



Heidelberg University Clinic

Heidelberg Universitätsklinik | Abteilung Neuroradiologie
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Department of Neuroradiology
Division of Immuno-Imaging
Emmy Noether Group Leader
Michael O. Breckwoldt, MD, Ph.D.

1x PhD position (3.5 year contract with possible extension) in the field of neuroimaging, neuroscience and brain tumor immunology in the Emmy Noether Group “Immuno-Imaging” (Head: PD Dr. Dr. Michael Breckwoldt) as part of **SFB 1389** in cooperation with Dr. Katharina Sahm (AG Prof. Michael Platten, DKFZ)

Project: VISUALIZATION AND CHARACTERIZATION OF IMMUNE RESPONSES IN H3K27M MUTANT GLIOMAS

H3K27M-mutant gliomas represent a brain tumor entity with unfavorable prognosis and intrinsic therapy resistance. H3K27M-mutant gliomas exhibit a heterogeneous appearance on routine MRI with currently limited sensitivity and specificity for initial diagnosis and therapy monitoring. We have previously shown that mutation-specific immunity associated with delayed tumor growth can be induced by a vaccine targeting H3K27M in a humanized mouse model and in adult patients. Imaging characteristics of H3K27M-mutant gliomas and biomarkers for response to T cell-based immunotherapies will be analyzed in orthotopic patient-derived tumor models and clinical cohorts of adult patients with H3K27M-mutant gliomas.

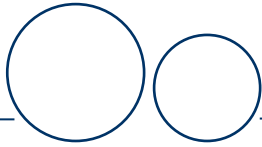
Specifically, this project aims to:

- Visualize the recruitment, infiltration and proliferation of mutation-specific T cell-receptor-transgenic T cells towards experimental tumors using correlative MRI and optical methods (light sheet microscopy and two-photon-microscopy)
- Spatially resolve and profile immune cell dynamics in the TME of H3K27M-mutant gliomas
- Develop imaging signatures of treatment response and resistance towards novel immunotherapy regimens for H3K27M-mutant gliomas

Background:

High field MRI is a versatile tool to monitor tumor infiltration and immune cell dynamics with high temporo-spatial resolution. The group combines advanced MRI techniques (immune cell tracking by nanoparticles, CEST, MR-elastography) and explores genetic and pharmacological means to manipulate the tumor microenvironment. Imaging approaches include high field MRI (**9.4 Tesla**) and correlative optical imaging (light sheet microscopy of cleared specimen, iDisco, vDisco) using **iron oxide nanoparticles** that are targeting innate immune cells or T-cells. Animal models of glioma will be employed to study cancer immunotherapies and its mode of action (e.g. targeted therapies, adoptive T-cell transfer, radioimmunotherapy). A second research line explores mechanisms of glioma cell invasion and imaging methods to visualize diffuse tumor cell infiltration in the adjacent brain parenchyma and its modulation during therapeutic intervention. Additional methods (light sheet microscopy of cleared specimen, immunohistochemistry and flow cytometry) will be employed to dissect molecular mechanisms of therapeutic efficacy and resistance.

A background in biophysics (MR physics), cancer biology, neurobiology or experimental medicine would be desirable but is not a prerequisite. Experience in imaging (MRI or optical), animal handling, molecular biology or immunological techniques would be a plus. We seek a highly motivated PhD candidate or Post-doctoral fellow with an interest in translational and multi-disciplinary research (neuroimmunology, biomedicine, imaging sciences). We offer a dynamic and supportive research



environment within the Collaborative Research Center (CRC 1389, Unite Glioblastoma, www.unite-glioblastoma.de) with access to additional training in the graduate school of Neurooncology, international cooperations and plenty of opportunities to perform cutting edge research in one of the leading biomedical centers in Germany. We are part of the University Clinic Heidelberg and the CRC 1389 with long standing cooperations within the Clinical Cooperation Unit Neuroimmunology and Brain Tumor Immunology (Head: Prof. Michael Platten, www.dkfz.de/de/neuroimmunologie/index.php) and the Clinical Cooperation Unit Neurooncology (Prof. Wolfgang Wick, Prof. Frank Winkler).

