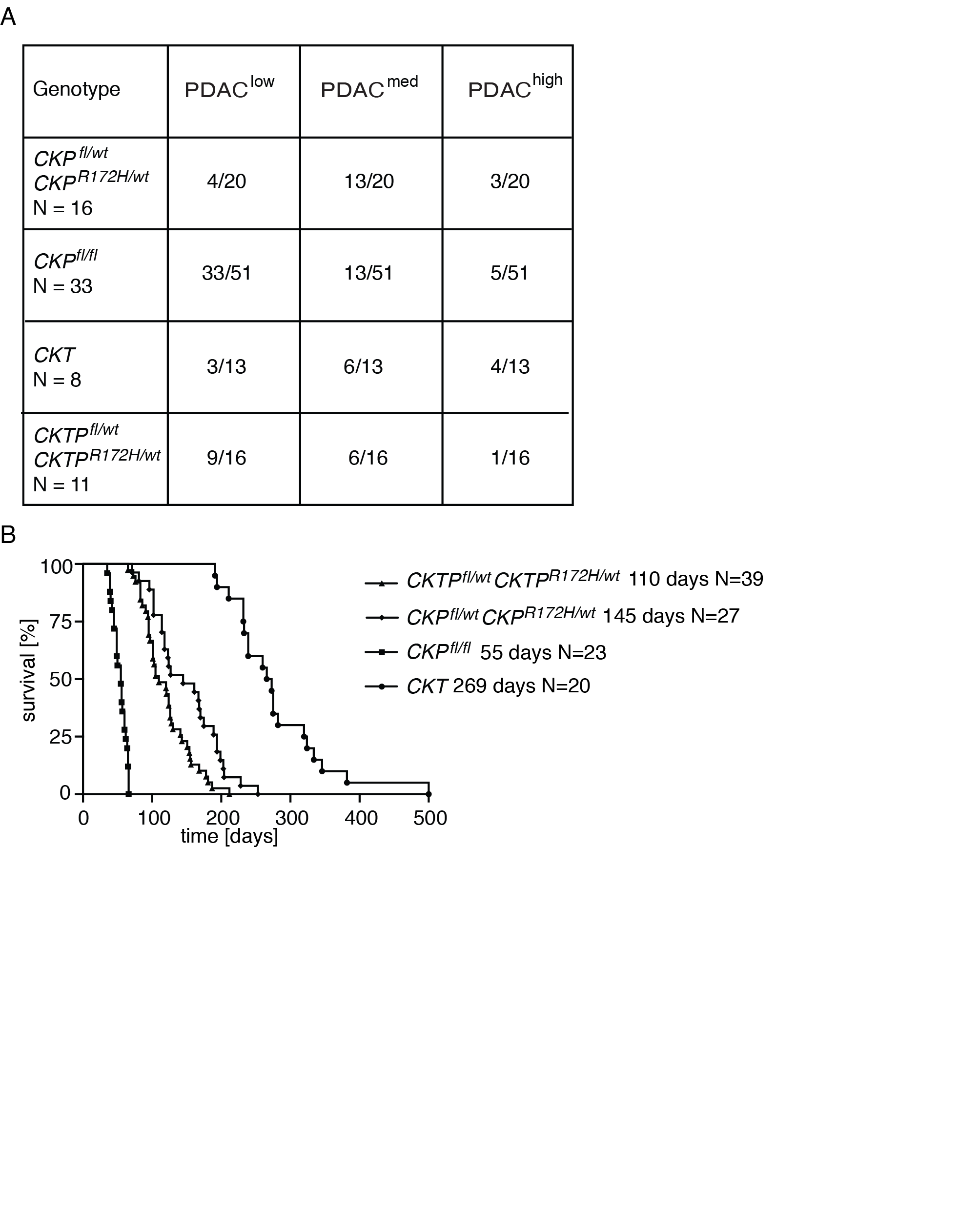
**Supplementary information for the manuscript:**

