PhD POSITION OFFER ASSOCIATED TO PROJECT "IMPACT"

Position

1. Project Title/ Job Position title: Hybrid nanoparticles for enhanced magnetic resonance imaging

2. Research project: Magnetic resonance imaging (MRI) is a non-invasive and non-radioactive technique for clinical diagnostic that provides information on the anatomy, function and metabolism of tissues. Unfortunately, the intrinsic contrast associated to a pathologic condition is often too limited to enable a sensitive and accurate diagnosis. For that reason, there is an increased use of MRI contrast agents (CA) that improve image resolution based on their selective accumulation in the Region Of Interest (ROI). Based on their relaxation activity, these CAs are classified as positive (T_1-weighted) or negative (T_2-weighted) image contrast promoters. At this point, the acquisition of MRI weighted in T_1 and T_2 could improve the safety of diagnosis and cross-validate the possible false-positive information. T_1-T_2 dual-modal strategy can provide complementary T_1 and T_2 MRI images, making it possible to isolate artifact signals from the contrast agents in the ROI. Our target in this research, is to develop novel nanoparticles presenting unique characteristics that allow exploiting the T_1-T_2 dual-mode CA concept.

3. Research Group: "Nanomedicine" is a multidisciplinary group in the ITQ. The general objective of the group is to develop novel therapeutic and diagnostic platforms based in nanomaterials and molecular recognition systems. The group's field of action involves: 1) Activities related to the development of nanomedicines with molecular recognition capabilities for the delivery and selective controlled release of therapeutic agents over pathology affected cells or tissues, in order to achieve efficient treatment with minimum side effects; 2) Activities related to the study of interactions between pharmacological platforms and biological systems, as well as the study of cell internalization mechanisms; and 3) Activities related to the development of imaging and diagnostic nanosystems for the early detection of diseases, both *in vitro* and *in vivo*.

4. Job position description: This job position deals with the development of novel, biocompatible, hybrid nanoparticles able to improve both positive and negative contrast T_1- and T_2- weighted magnetic resonance (MR) images, and its biological validation. The nanoparticles will be made of an internal metallic core of superparamagnetic iron oxide nanoparticles (SPIONs), and an external coating made of a ^{19}F-containing covalent organic framework (^{19}F-COF). This hybrid shows a high biosafety profile (e.g., SPIONs are approved for clinical use, and COF are organic fully biodegradable moieties), and has strong ability to incorporate organic

molecules on surface with variable functionality (e.g., therapeutic compounds, targeting molecules and imaging agents), displaying great potential for further clinical application. The resulting SPION@^{19}F-COF nanoparticles combines T_1- and T_2- magnetic centers closely packed, which is expected to promote a magnetic synergistic effect, resulting in significant improvement of longitudinal and transversal relaxivity. Furthermore, ^{19}F-MRI can be also used to quantify the number of cells in the Region of Interests, allowing excellent resolution of MR images. The position involves the training in synthesis protocols for the development of metallic nanoparticles, COF structures and the assembled hybrid materials, and its subsequent characterization by chemical, spectroscopic and magnetic techniques, and electronic microscopy. Subsequently, magnetic resonance capabilities of as-prepared contrast agents (CAs) will be monitored by obtaining phantoms in a microMRI facility. Finally, for the biological validation the candidate will receive specific training in *in vitro* testing (cytotoxicity, flow cytometry, confocal microscopy) and *in vivo* testing (mouse and rats models) models. Comparison of imaging performance of the obtained CAs will be carried out over commercial products currently at clinical used.

5. Period: 3 years (estimated starting at 2024-01-01).

Group Leader

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