RESEARCH PROJECT

“Fibrinogen uptake in cancer cells: good or bad?”

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Elite Graduate Program “Human Biology”

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Effect of Fibrinogen uptake on the expression of HMGB1 in different cell lines

Manasvini Sridharr is currently a student in the Elite Master of Science Program in Human Biology at Ludwig Maximilian University (LMU). In collaboration with the Walther Straub Institute of Pharmacology and Toxicology, she completed the following study during an 8-week internship under the guidance of Dr. Elmina Bach.

Introduction to PDAC – Pancreatic Ductal Adenocarcinoma

Pancreatic ductal adenocarcinoma (PDAC) accounts for more than 90% of pancreatic cancers and develops in the exocrine compartment of the pancreas. Surgery and chemotherapy can improve the survival of patients at the early stage of the disease; however these interventions in patients with late stages of the disease are often unsuccessful and the formation of distant metastases remains a challenge, as this constitutes the main cause of death in PDAC. The poor prognosis in PDAC patients is also often associated with delayed diagnosis and resistance to conventional therapies due to the immunosuppressive tumor microenvironment. The tumor microenvironment of PDAC is characterized by its multifaceted nature, involving dynamic interactions among neoplastic cells, stromal cells, inflammatory immune cells, myeloid-derived suppressor cells, and extracellular matrix proteins. Additionally, PDAC is associated with a hypercoagulable state, contributing to an elevated risk of venous thromboembolism. Fibrinogen has been proposed as a potential biomarker in the serum of PDAC patients compared to healthy subjects. Fibrinogen plays an important role in blood clotting and inflammation. Thrombin released from activated endothelium and platelets cleaves fibrinogen to fibrin, further inducing clot formation and recruitment of inflammatory immune cells. In line with elevated levels of fibrinogen, a strong deposition of fibrin was described in PDAC tumor tissues compared to normal pancreatic tissues. Although fibrin(ogen) levels were found elevated in advanced tumor stages in many solid cancer types, including PDAC, the molecular mechanisms of fibrinogen uptake and release remain elusive.

Aim of the study: The fibrinogen uptake capacity between normal pancreatic epithelial and PDAC cells

In this study, the fibrinogen uptake capacity between normal and PDAC tumor cell lines was analysed, using mouse and human PDAC, as well as normal pancreatic cell lines (HPDE, KPC and Panc1). Interestingly, a significant enhancement in FGN uptake in cancer cells was observed, highlighting the potential regulatory role of oncogenic pathways in this uptake mechansism. This research indicates that fibrinogen uptake mechanisms are differentally regulated between normal and pancreatic cancer cells, which may influence the fibrin(ogen) levels during cancer progression and metastasis, thereby modulating the response to the anti-cancer treatments

Future perspectives

Future studies will decipher the underlying molecular mechanisms, including the kinetics of fibrinogen uptake and release during PDAC tumor growth and progression. Additionally, the study will analyze the contribution of the uptake process to several hallmarks of tumor cells, including invasion, inflammatory cell recruitment, cytokine release, blood clotting and resistance to the anti-cancer therapies in PDAC.

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