

German Cancer Research Center | M123 | PO Box 101949 | 69009 Heidelberg | Germany

Position: PhD student – Biomarker identification from N²M² clinical study material to overcome resistance against targeted therapies in glioblastoma patients (m/w/d)

Research group: Clinical Cooperation Unit Neurooncology

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The German Cancer Research Center is the largest biomedical research center in Germany. With more than 3,000 employees, we run an extensive scientific program in the field of cancer research.

The Clinical Cooperation Unit Neurooncology at the DKFZ has research foci on molecular profiling-based multi-center clinical studies with consecutive biomarker profiling, cerebrospinal fluid liquid biopsies, characterization of glioblastoma (GB) stem cells and central nervous system (CNS) lymphomas as well as therapeutic CAR-T cell therapies.

We are recruiting a PhD student for the biomarker identification from a world-leading open-label, multi-center, phase I/IIa, umbrella NOA-20/N²M² patient study in which GB patients were assigned to one of eight different drug arms based on biomarker expression (<https://clinicaltrials.gov/ct2/show/NCT03158389?term=temsirolimus&cond=Glioblastoma+Multiforme&draw=3&rank=21>). The approximately 350 patients have already been recruited and study tissue is available for comprehensive analysis using a state-of-the-art multi-omic approach. The PhD student will characterize the tissues using single-cell RNA sequencing and proteomics. The resulting potential biomarkers that suggest response or resistance to the respective treatments are then spatially corroborated and finally functionally validated using CRISPR modifications and drug combination screens in high-throughput format. Established protocols for all methods are already in place and the PhD student will be initially taught these techniques.

Your tasks:

- Planning and execution of bulk RNA sequencing, single cell-RNA sequencing and proteomics for the characterization of patient GB tissues
- Application of modern multidimensional spatial methods (e.g. 10x Genomics Visium, Multiplex Ion Beam Imaging) for the validation of RNA and protein biomarkers from human and mouse tissue: paraffin/cryoembedding, preparation of slides on microtome/cryotome, acquisition of multi-color stainings on microscope

Foundation under Public Law

Management Board
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- State of the art cell culture techniques: Cultivation of GB cells as 2D monolayer on different *substrata*, 3D spheroids and organoid co-culture models, including thawing, splitting, modification and freezing of cells
- Functional *in vitro* analyses: Planning and execution of cell-based assays in high-throughput format, e.g. drug-screens
- Microscopic evaluation of genetic and pharmacological perturbations for correlation with the phenotype
- Molecular biology/protein chemistry: PCR, qRT-PCR, nucleic acid and protein isolation, Western blots
- Optional: Primary animal experimental GB research
- Code-writing/scripting and execution of image-based high-throughput screens and omics data
- Data-mining from publicly available datasets
- Statistical evaluation of results
- Documentation and critical evaluation of research results as well as preparation of publications, presentations and posters
- Preparation of the dissertation within the PhD project
- 65% Wet-lab, 35% Bioinformatics

Your profile:

Strong Requirements:

- Diploma or Master's degree in biological sciences (biology, biochemistry, biophysics, neuroscience, bioinformatics or related disciplines) and/or at least 10 semesters at a university
- Proficient in planning and conducting oncology, neurology and/or pharmacology experiments
- Profound scientific and technical expertise and experience in cell culture, cellular assays, cancer and neuronal cell biology, and pharmacologic compound studies
- Experience with a programming language (R, Python, Matlab, Java, etc.)
- Independent problem solving, collaboration and teamwork
- High degree of independence, motivation and interest in the development of modern methods and their application in translational cancer research

Plus:

- Familiar with scientific or technical literature within the scientific field and related areas
- Experience with high-throughput and omics technologies (RNA sequencing and proteomics) as well as imaging-based readouts e.g., widefield, confocal or light sheet microscopy
- Some experience in molecular cloning and genome editing
- Animal experimental experience (tumor implantation and drug treatment) and FELASA-B certificate

**We offer:**

- Highly clinically relevant projects at the crossroads of medicine, biology and bioinformatics with clinical-study patient material as the seed for hypothesis generation
- State-of-the-art omics technologies, high-throughput readouts and artificial intelligence-supported data analysis with high quality in-group bioinformatics support
- Hands-on wet-lab training of established workflows by trained biologists and interaction with trained bioinformaticians
- Multilayer supervision and guidance from renowned experts in the field (Prof. Dr. Wolfgang Wick, PD Dr. Tobias Kessler, M.Sc. Dirk Hoffmann)
- Integration into existing structures and collaborations within a leading glioblastoma consortium (UNITE-Glioblastoma; <https://www.unite-glioblastoma.de/>)
- Heidelberg campus with modern state-of-the art infrastructure and close collaboration of our research group with ones at other world-class institutes (Health and Life Science Alliance Heidelberg-Mannheim; <https://www.health-life-sciences.de/mitglieder/?lang=de>, <https://www.biorn.org/>)
- International research networks (Heidelberg-Harvard alliance)
- Doctoral salary (65%) and social benefits
- Several education and mentoring programs through the Helmholtz International Graduate School and UNITE-Glioblastoma consortium
- Flexible working hours
- Work within a warm-hearted, supporting, ambitious, international and freaking cool team

Please send your application to dirk.hoffmann@dkfz-heidelberg.de