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Protease-guided tumor targeting tools to revolutionize cancer diagnostics and treatment (OncoProTools)

Doctoral Candidate (DC4) – Innovative Target Modulators for FAP-targeting UniCAR T therapy

About OncoProTools

OncoProTools is an MSCA Doctoral Network that is currently starting up. The mission of OncoProTools is to develop tumor targeting strategies for cancer diagnostics and therapeutics, to make them more effective, selective, patient-friendly and personalized. Tumor targeted diagnostics and therapeutics are molecules that are typically equipped with a vector unit. The vector unit binds to a protein that is overexpressed on cancer cells or in the Tumor Micro-Environment (TME), causing the diagnostic or therapeutic payload to accumulate in the tumor. Exciting, recent innovations rely on small molecule vectors that target TME proteases. Proteases are ideal candidates for tumor targeting: they are often strongly overexpressed in the TME and possess an active site that allows high-affinity anchoring of vectors. Members of this consortium have played a leading role in these recent developments.

OncoProTools wants to force breakthroughs by:

1) Exploring innovative venues for protease targeting in cellular immunotherapy.
2) Discovering novel vectors that bind to other TME proteases, like cathepsins and granzymes.
3) Personalized applications of protease targeting: deliver innovative diagnostics through deeper understanding of TME biology.

OncoProTools will deliver a training program to 10 Doctoral Candidates that truly captures the MSCA values, hence providing them with all capabilities to become leaders of tomorrow's R&I in Europe.

About Helmholtz-Zentrum Dresden-Rossendorf

The Helmholtz-Zentrum Dresden-Rossendorf (HZDR) is a member of the Helmholtz Association of German Research Centres and strives for new knowledge to improve and sustain our livelihoods. The HZDR conducts research in the fields of Energy, Health and Matter in Dresden, Freiberg, Leipzig, Schenefeld, Görlitz and Grenoble. Our largescale facilities are also available to external guests from around the world. Establishing interdisciplinary research, focusing on the future, and thinking outside the box are all paramount to us. That is why we are working closely together with other research institutions within the Helmholtz Network. We also cooperate with universities and non-university partners to form strategic partnerships like DRESDEN-concept. The HZDR has 1400 employees including around 500 scientists and around 170 doctoral students from more than 60 nations. The HZDR considers it a duty to provide optimal working conditions for its staff. High scientific productivity is based on motivated and well-qualified personnel. The HZDR offers exciting science and excellent research infrastructures, interesting and highly diverse work, professional and family life compatibility, a gender equality plan, optimal support for young (international) staff and students, an international office, a guest house, German and English language courses, extensive opportunities for doctoral candidates, recurring awards for outstanding professional education and occupational health management.

The Institute of Radiopharmaceutical Cancer Research is engaged in Radiopharmaceutical Cancer Research. The institute's activities are focused on research and development towards radiolabelled compounds including immunotherapeutics for the functional characterisation and therapy of tumors but also other diseases such as autoimmune diseases and infections. Furthermore, computational methods for the quantitative characterisation of tumors by molecular imaging are developed. In particular, this includes mainly positron emission tomography and connected multimodal imaging techniques. **Prof. Dr. Michael Bachmann** (cumulative impact above 1100, h-factor 57) is one of two directors of the institute of Radiopharmaceutical Cancer Research. In parallel, he is a full Professor at the Medical Faculty of the "Technische Universität Dresden" and one of the Directors of the National Center for Tumor Diseases (NCT/UCC). He is an expert in the development of immunotheranostics including bispecific antibodies and cellular immunotherapies. For example two bispecific T cell engagers (BiTEs) designed and developed by him are currently tested in clinical phase 1 trials. In addition, he is the inventor of modular chimeric antigen receptor platforms including the UniCAR and RevCAR system. The UniCAR system is the first switchable CAR platform which has recently shown not only clinical efficacy but also full functionality including the proposed capability to repeatedly turn on and off the function of the genetically manipulated immune effector cells. Thanks to its modular character it can be adapted to almost all kinds of cancer diseases and also to autoimmune diseases, tissue rejection after transplantation and virus infections.

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Tasks description

This interdisciplinary doctoral position is hosted by the **Department Radioimmunology** of the Institute of Radiopharmaceutical Cancer Research at the Helmholtz Zentrum Dresden-Rossendorf. The Radioimmunology group has expertise in the development of novel strategies and technologies of antibody-based immunotherapies and cellular immunotherapies as well as diagnostics from bench to bedside. In particular, we further develop novel advanced and highly flexible modular and switchable chimeric antigen receptor platforms (UniCAR/RevCAR), novel technologies for molecular imaging during therapy (PET, SPECT) and/or novel radioimmunotherapeutic applications. The institute of Radiopharmaceutical Cancer Research has an overall research area of more than 3500 square meter well equipped including with a cyclotron for production of a variety of radionuclides (e.g., Cu64, F18, J123 etc.), PET, SPECT and MRT scanners for small animals, cLSM, SPR, animal facilities for labelled and unlabelled animals, conventional labs for chemical, biochemical, biological (cell biology, molecular biology (S1, S2 area)) and immunological labs. The latter ones are equipped with an automated cell processing machine for production of GMP grade CAR T cells (effector T cells, Tregs, NK cells), cell sorter including for GMP sorting, flow cytometer, and a GMP facility for routine production of radiolabelled and unlabelled molecules.

