Programma Operativo Fondo Sociale Europeo - Regione Liguria 2014-2020
ASSE 3 "Istruzione e formazione"

EXCERPT OF INFORMATION SHEET **HAEMATO-ONCOLOGY AND CLINICAL-TRANSLATIONAL INTERNAL MEDICINE**	
GENERAL INFORMATION STRUCTURE OF THE TRAINING PROJECT	
DURATION AND ORGANIZATION OF THE COURSE	The course starts officially on 1 of November 2018 and lasts three years. 1. At the end of each year, doctoral students shall present the Teaching Body with a detailed written account of the activities carried out. The Teaching Body may ask for the account to be discussed according to procedures it has established. **Coordinator of the course:** Prof. Edoardo Giovanni Giannini; **E-mail address:** egiannini@unige.it **Department coordinating for research:** Department of Internal Medicine and Medical Specialities (Dipartimento di Medicina interna e Specialità mediche – DIMI)
ARTICOLAZIONE E FREQUENZA	The following 3 projects/scholarships are activated: **Curriculum GERONTOLOGY, PATHOPHYSIOLOGY OF GERIATRIC DISEASES AND ANTI-AGEING MEDICINE (CODICE 7293):** **Project/scholarship No. 1: Promoting neurorigeneration through a fasting-mimicking diet in patients with mild cognitive impairment or mild Alzheimer's disease.** *Months abroad:* 0 *In cooperation with:* - LNI S.r.l. - Polo Ligure Scienze della Vita *Project/scholarship details:* Alzheimer's disease (AD) is the leading cause of dementia, burdened by an annual social cost that varies in Europe between 100 and 240 billion euros. Pharmacological treatments currently approved for AD (donezepil, galantamine, rivastigmine and memantine) have limited efficacy. Therefore, new treatments are urgently needed. Periodic cycles of a fasting-mimicking diet restricted in total porteins (RP-FMD) have been shown to reduce circulating levels of IGF-1, have surprising neurorigenerative effects, improve cognitive performance in healthy mice and slow cognitive decline in mouse models affected by AD. A 1 week PR-FMD has been shown to be well tolerated and to improve cognitive performance in healthy volunteers. It is hypothesized that repeated cycles of a non-calorie-restricted (non-CR) PR-FMD lasting one week (which will be developed and produced by LNI Srl, daughter company of the American spinoff, L-Nutra Inc.) followed by three weeks of a diet normal will be well tolerated and will be able to stabilize or even improve cognitive performance and quality of life (QoL) in patients with mild cognitive impairment (MCI) or with mild AD. It is also hypothesized that these effects will be associated with a reduction of the factors that promote AD and with a reduction in oxidative stress markers. The primary objectives of this project will be: 1) to perform a randomized, placebo-controlled, randomized phase I / II phase study of six cycles of a non-RC PR-FMD that will be developed and

