Table S1. Co-locolization of nanozyme with Lysotracker, ER Tracker, and MitoTracker in murine macrophages

Organelle	5 min	15 min	30 min	60 min
Acidified endosomes	59.5 ± 3.5[a]	87.2 ± 2.4	77.3 ± 3.7	77.0 ± 2.7
ER	6.5 ± 2.8	0.21 ± 0.09	0.94 ± 0.5	21.3 ± 8.7
Mitochondria	4.6 ± 1.3	3.2 ± 0.6	5.2 ± 0.9	9.2 ± 1.0

[a] Data represent means ± SEM (N = 40).

Table S2. Effect of PMA on nanozyme transfer from BMM to CATH.a neurons

Treatment	Accumulation (Arb U/10^6 cells)
Media	56.74 ± 0.6[a]
PMA	56.95 ± 0.3

[a] Data represent means ± SEM (N = 4).

SUPPLEMENTARY DATA

Figure S1. Inhibition of phagocytosis by disruption of actin microfilaments with cytochalasin b in murine macrophages. Murine macrophages were treated with cytochalasin b (10 µg/ml) for 2 hours, washed, and stained with Alexa Fluor-488-phalloidin. Confocal images clearly demonstrated disruption of actin microfilaments in the treated cells (**B**) in contrast to control untreated macrophages (A). Bar = 20 µm.

Figure S2. Internalization of nanozyme within human macrophages occurs in clatrin-coated pits with caveolae-mediated endocytosis involvement. Human monocyte-derived macrophages (HMDM) were incubated for different times with Alexa Fluor-649-labeled nanozyme, fixed, stained with FITC-anti clathrin heavy chain (**A**) or FITC-anti caveolae (**B**), and colocalization with nanozyme was evaluated by confocal microscopy. Significant colocalization of nanozyme with clathrin-coated pits and at lesser degree with caveolae antibody indicates that nanozyme enters mostly by clathrin-mediated endocytosis. Bar = 20 µm.

Figure S3. Colocolization of nanozyme with lysosomes, ER, and mitochondria in murine macrophages. Murine macrophages were incubated with Alexa Fluor-647-labeled nanozyme for different times, and stained with (**A**) LysoTracker Green (50 nM), (**B**) ERTracker Green (1 µM), or (**C**) MitoTracker Green (20 nM). Colocalization of nanozyme (red) and compartment staining (green) is shown in yellow. Nanozyme was predominantly localized in acidic endosomes, and at lesser degree in ER and mitochondria. Refer also to **Table S2** for quantitative colocalization. Bar = 20 µm.

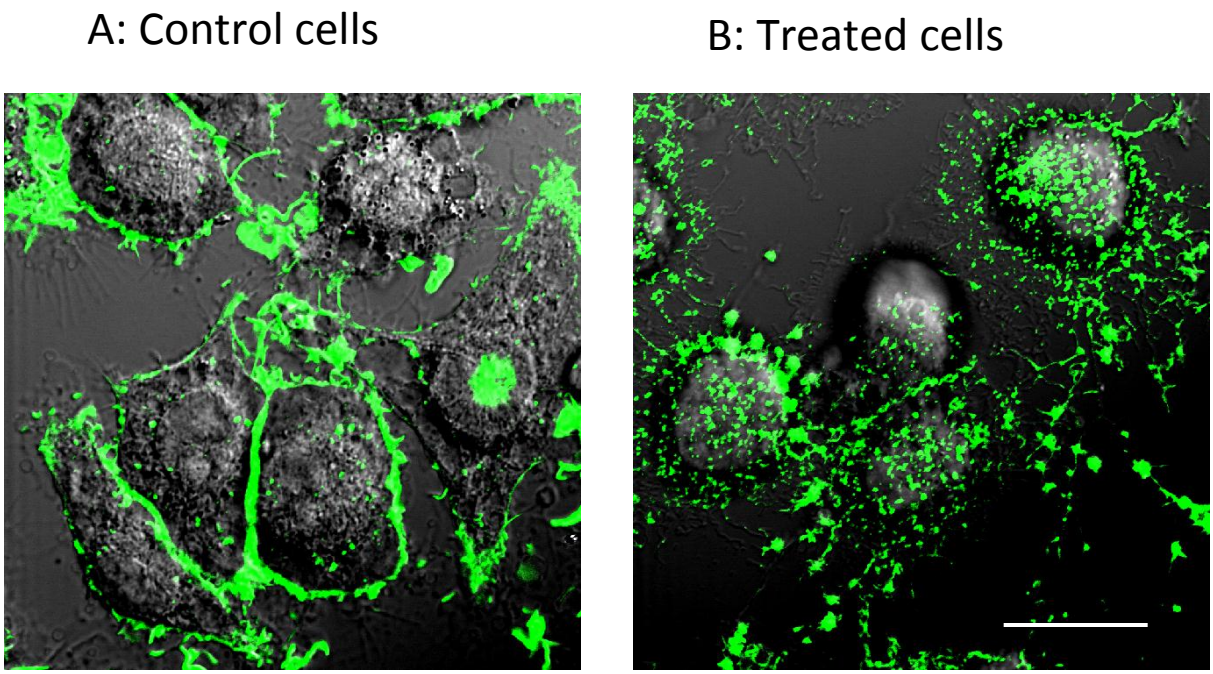
Figure S4. Colocalization of free nanozyme in HBMEC with endosomal conpartments. HBMEC were incubated with Alexa Fluor-647-labeled nanozyme for one hour, fixed,

