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Individual Research Project

Doctoral Researcher 4

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 chimeric antigen receptor (CAR)-T cell immunotherapies have shown outstanding results in hematologic malignancies. Nevertheless, the physical barriers represented by cellular and non-cellular components of the tumor microenvironment combined to the abnormal vasculature and high interstitial fluid pressure, hamper an efficient tumor infiltration of CAR-T cells in solid tumors. 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 disrupt these barriers, i.e. 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.

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DESCRIPTION OF THE INDIVIDUAL RESEARCH PROJECT

The purpose of this PhD project is to perform *in vitro* and *ex vivo* OMICS-based high-throughput assessment of toxicity and cellular interactions of engineered magnetic nanoparticles (NPs) to support rapid development and clinical uptake. This PhD project will utilize integrated novel methodologies, including 1. Advanced cell-based *ex vivo* and *in vitro* high-throughput screening using patient-derived primary tumor cell cultures and established cell lines for therapeutic potentiation of the uptake and efficacy of the NPs, 2. Toxicogenomics for modelling adverse outcome pathways and safety assessment; and 3. High-content imaging-based analyses to identify biological interactions of the NPs. The research will focus on cell-based toxicity and therapy efficacy assessment, and, significantly, on producing large volume of biological data on cellular processes affected by the iron carbide NPs using the Tox5 score developed by Misvik Biology. In addition, state-of-the-art organ-on-chip technologies and other new approach methodologies developed by the Melomanes partners will be used to validate findings to develop the best models into potential biomarkers and therapeutic strategies for the iron carbide conjugates for cancer therapy.

Objectives

- 1°) Develop and apply *ex vivo* tissue and cell models for the analysis of the safety of the magnetic nanoparticles.
- 2°) Assess and predict the toxicity and biological activity of the magnetic NPs.
- 3°) Identify combinatorial therapeutic strategies to potentiate the uptake and efficacy of the NPs.

Expected Results

- 1) Identification and characterization of cellular processes affected by the exposure of human cells and tissues to the multifunctional NPs.
- 2) Categorization of the nanotoxicology profiles of the new materials to existing nanosafety records of nanomedicines.
- 3) Identification of targets to be used for sensitising cancer cells with the multifunctional NPs.

Supervisors and host organisations

Main supervisors and recruiting organisation:

Dr. Juha K. Rantala, Misvik Biology Oy, Turku, Finland,

Dr. Vesa Hongisto, Misvik Biology Oy, Turku, Finland,

Misvik Biology is pre-clinical stage life science company specializing in precision oncology and nanotoxicology research. Misvik provides cell-based high-throughput-driven research services, cutting-edge imaging-based and high-throughput screening platforms as well as omics analysis services. Over the last eight years the company has developed laboratory technologies for single cell resolution analysis of drug response characteristics and regulatory safety testing of engineered nanomaterials. Misvik is partner



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in 4 ongoing EU funded large collaborative research project developing safety governance of engineered nanomaterials.

Co-supervisor (academic partner):

Prof. Davide Bonifazi (University of Vienna)

Dr. Emmanuel Donnadiou (National Institute of Health & Medical Research, INSERM)

Planned mobility track and secondments:

INSERM; France (6 months, M16-M21): Assessment of the safety of multifunctional iron carbide NPs using tumor slices.

University of Vienna; Austria, (4 months, M30-M33): Biodegradation of the NPs monitored by physicochemical characterization

Enrolment in Doctoral School:

University of Turku, Drug Research Doctoral Programme (DRDP), Turku, Finland

TERMS AND CONDITIONS FOR EMPLOYMENT

Duration

36 months

Salary

4 063 €/per month (gross, before compulsory employer contributions)

Other allowances

Mobility allowance 600€/per month, family allowance if applicable 660€/per month (both gross, before compulsory employer contributions)

THE CANDIDATE PROFILE

Academic prerequisite

We are looking for an excellent candidate interested in combining cell-based biological studies with bioinformatics analyses to advance the use and efficacy of the novel nanomaterials as new approaches for more effective cancer therapies. The successful candidate should hold a MSc degree in relevant biological sciences, biochemistry or a related discipline and preferably have previous experience in bioinformatics and next generation RNA/DNA sequencing.



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Technical skills and knowledge required

The successful candidate should preferably have previous experience in high-throughput screening and bioinformatics.

Soft skills

- Curiosity for science, creativity, and autonomy
- Great sense of thoroughness and organization
- Writing skills in English and ability to summarize are essential

Exclusion criteria

The candidate, at the time of recruitment, must hold a Master's degree.

The candidate must not have resided or carried out their main activity (work, studies, etc.) in Finland 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 Misvik Biology 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 September 2023;



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- 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: rantala@misvik.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.

Apply for this position before the 15.4.2023