Supplementary Information
For

Magnetic Manipulation of Bacterial Magnetic Nanoparticle-Loaded Neurosphere

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Uptake Efficiency of BMPs

The BMPs were added to 10^6 cells with serial concentration from 5 to 40 µg/ml. Figure S1 shows that the amount of uptake by SH-SY5Y cells after overnight incubation. In the concentration range, maximum amount of intracellular BMPs was 16.24 pg/cell when 40 µg/ml of BMPs was added to 10^6 cells. In addition, more BMPs were internalized in a cell as increasing quantity of adding particles.

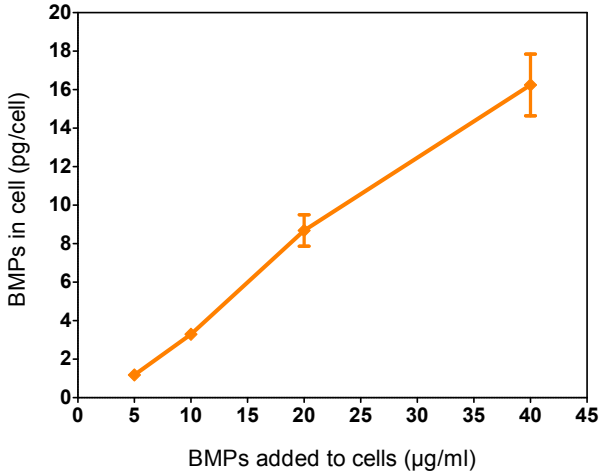

Fig. S1 Uptake ratio of BMPs by SH-SY5Y cells

SMF Exposure for Neuronal Differentiation

The SMF was applied constantly to cells as presented in Fig. S2 during the neuronal differentiation by RA treatment. The cells were placed in the magnetic field strength range of 100 to 220 mT (Fig. S3).

