



Development of Patient-Derived Xenograft (PDX) Models for Pancreatic Carcinoma as a Preclinical Platform for Drug Development

Abstract
No. 6444

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CONNECTING SCIENCE TO PATIENTS

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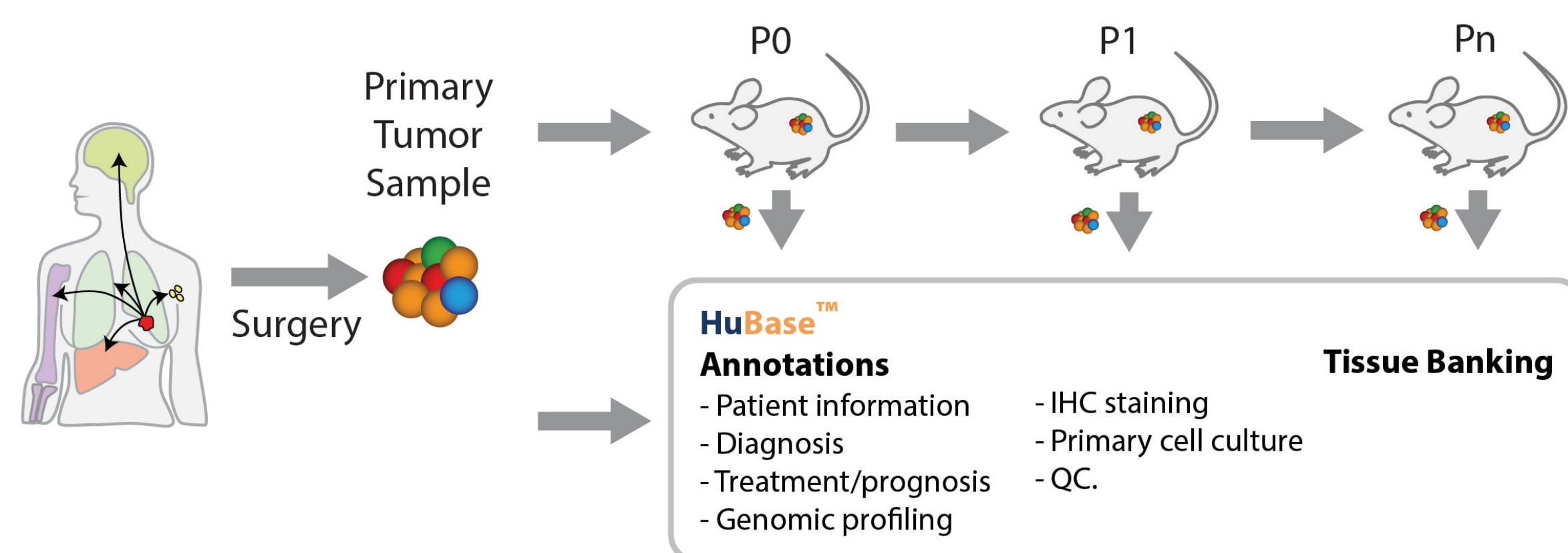
INTRODUCTION

Pancreatic ductal adenocarcinoma (PDA) remains one of the most aggressive tumors in humans. A notable feature of PDA is its innate resistance to many chemotherapies. In preclinical studies, Abraxane® showed antitumor activity as a single agent and synergistic activity in combination with gemcitabine in murine models of pancreatic cancer. In this study, we have developed and characterized multiple PDX models of pancreatic cancer. These models recapitulate major structural and genetic features noted in patient populations. Developed PDX models are from both prior treated and naïve patients with varying levels of resistance to gemcitabine. Here we have investigated the efficacy of standard of care (SoC) agents in these pancreatic models and demonstrated the potential utility of the pancreatic PDX models in oncology drug discovery to better position existing or identify novel treatments for pancreatic cancer.

METHODS

HuPrime® Depth and Diversity: CrownBio has built the largest commercially available PDX library of >2,500 models with genetic profiles of major cancer types. Cryopreserved cells from patient biopsies were injected into immunocompromized mice to develop the PDXs.

The HuPrime® Model



RESULTS

Table 1: Patient Clinical Pathology Information.

Model ID	Cancer Type	Sex	Age	Clinical Diagnosis	Prior Treatment	Previous Drugs
PA5312	Pancreatic (KRAS mut)	M	69.6	Adenocarcinoma	Unknown	--
PA5313	Pancreatic	F	68.8	Adenocarcinoma	Naïve	--
PA5314	Pancreatic	M	49.3	Adenocarcinoma	Naïve	--
PA5362	Pancreatic	F	58.5	Adenocarcinoma	Pretreated	Gemcitabine, Avastin®
PA5364	Pancreatic	F	77.5	Adenocarcinoma	Pretreated	--
PA5365	Pancreatic	F	54	Adenocarcinoma	Naïve	--
PA5366	Pancreatic	F	65.4	Adenocarcinoma	Pretreated	--
PA5379	Pancreatic	M	70.2	Adenocarcinoma	Pretreated	--
PA5410	Pancreatic	M	65.9	Adenocarcinoma	Pretreated	5-FU and Gemzar®
PA5415	Pancreatic	M	74.1	Adenocarcinoma	Naïve	--

Figure 1: Histology of the Pancreatic Patient-Derived Xenograft Tumors. Representative histological sections. Tissues were fixed and stained (H&E) to verify pathology diagnosis.

