Nucleic Acid-based Engineering of Iron Oxide Nanoparticles for Magnetic Hyperthermia Applications

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"Smart" multifunctional nanomaterials combine multiple tasks into a single nanoplatform and can be used as theranostic nanoprobes for simultaneous diagnostics and therapy.[1] Superparamagnetic iron oxide nanoparticles (SPIONs) are particularly interesting for this purpose, due to their ability to generate heat when exposed to alternating magnetic fields (magnetic hyperthermia). Hyperthermia using SPIONs is nowadays applied as adjuvant therapy in the treatment of cancer and is receiving increasing attention for hyperthermia-mediated drug delivery. Recently in our group we have designed a "molecular thermometer" based on SPIONs functionalized with complementary DNA strands of different lengths.[2] The heat generated by the DNA-SPIONs upon application of the magnetic field promoted the denaturation of the complementary nucleotides and enabled the accurate mapping of the temperature profile at different distances from the surface of the nanoparticle.

Here we report the use of DNA and peptide nucleic acids (PNAs) for the engineering of multifunctional iron oxide nanoparticles for hyperthermia-mediated drug delivery. Firstly, DNA and PNA (different ratios) were covalently conjugated to the surface of 12 nm SPIONs coated with an amphiphilic polymer bearing carboxyl groups, using standard peptide chemistry. An indirect method was used to assess the extent of functionalization, based on the hybridization with a complementary DNA strand bearing carboxyfluorescein (FAM). The amount of FAM-DNA released upon dehybridization was quantified by fluorescence spectroscopy. Our preliminary results indicate that the use of PNA increases the efficiency of the functionalization when compared to only DNA. We are currently working on the multifunctionalization of these DNA/PNA-SPIONs with complementary DNA chains bearing folic acid as tumoral marker and Doxorubicin as chemotherapeutic drug (*oligo-zipping strategy*). The release of Doxorubicin will be triggered by magnetic hyperthermia when the temperature in the vicinity of the nanoparticle will be higher than the melting temperature of the oligonucleotide (*oligo-unzipping*).

1 (a) Fratila, R. M.; Mitchell, S. G.; del Pino, P.; Grazu, V.; de la Fuente, J. M. *Langmuir* **2014**, DOI: 10.1021/la5015658. (b) Lee, D.-E.; Koo, H.; Sun, I.-C.; Ryu, J. H.; Kim, K.; Kwon, I. C. *Chem. Soc. Rev.* **2012**, *41*, 2656.

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