micromod Partikeltechnologie GmbH

modular designed particles

Publications and Reviews

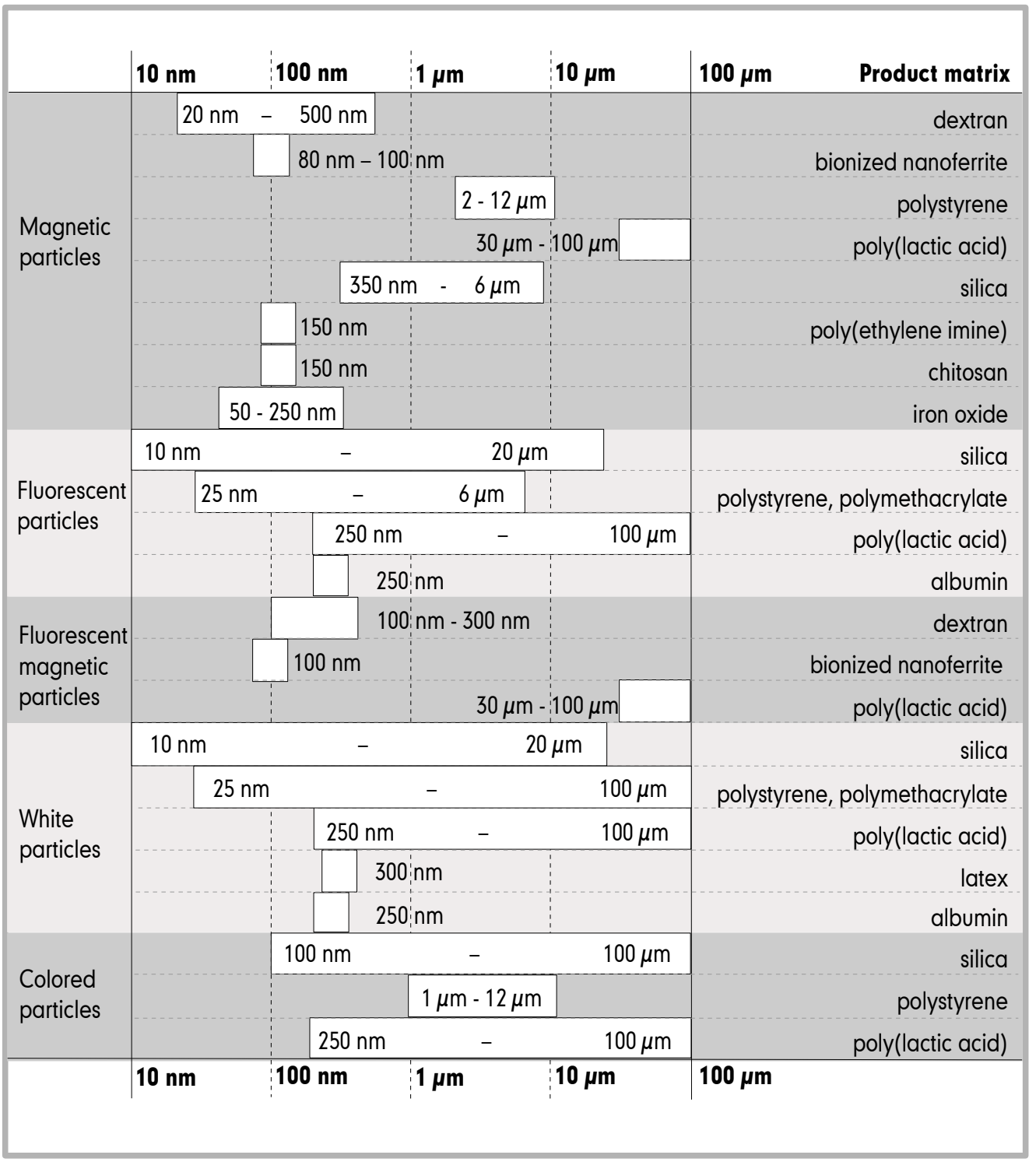
Technological Applications

Implementation in Life Sciences

magnetic micro- and nanoparticles

www.micromod.de

Product overview



micromod Partikeltechnologie GmbH
Friedrich-Barnewitz-Straße 4, D-18119 Rostock
Tel.:+49 381/54 34 56 10, Fax: +49 381/54 34 56 20
Technical Support Tel.: +49 381/54 34 56 14
E-mail: info@micromod.de, Internet: www.micromod.de