permeabilized, and stained with (**A**) FITC-conjugated EEA1 monoclonal antibody (to early endosomes), (**B**) mouse monoclonal antibody Rab7 (late endosomes), (**C**) mouse monoclonal antibody Rab11 (recycling endosomes), or (**D**) FITC-conjugated LAMP 1 monoclonal antibody (to lysosomes). Cells reacted with unconjugated primary mouse antibodies (**B, C**) were stained with FITC-conjugated secondary goat anti-mouse immunoglobulin G. Colocalization of nanozyme (red) and compartment staining (green) was manifested in yellow. Nanozyme was predominantly localized in lysosomes, and at lesser degree, if any, in early endosomes, recycling endosomes, followed by late endosomes. Bar = 20 µm.

Figure S5. Transfer of gold nanoparticles from murine macrophages into CATH.a neurons. CATH.a neurons were incubated for 18 hours with bone marrow-derived macrophages (BMM) loaded with gold nanoparticles, washed, stained and submitted for TEM and SEM image analyses. (**A**) TEM images of nanoparticles taken up by macrophages; TEM images of nanoparticles transferred from BMM (**B**) or from the media (**C**) to CATH.a neurons. Bar = 100 nm.

Media S1. Dynamics of nanozyme transfer from exosomes released by macrophages to CATH.a neurons. Confocal images of CATH.a neurons incubated with exosomes released from macrophages loaded with fluorescently-labeled catalase nanozyme (red) were taken at various times.