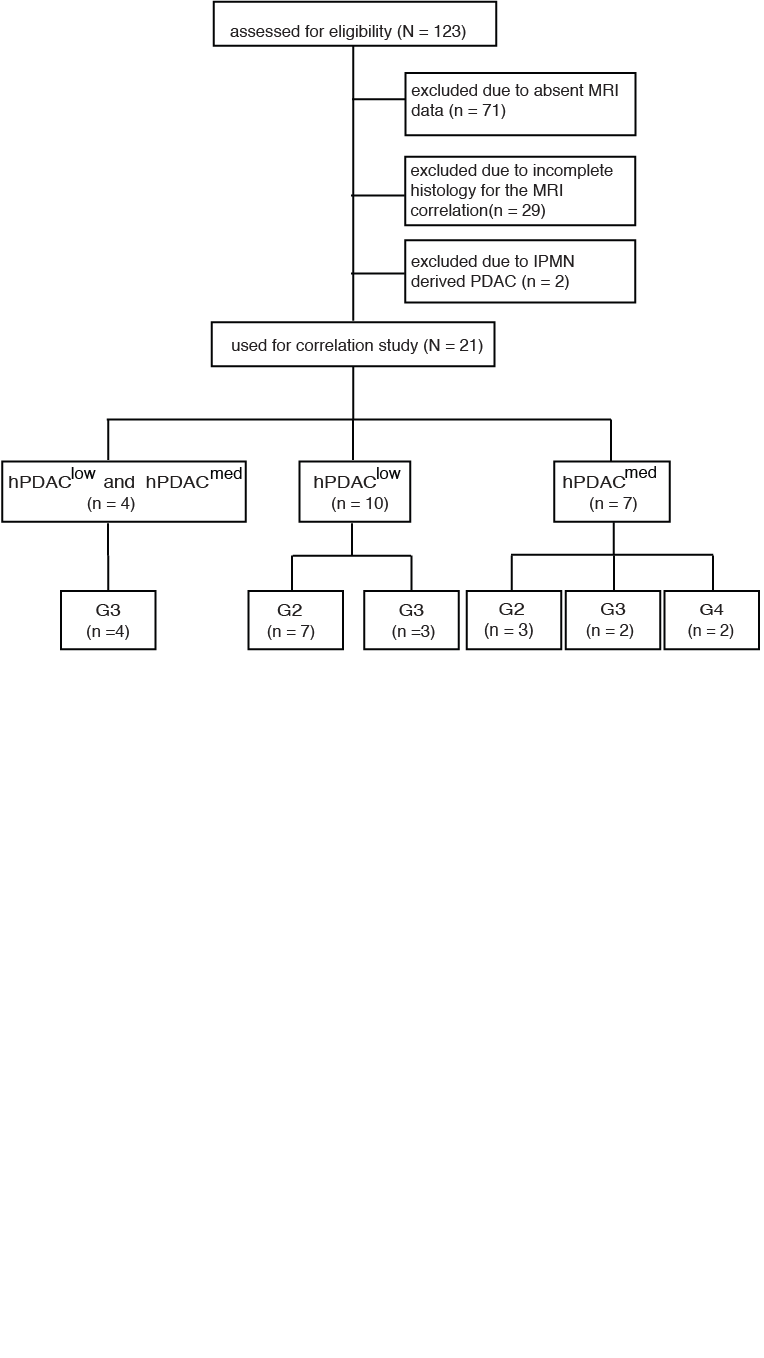
**Co-clinical assessment of tumor cellularity in pancreatic cancer**

Irina Heid1, 11, Katja Steiger2, 11, Marija Trajkovic-Arsic3, 11, Marcus Settles1, Manuela R. Eßwein1, Mert Erkan7, Jörg Kleeff4, Carsten Jäger4, Helmut Friess4, Bernhard Haller5, Andreas Steingötter8, Roland M. Schmid3,10, Markus Schwaiger6,10, Ernst J. Rummeny1, Irene Esposito9\*, Jens T. Siveke3,10\*, Rickmer F. Braren1\*

