MASTER THESIS

“Pancreatic cancer research”

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Elite Graduate Program “Human Biology - Principles of Health and Disease”

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Pancreatic Cancer, a Tough Challenge

Leon Heffinger studied in the Elite Master Program “Human Biology - Principles of Health and Disease” at Ludwig-Maximilians-University Munich. During his external Master’s Thesis at the Karolinska Institutet in Stockholm, he investigated sex differences in the tumor immune microenvironment in pancreatic cancer.

Pancreatic Cancer Is One of the Deadliest Cancers Pancreatic cancer ranks as the third leading cause of cancer-related death, and it is expected to become second by 2030. Additionally, it is one of the deadliest cancers, with an overall survival rate of only six months. Late diagnosis and resistance against common cancer therapies are the main reasons for a negative prognosis. Approximately 90% of pancreatic tumor mass consists of connective tissue, known as the stroma. The stroma serves as a mechanical barrier, preventing drugs from reaching the cancer cells. Another stroma characteristic is the suppression of the body’s own immune cells, hindering them from targeting and killing cancer cells. This immunosuppressive tumor microenvironment (TME) drastically reduces the efficiency of newly developed cancer immunotherapies.

Innovative, Sex-Related Cancer Research

In previous research projects, our group identified the Formyl Peptide Receptor 2 (FPR2) expressing macrophages as key immunosuppressors in pancreatic cancer. Increased expression of this receptor was associated with a significantly reduced survival rate in female pancreatic cancer patients. These findings raise the question of whether other sex-specific factors influence tumor immune microenvironment (TIME). Preliminary results from publicly available RNA sequencing data of pancreatic cancer patients revealed various differentially expressed signaling molecules in both sexes.

Leon Heffinger investigated some of the differentially expressed signaling molecules identified via RNA sequencing analysis. Consequently, he treated established female and male pancreatic cancer cell lines co-cultured with immune cells from healthy donors matching the respective sex with these molecules. The killing rates of the cancer cells and the frequency of different immune cell subsets were analyzed. This setup allowed us to identify sex-specific effects of the respective molecules on cancer cell killing and whether they induce a shift toward a tumor-promoting or tumor-suppressing TIME. Two molecules showed an effect in both sexes, whereas three molecules significantly influenced the killing rates only in females. These immunoregulatory molecules, along with their related signaling pathways, hold promise for further identifying possible biomarkers or treatment targets for developing sex-specific therapies in pancreatic cancer.

New therapeutic strategies are urgently needed to improve pancreatic cancer prognosis. Since pancreatic cancer research has not focused on sex differences, this could prove to be a promising approach to improve patient prognosis.

More on the Elite Graduate Program:

www.elitenetzwerk.bayern.de

https://www.mhb.uni-muenchen.de/index.html

https://ki.se/en/research/groups/tumor-immunology-and-immunotherapy-group-dhifaf-sarhan#tab-research-group-dhifaf-sarhan