

Synthesis of water soluble fluorinated gold nanoparticles and *in vivo* ^{19}F MRS.

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Organic fluorine is not naturally occurring in human biological media for which it constitutes an interesting label or reporter. The absence of background signal allows for fluorinated species to be studied unequivocally and quantitatively by magnetic resonance (MR) related techniques [1,2], as long as sufficient local fluorine concentration is available. In this sense, ^{19}F Magnetic Resonance Imaging (^{19}F MRI) based on imaging exogenous fluorinated probes, is a versatile diagnosis technique complementary to conventional ^1H MRI. However, the applicability of ^{19}F MRI is currently limited by the detection sensitivity of the MRI technique and the need for high local concentration of fluorine, for which the design of highly fluorinated probes is an active field of research. Despite its interesting features, the prospects of fluorine in nanoparticle (NP) design for nanomedicine are somehow limited by several reasons, namely, (i) the high hydrophobicity of fluorinated molecules, (ii) the sometimes challenging synthesis of those, (iii) the need of high local concentration of fluorine for magnetic resonance (MR) applications and (iv) the usually poor relaxation times due to NP structural design. Thus, examples of fluorinated NPs composed of a metal core and fluorinated ligands that are water soluble are scarce in the literature. Herein, two methodologies are presented for their preparation: (i) a direct synthesis method using ad hoc prepared fluorinated ligands [1-3] and (ii) a fluorine labelling strategy based on the conjugation of custom made small fluorinated building blocks, obtained by simple synthetic transformations, with carboxylated gold NPs through a convenient phase transfer process. For the latter method, the synthesis of four fluorinated building blocks with different chemical shift in ^{19}F

nuclear magnetic resonance and varied functionalities is presented, along with their conjugation onto NPs. Following these two synthetic methodologies, fluorinated NPs of small core size with very high (above the average) transverse relaxation times (T_2) ranging from 518 to 1030 ms and fluorine atoms per NP of up to 1260 atoms are obtained. Such T_2 and fluorine content values are challenging to achieve in fluorinated probes and make these NPs potential candidates for ^{19}F magnetic resonance related applications. Finally, non-targeted fluorinated NPs were probed *in vivo* by ^{19}F magnetic resonance spectroscopy (^{19}F MRS) in mice. NPs were clearly detected both at 1 hour and 2 hours after being injected and their fate was studied by analysing the gold content in tissues by ICP-MS.

References

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Figures

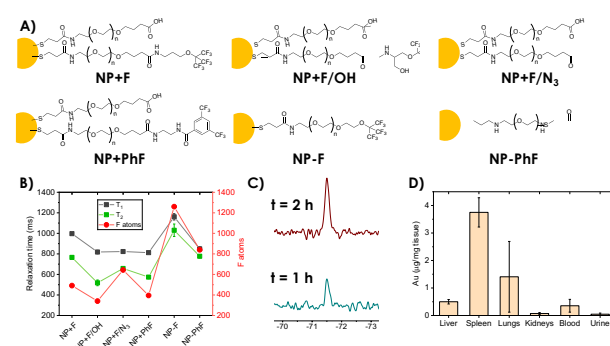


Figure 1: A) Fluorinated NPs prepared. B) Plot of relaxation times and number of fluorine atoms. C) *in vivo* ^{19}F MRS at 1 and 2 hours. D) ICP-MS analysis of extracted tissues and organs.