10 Doctoral Candidate Positions – Horizon Europe MSCA-DN NO-CANCER NET

CÚRAM, SFI Centre for Medical Devices and Lambe Institute for Translational Research

Ref. No. University of Galway xxx

Applications are invited from suitably qualified doctoral candidates for 10 doctoral candidate positions to pursue PhD education as part of NO-CANCER-NET. Two candidates will be located the SFI Centre for Research in Medical Devices (CÚRAM) and Lambe Institute for Translational Research University of Galway, Ireland, and 8 at our partner beneficiaries as listed below.

The positions are available for 36 months at 1.0 FTE and are funded through Horizon Europe MSCA DN grant number 101119873.

Organisation: CÚRAM, SFI Research Centre for Medical Devices is a national, SFI funded, research centre that brings together researchers from University of Galway and other leading universities from Ireland. The prime objective for CÚRAM is to radically improve health outcomes for patients by developing innovative implantable 'smart' medical devices to treat major unmet medical needs. Implants will be designed and manufactured to respond to the body's environment and to deliver therapeutic agents, such as drugs, exactly where needed. Lambe Institute for Translational Research was established in 2015 with the aim to translate basic research findings to clinical applications, in particular cancer research. The Lambe Institute boasts a state-of-the-art research infrastructure including imaging, histology, flow cytometry, molecular biology, gene vector and mammalian cell culture core facilities which are coordinated by a team of fully trained technical support staff.

Website https://www.universityofgalway.ie/cancercentre/research/no-cancer-net/

About NO-CANCER-NET:

Recently, Prof. Sharon Glynn, Principal Investigator (PI) at CÚRAM and the Lambe Institute, and colleagues in Italy, Denmark, France, Luxemburg and Spain have been awarded an EU-funded MSCA Doctoral Network Grant – NO-CANCER-NET: Advanced Engineering of Nitric Oxide Based Therapeutics for Triple Negative Breast Cancer Training Network.

NO-CANCER-NET represents a collaborative six-countries network, encompassing leading universities and government organizations. In addition to our consortium beneficiaries, NO-CANCER-NET has gathered a diverse group of companies, hospitals, and internationally renowned cancer institutions. These associate partners will play a vital role in translating and leveraging the project's outcomes over the medium to long term.

The overarching goal of NO-CANCER-NET is to establish an interdisciplinary, intersectoral, and international doctoral training and research programme. Our aim is to foster a new generation of leaders dedicated to advancing the treatment of triple-negative breast cancer (TNBC), emphasizing excellence in research and clinical practice.

NO-CANCER-NET will address three interconnected challenges aimed at identifying novel and effective nitric oxide (NO) based treatments for TNBC, including the discovery of selective biomarkers for effective patient stratification, the development of reliable 3D tumour models to investigate tumour biology and drug response and the development of novel NO-based treatment options. The 10 Doctoral Candidates (DC) will be hosted

across the network, and in addition to conducting an original research study they will participate in a 36-month network-wide training program, public engagement activities and collaboration with network members through short-term secondments in European intersectoral partner organisations. NO-CANCER-NET will provide enhanced career perspectives in academic and non-academic sectors for 10 DCs.

Projects	Title of Project	Institute (Beneficiaries)	Country
DC1	GSNOR as new diagnostic marker of cancer and inflammatory diseases	Danish Cancer Society	Denmark
DC2	Inflammatory caspases – regulators of NO levels during triple negative breast cancer	Trinity College	Ireland
DC3	Spatial modelling of cancer metabolic networks on multi-cell population level	University of Luxemburg	Luxemburg
DC4	Study of the combination of chemotherapy and NO donor for the treatment of TNBC	EPHE PSL Research University Paris – University of Burgundy	France
DC5	Novel TME responsive and targeted systems releasing NO, ROS or drugs upon external stimuli application	National Research Council of Italy	Italy
DC6	Study of NO conjugate photoactivable compounds for simultaneous oxidative stress-triggered cellular imaging and photodynamic therapy	University of Udine	Italy
DC7	Hydrogel delivery of NO scavenging therapeutics	University of Galway	Ireland
DC8	Cell interaction in the TME under pharmacological pressure by tyrosine kinase inhibitors in a 3D culture	University of Seville	Spain
DC9	Tumour-endothelial cell interplay under NO based drugs	University of Siena	Italy
DC10	3D spheroid models of Nitric Oxide Synthase biology in Triple Negative Breast Cancer	University of Galway	Ireland

The applicants, at the time for the application, should not have resided in the country where are applying to, for more than 12 months in the 3 years immediately prior to the reference date. **Start date is June 2024**.