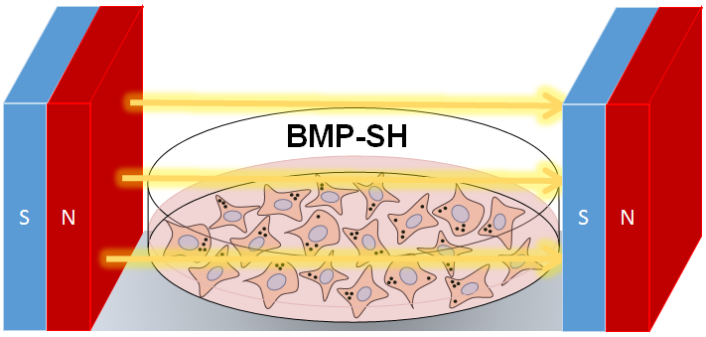

Fig. S2 Schematic of SMF exposure to cells during RA treatment

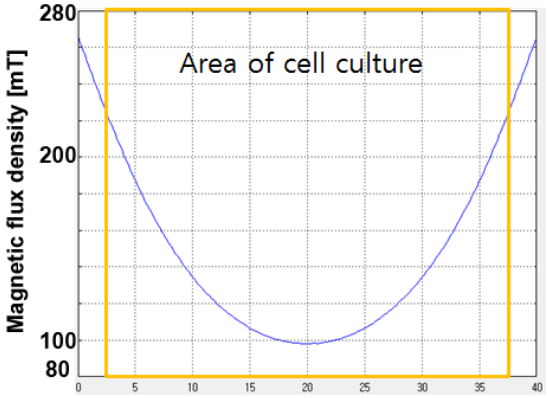

Fig. S3 Magnetic flux density in cell culture area

Attachment of a Neurosphere on surface

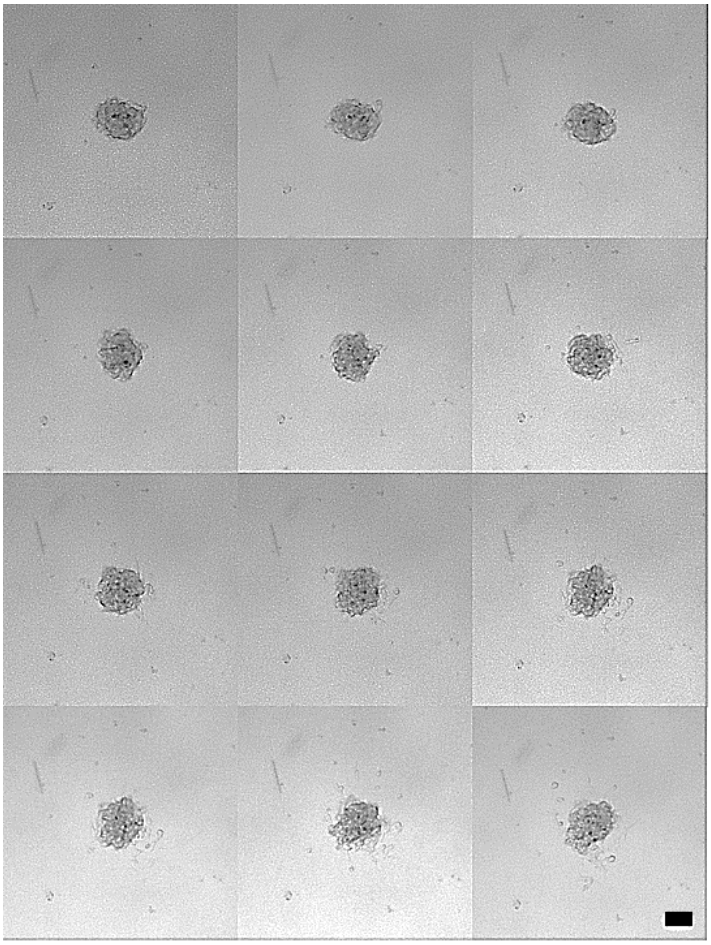

Fig. S4 attachment and spreading of a BMP-free neurosphere observed hourly for 11 h, scale bar: 100 µm

Calculation of Magnetic Field and Force

To understand physical effect of the internalization of BMPs with SMF exposure on a cell, magnetic force on a BMP was estimated using a magnetofection model. When the BMP is trasnfected into a cell and exposed to an SMF externally at the bottom of the cell, the environment is similar with magnetofection. Cytoplasm could be substituted for the transport fluid in the magnetofection model.[1] The magnetic force on a BMP is modeled using the effective dipole moment method in which a magnetic particle is replaced by an equivalent point dipole with a moment $m_{p,\mathrm{eff}}$.[1, 2] The force on the dipole (and hence on the particle) is given by

$$F_m = \mu_f m_{p,eff} \cdot \nabla H_a ,$$

where μ_f is the permeability of transport fluid, $m_{p,\mathrm{eff}}$ is the effective dipole moment of the particle, and H_a is the externally applied magnetic field intensity at the center of a particle, where the equivalent point dipole is located. The $m_{p,\mathrm{eff}}$ is depends on H_a as following equation.

$$m_{p,eff} = V_p f(H_a) H_a$$

where

$$f(H_a) = \begin{cases} \dfrac{3(\chi_p - \chi_f)}{(\chi_p - \chi_f) + 3} & if \quad H_a < \left(\dfrac{(\chi_p - \chi_f) + 3}{3\chi_p}\right) M_{sp} \\ \dfrac{M_{sp}}{H_a} & if \quad H_a \geq \left(\dfrac{(\chi_p - \chi_f) + 3}{3\chi_p}\right) M_{sp} \end{cases}$$

We assume that the cytoplasm is nonmagnetic ($\chi_f = 0$) with a viscosity and density equal to that of water. The BMP consists of Fe_3O_4 and have a density $\rho_p = 5170$ kg/m^3 and saturation magnetization $M_{\mathrm{sp}} = 4.52 \times 10^5$ A/m. When, $\chi_p >> 1$

$$f(H_a) = \begin{cases} 3 & if \;\; H_a < M_{sp}/3 \\ \dfrac{M_{sp}}{H_a} & if \;\; H_a \geq M_{sp}/3 \end{cases} .$$

In our SMF exposure condition, employing a rectangular neodymiumiron boron (NdFeB) magnet (50 x 25 x 25 mm), 1-D distribution of H_a is described as following equation which is provided from the international magnetic solutions (IMS).

$$H_a = \frac{M_s}{\pi}\left[\left[\tan^{-1}\frac{WL}{2x\left(4x^2 + W^2 + L^2\right)^{1/2}}\right] - \tan^{-1}\left[\frac{WL}{2(x+T)[4(x+T)^2 + W^2 + L^2]^{1/2}}\right]\right] H_a = \frac{M_s}{\pi}\left[\left[\tan^{-1}\frac{}{2x(4x}\right.\right.$$

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where W is width and L is length of the magnet. The Flux density H_a is calculated along the center axis at a distance x from the magnet and $M_{\mathrm{s}} = 9.09 \times 10^5$ A/m. When the distance from center of the magnet $x < 0.10$ m, $H_a \geq M_{\mathrm{sp}}/3$.