	produced by LNI Srl (Genoa) lasting one week and followed by three weeks of a normal diet in patients diagnosed with MCI or with mild AD (study approved by the ethics committee of the Liguria Region in May 2018). The primary endpoint of the study will be the feasibility and safety of the PR-FMD; 2) to monitor the effect of PR-FMD (compared to the placebo control diet) on cognitive performance, functional capacity, nutritional status, mood and quality of life of the patient, as well as on the stress of the caregiver; and 3) to determine the effect of PR-FMD on oxidative and inflammatory stress markers with a confirmed role in the pathogenesis of AD. The present experimental study provides a potential new non-pharmacological therapeutic approach that could slow down, minimize or even reverse the progression of MCI- or AD-associated cognitive impairment. **Curriculum TRANSLATIONAL ONCOLOGY (CODICE 7291)** **<u>Project/scholarship No. 2: Potentiation of anticancer treatments by a fasting-mimicking diet</u>** *Months abroad*: 0 *In cooperation with*: - LNI S.r.l. - Polo Ligure Scienze della Vita *Project/scholarship details*: Over three million new cases of cancer are diagnosed in Europe each year and their overall mortality is more than 1.5 million deaths per year (Ferlay, D. M. Parkin, E. Eur J Cancer 2010, 46: 765). Thanks to the availability of modern chemotherapeutic drugs, biological agents but also effective palliative treatments, cancer patients are cured in half of the cases and even if the patient relapses or progresses he/she can still enjoy long periods of symptoms-free survival. However, the prognosis of many neoplastic diseases, particularly those reaching the metastatic phase, remains unfavorable. Among the priorities identified in the field of cancer research there is the evaluation of new therapeutic approaches (including those based on diet and lifestyle) but also of new approaches to reduce the toxicity of treatments, including long-term side effects (Jaffee EM, et al., Lancet Oncol. 2017; 18: e653-e706). The vulnerability of cancer cells to nutrient deprivation and their dependence on specific metabolites are indeed emerging as hallmarks of many types of cancer. A project approved by the Ethics Committee of the Liguria Region in November 2017 (proponent Prof. Alessio Nencioni, DIMI UNIGE) proposes to conduct a single-arm phase II study of DMD in 60 patients suffering from solid or haematological tumors who undergo treatment with chemotherapeutic regimens, hormonal therapies, other molecular targeted therapies (including kinase inhibitors), biologicals (including trastuzumab, pertuzumab, cetuximab and bevacizumab) or inhibitors of immune checkpoints (e.g. Opdivo, Keytruda). Primary objectives of the study will be the feasibility and safety of cycles of a fasting-mimicking diet (FMD; ProlonTM by LNI S.r.l.) in these patients. The recruitment will take place at the Geriatric Clinic of the Dept. of Internal Medicine and Medical Specialties of the University of Genoa (center of Oncogeriatrics) and will see the collaboration of the Clinical Nutrition Unit of the Policlinico San Martino Hospital, IRCCS for Oncology. The successful candidate for this PhD project will take part in this clinical study with the task of evaluating and managing the recruitment of patients, collecting and analyzing clinical and nutritional data, carrying out and analyzing ex vivo laboratory tests on patient samples through methods such as ELISAs and to conduct correlation studies with parameters and clinical results. He/she will perform regular secondments at LNI S.r.l. (2 months every year) aimed, among other things, at the customization of DMD kits to improve patient compliance.

	Curriculum CLINICAL PATHOPHYSIOLOGY OF ENDOCRINE AND METABOLIC DISORDERS (CODICE 7292) **<u>Project/scholarship No.3: Study of long-term clinical outcomes in response to a fasting-mimicking diet in patients with metabolic syndrome.</u>** *Months abroad:* 0 *In cooperation with*: - LNI S.r.l. - Polo Ligure Scienze della Vita *Project/scholarship details:* The prevalence of metabolic syndrome (MetS) ranges from 2% to 15% depending on population and age, while in the United States it is estimated at around 22% (Long Mt et al., Nat Rev Endocrinol, 2016; 12: 177- 83). There is also a tendency to observe a high prevalence of metabolic syndrome in children and adolescents in Europe (including Italy) with percentages that, for example, reach 33% in the United Kingdom. Dietary approaches of chronic caloric restriction are generally very effective against metabolic syndrome, allowing to lose weight and to effectively reduce many risk factors (Cespedes EM et al., Rev Rev. Chronicle 2015; 11: 448-9). However, these approaches are hardly sustainable for patients over time and their benefits are therefore often transitory. Preclinical studies and a clinical study of a fasting-mimicking diet (FMD) by LNI S.r.l. (ProlonTM) that was recently completed, demonstrate that periodic cycles of DMD are extremely effective against MetS (Wei M et al. Sci Transl Med. 2017; 9: pii: eaai8700). Specifically, the FMD ProlonTM was shown to be particularly effective in reducing body mass index, blood pressure, fasting glucose, IGF-1, triglycerides, total cholesterol and LDL cholesterol, and C-reactive protein in participants who at the enrollment had high levels of these risk factors as compared to subjects in which these factors were not increased (Brandhorst S, et al. Cell metabolism 2015; 22: 86-99; Wei M et al. Sci Transl Med. 2017; 9: pious : eaai8700). For this project we propose to conduct a randomized clinical study in which adult patients diagnosed with MetS according to the NCEP-ATP III criteria and glycated hemoglobin (HbA1c) levels between 6% and 6.4% at the enrollment will be randomized to receive six bi-monthly ProlonTM cycles vs. a calorie restricted diet (for a total of 2,100 Kcal for men and 1,900 Kcal for women with the recommendation for foods to be eaten according to the Mediterranean diet). The primary efficacy endpoint of the study will be the serum HbA1c concentration as a reliable marker of the metabolic control over the previous three months. The successful candidate for this project. it will take part in this trial with the task of evaluating and managing the recruitment of patients, collecting and analyzing clinical and nutritional data, carrying out and analyzing ex vivo laboratory tests on patient samples through ELISA methods and conducting correlation with parameters and clinical results. He/she will perform regular secondments at LNI S.r.l. (2 months every year) aimed, among other things, at the customization of the FMD kits to improve patient compliance
PhD FUNDING	The annual gross amount of the grant, including social security expenses to be paid by the recipient, is € 16,500.00. The amount of the doctoral grant shall be increased by 50% for an overall period of not more than 18 months, if the graduate student is authorized to by the teaching body to carry out research abroad. Starting from the first year, each graduate student will have, besides the grant, a budget for research activities in Italy and abroad which will not be less than 10% of the grant.
ADMISSION REQUIREMENTS	
COURSE ADMISSION	Admission is subject to the passing of the selection tests and is conditioned by the positive outcome of the medical examinations, where required, that are carried out in health facilities and aimed at ascertaining the suitability for the