**Supplementary Figure 1.**

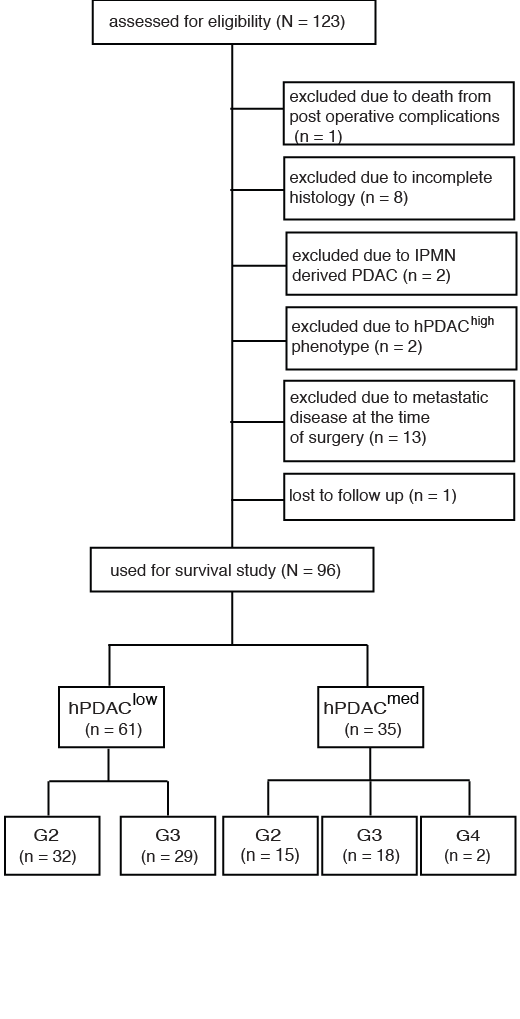
** Summary and survival of murine cohort used in the study.** (**A**) Distribution of the PDAC groups according to cellular content among the used genotypes. Only animals that received DW-MRI and were included into the study are described. n = number of animals per genotype, all other numbers represent the amount of analyzed lesions. Up to three lesions per animal (i.e. head, neck and/or tail region) were included. (**B**) Kaplan Mayer survival analysis of the genotypes used in the study.

**Supplementary Figure 2**

****

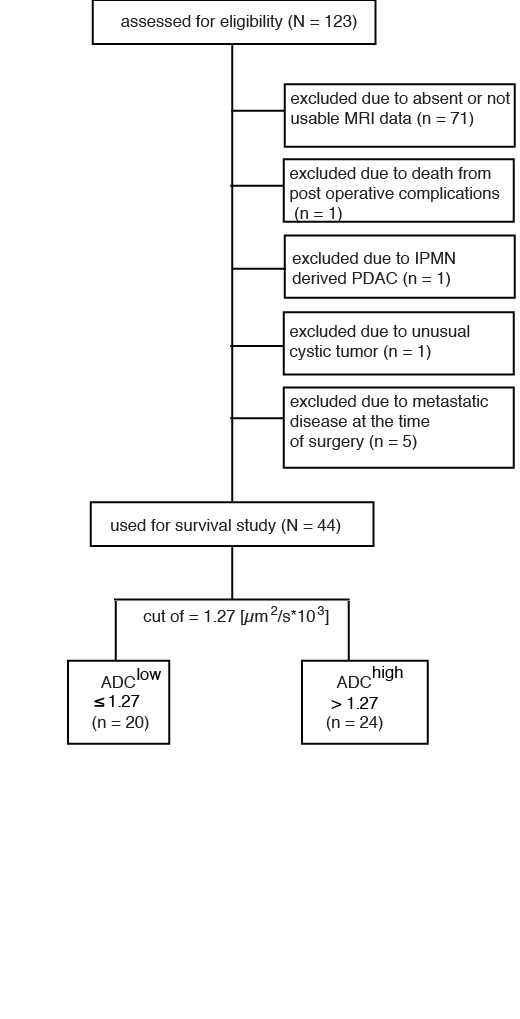
Consort diagram of the patient distribution of surgical subcohort 1.

