CSC-Tübingen PhD Scholarship Program

2024 application round: prospective PhD positions at the University of Tübingen

Faculty: Faculty of Medicine, Eberhard Karls University Hospital Tübingen

Institute / Section / Subject: Department of Dermatology & Werner Siemens Imaging Center / Therapeutic modulation of the pH within the tumor microenvironment to foster cancer immunotherapy

Supervising Professor(s): PD. Dr. Manfred Kneilling and Prof. Dr. Andre F. Martins

About the Supervisor(s): PD. Dr Manfred Kneilling is the head of the allergy section at the department of Dermatology and leads the team for inflammation and immunology at the Werner Siemens Imaging Center. Prof. Andre Martins leads the team Advance Metabolic Imaging and Cell Engineering (AMICI) at the Werner Siemens imaging Center.

Specification: Therapeutic modulation of the pH within the tumor microenvironment to foster Immune checkpoint inhibitor therapy and identification of *relevant metabolic biomarkers*

Topic Description: Immune checkpoint inhibitors (ICI) targeting CTLA-4 and PD-1/PD-L1 axis show promise in treating various solid tumors. However, only a fraction of patients experiences sustained responses, and many do not respond. Tumor stages, mutational burden, and heterogeneity contribute to ICI resistance, and the underlying mechanisms remain unclear. The tumor microenvironment's (TME) complexity and acidity, particularly in hypoxic regions, impact antitumoral immune responses. Acidosis, a prominent TME feature, increases PD-L1 expression on tumor cells and hinders T cell function. Our preliminary findings suggest that acidosis upregulates PD-L1 via the IFN-γ-STAT1 pathway, observed in specific tumor models. Investigating the interplay between TME acidity and immune checkpoint receptors is crucial to enhance ICI efficacy. We aim to explore acidity's effects on TME subtypes, normalize TME pH with targeted antibodies, and address anti-PD-L1 therapy resistance across cancer types, identifying predictive biomarkers using murine tumor models and multimodal hybrid imaging. The student will be supported by a strong team of interdisciplinary researchers;

Degree: PhD Exp. Med. / Dr. rer. nat.

Required Degrees: Master degree in Oncology, Medical Physics, Radiology, Biomedical Imaging, Biochemistry, biomedical technologies, or related degrees

Language Requirements: Excellent English communication skills are mandatory (high-level IELTS, TOEFL).

Notes: *The successful candidate will identify relevant metabolic biomarkers in immune-oncology. Ideally, the successful candidate has experience with: MRI, preclinical imaging, biostatistical analysis, and biochemistry techniques (cell culture, flow cytometry, qPCR, histology). Experience working with Matlab, R, and Python would be a plus but not mandatory. The candidate should integrate well into a multidisciplinary group of people aiming to translate technologies into the clinical setting.*