

TITLE

Identification of new lead compounds for drug-discovery from marine sources as a novel therapeutic opportunity to reinforce muscle function in Duchenne's muscular dystrophy (DMD)

DESCRIPTION

The research program will focus on the chemical investigation of marine natural products as an unpredicted opportunity to treat degenerative muscle disorders such as Duchenne's Muscle Disease. The research activity will be assessed in 3 milestones:

Milestone 1

- Identification of potential hits from a library of marine extracts by use of biological *in vitro* tests in murine skeletal muscle cells:

Chemical aspect:

- Library of marine natural products through fractionation of marine extracts on Solid Phase Extraction (SPE);
- Chemical characterization of the fractions by chromatographic and spectroscopic techniques (TLC, NMR, MS, LC-MS).

Biological aspect:

- Vitality cell assays (MTT, caspase-3, ROS activity etc.);
- Isolation and purification of mRNAs and proteins to measurement the effects of marine compounds on muscle cell proliferation and differentiation;
- Intracellular Ca²⁺ measurements;
- etc.

Milestone 2

- Isolation and purification of the active secondary metabolites by advanced chromatographic techniques;
- Structure elucidation of new chemical entities by spectroscopic techniques (NMR, MS, UV, CD, IR);
- Stereochemical analysis by physical and chemical methods;

Milestone 3

- Potential application of hits in dystrophic mice to evaluate the loss of muscle function measured by locomotor tests as well as histological and biochemical analysis.

Duchenne's muscle dystrophy (DMD) represents the most frequent form of hereditary myopathy affecting young boys with a rate of approximately 1:3500. The lack of functional dystrophin protein impairs the regenerative muscle capacity.

Despite great advances in searching for a long-term therapeutic approach to treat DMD, currently there is still no cure. Complementary and/or supportive therapies are hence currently used to delay and/or reduce the severity of symptoms.

In this scenario, the discovery of new drugs from marine sources have been described as "the last great frontier of Earth". The oceans have an enormous number and diversity of life forms. During the relatively few years that marine organisms have been mined for useful compounds, a large number of bioactive chemicals have been discovered. Natural products have provided inspiration for a large proportion of FDA-approved agents and continue to be one of the major sources of stimulation for successful drugs discovery.

Therefore, given the great need to find a cure for DMD, in the current PhD program we aim at searching for novel marine compounds to promote muscle cell regeneration, proliferation and differentiation.

Candidates should possess basic knowledge in System Biology and Organic Chemistry; they should be familiar with Molecular Biology, cellular and chromatographic and spectroscopic techniques.

SELECTION CRITERIA

Eligibility Criteria

- Academic degree: Applicants shall have a master degree **in Chemistry, Biology, Pharmacy or Pharmaceutical Chemistry** or related fields, corresponding to the second level of studies.
- Mobility rule: There will be no nationality restrictions. Applicants can be from any Country. However, according to the mobility rule, at the time of the application deadline researchers should not have resided or carried out their main activity (work, studies, etc.) in Italy for more than 12 months in the 3 years immediately prior to the reference date. Compulsory national service and/or short stays such as holidays will not be taken into account.
- Research experience: Applicants shall, at the time of the application deadline, be in the first four years (full-time equivalent research experience) of their research careers and not yet awarded a doctoral degree. Full-Time Equivalent (FTE) Research Experience will be determined from the date when a researcher obtained the degree which would formally entitle her/him to embark on a doctorate, either in the country in which the degree was obtained or in Italy, irrespective of whether or not a doctorate is or was ever envisaged.

Evaluation Criteria

Step 1 -Evaluation of documentation provided by the candidate: a) Academic record and training b) Research activities c) CV/motivation letter; d) Level of English; e) Reference letters.

Step 2 - Interview: a) Scientific knowledge in the field of interest; b) Research experience in the field of interest c), Motivation; d) English proficiency.

Supervisors

Dr. Jenny Nuzzo and Dr. Fabio Iannotti