SUPPLEMENTARY FIGURES



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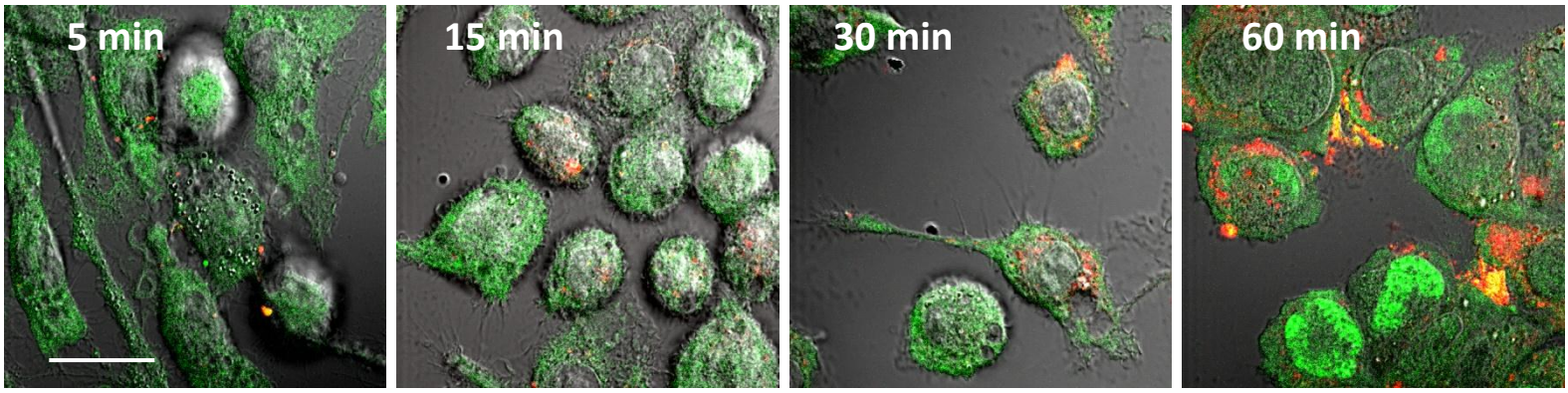
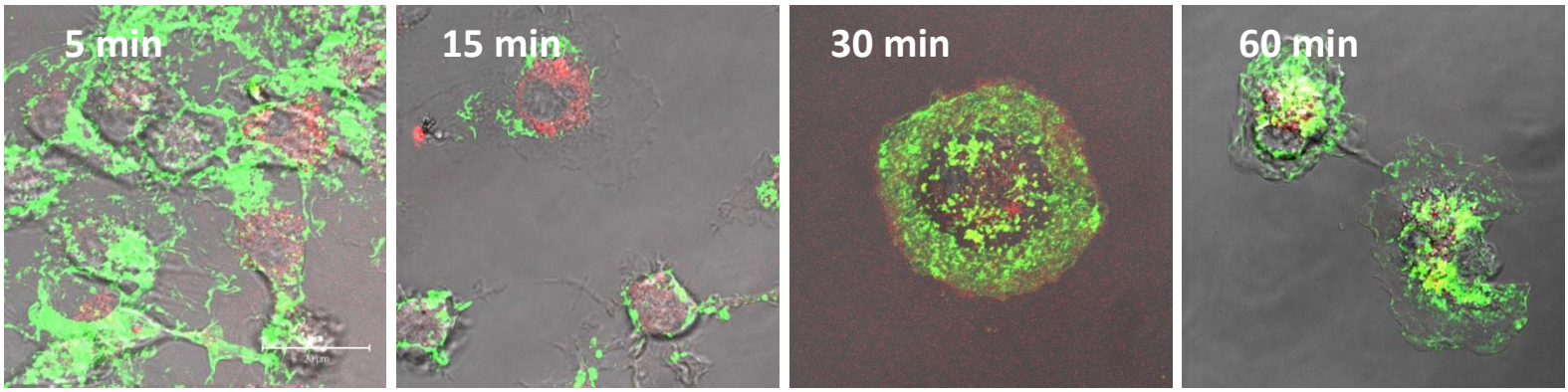
A: nanozyme/ clathrin



