## **Bioluminescent pancreatic cancer mouse models from genetically characterized primary cells:** a platform for drug discovery and toward personalized treatment in pancreatic cancer



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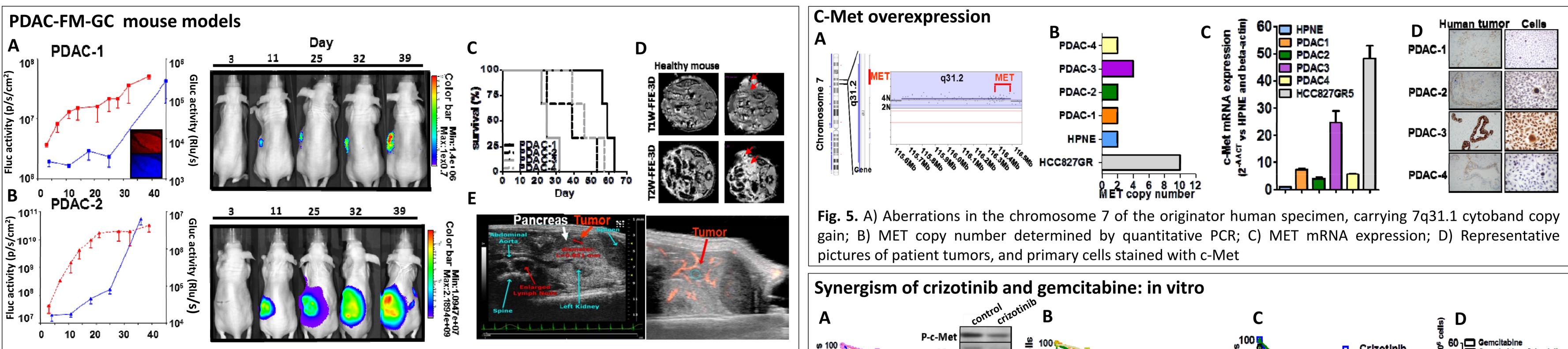
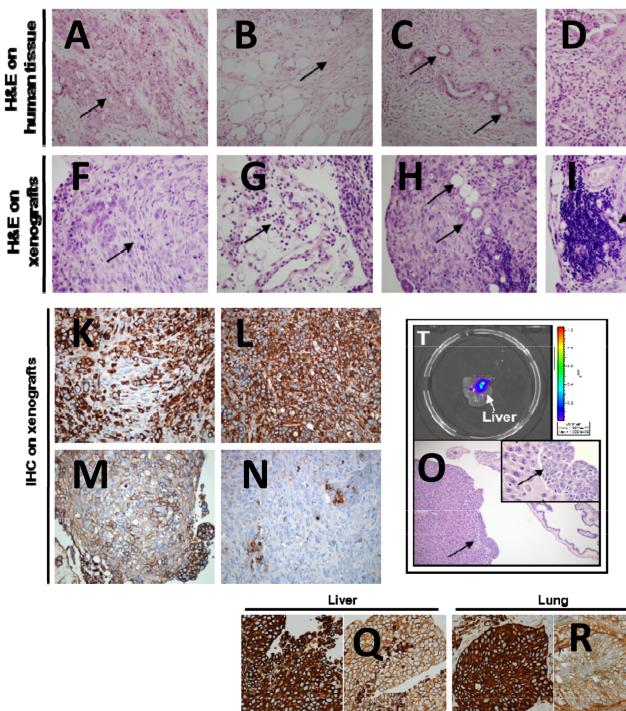


Fig. 2. A-B) Fluc (red curves) and Gluc (blue curves) activities of the PDAC-1/2-FM-GC mouse models. The insets show representative fluorescence microscopy images of PDAC-1-FM-GC cells; C) Kaplan-meier survival curves; (D) Magnetic resonance imaging (MRI)-images and (E) high-frequency ultrasound in 3D Power Doppler

