Development of hybrid bio-materials for theranostic applications

Regarding cancer treatment, the use of nanosized carriers seems appealing owing to their capacity to encapsulate drugs within their structure.

Mesoporous silica nanoparticles have been widely applied as carriers for cancer treatment. Among the different types of stimuli-responsive drug delivery systems, those sensitive to redox stimuli have attracted much attention.

Their relevance arises from the high concentration of reductive species that are found within the cells, compared to bloodstream, which leads to the drug release taking place only inside cells.

There are different types of gatekeepers that are able to open the pore entrances only upon application of reductive conditions will be introduced.

The rationale behind the use of nanoparticles (NPs) relies on the enhanced permeability and retention (EPR) effect, which promotes their passive accumulation in tumors.

In addition to this passive tumor targeting, NPs can be decorated with specific targeting ligands able to achieve selective recognition of cancer cells and their subcellular organelles, thereby releasing high concentration of drugs within such cells.

MSNs offer excellent physicochemical properties, namely a network of hollow cavities with tunable structures and narrow pore size distributions.

The open porous structure allows the loading of drugs by simple diffusion and, likewise, such compounds can easily diffuse out of the pores.

The production of reactive oxygen species (ROS) by aerobic cells is essential, as they mediate crucial intracellular signaling pathways and are vital for cell survival. However, excessive production of ROS, as it happens under conditions of cell injury, leads to cell damage and death. To overcome this, cells produce ROS scavengers (antioxidants). GSH plays a vital role in the maintenance of appropriate levels of ROS within cells. It is the most important non-enzymatic antioxidant in cells and GSH/GSSH is the major redox couple in animal cells.

Though it is true that tumor tissues present higher concentrations of GSH compared to normal tissues and would therefore constitute a differential feature that could be exploited to deliver drugs specifically at the extracellular tumoral matrix. It could be achieve using gatekeepers that present redox-cleavable bonds throughout their backbone.

In particular, we will focus on the synthesis and characterization of silica nanoparticles, followed by the loading of different type of therapeutic drugs. After the loading, NPs will be covered using specific coatings and then will be interesting to study drug release in function of the variation of environmental potential (due to the presence of GSH).

In the final part of the project should be interesting to conduce biological assay.