**Supplementary Figure 3.**

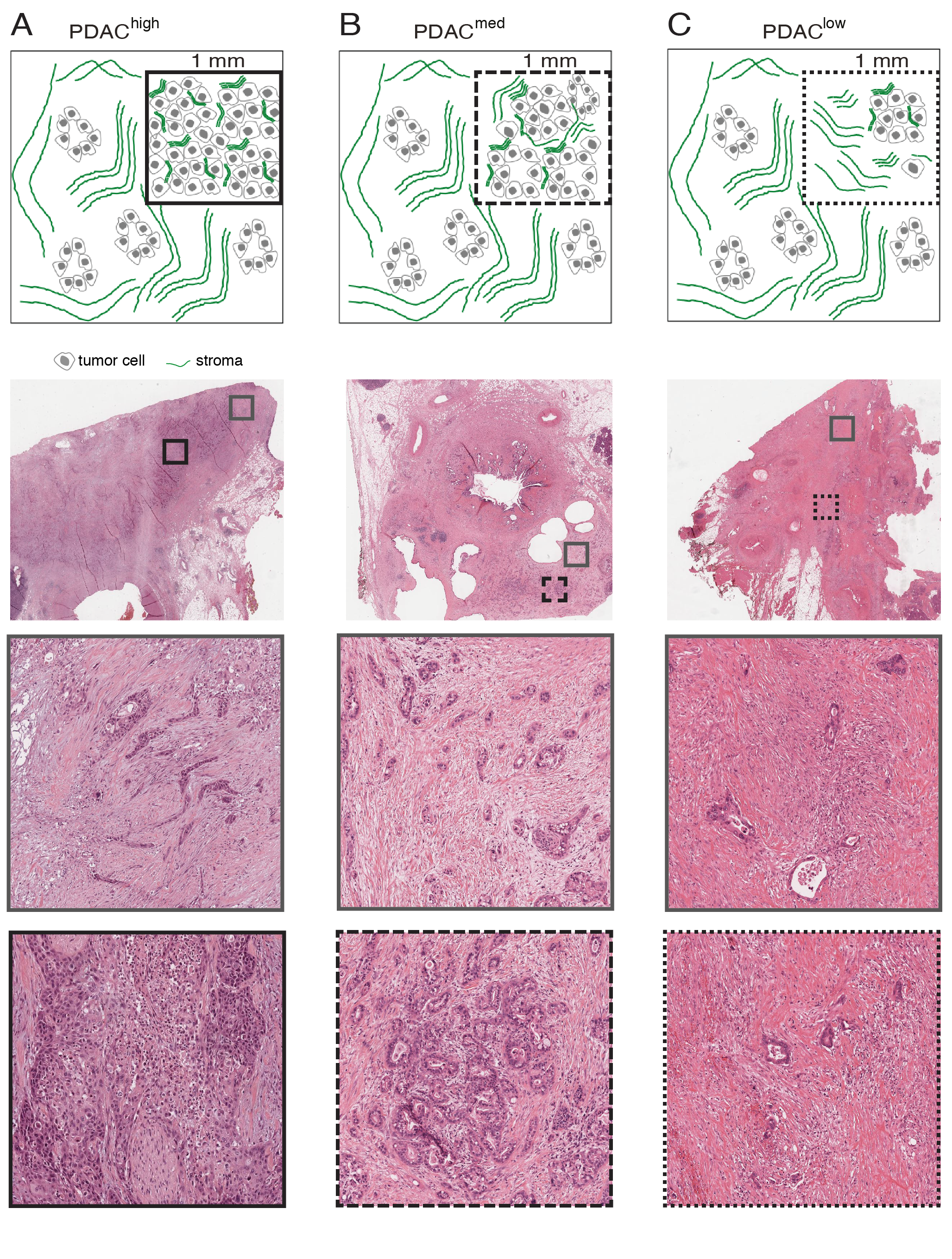
****

Consort diagram of the patient distribution of surgical subcohort 2.

**Supplementary Figure 4.**

****

Consort diagram of the patient distribution of surgical subcohort 3.

