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Individual Research Project

Doctoral Researcher 7

HORIZON EUROPE MSCA DOCTORAL NETWORK “MELOMANES”

Metastatic melanoma is a hard-to-treat disease and it remains as one of the most worrisome cancer. There is an urgent need to improve the current therapies (chemotherapy, radiotherapy) that have a limited efficacy. A single therapy is not efficient to tackle metastatic melanoma and a combination of therapies is thus emerging as a necessity to efficiently eradicate all cancer cells. Recently, the development of immunotherapies has shown promises, in particular chimeric antigen receptor (CAR)-T cells. Nevertheless, the physical barriers represented by cellular and non-cellular components of the tumor microenvironment combined to the abnormal tumor vasculature and high interstitial fluid pressure, hamper an efficient tumor infiltration of CAR-T cells. In this context, thanks to a network of 18 partners (including 10 non-academic partners), MELOMANES aims to train 12 doctoral researchers for the development of a combined therapy exploiting the properties of magnetic nanoparticles (NPs) to induce damage on the tumor microenvironment by magnetic and optic hyperthermia in order to facilitate the infiltration of CAR-T cells. Research and transferable training of the doctoral researchers will be performed in a highly interdisciplinary, intersectoral, and international environment. In addition to acquiring skills related to the research project, they will be trained also in open science, communication and dissemination, responsible research and innovation, circular economy, ethics, data management, entrepreneurship, marketing, intellectual property, and gender dimension in research. Their competences will be validated through certification and qualification examination, allowing a new generation of highly skilled doctoral researchers to emerge with a high-level training in particular in the multidisciplinary field of nanomedicine.

**Project funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the European Commission. Neither the European Union nor the European Commission can be held responsible for them.*

DESCRIPTION OF THE INDIVIDUAL RESEARCH PROJECT

Metastasis inhibition by iron carbide NPs targeting the metastatic vasculature

Objectives

- 1°) *Antitumor properties of the iron carbide NPs in primary tumours*
- 2°) *Targeting and antitumor properties of the iron carbide NPs in lung metastases developed in mice*
- 3°) *Investigation of the destiny of the conjugates, tumour evolution, and efficiency of the treatment*
- 4°) *Investigation of the (bio)degradation of the NPs at the tumour site*



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Methodology

- 1°) Primary tumours and lung metastases will be developed in C57BL/6 mice transplanted with melanoma B16-F10 cells as in previous studies
- 2°) Iron carbide NPs will be injected intravenously in melanoma-bearing mice +/- adjuvant treatments
- 3°) Destiny of the conjugates, tumour evolution, and efficiency of the treatment and (bio)degradation will be evaluated in post-mortem tissues by anatomopathological and histopathological techniques including transmission electron microscopy, magnetic resonance imaging, confocal Raman spectroscopy, and histopathology.

Expected Results

- 1) Evaluation of the targeting efficiency of vascular endothelial growth factor receptor-peptide conjugated iron carbide NPs *in vivo*;
- 2) Evaluation of the NP antitumor effect *in vivo*;
- 3) Identification of the NP biological fate after intravenous injection

Supervisors and host organisations

Main supervisors and recruiting organisation:

Monica López Fanarraga,

IDIVAL / UC, Santander, Cantabria

The IDIVAL research institute is the centre where all scientific research in the biomedical field is carried out at the Marqués de Valdecilla Hospital, which is an international reference institution. The IDIVAL building has 3000 m² of space dedicated to research laboratories and general. In March 2015 IDIVAL was awarded by the Institute of Health Carlos III as one of the reference Institutes for Health Research in Spain. IDIVAL. Please see more info at: <https://www.idival.org/en/about-us/>

Co-supervisor (non-academic partner):

Dr Florence Gazeau, CNRS, Paris

Co-supervisor (academic partner):

Tomasz Kostrzewski, CN Bio Innovations, Cambridge (UK)

Planned mobility track and secondments:

- 1) CN Bio (T. Kostrzewski, 3 months, M13-M15): Development of a melanoma tumor-on-chip based on the expertise of IDIVAL to develop a mouse malignant melanoma model;
- 2) Oslo University Hospital (Sébastien Wälchli, 3 months, M19-M21): Comparison of the use of HLA-G receptors vs. parts of the anti-HLA-G antibody used for generating the CAR-T cells to target HLA-G;
- 3) CNRS (F. Gazeau, 4 months, M25-M28): Assessment of the biodegradation pathways in macrophages



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Enrolment in Doctoral School:

PhD by the University of Cantabria. Doctorate in Molecular Biology and Biomedicine please see more info at: <https://web.unican.es/en/Studying/Academic-Offer/course-detail?plan=157&cad=2022>

TERMS AND CONDITIONS FOR EMPLOYMENT

Duration

36 months

Salary

2.017,24€/per month (gross) *Gross salary after employer taxes, pending deduction of employee contributions

Other allowances

Mobility allowance 454,89€/per month (gross), family allowance if applicable 500,38€/per month (gross)

THE CANDIDATE PROFILE

Academic prerequisite

We are looking for a student with a 5-years degree (Master) in Biology, Pharmacy, Biotechnology, Biomedicine, Chemistry, Nanomedicine or related fields.

All Grade/Master certificates/documents must be officially translated and formatted according to regulations described in the Spanish Ministry Platform <https://www.educacionyfp.gob.es/servicios-al-ciudadano/catalogo/gestion-titulos/estudios-universitarios/titulos-extranjeros/equivalencia-notas-medias.html>

Technical skills and knowledge required

Advanced knowledge of cellular/molecular biology, biochemistry and animal handling skills are required. It is absolutely necessary that the candidate is willing to work with mice. Other skills include: anatomopathology, histology, genetics, chemistry of nanomaterials, pharmacology, toxicology will be welcomed. Basic Spanish is preferred.

Soft skills

- Scientific integrity
- Intelligence, discipline, and productivity
- Writing skills in English and ability to summarize are essential
- Ability to teach/communicate with peers and with an audience



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Exclusion criteria

The candidate, at the time of recruitment, must hold a 5-years degree (Master level). The candidates must be willing to work with live animal models (mice).

The candidate must not have resided or carried out their main activity (work, studies, etc.) in Spain for more than 12 months in the 3 years immediately before the recruitment date. Compulsory national service, short stays such as holidays, and time spent as part of a procedure for obtaining refugee status under the Geneva Convention are not considered.

The candidate, at the time of recruitment by IDIVAL (Spain), must not be enrolled in a doctoral school or have been awarded a doctoral degree.

WHAT WE OFFER

- An enrolment in a PhD program;
- An international work environment, in which doctoral researchers can develop their skills and innovate within a competent team;
- An attractive 36 months' salary;
- An individual and well-structured scientific and transferable training (open science, responsible research and innovation, circular economy, ethics, data management, entrepreneurship, creativity, communication, career plans and gender balance in science) within the Melomanes network.

APPLICATION PROCEDURE

- Motivation letter (max. 2 pages);
- CV including the details of education/qualifications, work experience, language skills and other relevant skills; indication of at least two Scientists for reference letters (academic and/or non-academic);
- Certified/signed copy of a recent transcript of exams taken with relative mark. A certified/signed copy of Master of Science certificate or a letter from the Head of the degree course stating that the Student is going to finish before the end of 2022;
- A summary of your research projects (max. 5 pages).

Applicants can apply for up to 3 projects within the consortium, indicating the order of preference.

All applications will be checked for eligibility (in particular, the adherence to the mobility rule). Incomplete applications will be ignored. Shortlisted candidates will be invited for an interview. Candidates will be notified of the outcome. Start of employment is foreseen September-October 2023.

If you are highly motivated and interested in doing research in an internationally oriented and highly successful network, you should send your application to: fanarrag@unican.es and innovacion4@idival.org

Equal opportunities



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Equal opportunities policy without distinction on the grounds of gender, racial or ethnic origin, religion or belief, disability, age or sexual orientation will be applied.

The selection is not limited to EU citizens; therefore, candidates can be of any nationality.

Apply for this position at
<https://www.idival.org/en/employment/> before 15th
April 2023