Fe_3O_4@PNA nanoconjugates for miRNA dysregulation

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In the past decade, the non-coding microRNAs (miRNA) have emerged as a novel class of potent regulatory molecules that are found in a wide variety of organisms, able to modulate gene expression at the post-transcriptional level [1]. They are responsible for regulating many biological processes including differentiation, apoptosis, proliferation and cell-fate determination. 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 [2]. 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 in-vivo new miRNA targeting materials constituted by Peptide Nucleic Acids (PNAs, synthetic mimics of natural DNA and RNA, see Figure 1) [3]. Indeed, PNAs conjugate the effectiveness of the natural nucleic acids targeting with chemical/thermal stability and resistance to enzymatic biodegradation. In order to follow the fate of PNA and improve its solubility and permeability to cells, PNA has been linked to superparamagnetic iron oxide nanoparticles (SPIONs), affording new nanocomposites which will be exploited both as contrast agents for magnetic resonance imaging (MRI) and as sources of local overheating through the application of an alternating magnetic filed (Magnetic Fluid Hyperthermia, MFH).
SPIONs have been prepared by a slightly modified thermal decomposition method [4] (Scheme 1) in order to optimize in particular the hyperthermia effectiveness [5].
Then, the oleate layer has been replaced by dimercaptosuccinic acid (DMSA) which is a hydrophilic bifunctional small molecule, able to efficiently substitute the oleate capping agent (Scheme 1) [6]. This way both COOH and SH groups can be exploited to link PNA to the NP surface.

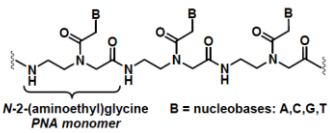
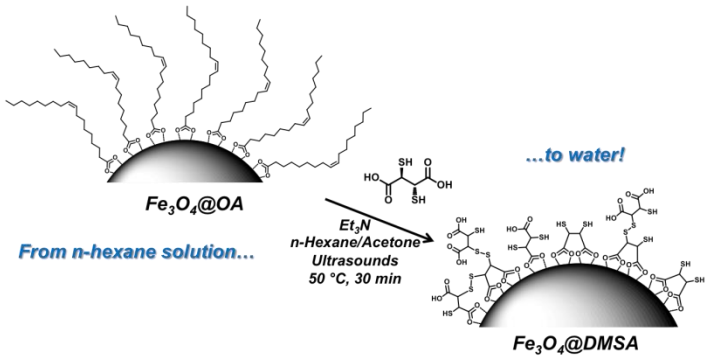


Figure 1. A peptide nucleic acid repeating fragment



Scheme 1: Exchanging of the stabilizing shell of oleic acid with the meso-*2,3*-dimercaptosuccinc acid (DMSA).

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