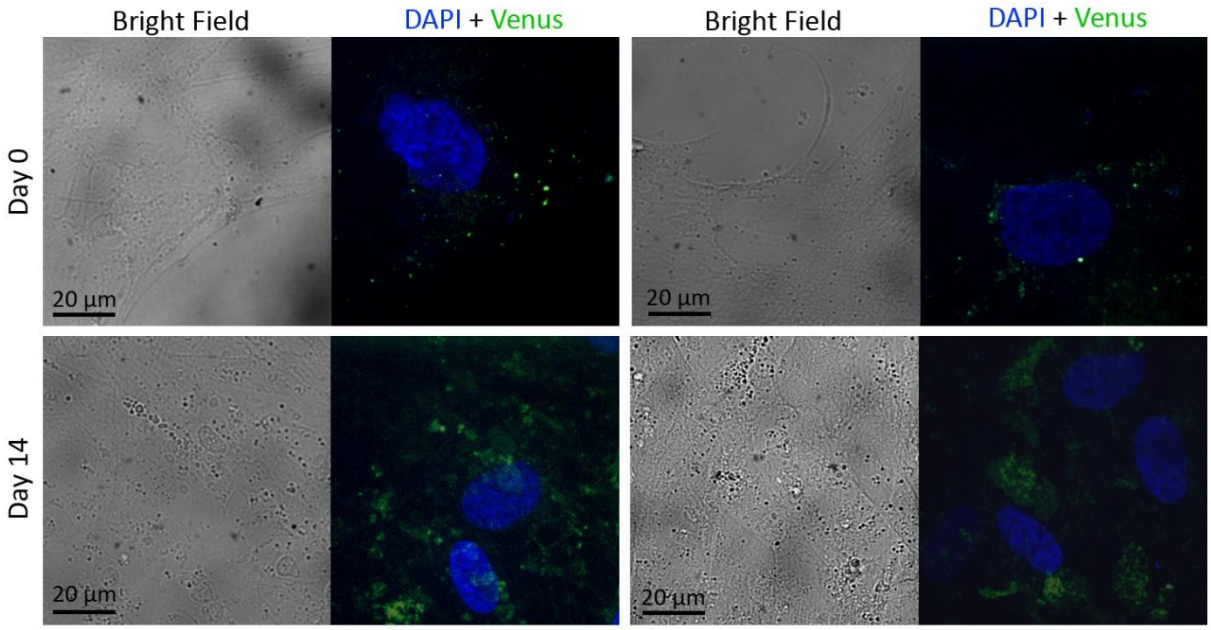

Figure S19: Confocal microscopy imaging of the stem cells right after internalization of the magnetosomes (day 0) or 2 weeks later (day 14). Bright field images are shown on the left, fluorescence images on the right (DAPI in blue, Venus in green). DAPI is a nucleus label and Venus is a fluorescent tag inserted within the membrane of the magnetosomes by genetic manipulation. Post internalization (day 0), the Venus tag is punctually located within the endosomes, while it is more diffuse on later days (day 14), suggesting a release of the magnetosome membrane from their core over time.

Sample	First coordination shell			Second coordination shell		
	S_0^2	R	σ^2	S_0^2	R	σ^2
Magnetite	1.1 (2)	1.98 (1)	0.011 (2)	1.2 (1)	3.37 (1)	0.013 (1)
D0	1.1 (1)	1.97 (2)	0.011 (2)	1.1 (1)	3.37 (1)	0.012 (1)
D3	1.2 (2)	2.00 (2)	0.011 (3)	0.8 (1)	3.34 (1)	0.010 (2)
D9	1.2 (1)	2.00 (1)	0.011 (1)	0.6 (1)	3.34 (1)	0.009 (1)
D21	1.2 (1)	1.99 (1)	0.010 (1)	0.5 (1)	3.33 (1)	0.009 (1)
Ferrihydrite	1.1 (1)	1.98 (1)	0.011 (1)	0.24 (4)	3.32 (1)	0.008 (1)

Table S1: Parameters of first and second coordination shell obtained from experimental EXAFS results for magnetite and ferrihydrite references and for sample evolving as a function of degradation time (D0 $\rightarrow$ D21). The amplitude reduction factor S_0^2, the interatomic distance R and the Debye-Waller (DW) factor σ^2 for the two shell distances are used as free parameters for each fitting