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**Liquid Biopsies for the analysis of KRAS mutations in circulating
DANN in patients with pancreatic carcinoma**

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The present work deals with the investigation of cell-free DNA (cf DNA) and KRAS mutations in the blood plasma of patients with pancreatic cancer as a marker to monitor treatment response.

The study is based on a biomaterial bank and the associated clinical documentation, which has been conducted since 2014. In the process, plasma samples were regularly taken from patients with gastrointestinal tumors in the course of their disease and used for the subsequent experimental evaluation of the study. The plasma of patients with pancreatic cancer was analyzed for the presence of cf DNA and the allele frequency of KRAS mutations using digital droplet PCR. The results were compared with the respective radiological re-staging examinations and the concentrations of known markers such as LDH, Ca19-9 and CEA. By correlating these data, it was investigated to what extent the cf DNA concentration and the allele frequency of the KRAS mutations in the plasma are suitable as prognostic markers for a therapy response or early progression.

In this study, the cf DNA concentration proved to be superior to the other markers in terms of correlation with radiological staging. Despite heterogeneous results, a clearly recognizable and significant tendency of the cf DNA concentration values to predict tumor progression was detected ($p=0.011$; $AUC=0.767$). The KRAS mutation frequency in cf DNA also showed a tendency to predict the course of the disease, but data were only available in 25 cases. The other already known markers LDH ($p=0.698$; $AUC=0.456$), CEA ($p=0.157$; $AUC=0.788$) and Ca 19-9 ($p=0.793$; $AUC=0.547$) did not provide significant benefit in terms of predicting tumor progression. However, only relatively few data were available for these markers, too. LDH values were available in 93% of cases, Ca 19-9 in only 43% and CEA in 30%. With regard to prediction of overall survival, cf DNA concentration showed a tendency, but no significant correlation (correlation coefficient = -0.078). No reliable correlation with overall survival could be found among the other markers either.

The cf DNA concentration in plasma proved to be the most trustworthy of all markers and should be tested for its validity in further studies. The KRAS mutation frequency in cf DNA also showed a tendency to predict the further course of the disease, but it should be tested with a larger cohort and possibly with more accurate analytical methods.