**Supplementary Figure 5.** 

**Schematic of relative tumor cell and stroma contribution in PDAChigh** (A), PDACmed (B) and PDAClow (C) groups and corresponding H&E stained examples (upper row: overview, areas of 1mm2 marked with rectangles, middle and lower row: close-up images of the areas marked in the overview). All tumors contain areas with only few tumor cells (grey rectangles). PDAChigh tumors display tumor cell clusters with >70% of tumor cells within an area of 1mm2 (solid line). Tumor cell cluster in PDACmed tumors contain between 30 and 70% of tumor cells (rough dotted line). In PDAClow tumors no tumor cell cluster area with more than 30% tumor cells within an area greater equal 1 mm2 are observed (fine dotted line).

**Supplementary Table 1.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Subcohort 1** | **PDAClow (N=10)** | **PDACmed (N=7)** | **PDAClow and PDACmed (N=4)** | **P-value**  **(X2- test)** |
|  |  |  |  |  |
| Sex |  |  |  | 0.82 |
| male | 6 | 5 | 3 |  |
| female | 4 | 2 | 1 |  |
|  |  |  |  |  |
| Age mean, (std. dev.) | 65.6 (36-75) | 70.2 (44-78) | 46.9 (43-58) | 0.09 (Mann-Whitney-U-Test) |
|  |  |  |  |  |
| T |  |  |  | 0.24 |
| 1 | 0 | 0 | 1 |  |
| 3 | 10 | 6 | 1 |  |
| 4 | 0 | 1 | 2 |  |
|  |  |  |  |  |
| N |  |  |  | 0.28 |
| 0 | 5 | 1 | 1 |  |
| 1 | 5 | 6 | 3 |  |
|  |  |  |  |  |
| G |  |  |  | 0.03 |
| 2 | 7 | 3 | 0 |  |
| 3 | 3 | 2 | 4 |  |
| 4 | 0 | 2 | 0 |  |
|  |  |  |  |  |
| R |  |  |  | 0.42 |
| 0 | 6 | 5 | 1 |  |
| 1 | 3 | 2 | 3 |  |
| X | 1 | 0 | 0 |  |
|  |  |  |  |  |
| Neoadjuvant CTx | 1 | 0 | 0 | 0.56 |
| Adjuvant CTx | 9 | 7 | 2 | 0.06 |

Statistics of the patients used in surgical subcohort 1.

HR = Hazard Ratio

CI = Confidence Interval

T= T-status

N = Lymph Node Infiltration

G = Grading

R = Resection Margin

R0 = microscopically free of tumor

R1 = microscopically **not** free of tumor

Rx = unknown

CTx = Chemotherapy

**Supplementary Table 2.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Subcohort 2** | **PDAClow (N=61)** | **PDAmed (N=35)** | **P-value**  **(X2- test)** |
|  |  |  |  |
| Sex |  |  |  |
| male | 32 | 22 | 0.32 |
| female | 29 | 13 |  |
|  |  |  |  |
| Age (mean, std. dev.) | 65.6 (11.4) | 64.1 (10.0) | 0.29 (Mann-Whitney-U-test) |
|  |  |  |  |
| T |  |  | 0.26 |
| 1 | 0 | 1 |  |
| 2 | 3 | 3 |  |
| 3 | 51 | 24 |  |
| 4 | 7 | 7 |  |
|  |  |  |  |
| N |  |  | 0.02 |
| 0 | 20 | 4 |  |
| 1 | 41 | 31 |  |
|  |  |  |  |
| G |  |  | 0.14 |
| 2 | 32 | 15 |  |
| 3 | 29 | 18 |  |
| 4 | 0 | 2 |  |
|  |  |  |  |
| R |  |  | 0.89 |
| 0 | 34 | 20 |  |
| 1 | 24 | 14 |  |
| 2 | 1 | 0 |  |
| X | 2 | 1 |  |
|  |  |  |  |
| Neoadjuvant CTx | 3 | 0 | 0.41 |
| Adjuvant CTx | 52 | 29 | 0.09 |

Statistics of the patients used in surgical subcohort 2.

