Gold Nanorods synthesis and scale-up for photoacoustic theranostic nanomedicine approach against bladder cancer

Despite years of awareness, as of today, there is no screening program for the early detection of bladder cancer (BCa). The unmet clinical needs in the management of BCa are the prevention of tumor onset, relapse and progression, and therapy of the aggressive bladder carcinoma in situ (Cis), requiring frequent and endless follow-up and weekly treatments, with a consequent poor quality of life and the highest cost per patient among all cancers. In this european funded project we propose an advanced transformative technology combining a novel high-resolution photoacoustic imaging on the bladder instilled with targeted plasmonic gold nanosensors.
Activities in charge to the fellowship holder: the synthesis and characterization of functionalized Gold nanorods (GNRs) for photoacoustic imaging applications, scaling up to 30 litres the whole process including GNRs functionalization with specific biomolecules to target bladder cancer. Shipment to the San Raffaele Hospital (Milano) where in vivo experiments will be carried out.

In detail the following activities are forecasted
- Nuclear magnetic resonance (NMR) 1H- and 13C- will be used for structural characterization and to check the good success of the chemical purity and coupling reaction.
- Structure and presence of organic backbone and various functional groups also in the final nanocarriers will be confirmed with a FT-IR analysis and CHN-elemental analysis.
- All the nanocarriers will be largely investigated especially in size, stability in buffered solutions, and stability in time: DLS (dynamic light scattering) will be used to determine size together with the PDI (polydispersity index).
- Morphology of nanoparticles will be explore using combined techniques like AFM (atomic force microscopy) and SEM (scanning electron microscopy) including an EDS (Energy- dispersive X-ray spectroscopy) probe to check the atomic composition, part of this will be carried out in collaboration.
- Uv-Vis (ultraviolet-visible spectrophotometric) analysis will be performed to check the absorption spectra and maximum wavelength of the GNRs, of the nanoparticles and to confirmed survivor of the same after the entrapment process. This technique coupled with colorimetric analytical tests can be also applied to biomolecules determination in the nanocarriers after coupling reaction.
- TGA (termo-gravimetric analysis) or DSC (differential scanning calorimetry) will be used to investigate the final composition of the metal-loaded nanoparticles in terms of ratio between metal phase and polymer one.
- At the end ICP-MS (Inductively coupled plasma mass spectrometry) or AAS (Atomic absorption spectroscopy) will be used for quantitative metal determination in the synthesized nanosystems.

Collaborations with a European/USA company to run the scale-up under GMP (Good Manufacturing Process) up to 30 L conditions is also a key step of the project.
Another important task will be the definition of the GMP regulatory requirements for the manufacturing, in collaboration with the company, and the definition of a Master Batch Record for the GMP process according to the requirements for clinical trials. The Master Batch Record will contain all information required to manufacture the product in GMP conditions. Final functionalized GNRs produced in 30L reactor under GMP requirements will be supplied to partners for effectiveness evaluation and for pre-clinical tests after having performed analytical tests for the certification ISO 21363:2020.

Final goal is to be ready for future clinical trials.

The fellowship may be renewed for additional 12+12 months.