Controlling the interaction of magnetic nanoparticles with human cells

M. Schwalbe, M. Vetterlein, C. Jörke, K. Pachmann, K. Höffken, J.H. Clement

Klinik für Innere Medizin II, Friedrich-Schiller-Universität Jena, Erlanger Allee 101, 07740 Jena;

There are several approaches to treat primary tumors or metastases by hyperthermia or drug targeting using magnetic nanoparticles. We focus on the tumor cells circulating in the peripheral blood. Our vision is to eliminate these cells quantitatively, because these disseminated tumor cells are suspected to be potential start points of metastasis formation at distant sites.

To achieve a more specific enrichment of distinct cell types magnetic nanoparticles are usually coated with biocompatible shells of organic and/or inorganic nature. These shells might then be used to attach other molecules in order to direct the nanoparticles towards specific destinations. A suitable material for this purpose is the polysaccharide dextran, which can be further functionalized by introduction of reactive groups like carboxymethyl residues.

In the presented work we focus on the control and optimization of the conditions which are suitable for effective interaction of magnetic nanoparticles and human cells. Using carboxymethyl dextran (CMD) coated magnetic nanoparticles we analyzed tumor cell lines and leukocytes from peripheral blood as test systems.

First, the duration of nanoparticle-cell interaction and the temperature were changed. We could show that after 4 to 12 minutes of incubation a significantly higher amount of the tumor cells was labeled with magnetic nanoparticles in comparison to leukocytes [1]. Reduction of the incubation temperature from 37 °C to 4 °C abolished the uptake of nanoparticles completely. In contrast, 24 °C or 40 °C did not alter the interaction kinetics of tumor cells as well as leukocytes.

Next, the pH and the osmolality were varied. Within a pH range from 6.8 to 7.5 the cell-type specific uptake of magnetic nanoparticles was not affected. In contrast, an increase of the osmolality from 0.24 to 0.56 osmol/kg reduced the labeling of the tumor cells by 50% whereas the amount of magnetically labeled leukocytes was reduced by 90%.

The supplementation of the incubation medium with various saccharides exerted different effects. The polysaccharide carboxymethyl dextrane increased the uptake of magnetic nanoparticles in a concentration-dependant manner, which might be due to the fact, that CM dextran is attractive for cellular uptake. Polysucrose and Methylcellulose did not affect the nanoparticle-cell interaction. The monosaccaride glucose increased the uptake of nanoparticles, especially in leukocytes, whereas fucose and mannose had no additive effect.

In concert with our previous observation that human plasma is able to modulate the nanoparticle-cell interaction in a concentration-dependant manner [2], we conclude, that the precise modulation of the incubation conditions allows a highly specific control of the interaction of magnetic nanoparticles with human cells.

This work was supported by DFG priority program 1104, grant CL 202/1-2

[1] Clement, J.H., Schwalbe, M., Buske, N., Schnabelrauch, M., Görnert, P., Kliche, K.O., Pachmann, K., Weitschies, W., Höffken, K. (2006) J. Cancer Res. Clin. Oncol.: in press

[2] Schwalbe, M., Jörke, C., Buske, N., Höffken, K., Pachmann, K., Clement, J.H. (2005) J. Magn. Magn. Mater. 293: 433-437