FLT3 RECEPTOR AS A POTENTIAL PROGNOSTIC BIOMARKER AND THERAPEUTIC TARGET IN PANCREATIC CANCER

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Pancreatic ductal adenocarcinoma (**PDAC**) is among the most aggressive and difficult to cure cancer types, therefore the discovery of possible diagnostic and treatment biomarkers and therapeutic targets is very important. One of the potential candidate biomarkers is receptor tyrosine kinase **FLT3**. FLT3 is mainly expressed in haematopoietic progenitor cells, but was also identified as a specific pancreatic cancer prognostic biomarker using proteomic analysis [1].

In this study we examined the level of FLT3 receptor in surgically removed PDAC tumors. Tissue samples obtained from surgery due to nonmalignant diseases of pancreas or duodenum were used as nonmalignant (healthy) control. Also primary cell cultures from PDAC tumors were obtained by outgrowth method. A correlation between better survival of PDAC patients and the FLT3 receptor expression in tumors as identified by mass spectrometry was observed. **PDAC-specific expression** of FLT3 receptor was confirmed by Western Blot analysis in tumor samples, compared to healthy pancreatic tissue, and in PDAC patient-derived primary cell lines. Next step was to evaluate the activity of FLT3 receptor. We showed the relative levels of FLT3 ligand expression in primary cell cultures utilizing the quantitative polymerase chain reaction (qPCR) method. Analysis indicated the **FLT3 ligand expression** and allowed us to confirm that FLT3 receptor can be activated in primary PDAC cultures. Finally, the effects on primary cell lines from FLT3 receptor inhibitor ASP2215 alone or in combination with other chemotherapeutic agents were measured. Analysis of cell dissemination from spheroids that mimics invasiveness showed that **ASP2215 can inhibit cancer cell invasiveness**. Several of primary cell cultures analysed were sensitive to FLT3 inhibition by ASP2215. Moreover, we demonstrated that a combination of ASP2215 with FGF (fibroblast growth factor) receptor inhibitor BGJ398 is **cytotoxic to all primary PDAC cell cultures** analysed.

These findings led us to propose FLT3 receptor as a potential prognostic biomarker and therapeutic target in pancreatic ductal adenocarcinoma.

[1] Ger et. al. (2018); *Proteomic Identification of FLT3 and PCBP3 as Potential Prognostic Biomarkers for Pancreatic Cancer*; Anticancer Research, 38(10), 5759–5765.