B: nanozyme/ caveolae



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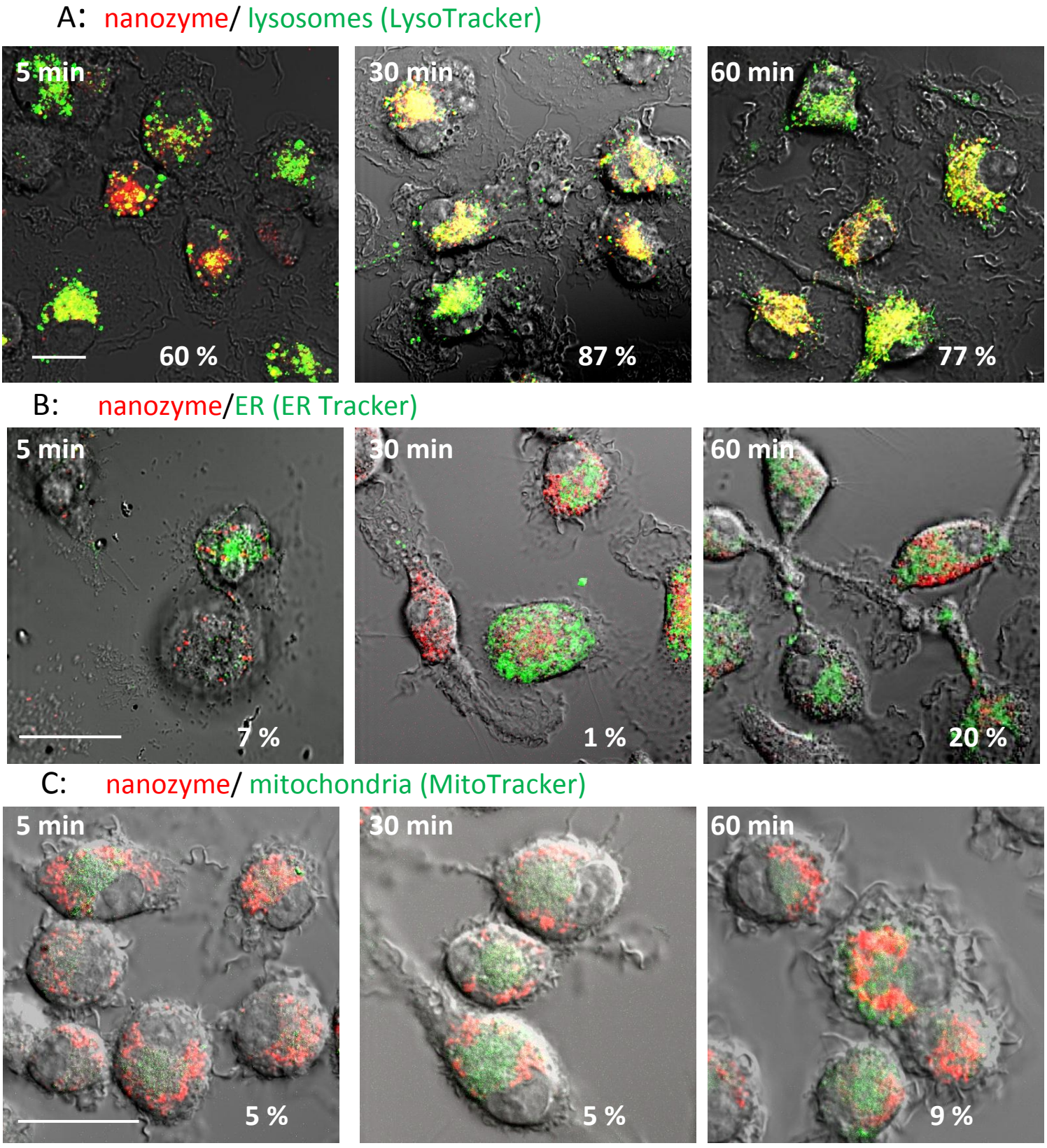

