CROWN BIOSCIENCE

Pretreated PDX Models

Evaluate your next-generation therapeutics with the most clinically relevant models reflecting the patient population and cancer treatments of today.

A JSR Life Sciences Company

FACTSHEET

V1.0

Pretreated PDX Models

Evaluate your next-generation therapeutics with the most clinically relevant models reflecting the patient population and cancer treatments of today.

Drug resistance, relapse, and the resulting ineffectiveness of drug treatments are responsible for up to 90% of cancer related deaths[1]. Patient-derived xenografts (PDX) are the gold standard in preclinical models for their proven translational relevance to human disease. However, researchers and drug developers need access to the most clinically relevant PDX models that accurately reflect the patient population and cancer treatments currently in use. To understand the underlying mechanisms of tumor resistance to treatments, it is necessary to support the development of targeted treatment strategies and model resistance to standard and new therapeutics. Crown Bioscience's unique collection of pretreated PDX includes several models derived from patients who relapsed or experienced resistance to the current lines of treatments that are failing today due to drug resistance.

Advantages of our Pretreated PDX Models

- **Models that reflect the patient populations and treatments currently in use today**
  Crown Bioscience's pretreated PDX collection carries a wide selection of models coming from patients with different treatment histories, including those that are relevant to today's therapies, including KRAS inhibitors and immune checkpoint inhibitors. Furthermore, we carry models reflecting disease states with the highest unmet need, including advanced metastatic cancer.

- **Quickly find pretreated models for your research needs**
  Crown Bioscience provides you with the tools to quickly identify the most relevant pretreated models for your specific patient profiles and test your next-generation drug candidates with confidence. Use our curated and searchable online PDX database (HuBase™) to identify your pretreated model by indication, or other criteria.

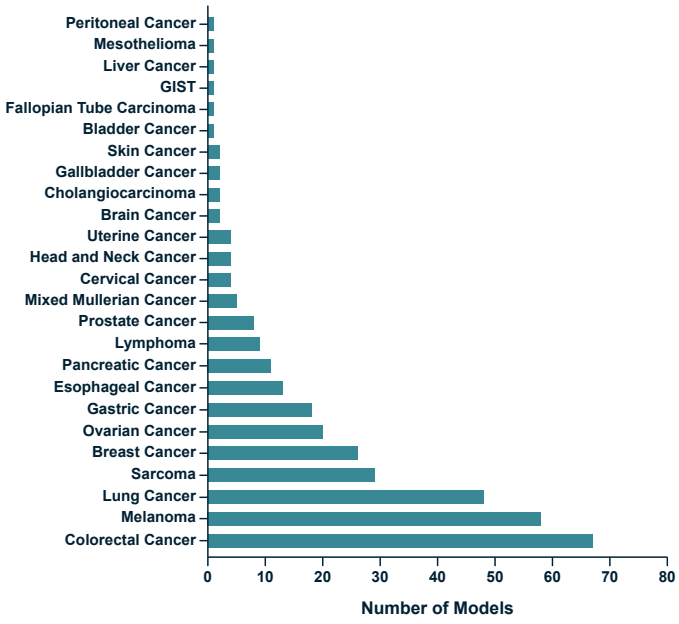
- **Flexibility and more preclinical options to boost your study (upstream and downstream capabilities)**
  Crown Bioscience offers relevant services like mouse clinical trial support for stratifying patients, matching patient-derived xenograft organoids (PDXO) for screening and immuno-oncology platforms for the evaluation of immunotherapeutics, as well as genomic, proteomic, bioinformatic, and biomarker discovery support.

- **Reduce your project timelines with faster study initiation times**
  Our scientific project managers work with you to quickly set up your study with our pretreated PDX models that are maintained and kept alive, making them ready for service to you - no tissue revival required.

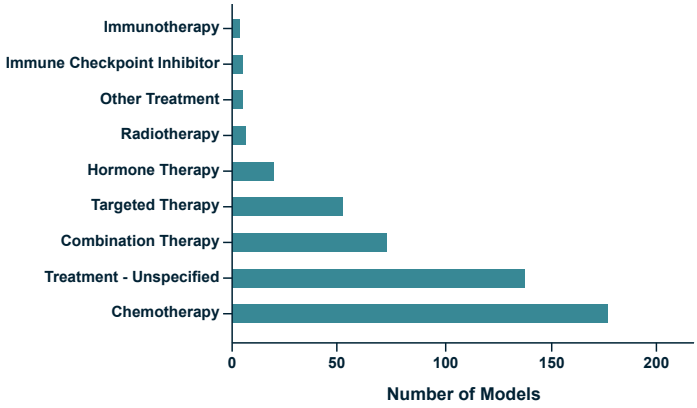
Pretreated PDX Models Key Facts

- Over 300 pretreated PDX models covering 25 cancer types derived from patients with different drug treatments.
- Treatments include immune checkpoint inhibitors, 3rd generation EGFRi, PARPi, KRASi, CDK4/6i, BTKi, and MEKi.
- 75+ pretreated PDX modeling advanced, metastatic disease with samples collected from various biopsy sites.
- Models from serial (longitudinal) biopsies from patients receiving sequential treatments (including investigational drugs).