## Histopathology and immunohistopathology Genetic characteristics of the orthotopic PDAC of the orthotopic PDAC mouse models mouse model compared to their human originator tumors (array-CGH) 1 2 3 4 5 6 7 8 10 12 1416 1820 23 1 2 3 4 5 6 7 8 10 12 1416 1820 23 1 2 3 4 5 6 7 8 10 12 1416 1820 Fig.3. Infiltration (A, F, arrows,) PDAC-associated desmoplastic reaction (B, G,), well-defined glandular pattern, with differentiated duct formations (C, H, arrows,), and inflammatory reaction (D, I, arrows,). IHC for (K) Ck 8/18, (L) CK7, (M) EGFR, (N) CEA; (O,Q); liver, **Fig. 4.** H:human; C:cells; M:mouse and (P,R) lung metastases

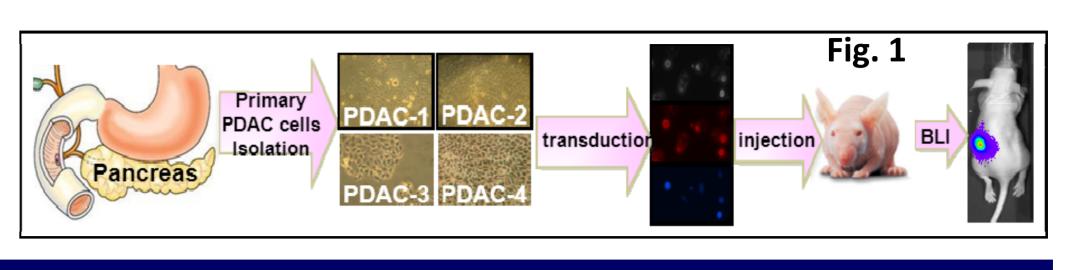


>Our orthotopic PDAC imaging models showed genetic, histopathological and metastatic features similar to their originator tumors >One of our models identified c-Met as a potential therapeutic target

## **PRELIMINARY RESULTS**

## **CONCLUSIONS & FUTURE STUDIES**

- To develop orthotopic mouse models (Fig.1) from primary pancreatic tumor cells and optimize bioluminescent imaging - To test new targeted drugs in vitro and in vivo



