



PhD in CHIMICA INDUSTRIALE E INGEGNERIA

CHIMICA / INDUSTRIAL CHEMISTRY AND CHEMICAL ENGINEERING - 39th cycle

THEMATIC Research Field: DEVELOPMENT OF FLUORINATED LIPID NANOPARTICLES AS THERANOSTIC DRUG DELIVERY VECTOR

Monthly net income of PhDscholarship (max 36 months)

€ 1400.0

In case of a change of the welfare rates during the three-year period, the amount could be modified.

Context of the research activity

Motivation and objectives of the research in this field

Titolo: Lipid Nanovectors for the Delivery of Nucleic Acids: a Composition-Structure-Function Relationship Approach
 Acronimo: Lancelot
 CUP: D53D23017190001
 Decreto di Concessione: Decreto Direttoriale n. 1409 del 14-09-2022

Since the successful use of mRNA vaccines against SARS-CoV-2, nucleic acid (NA) therapeutics have gained renewed and growing interest. The highly charged nature of NAs prevents efficient cell entry. The development of biocompatible vectors for NAs is a top priority in this area. Nanoformulations based on lipids and polymers are the most used and developed nonviral vectors. Of note, only lipid nanoparticles (LNPs) have been used in clinics to deliver RNAs. Even if LNPs have proven their versatility and efficacy, their cellular internalization, intracellular fate, and targeting mechanism are far from being understood and the delivery percentage into the cytosol (1-2%) is still very low. To fill this gap, we will develop fluorinated lipid nanovectors (NVs) for NA with improved therapeutic efficacy by a systematic approach, where the investigation of their internal structure as a function of lipid composition, by state-of-the-art physico-chemical techniques, will be the guiding design principle to increase their performance.



	<p>In summary, starting from these premises, the goal of this project is developing more efficient lipid NVs for NA delivery through the following three objectives:</p> <ol style="list-style-type: none"> 1) Synthesis and characterization of cationic fluorinated lipids; 2) Study the effect of fluorinated lipids on internal structure of lipid based NVs, NA encapsulation efficiency and affinity to lipid membranes; 3) Understand how the internal structure of NA loaded lipid NVs affects the interaction with membrane model systems and cells in relation to cellular internalization and NA release.
<p>Methods and techniques that will be developed and used to carry out the research</p>	<p>This research project will include the synthesis and characterization of cationic fluorinated lipids. The self-assembling behavior of these lipids will be studied in physiological conditions by dynamic light scattering (DLS) and small angle x-rays scattering. These lipids will be formulated with other lipids to obtain LNP which will be characterized in terms of colloidal stability, morphology and nucleic acid encapsulation efficiency. ¹⁹F-NMR measurements will be also performed for evaluating their imaging features (relaxation times, sensitivity, etc.). LNP interactions in the biological environments will be studied by physical chemical techniques and proteomics. LNP interactions with membrane model systems will be studied by quartz crystal microbalance (QCM-d), Raman imaging and neutron reflectometry (NR). Finally, cellular uptake and citotoxicity studies will be done by immunohistochemistry and immunofluorescence and LNP intracellular localization will be determined by confocal microscopy and flow cytometry.</p>
<p>Educational objectives</p>	<ul style="list-style-type: none"> •Learn how to design and develop drug delivery vectors •Learn how to design and develop gene delivery vectors •Learn how to characterize nano-scaled materials •Learn how to develop ¹⁹F-MRI active imaging agents •Learn the fundamental molecular and cellular techniques
<p>Job opportunities</p>	<ul style="list-style-type: none"> •R&D positions in biotech or pharmaceutical companies



	<ul style="list-style-type: none"> •Biomaterial engineer in chemical and biomedical companies •R&D positions in Drug and Gene Delivery Technology companies •Researcher in IRCCS or similar biomedical research institutes/Hospitals •Product Application Specialist in biochemical or pharmaceutical companies
Composition of the research group	2 Full Professors 3 Associated Professors 5 Assistant Professors 9 PhD Students
Name of the research directors	Prof. Francesca Baldelli Bombelli

Contacts
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Additional support - Financial aid per PhD student per year (gross amount)	
Housing - Foreign Students	--
Housing - Out-of-town residents (more than 80Km out of Milano)	--

Scholarship Increase for a period abroad	
Amount monthly	700.0 €
By number of months	6

Additional information: educational activity, teaching assistantship, computer availability, desk availability, any other information
<p>Educational activities (funding for participation in courses, summer schools, workshops and conferences) - financial aid per PhD student per year:</p> <p>1st year: around 1.900 euros per student 2nd year: around 1.900 euros per student 3rd year: around 1.900 euros per student</p> <p>Teaching assistantship: availability of funding in recognition of supporting teaching activities by the PhD student:</p> <p>There are various forms of financial of for activities of support to the teaching practice. The PhD</p>



student is encouraged to take part in these activities within the limits allowed by the regulation.