	specific task in accordance with D. Lgs. No. 81/08.
REQUIRED QUALIFICATION	Degree which has been conferred according to the rules and regulations in force prior to the reform of didactic freedom in universities, or a specialist/II level degree or an equivalent foreign academic qualification.

SELECTION PROCESS	
SELECTION COMMITTEE	The committees are made up of at least 3 university professors for each course; they may be integrated by not more than 2 experts, who may also be foreign nationals, from public and private research institutions and structures.
ADMISSION TEST VENUE	Department of Internal Medicine and Medical Specialities (Dipartimento di Medicina interna e Specialità mediche – DIMI)
TYPE OF ADMISSION TEST	• Comparative assessment of the qualifications/publications. • Written test (research project). • The interview consists in the discussion of the written test (research project) and the description of the candidate's research area of interest, also on the basis of previous activities stated in his/her scientific-professional curriculum The tests are focused on confirming the candidates' aptitude for scientific research.
METHODS FOR INVITING THE CANDIDATES AND COMMUNICATING THE OUTCOMES OF THE TESTS	The **examination schedule** is as follows: • Evaluation of qualifications, curriculum and written test (research project): **30.7.2018, 9.00 am** • Interview: **30.7. 2018, 3.00 pm** at Department of Internal Medicine and Medical Specialities (Dipartimento di Medicina interna e Specialità mediche – DIMI), room B (1st floor- avancorpo), viale Benedetto XV 6, Genova. **Candidates can use video conference mode; and, for identification purposes, the candidate must show the original document of which he has deposited a certified copy at the time of application.** The list of those admitted to the interview will be affixed at the Department of Internal Medicine and Medical Specialities (Dipartimento di Medicina interna e Specialità mediche – DIMI), room B (1st floor- avancorpo), viale Benedetto XV 6, Genova. The **final lists** shall be announced on **10th August 2018**, and will appear solely on: • the noticeboard of the relevant research Departments/facilities for the research courses; • the noticeboard of the University; • on the Internet address https://unige.it/usg/it/dottorati-di-ricerca No information whatsoever shall be posted to candidates' domicile.
WRITTEN TEST	The research project (10 pages maximum) has to be attached to the online application form, and it must concern one or more research Projects/grants highlighted in the section "TRAINING PROJECT". The research project will be evaluated as practical test for the selection, together with the evaluation of the qualifications and the scientific-professional curriculum, in order to identify the candidate's aptitude for scientific research in terms of originality, feasibility, clarity in the definition of objectives, methods and expected results.
INTERVIEW	The interview consists in the discussion of the written test (research project)

	and the description of the candidate's research area of interest, also on the basis of previous activities stated in his/her scientific-professional curriculum During the interview, the candidate shall also prove his/her proficiency in the following foreign language: English. Non-Italian candidates will also have to prove knowledge of the Italian language.
PERCENTAGE VALUES OF TO EACH TEST	To each candidate can be assigned a maximum of 150 points, divided as follows: - comparative assessment of the qualifications/publications: max score 30/30, pass mark 20/30. - Written test (research project):max score 60/60, pass mark 40/60. - Interview: max score 60/60, pass mark 40/60. The final ranking will be drawn up by adding the scores assigned in comparative assessment, written test and interview. Candidates will be selected in compliance with the principles of equal opportunities.
ADDITIONAL CRITERIA FOR ADMISSION TO THE COURSE	In the case of equal grades, the evaluation of candidates' incomes prevails for the assignation of grants, as per D.P.C.M. 9 April 2001

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