ImmunoTools *FlowISiAM* Award 2024

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Intracellular proteins in activated blood monocytes as potential biomarkers for the differential diagnosis of pancreatitis and pancreatic cancer.

Pancreatic cancer is a significant global health issue. It ranks as the fourth and seventh leading cause of cancer-related death in Western countries and China, respectively. Despite advances in disease management, the overall 5-year survival remains low at 5 – 9%. Smoking, diabetes, chronic pancreatitis, family history, obesity, and heavy alcohol consumption are major risk factors. Diagnosis relies on imaging (MRI, CT) and pathological examination. The most common pancreatic tumor is pancreatic ductal adenocarcinoma (PDAC), accounting for 90–95% of cases. Surgery remains the primary therapeutic option. Despite decades of research, no reliable diagnostic test exists for early pancreatic cancer detection. Challenges include nonspecific symptoms, lack of reliable biomarkers, and limited imaging resolution due to the pancreas's retroperitoneal position. However, early molecular detection is feasible, requiring better disease markers. Identifying relevant mutations and monitoring cellular changes could aid in identifying at-risk individuals.

In this project we will investigate the extent to which monocytes that have phagocytosed proteins derived from PDAC or from pancreatitis can be detected in peripheral blood from patients. Subsequently, we will investigate whether a monocyte-based diagnostic approach can be developed, that allows to detect PDAC and/or pancreatitis and that can distinguish the two conditions.

We can build on previous collaborative work with INVIGATE (Dr. Andreas Wohlmann) and will evaluate phagocytosed biomarkers in defined monocyte subpopulations and correlate them with expert pathological and clinical results.

Experimental Design & Methods: We will analyze a cohort of patients (n = 50 - 60) from our clinic with suspected diagnosis of pancreatic cancer (PDAC) or pancreatitis. The results

obtained will be most accurate compared with the final diagnosis from the Institute of Pathology. Moreover, tissue and further blood samples will be processed and stored in the BioBank Rostock for subsequent analyses on further solid and liquid biomarkers.

Impact: The intended investigations will provide novel insights into whether phagocytosed epitopes from pre-selected biomarkers can be detected by *FlowISiAM* analysis and how they correlate with presence of PDAC individual levels in CSF. Furthermore, we look forward to obtain confirmation of recently obtained results for principal traceability of AD related markers by *FlowISiAM* in peripheral blood monocytes/macrophages. If successful, we anticipate a promising foundation for a novel blood-based test concept early diagnosis of AD.

Cooperation partner: The group of Privatdozent Dr. Michael Linnebacher will work together with ImmunoTools to adjust the experimental and instrumental set-up to conduct *FlowISiAM* analysis. Furthermore, ImmunoTools and INVIGATE will provide previously developed molecular probes from a proprietary collection of mAbs to antigens specific for cancer, for gastrointestinal tissues as well as other antibody reagents for *FlowISiAM* analysis. Privatdozent Dr. Michael Linnebacher and Dr. Andreas Wohlmann (INVIGATE) intend to intensify the preexisting and further expand the work on the development of optimized monoclonal antibodies for detection of cancer and inflammation related molecular signatures within the *FlowISiAM* setting.

ImmunoTools *FlowISiAM* AWARD for **Michael Linnebacher** includes

antibodies for *FlowISiAM*, know how transfer and protocol, support regarding selection of specific antibodies against specific biomarkers from INVIGATE, expert assistance in evaluating the results obtained, and integration into the ImmunoTools *FlowISiAM* network.

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