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Magnetic iron oxide nanoparticles with hyperthermia-induced drug release ability by using click chemistry

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We report a method for the production of novel functional iron oxide magnetic nanoparticles (IONPs) showing unprecedented, active control over drug release using hyperthermia effects. The preparation of this new class of functional IONPs relies on a versatile methodology that employs a combination of orthogonal click reactions: copper-catalyzed azide-alkyne cycloaddition (CuAAC) and thermoreversible Diels-Alder (DA) reaction. We designed a versatile multifunctional ligand that contains a phosphonic acid group which strongly binds to the iron oxide surface of IONPs, and two orthogonal clickable groups: an alkyne moiety for installing an azide end-functionalized hydrophilic polymer through CuAAC to impart aqueous dispersability/stability, antifouling property, and biocompatibility to the IONPs, and a furan ring that serves as a thermoreversible linker for a biologically active molecule (probe or drug) through reversible DA reaction: This synthetic design allows us to control the release of the conjugated drug whilst maintaining the colloidal stability and magnetic properties of the IONPs. Upon alternating magnetic field (AMF) exposure, the retro-DA reaction enables the release of the conjugated drug without any significant heating of the medium. Our results thus demonstrate that sufficient energy can be brought in close proximity to the cycloadduct to initiate the retro-DA reaction without more delocalized overheating. This method has the potential to improve hyperthermia therapies by expanding the range of polymers and molecules (drugs, dyes, etc) that can be used. This class of functional IONPs may become important tools for preparing the next generation of controlled-release devices and nanomedicines for *in vitro* and *in vivo* applications.

Biography

Laurent Fontaine has completed his PhD and Habilitation from Université du Maine (Le Mans, France). He is the head of the "Methodology and Polymer Synthesis" group at Institut des Molecules et Matériaux du Mans, a CNRS-Université du Maine joint laboratory. He has published more than 75 papers in reputed international journals.

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