**Supplementary Methods**

*Mouse models*

*KC model -* K-rasLSL.G12D/+; PdxCretg/+ mice (N = 24), also called KC mice, are prone to spontaneous pancreatic inflammation with mild fibrosis. This inflammation was shown to potentially lead to PDA at advanced ages (1).

*KPC model -* A total of 30 K-rasLSL.G12D/+; p53R172H/+; PdxCretg/+ (KPC) mice were also used in this study. The KPC mice tend to develop pancreatic tumors with pathophysiological and molecular features resembling those of human PDA (2). This model is based on the pancreas–specific, endogenous expression of point-mutant K-ras and p53, reflecting cognate mutations that are found in over 95% and 75% of PDA patients, respectively. KPC mice are born with normal pancreata and then develop progressively more severe pathology over several months, beginning with acinar-to-ductal metaplasia (ADM) and pancreatic intraepithelial neoplasia (PanIN) lesions and progressing to overt ductal adenocarcinoma. These changes are accompanied by an increasingly complex and fibrotic extracellular matrix composition.

*KPCB2F/F model –* An additional genetic mutation was performed for these mice (N = 6). The Brca2 gene was inactivated in the pancreas to reflect a particular case of PDA. Deleterious Brca2 mutations generally induce an increased risk of developing PDA (3). In addition, several studies indicate that Brca mutation sensitizes the tumor to cisplatin treatment, although the exact mechanism is still under investigation (4–6).

*IL-1b –* Transgenic mice expressing the IL-1beta gene (7) were included in this study (N = 8). These mice commonly develop mild chronic inflammation with edema. As pancreatitis is a risk factor of PDA, these mice were used to evaluate HMI potential of staging the pancreatic deterioration leading to cancer.

*Histological analysis*

The pancreatic specimens were immediately fixed in cold 4% PBS/formalin solution at 4°C, routinely processed for paraffin embedding, and sectioned 4μm. Tissue sections were stained using ST Infinity H&E staining kit (Leica) or Masson’s Trichrome Staining Kit (Sigma-Aldrich, St Louis, MO, USA).

Picrosirius Red (PSR)

The slides were incubated in a 0.1% Sirius Red solution dissolved in aqueous saturated picric acid for 1.5 hours, washed with 100% ethanol twice and dehydrated and mounted with Permount. Picrosirus red stained sections were examined under polarizing light microscopy (Olympus BX41 TF) at a magnification of x4. Halogen lamp intensity was kept constant for all images, and an exposure time that optimized the signal-to-noise ratio was chosen and kept constant within each image type. All images were digitally captured using cellSens acquisition platform (Olympus Corp.) and analyzed using ImageJ software.

**References**

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