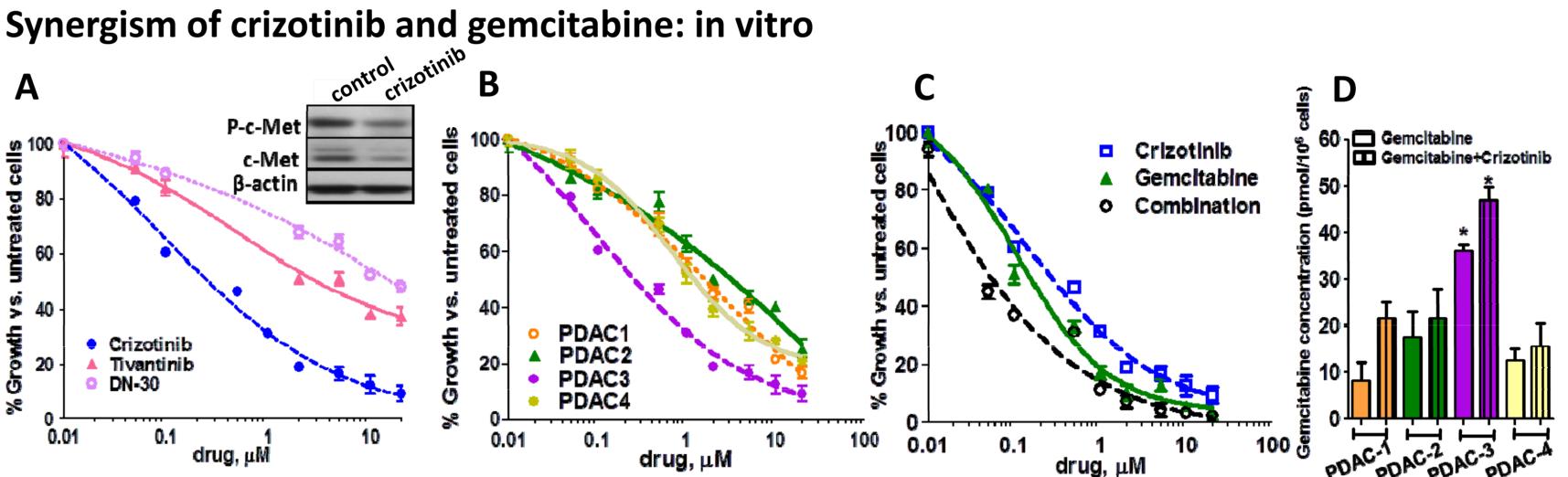
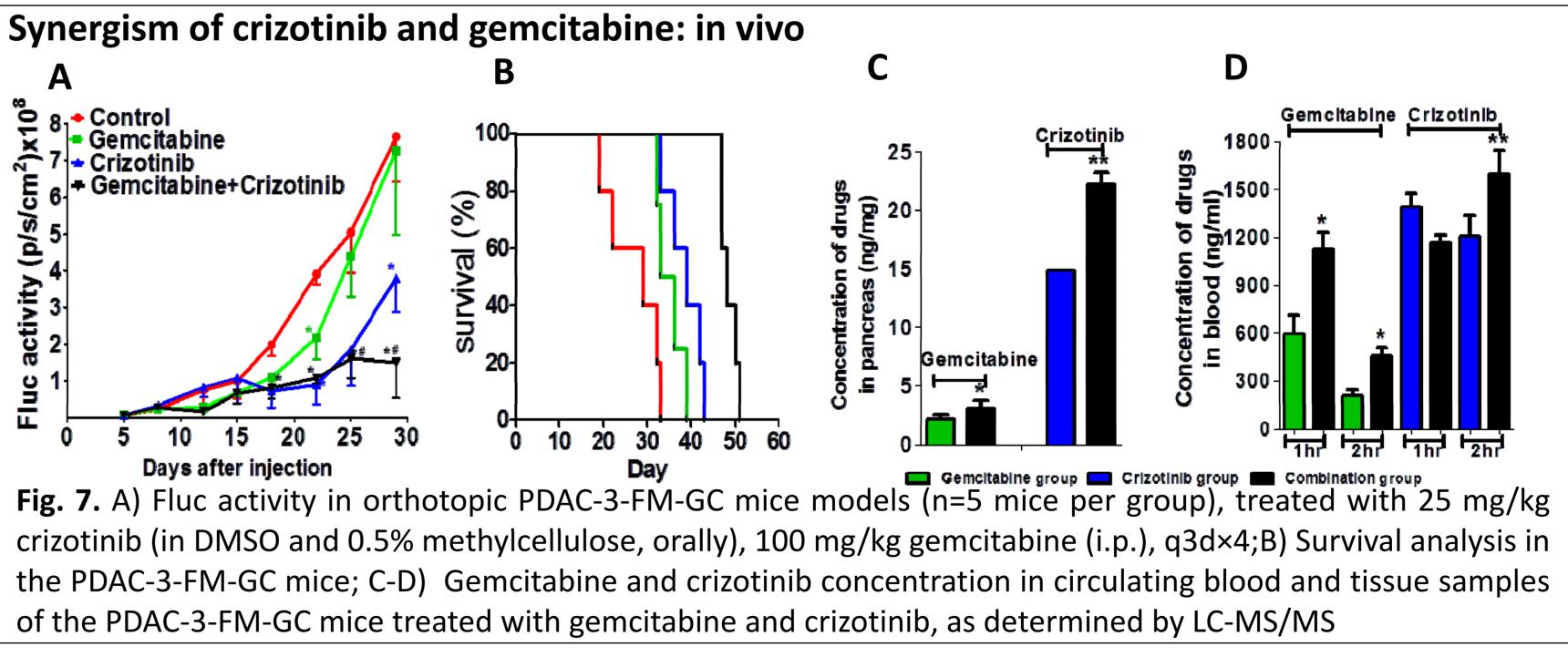


Fig. 6. A) Growth inhibitory effect of c-Met inhibitors, crizotinib, tivantinib and DN-30 in PDAC-3 cells; inset, modulation of protein expression of c-Met and phospho-c-Met; B) Growth inhibitory effect of the c-Met inhibitor crizotinib in PDAC-1/2/3/4 cells, as determined by SRB assay; C) Growth inhibitory effect of crizotinib, gemcitabine and their combination in PDAC-3 cells; D) Intracellular accumulation of gemcitabine after exposure to 10 µM gemcitabine for 4 hours, as determined by LC-MS/MS



Crizotinib and gemcitabine were synergistic in vitro and in vivo Crizotinib increased blood, tumor cell and tissue concentrations of gemcitabine > These models provide a platform to test the efficacy of targeted innovative anticancer drugs