P16: Superparamagnetic iron oxide nanoparticles functionalized by peptide nucleic acids

M. Galli [a], A. Guerrini [b], S. Cauteruccio [a], P. Thakare [a], D. Dova [a], F. Orsini [c], P. Arosio [c], C. Carrara [a], C. Sangregorio [d, e], A. Lascialfari [c,e], D. Maggioni [a, e,*], E. Licandro [a, e]

[a] *Dip. di Chimica, Univ. degli Studi di Milano, Via Golgi 19, 20133 Milano, Italy.*
[b] *LA.M.M. c/o Dip. di Chimica, Univ. degli Studi di Firenze, Via della Lastruccia 3, 50019 Sesto F.no (FI), Italy*
[c] *Dip. di Fisica, Univ. degli Studi di Milano, Via Celoria 20, 20133 Milano, Italy*
[d] *ICCOM – C.N.R., via Madonna del Piano 10, 50019 Sesto F.no (FI), Italy*
[e] *Consorzio INSTM, via G. Giusti 9, 50121, Firenze, Italy*
[*] *daniela.maggioni@unimi.it*

The dysregulation of microRNAs (miRNAs) has been implicated in a variety of pathologies, such as inflammatory and autoimmune diseases, neurological disorders, as well as several types of cancer. Anti-miRNA platforms highly effective in in-vitro cell assays have been reported, but translation to the clinic is hampered by poor in-vivo stability of nucleic acids and ineffective uptake of nucleic acids by target cells. This study aims to overcome these obstacles by designing, producing and testing new miRNA targeting materials constituted by Peptide Nucleic Acids (PNAs, synthetic mimics of natural DNA and RNA) [1]. Indeed, PNAs conjugate the effectiveness of the natural nucleic acids targeting with chemical/thermal stability and resistance to enzymatic biodegradation.
A novel efficient method has been developed for covalently linking Peptide Nucleic Acid (PNA) oligomers and superparamagnetic iron oxide nanoparticles (SPION), to produce water soluble hybrid nanomaterials that can act as MRI contrast agents, as hyperthermia promoters and as PNA carriers. The multistep procedure involveed: (i) preparation of oleate-stabilized SPION by using the thermal decomposition method, to control the size of the magnetic core; (ii) exchange of the oleate layer by dimercaptosuccinic acid (DMSA), to impart water solubility and to provide functional groups for PNA grafting; (iii) functionalization of a PNA oligomer with a terminal maleimide moiety, to allow SPION–PNA conjugation by thiol-maleimide Michael addition reaction, exploiting the SH groups of DMSA on the SPION surface. The method was tested using a model PNA decamer containing all four nucleobases (–CTAGATCACT–). SPION–PNA conjugation by SH addition was found more efficient than conjugation through amide bond between the COOH groups of DMSA and the terminal NH_2 groups of PNA. Elemental analysis, UV-Vis and IR spectra, ζ-potential, TEM, AFM, relaxivity and magnetic measurements of the SPION used for PNA binding is reported, and compared to the one relative to the SPION–PNA conjugate.

Reference

[1] P. E. Nielsen, M. Egholm, R. H. Berg, O. Buchardt, *Science* **1991,** *254,* 1497;