**Supplementary Figures**

**Table S1. Proteomics data**

**Figure S1**

**Urine proteome analysis**. **A**, schematic outline of the study. **B**, classification of total identified proteins according to sub-cellular localisation and **C**, functional activity determined by Ingenuity Pathway Analysis. H: healthy, CP: chronic pancreatitis, PDAC: pancreatic ductal adenocarcinoma, GeLC/MS/MS: SDS-PAGE-Liquid Chromatography-Tandem Mass Spectrometry.

**Figure S2**

**Correlation of the three urinary biomarkers and plasma CA19.9 (CA19.9p). A**, Correlation plots (Navy blue: Healthy; Turquoise: chronic pancreatitis (CP); Purple: pancreatic adenocarcinoma (PDAC). **B**, Pearson correlation coefficients and corresponding significance (NS: non-significant, \*: p<0.05, \*\*: p<0.01, \*\*\*: p<0.001).

**Figure S3**

**Diagnostic performance of urine biomarkers in discriminating pancreatic adenocarcinoma all stages (A-C) and stage I-II (D-F) from chronic pancreatitis patients**. **A,** ROC curves of PDAC (n=143) versus CP (n=62) patients for individual urine biomarkers in the training set (70% of the data). **B**, ROC curves of PDAC versus CP patients for the panel in the training set and in the independent validation set (30% of the data, PDAC n=49, CP n=30). **C**, Summary table. **D**, ROC curves of individual urine biomarkers in training dataset (70%, PDAC stage I-II n= 56, CP=66). **E**, ROC curves of the panel in training and validation (PDAC stage I-II n=15, CP n=26) dataset. **F**, Summary table. Cnorm, creatinine-normalised, creat, creatinine, AUC: area under the curve SN: sensitivity, SP: specificity with 95% Confidence Interval (CI). SN and SP in the validation set were derived for optimal cutpoint determined in the training dataset.

**Figure S4**

**Exploratory comparison of plasma CA19.9 and the urine biomarker panel in discriminating early pancreatic adenocarcinoma from chronic pancreatitis patients. A**, ROC curves of the biomarker panel with corresponding plasma CA19.9 alone and in combination comparing CP urine (n=50), and urines from PDAC stages I-II (n=71) and, I-IIA (n=16) (**B**). **C**, Summary table. AUC: area under the curve, SN: sensitivity, SP: specificity with 95% Confidence Interval (CI). SN and SP in the validation set were derived for optimal cutpoint determined in the training dataset.

**Figure S5**

**Urine biomarker concentrations in different tumours**. Scatter dot plots of urine LYVE1, REG1A and plasma CA19.9 in different hepatobiliary pathologies and early stages of pancreatic adenocarcinoma (I-IIA, n=16) and I-II (n=71). The level of TFF1 protein was not measured in these samples due to substantial modifications made to the original ELISA assay by the source company at the moment of this analysis. IPMN (n=33): intraductal papillary mucinous neoplasm, AMP (n=26): ampullary cancer, NET (n=18): neuroendocrine tumour, CHL (n=24): cholangiocarcinoma, DuCA (n=16): duodenal cancer. Bars indicate median and IQR values. Upper bars: Kruskal-Wallis/Dunn’s post test, \*: p<0.05, \*\*: p<0.01, \*\*\*: p<0.001; where not shown, p>0.05 (no adjustment for multiplicity was made).

**Figure S6**

**Expression of the protein biomarkers in pancreatic cancer tissues**. **A**, Immunohistochemical analysis of REG1A: i) REG1A in poorly differentiated PDAC, ii) luminal REG1A in malignant glands. **B**, TFF1: i) heterogenous expression in cancer,, ii) luminal TFF1 in malignant gland**. C**,LYVE1 expression in the scattered lymphatic vessels i) in the muscle layer and ii) in the stroma surrounding malignant gland. **D**, The biomarker levels during monitoring of pancreatic adenocarcinoma patients: LYVE1, REG1A and TFF1were measured using ELISA in urine samples collected before surgery and during the patient’s follow up. Each point represents log-transformed ELISA values at a particular time point (x-axis).