10 Applications of fluorescent magnetic particles

Cordula Grüttner

micromod Partikeltechnologie GmbH, Friedrich-Barnewitz-Str. 4, 18119 Rostock, Germany

10.1 Combination of optical imaging with Magnetic Resonance Imaging (MRI) or Magnetic Particle Imaging (MPI)

The combination of fluorescent and magnetic properties allows the design of nanoparticles for individual multimodal applications. Here we introduce highly specific applications of fluorescent magnetic nanoparticles that combine optical imaging and different magnetic techniques.

This combination allows for detection of fluorescent magnetic nanoparticles (MNPs) in a variety of biomedical applications. Rimkus et al. have studied the selective cell binding of fluorescent MNPs to endothelial cells as response to inflammatory factors. Functionalized nanomag®-CLD-spio particles were conjugated with antibodies that are directed to the cell-surface molecule VCAM-1 on. The antibodies were labelled with a near-infrared fluorochrome (DY-649) before conjugation (Fig. 1). Cell-binding properties of the targeted opto-magnetic probes were successfully evaluated on murine endothelial cells by fluorescence and MR imaging [1].

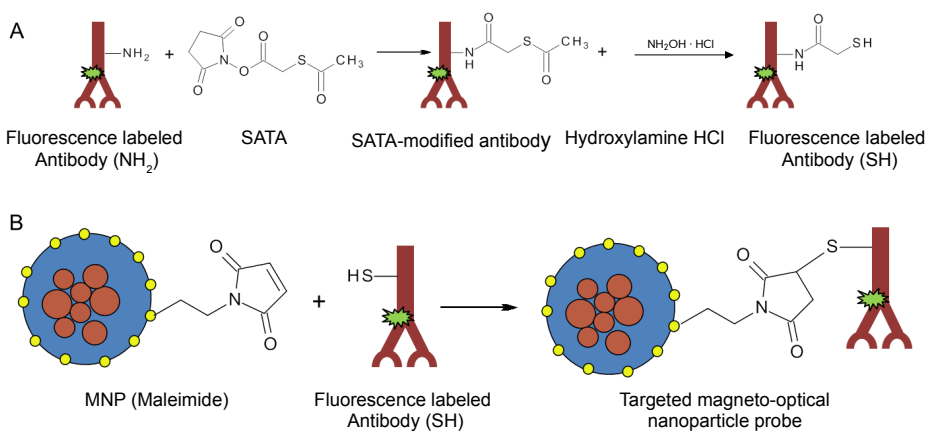


Figure 1: Reaction scheme of antibody-MNP conjugation using maleimide chemistry

MNPs are an interesting tool for labelling of stem/ progenitor cells for their homing and tracking by MRI or MPI in the field of regenerative medicine. Additional fluorescence labelling of the particles allows the visualization of the MNPs in the cell compartments to provide insight into the mechanism of particle-cell interaction. Kasten et al. labelled adipose tissue-derived progenitor cells with plain nanomag®-CLD-redF or BNF-Starch-redF particles for MR tracking. Poly-L-lysine (PLL) was used as transfection agent known for promoting cell adhesion. No co-localization between nanoparticles and mitochondria or nuclei was found. Both nanoparticle types appeared to be associated with lysosomes (Fig. 2) [2]. Cells were seeded onto collagen scaffolds and subcutaneously implanted into severe combined immunodeficient (SCID) mice. MRI analyses were performed visualizing nanoparticle-labelled cells using T2-weighted sequences over 28 days [3].