HR = Hazard Ratio

CI = Confidence Interval

T= T-status

N = Lymph Node Infiltration

G = Grading

R = Resection Margin

R0 = microscopically free of tumor

R1 = microscopically **not** free of tumor

Rx = unknown

CTx = Chemotherapy

**Supplementary Table 3.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Subcohort 3** | **ADChigh (N=24)** | **ADClow (N=20)** | **P-value**  **(X2- test)** |
|  |  |  |  |
| Sex |  |  |  |
| male | 14 | 13 | 0.65 |
| female | 10 | 7 |  |
| Age (mean, std. dev.) | 65.2 (9.3) | 64.9 (13.7) | 0.55 (Mann-Whitney-U-test) |
|  |  |  |  |
| T |  |  | 0.55 |
| 1 | 1 | 2 |  |
| 3 | 20 | 14 |  |
| 4 | 3 | 4 |  |
|  |  |  |  |
| N |  |  | 0.06 |
| 0 | 8 | 2 |  |
| 1 | 16 | 18 |  |
|  |  |  |  |
| G |  |  | 0.18 |
| 1 | 0 | 1 |  |
| 2 | 15 | 7 |  |
| 3 | 9 | 11 |  |
| 4 | 0 | 2 |  |
|  |  |  |  |
| R |  |  | 0.50 |
| 0 | 14 | 10 |  |
| 1 | 9 | 10 |  |
| X | 1 | 0 |  |
|  |  |  |  |
| Neoadjuvant CTx | 3 | 0 | 0.26 |
| Adjuvant CTx | 20 | 16 | 0.77 |

Statistics of the patients used in surgical subcohort 3.

HR = Hazard Ratio

CI = Confidence Interval

T= T-status

N = Lymph Node Infiltration

G = Grading

R = Resection Margin

R0 = microscopically free of tumor

R1 = microscopically **not** free of tumor

Rx = unknown

CTx = Chemotherapy

**Supplementary Table 4.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **P-value** | **HR** | **95.0% CI** | |
| **lower** | **upper** |
| PDAClow versus PDACmed | 0.034 | 1.730 | 1.043 | 2.868 |
| Age | 0.253 | 1.014 | 0.990 | 1.039 |
| Sex | 0.991 | 1.003 | 0.637 | 1.577 |
| T1 + T2 + T3 +T4 | 0.367 |  |  |  |
| T1 + T2 | 0.970 | 0.983 | 0.406 | 2.382 |
| T3 + T4 | 0.365 | 1.683 | 0.563 | 4.770 |
| N | 0.276 | 1.376 | 0.775 | 2.443 |
| G all | 0.000 | 2.744 | 1.599 | 4.709 |
| R all | 0.587 |  |  |  |
| R0 | 0.802 | 0.933 | 0.541 | 1.608 |
| R1 + R2 | 0.335 | 1.812 | 0.541 | 6.067 |
| CTx | 0.037 | 0.515 | 0.276 | 0.961 |

HR = Hazard Ratio

CI = Confidence Interval

T= T-status

N = Lymph Node Infiltration

G = Grading

R = Resection Margin

R0 = microscopically free of tumor

R1 = microscopically **not** free of tumor

R2 = macroscopically **not** free of tumor

CTx = Chemotherapy

Results of a multivariable Cox regression model fit to the data of subcohort 2 that assess whether PDAC is associated with overall survival after adjustment for common predictors.

**Supplementary Table 5.**

|  |  |  |
| --- | --- | --- |
|  | **P-value** | **estimated cut off** |
| Lowest ADC | 0.055 | 1.08 |
| T | 0.113 | 1.08 |
| N | 0.076 | 1.08 |
| G1 + G2 vs. G3 + G4 | 0.068 | 1.08 |
| R | 0.068 | 1.08 |
| CTx | 0.024 | 1.08 |

T= T-status

N = Lymph Node Infiltration

G = Grading

R = Resection Status

CTx = Chemotherapy

The permutation test analysis revealing association between overall survival and lowest ADC stratified by each of the relevant categorical variables. Data used for analysis are derived from surgical subcohort 3.