In this position, you will:

- Generate and characterize innovative UniCAR target modules (TMs) that allow bimodal cancer therapy (CAR T cell immunotherapy and radiotherapy).
- Perform analytical, biochemical and biological investigations on the UniCAR TMs.
- Set up advanced cellular evaluation models and deliver preclinical proof (cell, in vivo) of efficacy for newly designed UniCAR TMs.
- Write project reports for your local and network supervisors on a regular basis
- Successful candidates will apply in one of two graduate schools at the medical faculty of TU Dresden (e.g. DIGGS-BB)
- Participate actively to OncoProTools' training, dissemination, communication and valorization program.
- Prepare a doctoral thesis, and publish scientific articles related to the research project.

Furthermore, the selected candidate will take part in the following planned secondments:

- Academic secondment at University of Copenhagen (6 months, Denmark) to synthesize UniCAR TM1.
- Industrial secondment at CROmed (5 months, Hungary) for the *in vivo* evaluation of TM1.

Profile & requirements

- Applicants must hold a master's degree or equivalent in the field of Biology, Biotechnology, (Bio-) Chemistry or equivalent e.g. must have completed their medical studies
- Master students in their final year may apply. Final selection under the condition of showing transcripts of their master's degree in July (July 15th at the latest).
- Applicants must have a solid knowledge of immunology and/or protein biochemistry
- Applicants have obtained outstanding academic results
- Applicants must have an ability to understand and express themselves in both written and spoken English to a level that is sufficiently high for them to derive the full benefit from the network training.
- Applicants must be eligible to enrol on a PhD programme at the host institution (or at a designated university, in case the host institution is a non-academic organisation).
- Applicants must have the necessary academic skills and background to make the success of a doctoral degree.
- Applicants can be of any nationality but must comply with the Horizon Europe MSCA eligibility criteria:

HORIZON MSCA Mobility Rule: researchers must not have resided or carried out their main activity (work, studies, etc.) in the country of the host organisation 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 by the researcher as part of a procedure for obtaining refugee status under the Geneva Convention are not taken into account.

HORIZON MSCA eligibility criteria: supported researchers must be doctoral candidates, i.e. not already in possession of a doctoral degree at the date of the recruitment. Researchers who have successfully defended their doctoral thesis but who have not yet formally been awarded the doctoral degree will not be considered eligible.

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Benefits

- ✓ The selected candidate will be employed by the host organisation for **36 months.** In line with regulations and following a positive evaluation by the doctoral committee, HZDR may provide funding for an additional period of 6 months that may be further extended to a maximum of 12 months to complete a doctoral degree.
- ✓ **The start date will be from January, 1st 2023 onwards.**
- ✓ HZDR has received the following EU-grant to recruit a Doctoral Candidate (DC): monthly Living Allowance € 3.342,2; monthly Mobility Allowance € 600; and monthly Family Allowance € 660 (only if applicable). Please note that the final monthly, gross salary will result from deducting (from the mentioned amounts) all compulsory national labour taxes (social security, etc.) to be borne by the employer. More information: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/wp-call/2021-2022/wp-2-msca-actions_horizon-2021-2022_en.pdf. Moreover, funding is available for technical and personal skills training and participation in international research events.
- ✓ the opportunity to be part of an MSCA Doctoral Network: the selected candidate will benefit from the designed training programme offered by the host organisation and the OncoProTools consortium.
- ✓ The selected candidate will participate in international secondments to other organisations within the OncoProTools network and in outreach activities targeted at a wide audience.

Please, find additional information in the Horizon Europe Work Programme MSCA from p.75 onwards.

Application

- Interested candidates are invited to apply for this position by filing in the application form on our website (www.oncoprotools.eu), via this link: https://www.uantwerpen.be/en/projects/protease-guided-tumor-targeting-tools/job-openings/submit-your-applicat/ .
- The closing date for applications is **July 15th 2022**.
- The selection committee will review all of the applications as soon as possible after the application deadline. As soon as a decision has been made, we will inform you about the next steps in the selection procedure.
- Pre-selected candidates will be invited to take part in the recruitment event in Antwerp (Belgium) on October 6th, 2022. OncoProTools will offer a financial support of max. € 200 to attend this physical event.
- The recruitment process of DCs within OncoProTools is in line with the principles set out in the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers.
- Ukrainian researchers are eligible to benefit from the Science4Refugees initiative without the need of holding the refugee status.

Additional information

For additional information about the research project and this individual position, please contact:

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HZDR HELMHOLTZ ZENTRUM DRESDEN ROSSENDORF

science4refugees

Disclaimer: please note that this offer is subject to the signature of the grant agreement nr° 101073231 expected by mid July 2022