Finally, the magnetic force on a BMP could be described as following.

$$F_m(x) = \mu_f V_p \left(\frac{M_{sp}}{H_a}\right) H_a \cdot \nabla H_a = \mu_f V_p \left(\frac{M_{sp}}{H_a}\right) H_a \frac{dH_a}{dx} = \mu_f V_p M_{sp} \frac{dH_a}{dx}$$

We assumed the distance x is 1 mm which is the thickness of the culture dish we used. The BMPs internalized cells attached right on the dish and ignored the height of a cell. Based on our experiment condition, the magnetic force on a BMP was 0.81 *f*N toward the magnet.

μ_f : permeability of transport fluid $\approx \mu_0$

$m_{p,\text{eff}}$: effective dipole moment of the particle

H_a : externally applied magnetic field intensity at the center of the particle

V_p : volume of a magnetic nanoparticle, 6.54×10^{-23} m^3

r_p : radius of a magnetic nanoparticle, 25 nm

χ_p : magnetic susceptibility of the particle

χ_f : magnetic susceptibility of the fluid

M_{sp} : saturation magnetization of the particle

M_{s} : saturation magnetization of the magnet

Stopper effect of captured BMP-NSs

Figure S5 shows that reduced speed of a BMP-NS as faced stopper BMP-NSs which was captured earlier. The yellow circle indicates positions of a BMP-NS every 2 s. A video is also available in the web.

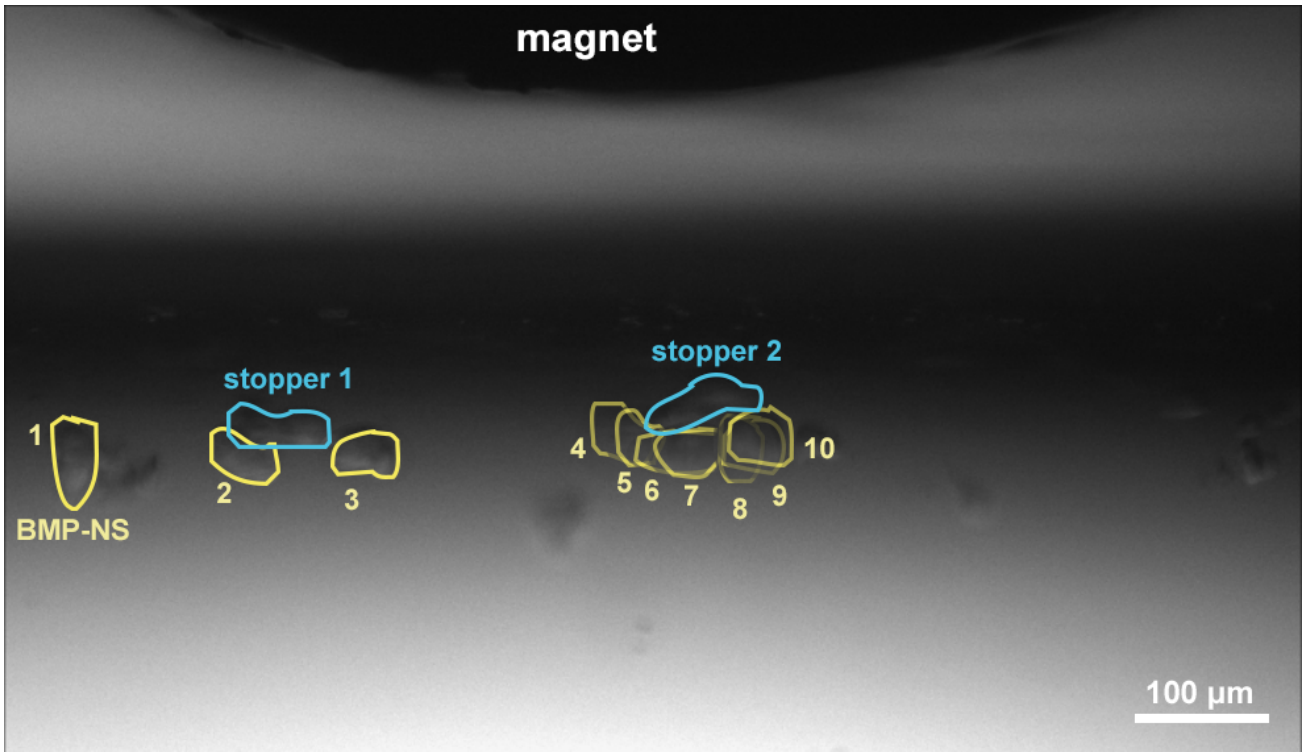

Fig. S5 Tracking a BMP-NS every 2 s (yellow)

Reference

1. E. P. Furlani and K. C. Ng, *Physical Review E*, 2008, 77, 061914.
2. E. Furlani and K. Ng, *Physical Review E*, 2006, 73, 061919.