Doctoral Candidate Posts

DOCTORAL CANDIDATE 1

Host: Danish Cancer Institute (DCI), Copenhagen Denmark
Primary Supervisor: Professor Giuseppe Filomeni
Co-supervisors/mentors: Dr. Salvatore Rizza (DCI), Dr. Chiara Pecorari (DCI);
Duration: 36 months
Required applicant profile: Master's in Biology/Biotechnology/Biochemistry, or related topics
Desired Skills: Basic techniques of Biochemistry, Molecular and Cellular Biology (biochemical assays, Western blot, real time, cellular assays), Microscopy, Cell culturing, Cloning, FACS, basic knowledge of bioinformatics (R, pithon,)
Project Objectives: Growing evidence supports the idea that tumour metabolic rewiring and is implicated in cancer progression. Interestingly, in breast cancer patients, this is associated with a significant decrease in the expression of the denitrosylase S-nitrosoglutathione reductase (GSNOR). In this DC we aim at: 1) Identifying and characterizing a novel role for GSNOR as onco-suppressor and metabolic regulator of breast cancer progression. 2) Understanding the effects produced by GSNOR-deficiency to be exploited as potential druggable targets for new therapeutical applications.
Secondment(s): EPHE-PSL (3 months); University of Galway (3 months) and University of Luxemburg (3 months).
For more information, contact: Professor Giuseppe Filomeni: giufil@cancer.dk

Lab Website: https://www.cancer.dk/research/dci-research/redox-biology/
Link to Advert:
https://www.linkedin.com/company/danish-cancer-institute/?originalSubdomain=dk
https://www.linkedin.com/in/giuseppe-filomeni-2418ba89/

DOCTORAL CANDIDATE 2

Host: Trinity College Dublin (TDC), Ireland
Primary Supervisor: Professor Emma Creagh
Co-supervisors/mentors: Profs Thomas Sauter (UL) and Lucia Morbidelli (UNISI)
Duration: 36 months
Required applicant profile: Prospective candidates should hold an MSc degree (or BSc (minimum 2.1 grade, with additional lab-based research experience) in biochemistry, molecular biology, immunology or related disciplines.
Desired Skills: Basic techniques of Biochemistry, Molecular and Cellular Biology (biochemical assays, Western blot, real time, cellular assays, ELISAs), Microscopy, Primary cell culture, experience with animal models desired but not essential.
Project Objectives: The objectives are to 1. Confirm whether inflammatory enzymes/markers (e.g., caspases/IL-1alpha) have potential as diagnostic markers for TNBC. 2. Determine the influence of inflammatory caspases on NO production in both tumour and stroma, using 2D cell models and co-culture models. 3. Optimise and establish a TNBC model in wild type and inflammatory caspase-deficient C57/BL6 mice. 4. Use the murine TNBC model to determine the effect of stromal and tumour caspase expression on NO production and tumour progression
Secondment(s): Luxemburg University (1 months); University of Galway (3 months); EPHE-PSL (2 months).
For more information, contact: Professor Emma Creagh; ecreagh@tcd.ie
Lab Website: Emma Creagh'Trinity Research - Trinity College Dublin (tcd.ie)
Link to Advert: Search Vacancies (corehr.com)

