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Synthesis and study of multifunctional hybrid nanoparticles

for X-rays based imaging and treatment.

Keywords : Nanoparticles, functionalization, organic moieties, solvothermal, spectroscopy.

Cancer is one of the major societal issues of the century and accounts for the second cause of death in Europe. Even if several strategies of treatments exist, the conditions of life of the patient during and after the treatment are deteriorated by side effects of therapies such as radiotherapy for example (use of X rays of High energy). The possibility to use new treatments such as X-Ray activated Photodynamic Therapy (XPDT) is therefore raising a great interest. PDT alone is a very efficient strategy for cancer treatment but unfortunately, the strong absorption of light by tissues limits its use to rather superficial tumors. In that context X-PDT appears as a new technology involving the same mechanisms but spreading the potential of treatment.

The principle of XPDT is to irradiate with low energy X-Rays hybrid nanoprobes consisting in an inorganic core functionalized with organic moieties (Photosensitizers-PS). Upon excitation the inorganic particle will emits light (scintillation) which will be absorbed by the PS. The latter will reach an excited state, making it able to react with surrounding oxygen and leading to the production of reactive oxygen species able to kill tumor cells. **Figure 1** illustrates the principle of this technique.

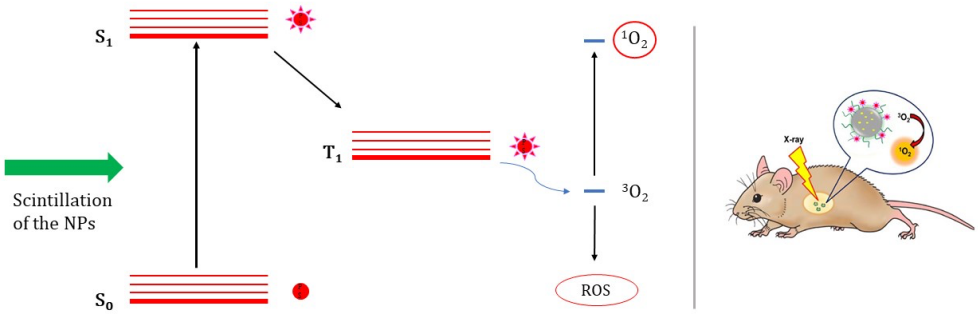

Figure 1. XPDT principle. On the left PS is excited by the scintillation of the particle, intersystem crossing allows conversion of the singlet state into triplet state which is able to generate ROS or singlet oxygen. On the right, a complex nanosystem is irradiated by X-Ray to treat deep-seated tumor by XPDT.

Based on the strong experience in the laboratory concerning the design of nanoparticles in suspension, their functionalization with various organic moieties and their analysis, the thesis will be divided into two main parts:

- The synthesis of scintillating inorganic nanoparticles (Fluorides, phosphates, oxides for example) by different production processes (solvothermal, coprecipitation, thermolysis…).
- The functionalization of the obtained nanoparticles through grafting of organic moieties on their surface. Theses reactions will take place in solution, with specific molecules or macromolecules to ensure biocompability on one side and generation of singlet oxygen for XPDT treatment on the other side.

The different systems will be characterized by several techniques such as FT-IR, DLS, XRD, Microscopy (TEM and SEM) but also by spectroscopic analysis (UV/Visible, fluorescence). Characterizations in cellulo and in vivo could also be done during this PhD. **Figure 2** illustrates some of the characterizations that have been done on previous systems.

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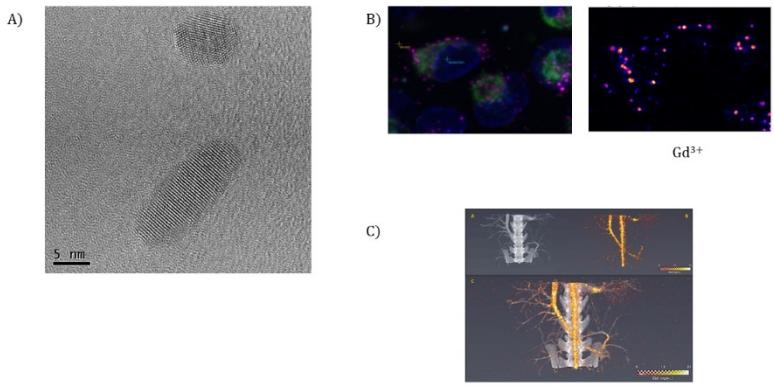

Figure 2. A) HR-TEM imaging of nanoparticles of $Gd_{1-x}Tb_xF_3$; B) Cellular uptake of $Gd_{1-x}Tb_xF_3$ NPs, Gadolinium is quantified inside the cell ; C) In vivo imaging of a abdomen of a rat, on the upper left standard CT imaging, on the upper right K-edge imaging which allow to quantify Gd^{3+} in vivo.

As this project involves strong partnership with radiologists, biologists and physicists, the PhD student will have the opportunity to make experiment at CERMEP (Hospices Civiles de Lyon) on clinical scanner with radiologist and engineer specialized in biomedical imaging.

The candidate will be a chemist with great interest in colloidal chemistry, organic synthesis and interface chemistry/surface functionalization. He/She will also have some experience in all basic characterization techniques (infrared and UV/Visible spectroscopy, thermal analysis, X-ray diffraction, DLS...).

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