Politecnico di Torino

CHEMICAL ENGINEERING

Multimodal innovative theranostic nanoparticles

Funded By	Dipartimento DISAT FONDAZIONE CRT CASSA DI RISPARMIO DI TORINO [P.iva/CF:06655250014]
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Context of the research activity	Research activity will focus on: Doped zinc oxide nanocrystal synthesis and functionalization, loading with anticancer drug and coating with organic biomimetic shells. Characterization of such nanoconstructs, evaluation of their behavior in terms of cellular uptake and of reaction towards external stimuli. Evaluation of the efficacy of the system as a whole in terms of in vitro cellular viability, biostability over time, imaging and therapeutic capabilities, targeting efficacy
Objectives	The PhD student will be involved in the collaborative research project MITHoS, funded by the Italian Ministry for Instruction, University and Research (MIUR) under the PRIN 2020 call. The project proposes to develop a Multimodal Innovative THeranostic nanoSystem (MITHoS) to cover the gap between the present anticancer nanomedicine tools and the clinical requirements. Despite the intense research development of nanotheranostic tools, the deal with the complexity of these multi-component nanostructures in the biological environment is still an open challenge. Nanotheranostic agents, which act at the same time for therapy and diagnosis, are based on the concerted actions of inorganic, organic and biological nanomaterials. Their effectiveness critically depends on the physico-chemical characteristics of their interfaces and on their behavior in physiological conditions and biological environment. When considering drug delivery nanosystems or therapeutic nanoparticles activated by the action of external stimuli, there is currently scarce understanding and control of the fundamental physical, chemical and biological processes that are involved. This gap of knowledge has so far impaired the translation of research efforts towards in vivo testing and finally to clinical practice. MITHoS will be a hybrid theranostic nanosystem: a stimuli responsive core-shell nanoparticle, coupled to a pharmaceutically-relevant anticancer cargo, embedded in a cell-derived lipid bilayer shell and finally equipped by targeting ligands. MITHoS will be validated against multiple myeloma, a tumor for which relapses and disease progressions are common among affected patients, owing to innate or acquired drug resistance. It will overcome the limitations of the current approaches with a bottom-up strategy: on the foundations of new,

	fundamental knowledge concerning nano/bio interfaces, we will build a finely tuned, multi-purpose and time-controlled theranostic nanotool against cancer. We will use cutting-edge molecular simulation techniques to characterize all the involved nano/bio interfaces and develop predictive computational tools for the guidance of the experimental investigations. At the same time, the experimental synthesis, characterization and test of the MITHoS nanosystem will evolve from simple, model systems to more complex nanostructures employing a variety of forefront techniques, from high resolution microscopy to X-ray and neutron scattering, until the final goal of in-vivo testing of the MITHoS system. Furthermore, novel methodologies for stimuli-responsive and remotely-controlled diagnosis and therapy will be developed. MITHoS concept will thus open new horizons in the nanomedicine field, proving how the synergic action of competences in the fields of physics, chemistry, material science, engineering, biophysics and biology can finally translate basic understanding into effective cancer treatment and overcome current barriers towards clinical translation. In particular, the role of PoliTO will focalize on the synthesis of the nanoparticles and of their functionalization, on drug uptake and release control, on cell culturing and in vitro testing of the efficacy of the MITHoS system, comprising the actuation of several external stimulation to allow therapeutic and diagnostic intervention.

Skills and competencies for the development of the activity	Experience in inorganic nanoparticle wet-chemical synthesis, preferably metal oxides; Experience in surface coating and chemical functionalization functionalization of metal oxide systems; Necessary characterization techniques: optical fluorescence and microscopy, dynamic light scattering and zeta potential measurements, UV- visible spectroscopy, Nanoparticle Tracking analysis, X-Ray diffractometry (XRD), Cytofluorimetry Optional techniques giving an added value: Electron Paramagnetic Resonance (EPR) Spectroscopy, skills in cell culture, cell viability measurements and flow cytometry.