DOCTORAL CANDIDATE 3

Host: Université du Luxemburg, Luxemburg
Primary Supervisor: Professor Thomas Sauter
Duration: 36 months
Required applicant profile: MSc in Systems Biology, Computational Biology, Bioinformatics or equivalent
Desired Skills: Strong background in computational and molecular biology, especially data, network and image analysis, as well as in biochemistry.
Project Objectives: Methodological advances enable a deeper characterization of tumour tissues on the cellular (single-cell omics) and spatial level (imaging). Computational methods are needed for data integration and for gaining deeper insights, e.g., into tumour metabolic rewiring. In this DC we aim to: 1. Develop a novel computational approach for the integration of single-cell RNA-Seq and imaging data towards the detailed metabolic network modelling of cancer tissue on a multi-cell population level. 2. Together with consortium partners, apply this framework for the deeper characterization of metabolic alterations in TNBC and for the prediction of novel drug candidates and combinations.
Secondment(s): University of Galway (3 months) and University of Siena (3 months).
For more information, contact: Professor Thomas Sauter; thomas.sauter@uni.lu
Lab Website: https://www.uni.lu/fstm-en/research-groups/systems-biology/research/
Link to Advert:
https://recruitment.uni.lu/en/details.html?nPostingId=89056&nPostingTargetId=129739&id=QMUFK026203F3VBQB7V7VV4S8&LG=UK&languageSelect=UK&sType=Social%20Recruiting&mask=karriereseiten

DOCTORAL CANDIDATE 4

Host: EPHE-PSL Paris / University of Burgundy Dijon - France
Primary Supervisor: Dr. Stéphanie Plenchette

Co-supervisors/mentors: Lucia Mordibelli (UNISI) and Guiseppe Filomeni (DCI)
Duration: 36 months
Required applicant profile: MSC in Molecular and Cellular Biology, Biochemistry, Immunology or related fields.
Desired Skills: Required skills in cell culture, molecular and cellular biology, western blot, immunocytochemistry, biochemistry assays. The applicant should have knowledge in microscopy, flow cytometry and in vivo assays. A strong interest in research focusing on tumor microenvironment signaling and therapeutics in cancer is expected.
Project Objectives: The overall objective of this DC is to use NO-donors to harness the paradox action of the TNF ligands TNFα, FasL and TRAIL (pro- versus anti-tumour effects) to improve the efficacy of conventional anti-cancer therapies. The objectives are to 1.) Potentiate the anti-tumour efficacy of conventional chemotherapies for TNBC treatment (paclitaxel, carboplatin) with an NO donor (glyceryl trinitrate (GTN)) using various TNBC murine models based on TNF ligands levels. 2.) Determine the impact of NO on the specific contribution of the TNF ligands/receptors axis (*in vitro* and *in vivo*) in regulating the anti-tumour response. 3) Identify new NO targets in the tumour microenvironment.
Secondment(s): University of Siena (3 months); Université du Luxemburg (1 month), Trinity College of Dublin (3-4 months).
For more information, contact: Associate Professor Stéphanie Plenchette; stephanie.plenchette-colas@ephe.psl.eu
Lab Website: https://www.liic.fr/
Link to Advert: https://www.linkedin.com/school/%C3%A9cole-pratique-des-hautes-%C3%A9tudes/

