Self-Assembled Magnetic Gene Delivery Vectors: Physico-chemical and biophysical aspects

Mykhaylyk, O.[1]

[1] *Institute of Experimental Oncology and Therapy Research, Klinikum rechts der Isar, Technische Universität München, Ismaninger Str. 22, 81675 Munich, Germany*

To localize delivery of active agents, predominantly nucleic acids or viral particles, we associated them with suitable magnetic nanoparticles (MNPs) and accumulate them at target sites with gradient magnetic fields. Applied to nucleic acid delivery, this concept of magnetic drug targeting is known as Magnetofection [1]. We have exploited magnetofection to generate an integrated method of magnetic cell separation and genetic modification that we called Magselectofection, and to boost the efficacy of oncolytic adenovirus. MNPs of the core-shell type stabilized and "decorated" with self-assembled layers of surfactants and charged polymers were self-assembled with viral particles (vectors) into magnetic vectors [2-4]. We have found the optimal magnetic vector formulations for plasmid, siRNA and viral vector delivery that are stable in concentrated serum and cerebrospinal fluid. Electron and atomic force microscopy data showed structurally intact viruses surrounded or decorated by multiple MNPs. We have also developed and implemented a simple method for evaluating magnetophoretic mobility of the complexes, magnetic microbubbles or magnetically labelled cells [4,5] in defined magnetic fields to experimentally estimate the kinetics of magnetic sedimentation for any new magnetic complex. Optimized formulations of the magnetic viral vectors demonstrate significantly increased vector internalization, magnetotransduce numerous cell lines and primary cells with high efficiency and possess magnetic responsiveness promising to allow trapping of the vectors at the target sites and to achieve localized gene delivery at relatively low vector dosage. Importantly, analysis of the effect against internalized virus dose suggests that optimized decoration with MNPs dose not inhibit inherent virus infectivity. [1] C. Plank et al. Adv. Drug. Deliv. Rev. 63, 1300 (2011). [2] N. Tresilwised et al. Biomaterials 33, 256 (2012). [3] N. Tresilwised et al. Mol. Pharm. 7, 1069 (2010). [4] O. Mykhaylyk et al. Methods Mol. Biol. 487, 111 (2009). [5] O. Mykhaylyk et al. Curr. Opin. Mol. Ther. 10, 493 (2008).