Introduction
Pancreatic cancer is the fourth leading cause of cancer-related deaths in the Western world, and less than 5% of the patients survive longer than five years. With access to antibodies produced within the Human Protein Atlas [1], we have applied a multiplexed antibody bead array for high-throughput protein profiling of plasma [2]. We investigated the plasma proteomes of pancreatic cancer patients with the aim of identifying organ-specific proteins that are associated to advanced pancreatic cancer. The candidate proteins could complement existing tools for the early detection of pancreatic cancer, assessment of tumor stages, and for predicting patient survival.

Methods
Protein profiles were generated with multiplexed assays and 10,000 antibodies to identify promising proteins (Figure 1A). Antibody selectivity was then validated using immunocapture mass spectrometry (IC-MS, Figure 1B). Validated antibodies were chosen to build a dual-binder ELISA-type assay (Figure 1C), with the aim to quantify the protein concentrations in plasma.

Age and gender matched samples from the EndoTAG study (Table 1) [3] were analyzed for contrasting patients with locally advanced cancer and patients with metastatic cancer. In an extended discovery screening, a second independent set of 399 plasma samples from the BIOPAC study (Table 2) [4] were profiled.

Results
Among several candidate proteins with a significant association to cancer stage, we found Fibrinogen-like protein 1 (FGL1) to be associated with survival (Figure 2A). Plasma levels of this pancreas- and liver-specific protein correlated with clinically measured markers of inflammation, liver damage, and cancer cell proliferation including serum IL-6 (p=8.10-16), BASP (p=1.5.10-10), CRP (p=3.3.10-14), and YKL40 (p=4.2.10-11) (Figure 2B). The target was highly enriched by the antibody (Figure 2C). We further built dual-binder assays that confirmed our discovery data.

Conclusion
We have investigated two independent study sets for pancreas-specific proteins in plasma associated with pancreatic cancer. We found FGL1 as a protein expressed by the pancreas that was significantly linked with survival and clinical markers indicative for inflammation. Upon evaluation in further sample sets, the current findings could serve as a potential complementing tool for prognosis and monitoring of tumor progression in pancreatic cancer.

References

Profiling of plasma for proteins associated to pancreatic cancer
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