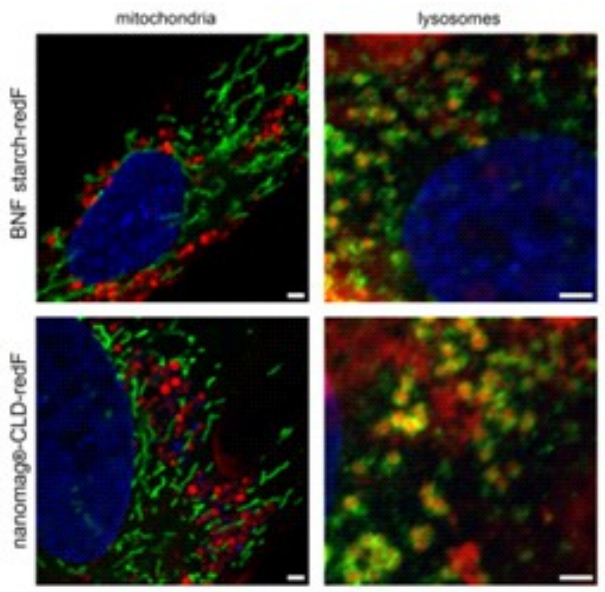
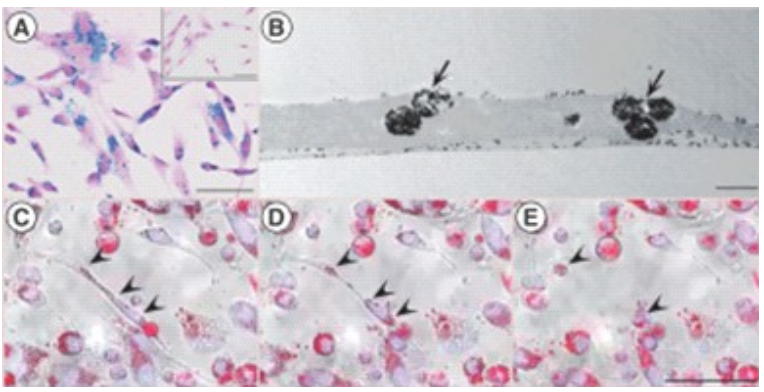


Figure 2. Intracellular localization of nanoparticles. Confocal laser scanning images of stem cells labeled with BNF-Starch-redF or nanomag®-CLD-redF and stained for mitochondria and lysosomes (both shown in green). Cell's nuclei were counterstained with Hoechst 33342 (blue).

To allow a direct labelling of stem cells without the use of any transfection agents perimag® particles with a medium positive zeta potential were developed (research name: M4A (plain), M4E (NH2), M4G (red fluorescent)). Kilian et al. analyzed the suitability of aminated perimag® (M4E) for safe human mesenchymal stem cell (hMSC) labeling and determined cell labeling maintenance in 2D and 3D culture (Fig. 3) as well as the cell tracking possibility by MPI [4].

Figure 3. Microscopic characterization of labeled cells. (A) Prussian blue staining of M4E-labeled human mesenchymal stem cells revealed successful cell–particle interaction. Nonlabeled controls were Prussian blue, negative (A, inset). M4E particles were mostly found in lysosomes (B, arrows). Live cell imaging showed fluorescent M4G particle distribution in the course of human mesenchymal stem cell division (C–E, arrowheads). (C–E) Represent overlays of transmission light and fluorescent images and indicate different time points during cell division. Scale bars: (A, inset; E): 100 µm; (B): 1000 nm.



Multi-echo susceptibility weighted imaging (SWI) in combination with optical imaging was applied to monitor the transportation of dextran-iron oxide nanoparticles (nanomag®-CLD-redF) in normal and hydrocephalus rat brains via intrathecal delivery [5]. Hydrocephalus can be experimentally induced by producing a sustained increase in cerebrospinal fluid (CSF) osmolarity. This implies that the macromolecular content in the CSF is critical in determining the ventricular volume. Krishnamurthy et al. confirmed that intraventricularly injected nanomag®-CLD-redF particles are transported into the brain tissue prior to clearance into the vascular system [5].

