



PhD in CHIMICA INDUSTRIALE E INGEGNERIA

CHIMICA / INDUSTRIAL CHEMISTRY AND CHEMICAL ENGINEERING - 39th cycle

PNRR 117 Research Field: DEVELOPMENT OF RNA-BASED NANOVECTORS FOR MOTOR NEURON DISEASES

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

Motor neuron diseases (MNDs) are a heterogeneous group of rare disorders characterized by degeneration of motor neurons. Motor neuron loss results in progressive and irreversible loss of motor function, muscle weakness and wasting, and ultimately death, usually due to respiratory failure. The spectrum encompasses different phenotypes, depending on the involvement of upper and/or lower motor neurons. Despite variability in onset, progression, and genetics, they share common disease mechanisms, specifically, data indicate that alteration of RNA metabolism is a crucial event in MND. Non-coding RNAs, functional RNA molecules that are not translated into proteins, seem to be highly implicated in MND, since they are important regulatory molecules of many cellular processes and have been identified as the key gene expression regulators. Based on this knowledge, more extensive studies on animal models and humans are needed to better understand the involvement of non-coding RNAs in muscle or motor neuron remodeling in MND during disease progression, and their potential as molecular targets of effective treatments for these conditions. The final goal of this project is to devise fluorinated molecules able to self-assemble into highly efficient miRNA nanovectors (NVs) that specifically target motor neurons and are also traceable *in-vivo* by Fluorine-19 Magnetic Resonance Imaging (^{19}F -MRI).



<p>Methods and techniques that will be developed and used to carry out the research</p>	<p>This research project will include the development and physical chemical characterization of the NVs and the evaluation of its biological efficiency in MNs by molecular and cellular methodologies. In particular, the candidate will prepare fluorinated ionizable dendrimers able to complex miRNA forming nano-scale objects that will be characterized by dynamic light scattering (DLS), small angle X-ray scattering and electron microscopy to determine their morphology and colloidal stability (also in the biological environment). ^{19}F-NMR measurements will also be performed for evaluating their imaging features (relaxation times, sensitivity, etc.). NV cellular uptake and cytotoxicity studies will be carried out by immunohistochemistry and immunofluorescence and NV intracellular localization will be determined by confocal microscopy in motor neurons and muscle cells from animal ALS models. miRNA expression and gene targeting activity will be evaluated by PCR and qPCR. The NV formulation will be optimized through this first phase and then tested in-vivo. miRNA-based treatment in mice will be performed by intrathecal or systemic administration of the miRNA-nanovectors in control and diseased animals. Disease progression will be evaluated by 7 Tesla MRI, histological and molecular analyses of brain, spinal cord and muscle tissues.</p>
<p>Educational objectives</p>	<ul style="list-style-type: none"> • Learn how to design and develop non-viral RNA delivery vectors • Learn how to characterize nano-scale materials • Learn how to develop ^{19}F-MRI agents • Learn the fundamental molecular and cellular techniques • Learn the immunohistochemical techniques
<p>Job opportunities</p>	<ul style="list-style-type: none"> • R&D positions in biotech or pharmaceutical companies • Biomaterial specialist in chemical and biomedical companies • R&D positions in Drug and Gene Delivery Technology companies



	<ul style="list-style-type: none"> •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 6 PhD Students
Name of the research directors	Proff. Baldelli Bombelli, Metrangolo

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

National Operational Program for Research and Innovation	
Company where the candidate will attend the stage (name and brief description)	Fondazione Istituto Neurologico Carlo Besta (FINCB) IRCCS Via Giovanni Celoria, 11, 20133 Milano (MI) https://www.istituto-besta.it/
By number of months at the company	6
Institution or company where the candidate will spend the period abroad (name and brief description)	Laboratory of general biochemistry and physical pharmacy , Ghent University, Belgium Ottergemsesteenweg 460, 9000 Gent, Belgium https://www.ugent.be/fw/pharmaceutics/biochemphypharm/en
By number of months abroad	6



Additional information: educational activity, teaching assistantship, computer availability, desk availability, any other information

Confidentiality (in case of DM 117 – Agreement with company): since this is a thematic scholarship, the management of Confidential Information, Results and their publication is subordinate to the restrictions agreed upon with the funding company. Upon acceptance of the scholarship, the beneficiary must sign a specific commitment. **Individual budget for research (5.700 euro):** 1st year: 1.900 euro; 2nd year: 1.900 euro; 3rd year: 1.900 euro **Teaching assistantship (availability of funding in recognition of supporting teaching activities by the PhD student):** there are various forms of financial for activities of support to the teaching practice. The PhD student is encouraged to take part in these activities within the limits allowed by the regulation.