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melomanes

CN-BIO

Individual Research Project

# Doctoral Researcher 12

## 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 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

**Project title: development of metastatic melanoma-on-chip systems to assess the efficacy and safety of CAR-T cell therapy combined to hyperthermia.**

Microphysiological systems, colloquially referred to as organs-on-chips, are designed to recapitulate human organ function, using proprietary microfluidic instrumentation that functions in common laboratory settings. They can be utilized alone but can also be connected through fluidic circuits to create advanced multi-organ microphysiological systems that can model the interactions between organ systems, allowing greater analysis of molecular pathways and disease mechanisms. CN Bio has extensive experience with its PhysioMimix® technology, launched in 2018, the platform has been used for a range



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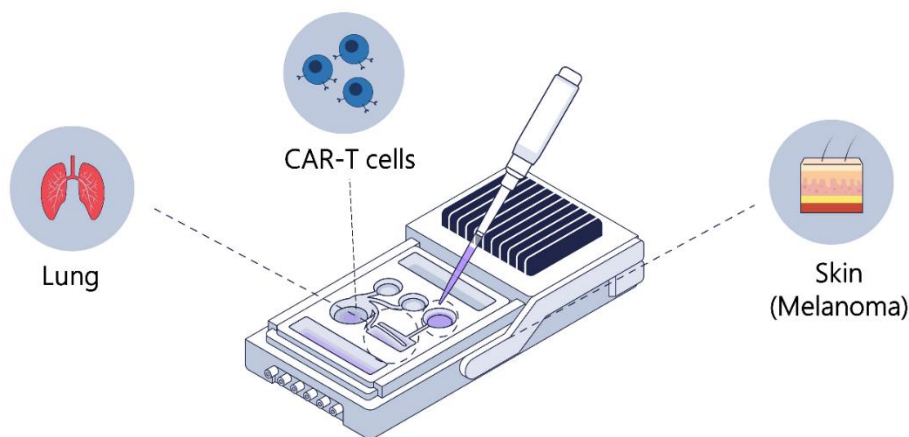
of applications, from toxicology to complex disease models, including models of non-alcoholic steatohepatitis (NASH) and a 10-organ “Body-on-a-Chip”.

## Objectives

- 1°) To develop a 3D perfused model of metastatic melanoma.
- 2°) To model the mechanisms of metastasis with the addition of a second organ model, most likely to the lungs and/or liver.
- 3°) To study the potential toxicity and therapeutic effects of magnetic nanoparticles, the CAR-T cells and hTERT-specific T-cell receptor T cells on tumor cells, and additionally any off-target toxicity effects on lung and liver tissue.

## Methodology

This project will aim to develop a 3D perfused model of metastatic melanoma, initially a healthy skin epithelium model will be developed and validated on the PhysioMimix® platform. This will then be induced to generate a melanoma (skin cancer) model, with different melanoma cells lines tested for their ability to invade and proliferate in the skin layers. If successful the model will be further developed to include a second organ model to allow the process of metastasis to be model, most likely to the lungs and/or liver (Figure 1). These models will be used to study the effects of the iron carbide nanoparticles and CAR-T cells on tumour cells but additionally any off-target toxicity effects on lung and liver tissue (Figure 1). The infiltration of CAR-T cells into the skin melanoma tissue will be an important feature to be analysed.



**Figure 1 – Microphysiological systems (MPS) model of metastatic melanoma used to assess efficacy and toxicity of CAR-T cells and magnetic nanoparticles.** The MPS model will be developed in a number of stages, starting with a healthy skin model, advancing this to a melanoma skin cancer model. This will then be combined with a lung (or liver) model to potentially study metastasis and all models will be used to test the efficacy and safety of CAR-T cell therapies in combination with magnetic nanoparticles.



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## Expected Results

- 1°) Development of a healthy human skin model on the PhysioMimix® platform and interactions with the nanoparticles.
- 2°) Development of a melanoma cancer model within the human skin model and response to hyperthermia.
- 3°) Assessment of hyperthermia and CAR-T therapy efficacy on melanoma model, including assessment of CAR-T cell infiltration.
- 4°) Development of a multi-organ melanoma plus lung/liver model, allowing determining on and off target effects of the treatments and modeling the potential for melanoma metastasis.