10.2 Visualization of MNPs at controlled apoptosis by nanoparticle rotation in dynamic magnetic fields

Zhang et al. have designed a unique dynamic magnetic field (DMF) generator that can induce rotational movements of superparamagnetic iron oxide nanoparticles (SPIONs). It was examined whether the rotational nanoparticle movement could be used for remote induction of cell death by injuring lysosomal membrane structures. For this study **micromod** has conjugated 20 nm nanomag®-CLD-redF particles with antibodies targeting the lysosomal protein marker LAMP1. Remote activation of slow rotation of LAMP1-conjugated particles significantly improved the efficacy of cellular internalization of the nanoparticles. Confocal imaging of nanoparticle location in rat insulinoma cells demonstrated that the efficacy of cellular internalization of the particles was significantly improved and that cell apoptosis can be controlled by nanoparticle rotation via dynamic magnetic fields [6].

10.3 Nanoparticle-assisted optical tethering of endosomes (NOTE)

Chowdary et al. have developed a microfluidic platform that allows to visualize retrograde axonal endosome transport using ligand-bound quantum dots and oblique illumination imaging in microfluidic neuron cultures. This microfluidic platform was refined to study a novel phenomenon termed nanoparticle-assisted optical tethering of endosomes (NOTE) that made it possible to study the collective function of dyneins on retrograde axonal endosomes in live neurons [7]. To answer the question if the velocity of retrograde endosomes in axons reflects the number of dyneins on the endosomes, the retrograde axonal transport of Alexa-wheat germ agglutinin (WGA) (~2 nm), WGA-coated quantum dots (QDs, ~15 nm) and WGA-coated fluorescent iron oxide nanoparticles of different sizes (INPs, 30, 50, 100 nm) were analysed. Streptavidin coated 100 nm BNF-Starch-redF particles were conjugated with biotin-WGA as largest nanoparticles as model particles for this study [7].

References

[1] Rimkus, G., et al., *mVCAM-1 specific iron oxide nanoparticles based probes for multimodal imaging purposes.* Biomed Tech, 2012. **57**: p. 77-80.

[2] Kasten, A., et al., *Comparative In Vitro Study on Magnetic Iron Oxide Nanoparticles for MRI Tracking of Adipose Tissue-Derived Progenitor Cells.* PloS one, 2014. **9**(9): p. e108055.

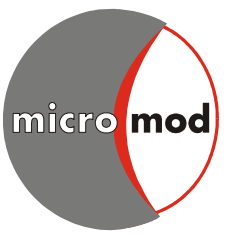
[3] Kasten, A., et al., *Tracking of adipose tissue-derived progenitor cells using two magnetic nanoparticle types.* Journal of Magnetism and Magnetic Materials, 2015. **380**: p. 34-38.

[4] Kilian, T., et al., *Stem cell labeling with iron oxide nanoparticles: impact of 3D culture on cell labeling maintenance.* Nanomedicine, 2016. **11**(15): p. 1957-1970.

[5] Krishnamurthy, S., et al., *SWI monitoring iron tagged dextran transportation in normal and hydrocephalus rat brains via intrathecal delivery.* Proc. Intl. Soc. Mag. Reson. Med., 2015. **23**: p. 0237.

[6] Zhang, E., et al., *Dynamic Magnetic Fields Remote-Control Apoptosis via Nanoparticle Rotation.* ACS Nano, 2014. **8(4):3192-201**(8(4)): p. 3192-201.

[7] Chowdary, P.D., et al., *Nanoparticle-assisted optical tethering of endosomes reveals the cooperative function of dyneins in retrograde axonal transport.* Scientific Reports, 2015. **5**: p. 18059.



Editor:
micromod Partikeltechnologie GmbH

Registergericht: Amtsgericht Rostock HRB 5837
Steuernummer: 4079/114/03352
Ust-Id Nr. (Vat No.): DE167349493

Compilation date - May the 10th, 2017
micromod Partikeltechnologie GmbH

www.micromod.de