DOCTORAL CANDIDATE 5

Host: Consiglio Nazionale delle Ricerche – Istituto per la Sintesi Organica e la Fotoreattività, Bologna Italy
Ph.D. course hosting Institution: University of Bologna (associate partner); Ph.D. course in "Nanoscience for Medicine and the Environment"
Primary Supervisor: Dr. Greta Varchi
Co-supervisors/mentors: Co-supervisor Dr. Claudia Ferroni
Duration: 36 months
Required applicant profile: A candidate with an above-average MSc (or equivalent degree) in chemistry, industrial chemistry, pharmaceutical/medicinal chemistry, or related fields. We expect a strong interest in research focusing on developing and characterizing novel molecular scaffolds and nanosystems delivering nitric oxide. Required skills include knowledge of the literature on these and related topics, and ability to carry out chemistry lab research.
Desired Skills: The applicants should have experience in synthetic organic chemistry, purification and characterization of complex organic molecules, nanoparticles preparation and characterization. Knowledge of analytical techniques, such as HPLC-UV/MS, NMR, UV/VIS, IR, Mass Spectroscopy, CD and SEC, DLS, DSC, would be a plus. Excellent knowledge of English is a requirement. Any peer-reviewed publications will be considered an advantage.
Project Objectives: The use of light or ultrasounds to selectively induce the generation of reactive oxygen and nitrogen oxygen species such as singlet oxygen ($^1O_2$) and nitric oxide (NO) represents a fascinating and powerful mean to spatiotemporally control the release of photo- toxic species. The DR will design and develop novel molecular conjugates combining near infrared light activatable NO donors and properly selected photosensitizers to induce the concomitant formation of high local concentration of NO and ROS. In parallel, DR5 will design and develop innovative molecular conjugates made of a LNOD unit connected through a TME-responsive linker with a cytotoxic drug to assess the effect of this combination on tumour cells growth. To further enhance the treatment selectivity and with the aim of specifically relief the hypoxic condition of the tumour microenvironment, DR5 will also incorporate the conjugates into biocompatible and oxygen-donating nanoparticles.
Secondment(s): Innovamol Consulting (1 month); University of Udine under (3 months), University of Galway (3 months).

For more information, contact: Dr. Greta Varchi, greta.varchi@isof.cnr.it
Lab Website: www.isof.cnr.it

DOCTORAL CANDIDATE 6

Host: University of Udine, Italy
Primary Supervisor: Professor Valentina Rapozzi
Co-supervisors/mentors: Co-supervisor: Dr. Eros Di Giorgio
Duration: 36 months
Required applicant profile: A candidate with an above-average MSc (or equivalent degree) in Biology, Biotechnologies, Pharmacy, pharmaceutical/medicinal chemistry, Medicine. We expect a strong interest in research focusing on cellular/molecular mechanisms involved in tumour response to photoactivable compounds. Required skills include knowledge of the literature on these and related topics, and ability to carry out biology lab research.
Desired Skills: Cell culture, molecular biology and biochemical assays, in vitro safety and efficacy tests for anticancer drugs.
Project Objectives: 1. To identify the subcellular compartmentalization of NO conjugated photoactivatable compounds. 2. Investigate the release of NO from the conjugates to evaluate the development of ROS/RNS species. 3. Evaluation of toxicity in the dark compared to phototoxicity Identification of the mechanism of cell death. 4. Evaluation of the antitumour activity of NO conjugates of photoactivatable compounds on breast cancer cells with varying degrees of malignancy compared to healthy normal breast cells. 5. Evaluation of molecular signalling pathways involved in tumour response to photodynamic therapy using iNOS inhibitor and scavenger NO.
Secondment(s): Danish Cancer Institute (3 months); University of Siena (3 months); Trinity College Dublin (4 months).
For more information, contact: Professor Valentina Rapozzi, valentina.rapozzi@uniud.it
Lab Website:www.uniud.it-

DOCTORAL CANDIDATE 7

Host: University of Galway, Ireland
Primary Supervisor: Professor Abhay Pandit
Co-supervisors/: Professor Sharon Glynn
Duration: 36 months
Required applicant profile: Masters in Biomedical Sciences/Engineering
Desired Skills: A range of basic techniques of in the areas such as Biochemistry, Molecular and Cellular Biology (biochemical assays, Western blot, real time, cellular assays), Microscopy, Cell culturing, Cloning, FACS, basic knowledge of bioinformatics (R, pithon), Biomaterials, Chemical Synthesis
Project Objectives: The overall objective of this project is to continue development of nitric oxide scavenging agents and their incorporation in optimal hydrogel delivery systems for the treatment of TNBC. 1) To assess and understand the mechanism of cellular uptake of a variety of hemin derivatives across TNBC subtype and understand the factors that influence the success of uptake. 2) To optimize the formulation of injectable hydrogel towards a continuous release of active NO-scavenging compound. 3) To identify the effects of hydrogel degradation products on the NO-induced migration from molecular perspectives.
Secondment(s): University of Siena (3 months), and University of Seville (3 months).
For more information, contact: Professor Abhay Pandit; Abhay.pandit@universtyofgalway.ie
Lab Website: https://www.universityofgalway.ie/curam/about-us/our-people/director/prof-abhay-pandit.html