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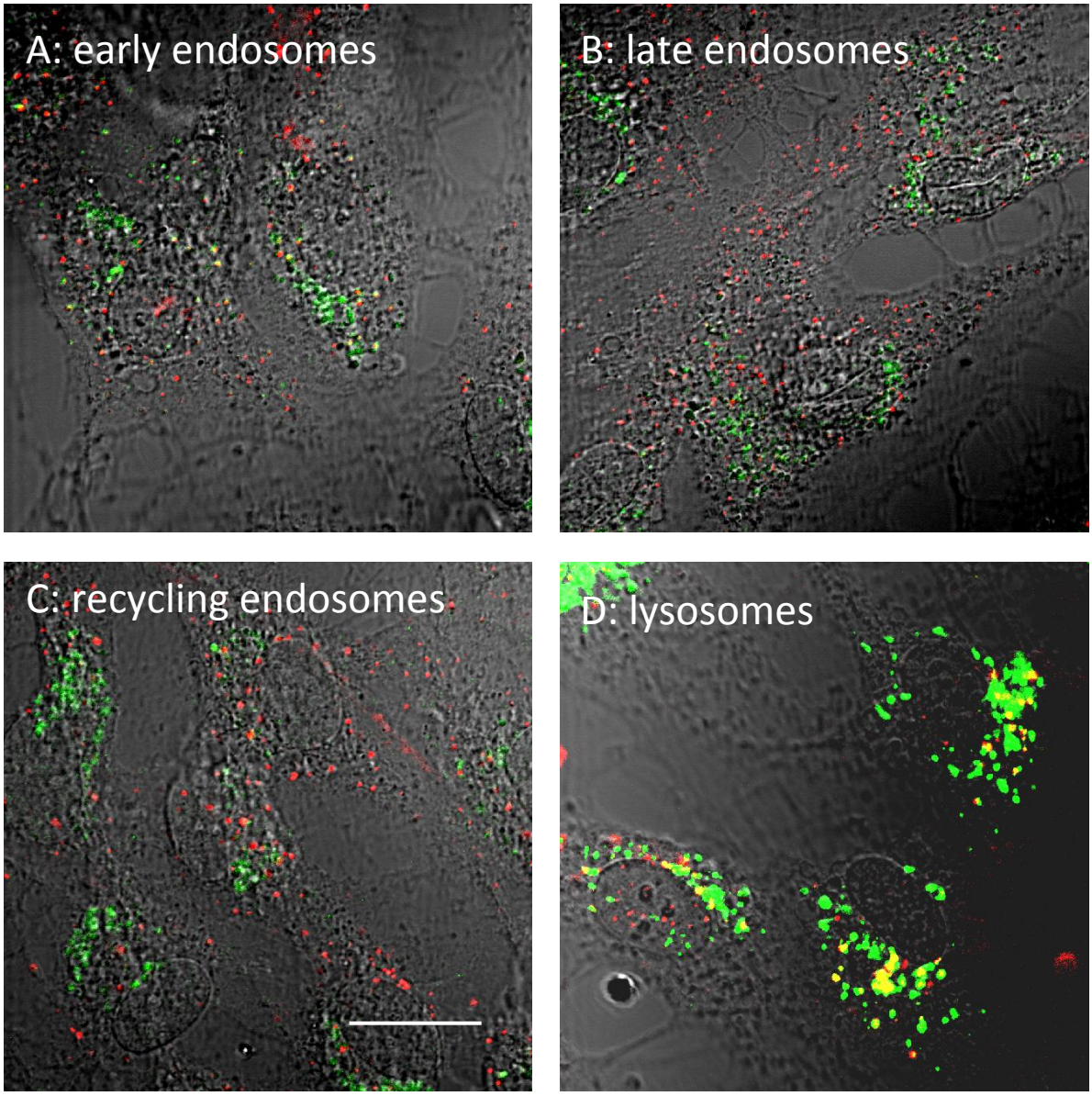