Please send your application to Dr. Michael Breckwoldt (Michael.breckwoldt@med.uni-heidelberg.de) including a CV, letter of motivation and 2 references.

Contact:

Michael Breckwoldt, MD, Ph.D.
Emmy Noether Group leader: Immuno-imaging
Clinical Attending

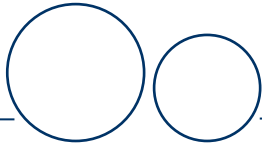
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References:

1. Grassl N, Poschke I, Lindner K, Bunse L, Mildenerger I, Boschert T, Jähne K, Green EW, Hülsmeier I, Jünger S, Kessler T, Suwala AK, Eisele P, **Breckwoldt MO**, Vajkoczy P, Grauer OM, Herrlinger U, Tonn JC, Denk M, Sahm F, Bendszus M, von Deimling A, Winkler F, Wick W, Platten M, Sahm K, A H3K27M-targeted vaccine in adults with diffuse midline glioma. **Nature Med.** 2023
2. J Hunger, K Schregel, B Boztepe, DA Agardy, V Turco, K Karimian-Jazi, I Weidenfeld, Y Streibel, M Fischer, V Sturm, R Santarella-Mellwig, M Kilian, K Jähne, K Sahm, W Wick, L Bunse, S Heiland, T Bunse, M Bendszus, M Platten and **MO Breckwoldt**, In vivo nanoparticle-based T cell imaging can predict therapy 1 response towards adoptive T cell therapy in experimental glioma, **Theranostics** 2023

V Turco, K Pfeleiderer, J Hunger, NK Horvat, K Karimian-Jazi, K Schregel, M Fischer, G Brugnara, K Jaehne, V Sturm, Y Streibel, D Nguyen, S Altamura, DA Agardy, Shreya S. Soni, A Alsasa, T Bunse, M Schlesner, MU Muckenthaler, R Weissleder, W Wick, S Heiland, P Vollmuth, M Bendszus, CB Rodell, **MO Breckwoldt**[#] and M Platten[#], T cell-independent eradication of experimental glioma by intravenous TLR7/8-agonist-loaded nanoparticles, **Nature Commun**, 2023, 14:771
3. K Schregel[#], L Heinz, J Hunger, C Pan, J Bode, M Fischer, V Sturm, V Venkataramani, K Karimian-Jazi, D Agardy, Y Streibel, R Zerelles, W Wick, S Heiland, T Bunse, B Tews, M Platten, F Winkler, M Bendszus, and **MO Breckwoldt**[#], A cellular ground truth to develop MRI signatures in glioma models by correlative light sheet microscopy and atlas-based co-registration, **J Neurosci**, 2023 7:JN-RM-1470-22



4. D Hausmann, DC Hoffmann, V Venkataramani, E Jung, S Horschitz, SK Tetzlaff, A Jabali, L Hai, T Kessler, DD Azorín, S Weil, A Kourtesakis, P Sievers, A Habel, **MO Breckwoldt**, MA Karreman, M Ratliff, JM Messmer, Y Yang, E Reyhan, S Wendler, C Löb, C Mayer, K Figarella, M Osswald, G Solecki, F Sahm, O Garaschuk, T Kuner, P Koch, M Schlesner, W Wick, F Winkler, Autonomous rhythmic activity in glioma networks drives brain tumor growth, **Nature**, 2023 Jan;613(7942):179-186
5. M Platten, L Bunse, A Wick, T Bunse, L Le Cornet, I Harting, F Sahm, K Sanghvi, C Leng Tan, I Poschke, E Green, S Justesen, G Behrens, **MO Breckwoldt**, A Freitag, LM Rother, A Schmitt, O Schnell, J Hense, M Misch, D Krex, D Stevanovic, G Tabatabai, JP Steinbach, M Bendszus, A von Deimling, M Schmitt, W Wick, Phase 1 trial of IDH1-vac, a peptide vaccine for IDH1R132H glioma, **Nature**, 2021, 592, 463–468