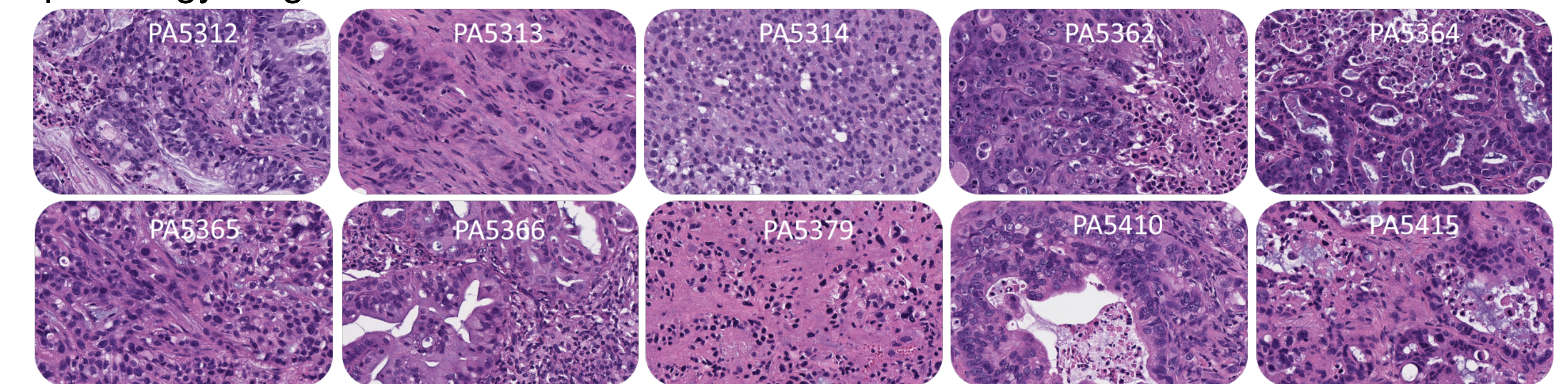


Figure 2: Dose Response of Abraxane (i.v.) in Pancreatic PDX Models.

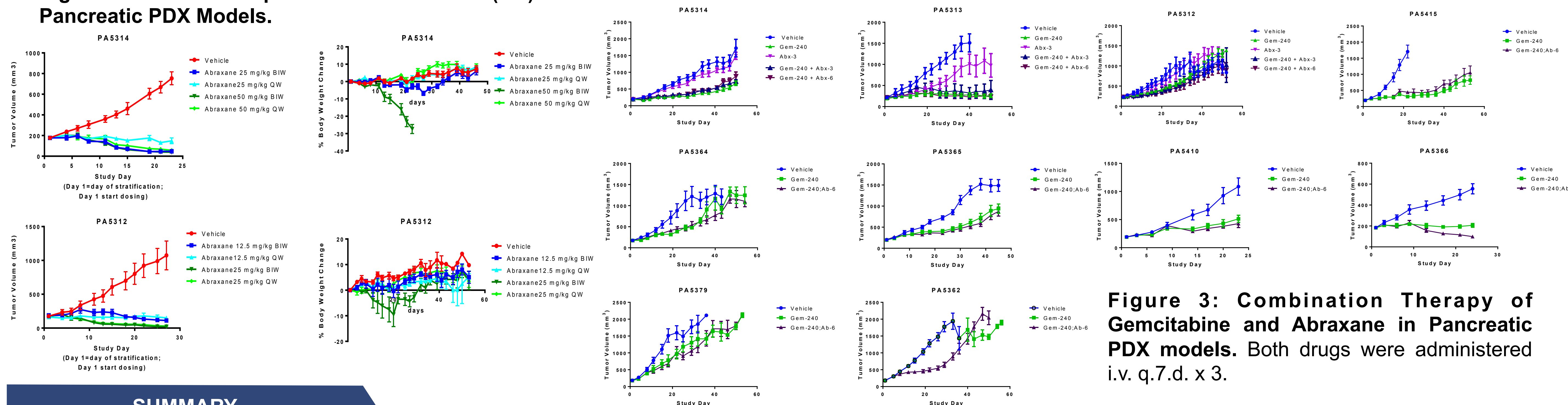


Figure 3: Combination Therapy of Gemcitabine and Abraxane in Pancreatic PDX models. Both drugs were administered i.v. q.7.d. x 3.

SUMMARY

- CrownBio's tumor bank is a reliable source of patient-derived tumor cells for drug testing.
- Pancreatic models have been verified and SoC data is available and continues to be generated.
- CrownBio's tumor bank demonstrates varying sensitivity and resistance to SoC drugs both *in vitro* and *in vivo*.
- Further characterization of these pancreatic models is currently in progress.