DOCTORAL CANDIDATE 8

Host: University of Seville, Spain
Primary Supervisor: Professor Jordi Muntané
Co-supervisors/mentors: Jordi Muntané

Duration: 36 months
Required applicant profile: A candidate with an above-average MSc (or equivalent degree) in Biology, Biochemistry, Biotechnology and Biomedicine. We expect a strong interest in research focusing on developing and characterizing novel cellular and molecular interactions among cells in 3D culture.
Desired Skills: The applicant will develop different protocols of cell fluorometric-based labelling of cells to be used in cell culture. Different variables will be in situ determined, as well as by western-blot and inmunocytochemistry. So, she/he should know different 3D cell culture, proteins analysis and molecular biology protocols
Project Objectives: 1) Cell specific antitumoural activity of tyrosine kinase inhibitors (TKI) in TNBC and liver cancer cells in different cell differentiation stages in coculture with inflammatory and other mesenchymal cells in 3D models. 2) Impact of the overexpression or deficiency of redox regulatory proteins (tiorredoxin-1 and GSNOR) in TKI-induced oncogenic properties in 3D cultured liver cancer cells. 3) Assess the effect of NO and oxidative stress related interventions in TKI treatment. 4) Spatial functional interaction among cancer cells and other stromal cells and their impact on drug effectiveness in combination with NO therapeutics in metastatic setting.
Secondment(s): Danish Cancer Institute (3 months); Houston Methodist (3 months).
For more information, contact: Professor Jordi Muntané; jmuntane-ibis@us.es
Lab Website: www.liverresearchunit.org

DOCTORAL CANDIDATE 9

Host: University of Siena, Italy
Primary Supervisor: Professor Lucia Morbidelli
Co-supervisors/mentors: Prof. Sandra Donnini, Dr. Valerio Ciccone
Duration: 36 months
Required applicant profile: MSc in Biology, Biotechnologies, Pharmacy, Medicine
Desired Skills: Cell culture, drugs and biomaterial handling, molecular biology, in vitro safety and efficacy tests for anticancer drugs
Project Objectives: 1. Safety issues of novel drugs/drug combinations and drug delivery systems: basic survival/apoptosis assays and cell selectivity tests (tumour vs normal cells) with new drugs or drug combination and their relative delivery systems will be run on different TNBC cells, normal endothelial and stromal cells (fibroblasts). These tests will be run in 2D culture systems, allowing to select the most promising active principles and their formulation to be further tested in more complex assays. 2. Set up and validation of multicellular 3D spheroids. Complex multicellular spheroids will be set up by adding TNBC cells, endothelial cells and fibroblasts to recreate the complexity of TME. Single cell types will be marked with fluorescent dyes or genetic constructs to monitor their 3D organization and to allow cell sorting upon drug exposure. The single cell types composing the multicellular organoid will be analyzed for functional/ molecular/ genetic/ epigenetic responses following exposure of the 3D organoids to NO based drugs. Both conventional techniques (WB, ELISA, immunohistochemistry and immunofluorescence) and innovative imaging and functional omics will be applied to the samples. Drug penetrance inside the organoids will be followed too. 3. The specific interaction between tumour and endothelial cells and the molecular mechanisms governing it (as IL-8/NOTCH signalling cascade; TGFbeta, HIF-1/VEGF, etc..) will be studied in response to NO based drugs. The effect of NO based drugs (or other drugs developed in WP2) will be assessed on the activation of endothelial cells toward a mesenchymal phenotype inside the organoids and in 2D tumour-endothelial cell co-culture systems.
Secondment(s): University of Galway (6 months); Université du Luxemburg (3 months).
For more information, contact: Professor Lucia Morbidelli; lucia.morbidelli@unisi.it
Lab Website: https://docenti.unisi.it/en/morbidelli; https://www.dsv.unisi.it/en

