Scientific report on the implementation of the project
PN-III-P1-1.1-PD-2016-1642 (contract no. 110／2018) entitled *Development of a multifunctional radiolabelled hybrid magnetic nanoparticle agent for dual-modality (SPECT and MRI) medical imaging*
(Acronim: NANOIMAG)" Phase 1-2018

Phase 1- Investigate multifunctional hybrid magnetic nanoparticles structure-property relationship

Related delivered activities:

Activity 1.1 - Design and optimize multifunctional hybrid magnetic nanoparticles preparation

Activity 1.2 - Evaluation of the experimental synthesis parameters. Selection of the optimum formulation

Activity 1.3 - Investigate the nanoparticles characteristics

Over the last decade, the field of molecular imaging in living systems has expanded tremendously.[1] In general, molecular imaging modalities include for example, magnetic resonance imaging (MRI), optical bioluminescence, optical fluorescence, targeted ultrasound, single-photon emission computed tomography (SPECT), and positron emission tomography (PET).[2] Although all these molecular imaging modalities are available in the clinic today, there is not a single modality that is perfect and sufficient to obtain all necessary information for a particular question.[3]

An ideal nanoparticle imaging probe for next-generation, multifunctional radiotracer should include the following functionalities: easy administration; excellent *in vivo* and radiolabeling stability;[4] biocompatibility;[5] selectivity; sensitivity;[6] ability to observe its accumulation in real-time and to monitor disease progression;[7] biodegradable or rapidly excreted after the imaging is complete; minimal to no side effects, and cost-effectiveness, while producing a strong imaging signal.[8]

In this context, the main objective of this project is to design a new multifunctional radiolabeled hybrid magnetic nanotracer as dual-modality SPECT and MRI imaging probe.

During the phase 1-2018, 3 types of hybrid nanoparticles were prepared, namely:

- magnetite nanoparticles obtained by coprecipitation of iron ions, subsequently coated with 3-aminopropyl triethoxysilane (batch M3);
- magnetite nanoparticles obtained by partial oxidation of iron ions, subsequently coated with 3-aminopropyl triethoxysilane (batch MO12);
- magnetite nanoparticles obtained by partial oxidation of iron ions in tetraethyl orthosilicate and 3-aminopropyl triethoxysilane medium (batch MOS 3);

The proposed strategy for achieving dual-modality candidate involved an innovative joint partial oxidation-condensation modified method. The hybrid magnetic nanoparticles were prepared using magnetic core (iron oxide), multifunctional silica shell chain (tetraethyl orthosilicate and 3- aminopropyltriethoxysilane) using very simple methodology (Figure 1).

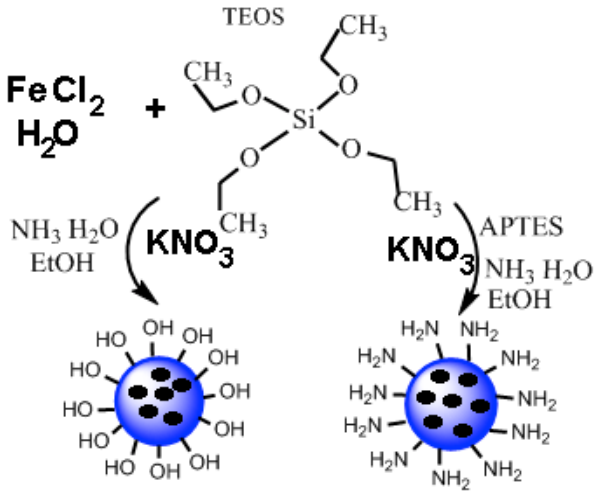

Figure 1. Reaction method

Conclusions phase 1

The deliverables associated with each activity that were obtained:

- 3 types of multifunctional hybrid magnetic nanoparticle optimized for *in vitro* and *in vivo* studies;
- characterization data for raw and multifunctional hybrid magnetic nanoparticles:
  - structural composition determined by FTIR-ATR where all the related peaks for Fe_3O_4, silica and amino moieties were found;
  - size distribution, homogeneity and zeta potential measured by DLS: The hydrodynamic diameters and polydispersity index of the nanoparticles were found to be in the range of 80-130 nm with a PDI in the range of 0.7-0.9;

  - saturation magnetization measured on magnetometer: in the range of 65-88 emu/g;
  - X-ray diffraction patterns: reveals the formation of magnetite with well-defined crystallinity;
  - the morphology and structural organization evaluated by TEM: nearly spherical in shape with an average diameter in the range of 14- 120 nm;
- 1 Radiopharmaceutical training Course at University of Helsinki, Tracers in Molecular Imaging group, Department of Chemistry, Kumpula Science Campus, Helsinki, Finland;
- Course on Radiochemistry- from basic to pre-clinical studies by Gianina Dodi at Advanced Research and Development Center for Experimental Medicine (CEMEX), Iasi, Romania.
- 1 paper submitted for publication: Chitin: revival of a long-lost polysaccharide, Authors: Gianina Dodi, Vera Balan, Dan Draganescu, Bogdan Ionel Tamba, Cristina Mariana Uritu, Under review at Carbohydrate Polymers;
- 1 activity report (WP1)

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