Proposed Projects

for the application as a Postdoc within the Medical Scientist Programme *InFlame*

P1 *Group of Benjamin Risse, Computer Science & Geospatial Data Science, Faculty of Geoinformatics & Mathematics and Computer Science*

Multimodal data integration and analysis of inflammation dynamics using deep learning and large language models

Imaging techniques such as molecular/cellular live-imaging systems and genetic tools are increasingly applied to study inflammatory processes. Yet, systematic quantitative evaluation remains challenging due to the need for interdisciplinary expertise. We implemented an annotation tool enabling efficient interaction with clinical data and are currently evaluating and expanding eye-tracking–based annotation strategies to further improve annotation efficiency, quality, and scalability. Applied successfully to inflammation datasets, these approaches facilitate the generation of curated resources that are subsequently analyzed using modern representation learning methods to uncover temporal patterns in inflammation dynamics. We will next extend this work through multimodal machine learning models that integrate imaging, genetic, and clinical metadata. We will investigate architectures that jointly embed heterogeneous data streams and capture temporal dependencies, enabling richer cross-modal representations. Large language models (LLMs) will serve as semantic integration layers, linking quantitative image-derived features with unstructured textual data such as clinical reports, experimental protocols, and biomedical literature. This approach aims to enhance interpretability, enable automated hypothesis generation, and improve predictive performance in inflammation research.

P2 *Group of Michael Schäfers, Molecular Imaging/Nuclear Medicine, Faculty of Medicine*

Deciphering molecular and cellular dynamics of Inflammation in tumors through multiscale imaging

Tumors possess a complex interplay between innate and adaptive immune cells within their immune-suppressive microenvironment. The synergetic effect of the different immune escape mechanisms employed by tumor cells, including modulation of innate immunity and inhibition of the adaptive response, hinders the effectiveness of new therapeutic strategies. Within the InFlame program, we aim to assess the spatial and temporal heterogeneity of the pro-tumorigenic inflammatory environment and challenge tumor progression with targeted therapies in animal models. In vivo molecular imaging spatial transcriptomics, and multispectral flow cytometry will be used to decipher the dynamics and interplay between tumor and recruited immune cells, and assess the inflammatory response following innovative treatment strategies, e.g., focused ultrasound in brain tumors, immunomodulatory regimes, neo-adjuvant vaccines, etc., aiming to

reprogram the tumor microenvironment. Identification of time-dependent molecular signatures of brain tumors will further support the development of targeted therapeutic regimens toward a more effective clinical application.

P3 *Group of Oliver Söhnlein, ZMBE, Faculty of Medicine*

Neutrophil dynamics in acute and chronic inflammation

Neutrophils, the most abundant white blood cells in humans, are produced in the bone marrow in a process termed granulopoiesis. Among all cells in the human body, neutrophils have the highest turnover, but their production kinetics and the adaptation of granulopoiesis to inflammatory insults remain unknown. Here we will use a combination of scRNAseq to assess trajec-tories of granulopoiesis, EdU/BrdU pulse chasing to time stamp proliferating progenitors, and fate mapping approaches to study transitions of neutrophil progenitors. These approaches will be used in steady state to generate a mathematical model of baseline circadian neutrophil production rates and transition times between the maturation stages. This model will then be applied to settings of acute bacterial and viral infection, as well as to systemic inflammation, to assess the short- and long-term adaptation of granulopoiesis to infection and inflammation. In addition, we will use a model of high-fat diet-induced hyperchole-sterolemia to assess the impact of chronic metabolic challenges on the kinetics of granulopoiesis.

P4 *Group of Tim Lämmermann, Medical Biochemistry, ZMBE, Faculty of Medicine*

Dissecting multilayer cell-cell communication between inflammatory cells

In response to tissue injury or infection, various immune cell types initiate a complex, multilayered inflammatory response aimed at containing damage and protecting surrounding healthy tissue. Key players such as neutrophils, macrophages, monocytes, and mast cells accumulate at sites of inflammation, where they exhibit distinct and dynamic behaviors, ranging from rapid movement to a more stationary presence. These cells also release specific inflammatory mediators that facilitate communication between different immune cell populations. In this project, we will employ live-cell imaging to unravel the complexity of immune cell dynamics at sites of inflammation. Using both in vitro and tissue-based live-cell microscopy, we aim to analyze the interactions and behavioral patterns among various immune cell populations. By targeting key processes such as actin cytoskeleton remodeling, chemotactic signaling, and metabolic pathways, we will investigate the migration strategies and intercellular communication mechanisms that drive the coordinated inflammatory response. This will allow us to define the functional roles of individual immune cell types within this multilayered system. Our focus will be on models of sterile inflammation, providing a foundational understanding that can be extended to studies of multicellular immune responses against bacterial and viral infections.

P5 *Group of Stephan Ludwig, Virology ZMBE, Faculty of Medicine, affiliated with Faculty of– Biology*

Host-targeted strategies to fight hyperinflammatory respiratory virus diseases

In acute respiratory viral infections, such as influenza or COVID-19, not only does the direct damage to the respiratory tract by the cytolytic activity of the pathogens play a role, but also an excessive immune reaction that turns against the organism in an immunopathological manner. This includes the triggering of a "cytokine storm," which is responsible for infections progressing to severe courses. These mechanisms will be investigated in cell culture, ex vivo tissue models, and animal models. In addition to capturing the dynamics of viral replication, immune responses

and metabolic changes during mild vs. severe respiratory viral infections or bacterial co-infections, we will focus on possible interventions. A significant emphasis will be on approaches that have both antiviral and immunomodulatory activities, thus representing a new concept in anti-infective therapy.

P6 *Group of Kerstin Steinbrink, Dermatology, Faculty of Medicine*

Mechanisms of innate immunity as interventional targets for inflammatory skin diseases

The worldwide increase in allergic, autoimmune, and inflammatory skin diseases - driven by rising incidences and demographic changes - highlights a major unmet therapeutic need. While most treatments target the adaptive immune system, new evidence shows that innate immune mechanisms, particularly those involving myeloid cells and their crosstalk to other immune and resident cells, including fibroblasts and sensory neurons, play crucial roles in disease onset and persistence. However, therapies targeting these pathways are lacking, which could be an important addition to the existing therapy portfolio. To address this gap, in the InFlame project, we will investigate how myeloid cells interact with their environment in in vivo models of inflammatory and autoimmune skin diseases. Our approach integrates advanced imaging techniques, spatial proteomics, and RNAseq combined with bioinformatic methods. Key findings will be translated to corresponding patient cohorts, ensuring clinical relevance.

P7 *Group of Alexander Zarbock, Anesthesiology, Intensive Care and Pain Medicine, Faculty of Medicine*

Analysis of the Immune Response during Sepsis

Sepsis is a severe, life-threatening condition and remains a leading cause of mortality in intensive care units. An inappropriate host immune response to infectious pathogens results in progressive organ failure, hematological abnormalities, and metabolic dysregulation. During sepsis, both immune cell-specific and organ-specific immune responses contribute to the disease phenotype.

This research project will investigate the systemic inflammatory response, including the interactions and signaling events of distinct immune cell types during sepsis. Using animal models as well as established in vitro approaches, we will investigate immune cell recruitment and the molecular mechanisms underlying the inflammatory response during sepsis in detail. High-resolution microscopy, flow cytometry, biochemical analyses, and (single-cell) RNA sequencing will be used to visualize and characterize the dynamics and activation of recruited immune cells in various organs. We aim to validate and translate the insights gained from basic research into clinical studies. Furthermore, we will collect biomaterials to enable reverse translational research.

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