DOCTORAL CANDIDATE 10

Host: University of Galway, Ireland
Primary Supervisor: Professor Sharon Glynn

Co-supervisors/mentors: Professor Abhay Pandit
Duration: 36+12 months
Required applicant profile: BSC and/or MSc in Biology/Medicine/Life Science/Bioengineering/Chemistry
Desired Skills: A range of basic techniques of in the areas such as Biochemistry, Molecular and Cellular Biology (biochemical assays, Western blot, real time, cellular assays), Microscopy, Cell culturing, Cloning, FACS, basic knowledge of bioinformatics (R, python), Biomaterials, Chemical Synthesis
Project Objectives: The overall objective of this DC is to develop 3D models of triple negative breast cancer (TNBC) that recapitulate a patient's individual tumour, which can be used for therapeutics assessment and to understand the contribution of the tumour microenvironment in TNBC to therapeutic response and drug resistance. (1) Using pathological and molecular data from our TNBC patient cohort of over 350 patients, the candidate will develop 3D models representing different TNBC subtypes (mesenchymal, basal, and androgen receptor luminal) with and without iNOS overexpression that recapitulate aspects of iNOS in TNBC. (2) To assess the impact of iNOS on endothelial-fibroblast-tumour interactions in 3D and the consequences for tumour angiogenesis and fibroblast activation. (3) To discover the effects of iNOS on lymphocytes polarisation and activation in 3D tumour microenvironment. The Glynn lab has demonstrated that iNOS is a key contributor to poor outcomes in TNBC.
Secondment(s): Houston Methodist Research Centre (2 months); Université du Luxemburg (2 months), and Consiglio Nazional delle Ricerche (approx. 2 months).
For more information, contact: Professor Sharon Glynn; sharon.glynn@universityofgalway.ie
Lab Website: https://www.universityofgalway.ie/our-research/people/sharonglynn/

Benefits
Marie Sklodowska-Curie Doctoral Candidates are paid a competitive gross salary of 3,400 €/month, adjusted for their host country, a Mobility Allowance of 600 €/month and, for researchers who have a family, a Family Allowance of 660 €/month. All amounts are subject to deductions and taxes. Family is defined as persons linked to the researcher by (i) marriage, or (ii) a relationship with equivalent status to a marriage recognised by the national legislation of the country of the beneficiary or of nationality of the researcher, or (iii) dependent children maintained by the researcher. Should the fellow's personal status (marriage, children) change during the action, they will become eligible for family allowance.

Eligibility criteria
To apply for one of these PhD positions, the applicant should fulfil the following conditions:

- Have — **at the date of recruitment (start date of June 2024)** — a Bachelors and/or Master's degree in a discipline as indicated in the project description specific to the beneficiary to which you are applying.
- **Trans-national mobility:** The applicant — **at the date of recruitment** — should not have resided in the country where the research training takes place for more than 12 months in the 3 years immediately prior to recruitment, and not have carried out their main activity (work, studies, etc.) in that country. For refugees under the Geneva Convention (1951 Refugee Convention and the 1967 Protocol), the refugee procedure (i.e. before refugee status is conferred) will not be counted as 'period of residence/activity in the country of the beneficiary'.
- Be able to communicate fluently in English (speaking and writing). Oral interview with the prospective advisor may be required.

Note: A Master's degree (or equivalent) is not necessary at the time of the application, but will be required at the date of recruitment (in June 2024).

For informal enquiries about these posts please contact the supervisor associated with the project of interest above (contact details provided above). General enquiries may be made to NOCancerNet@universityofgalway.ie

To Apply:
Applications are to include (1) a letter of motivation describing why you wish to apply to NO-CANCER-NET and your specific project of choice, (2) an up to date CV, and (3) the contact details of three referees should be submitted via Google Application form https://forms.gle/x2qQrv1p7Bb7PKWU6. Please be aware that your application may be shared amongst the beneficiaries.

Please put reference number **University of Galway xxxxx** in subject line of all e-mail applications or enquiries.

Closing date for receipt of applications is 5.00 pm on February 29th 2024

All positions are recruited in line with Open, Transparent, Merit (OTM) and Competency based recruitment.

University of Galway, Galway is an equal opportunities employer