## Supervisors and host organisations

### Main supervisors and recruiting organisation:

*Yassen Abbas*

*CN Bio Innovations, Cambridge, United Kingdom*

CN Bio Innovations is a leading biotechnology company that has developed disruptive single and multi-organ MPS to improve the accuracy and efficiency of drug discovery. With more than a decade of research and development experience in multi-organ MPS, we aim to transform the way human relevant pre-clinical data is generated through the development of the most complete model of the human 'Body-on-a-chip' in the laboratory. Our mission is to be the world's leading provider of organ-on-a-chip solutions which accurately predict human responses to medicines.

### Co-supervisors (academic partner):

*Florence Gazeau*

*Centre national de la Recherche Scientifique, Université Paris Cité, Paris, France*

*<https://msc-med.u-paris.fr/>*

*Emmanuel Donnadieu*

*Institut National de la Santé et de la Recherche Médicale (INSERM), Université Paris Cité, Paris, France*

*<https://institutcochin.fr/en/team/cancer-and-immune-response>*

### Co-supervisor (non-academic partner):

*Tomasz Kostrzewski*

*CN Bio Innovations, Cambridge, United Kingdom*



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### Planned mobility track and secondments:

1) INSERM (E. Donnadieu, 4 months, starting May 2025): Combination of the microfluidic melanoma on-the-chip model with dynamic imaging to monitor CAR-T cell responses and examination of the consequences of magnetic nanoparticles on these responses;

2) CNRS (F. Gazeau, 6 months, starting December 2025): Local hyperthermia by MH and/or PTT on the melanoma on-the-chip model and multi-organ models

### Enrolment in Doctoral School:

Université Paris Cité, Paris, France

Doctoral School ED 564 Physique en Ile de France

## TERMS AND CONDITIONS FOR EMPLOYMENT

### Duration

36 months

### Salary

55,855.20€/per annum (gross, before compulsory employer contributions)

### Other allowances

Mobility allowance 600€/per month (gross, before compulsory employer contributions)

Family allowance if applicable 660€/per month (gross, before compulsory employer contributions)

## THE CANDIDATE PROFILE

### Academic prerequisite

5-years degree (Master level) in Biology/Immunology/Bioengineering or related field

### Technical skills and knowledge required

#### ***Essential:***

- Expertise in a broad array of relevant lab techniques (molecular biology, immunoassays, cell culture).

#### ***Desirable:***

- Experience in primary cell culture, ELISAs, qPCR and microscopy.
- Experience in organ-on-a-chip technology
- Understanding of the drug discovery process, and the pharmaceutical industry.



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### Soft skills

- Strong interpersonal and communication (oral and written English) skills.
- Highly analytical, able to interpret complex sets of data with excellent attention to detail.
- Problem-solver, uses experience to identify problems and developing proposed solutions that minimise risk and ensure delivery.
- Self-motivated, confident, reliable, open-minded, and enthusiastic.
- A genuine team player, providing support to your colleagues with a proactive and friendly attitude, and able to work autonomously as required.
- Flexible and able to respond in a fast-evolving organisation.

### Exclusion criteria

The candidate, at the time of recruitment, must hold a 5-years degree (Master level).

The candidate must not have resided or carried out their main activity (work, studies, etc.) in **United Kingdom** 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 CN Bio Innovations (UK), must not be enrolled in a doctoral school or have been awarded a doctoral degree.

### VISA

The PhD candidate will need to apply for a VISA (with their costs covered by the grant).

UKRI recommends the Global Talent VISA:

[https://www.ukri.ac.uk/mariecurie/Documents/factsheet\\_heu\\_msca\\_mobility.pdf](https://www.ukri.ac.uk/mariecurie/Documents/factsheet_heu_msca_mobility.pdf)

## 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,



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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 September 2023;
- 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 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: **[careers@cn-bio.com](mailto:careers@cn-bio.com)**

### Equal opportunities

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.

**Send your application to [careers@cn-bio.com](mailto:careers@cn-bio.com)**

**before the 15<sup>th</sup> April 2023**