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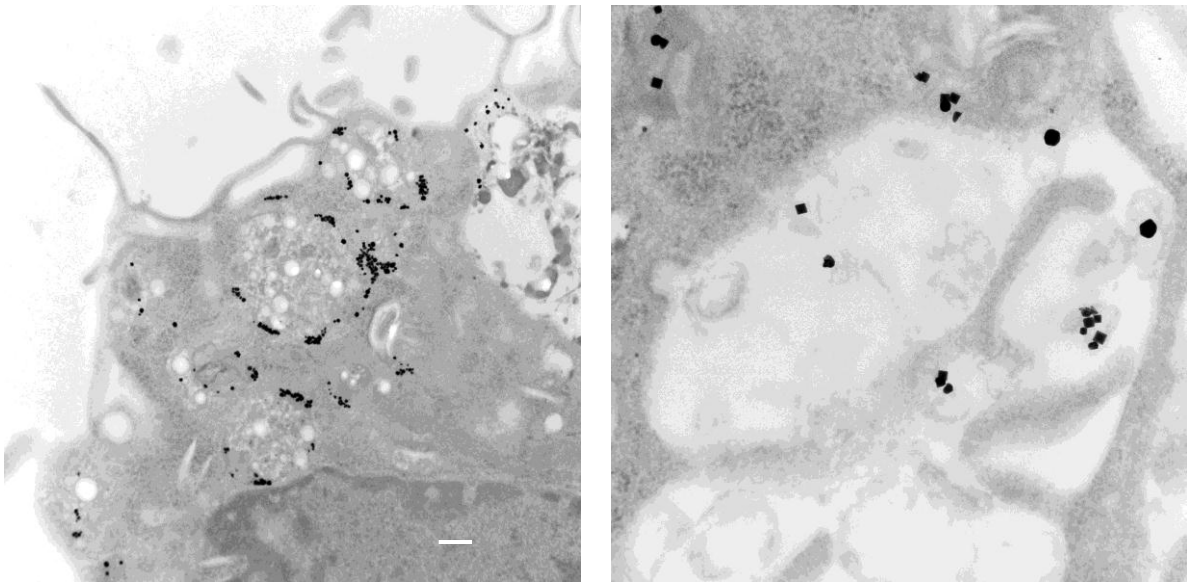
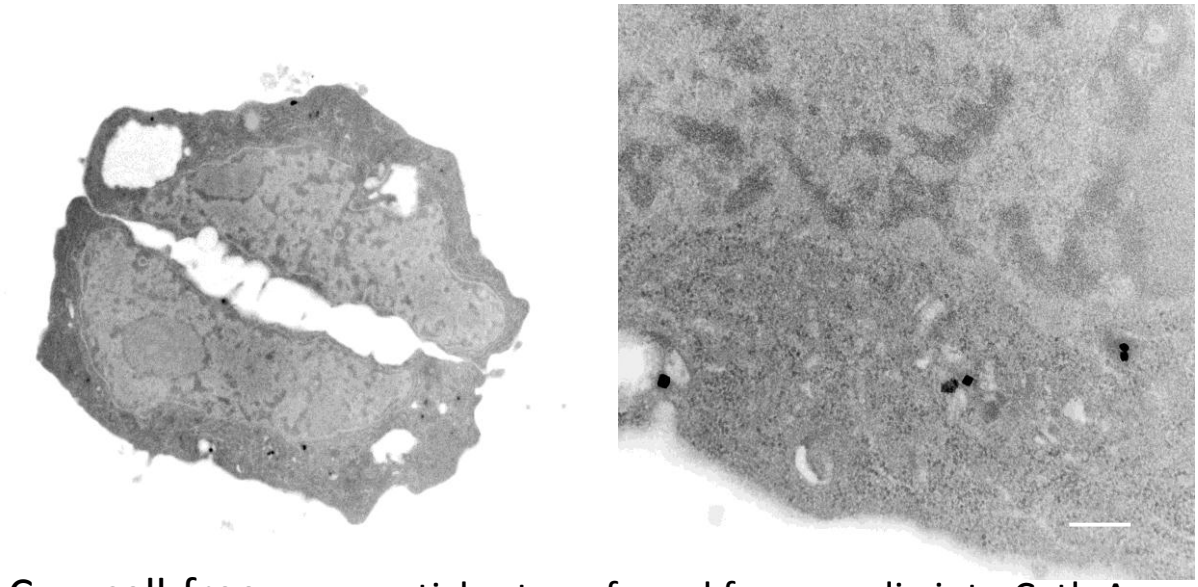
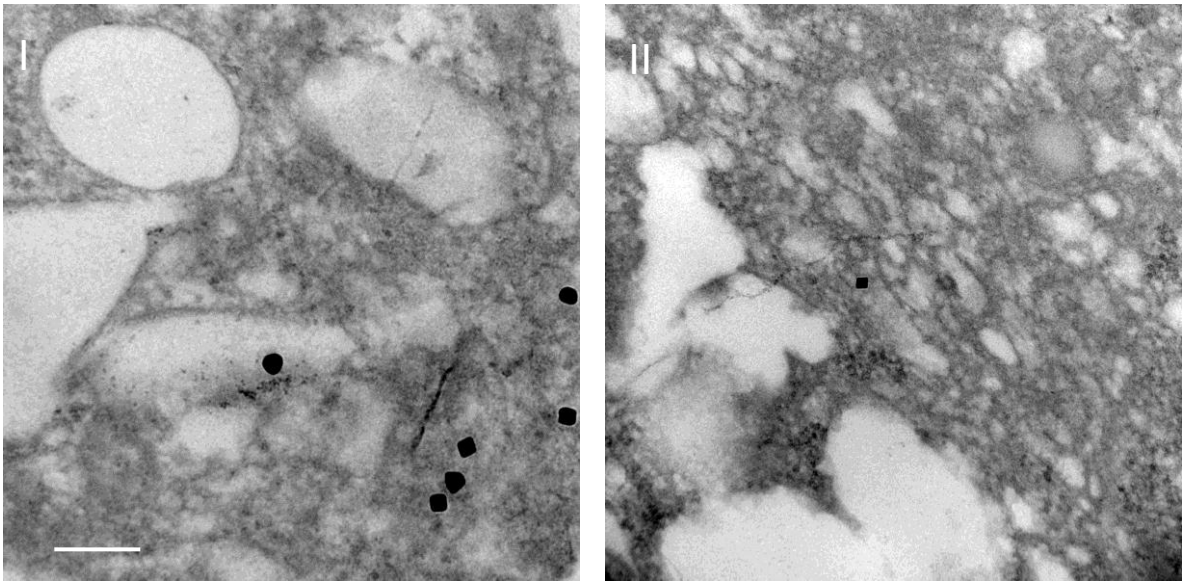
A: golden nanoparticles accumulated in murine macrophages



B: nanoparticles transferred from macrophages into Cath.A neurons



C: cell-free nanoparticles transferred from media into Cath.A



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