Pretreated Models by Indication

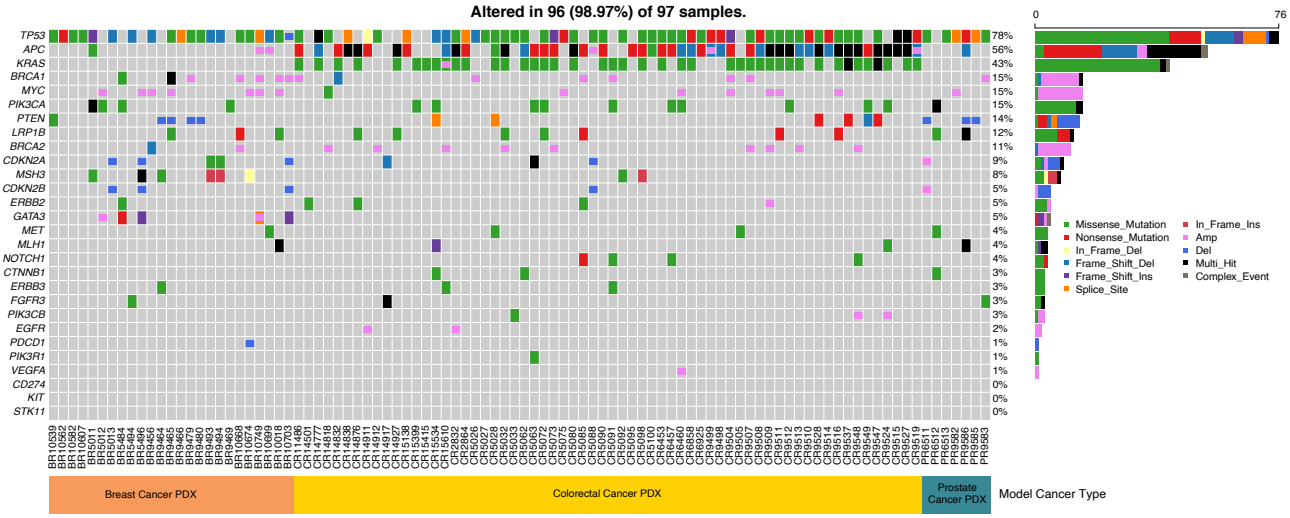


Pretreated Models by Treatment



Multiomic Profiling of Pretreated PDX Models

Crown Bioscience performs deep characterization of our PDX models, which includes multiomic profiling: RNAseq, WES, WGS, and 4D-DIA proteomics. The genomic oncoplot below shows mutations found in a subset of our PDX pretreated models. All available multiomic data for the pretreated PDX models can be found in our online PDX database HuBase.



Pretreated PDX Models with KRAS Mutations and Modeling Drug Resistance (KRAS Inhibitors)

Crown Bioscience has pretreated PDX models harboring specific KRAS mutations and models derived from patients who received targeted KRAS inhibitor treatments, and in some cases with documented response/resistance. The table below also shows the availability of matched PDXO, which enable upstream screening.

Model ID	Cancer Type	Patient Treatment History	Comments	PDXO Available
CR9505	Colorectal	1st: Oxaliplatin 2nd: FOLFIRI + Bevacizumab	KRAS G12D	Yes
CR9507	Colorectal	1st: FOLFOX+ Avastin 2nd: Xeloda 3rd: FOLOFIRI + Avastin	KRAS G12C	Yes
CR9508	Colorectal	1st: FOLFOX+ Avastin 2nd: XELIRI + Avastin	KRAS G12S	Yes
CR9511	Colorectal	1st: FOLFOX 2nd: FOLFIRI	Genetic Results KRAS G12D missense	--
CR9512	Colorectal	1st: FOLFOX 2nd: FOLFIRI 3rd: Avastin	KRAS Expression G12D	Yes
CR9513	Colorectal	1st: FOLFOX 2nd: FOLFIRI + Bevacizumab	KRAS Q61H	Yes
CR9516	Colorectal	1st: FOLFOX 2nd: FOLFIRI	KRAS G12D, Complete Responses to Investigational + Pembrolizumab – Became Resistant 2 Years Later	--
CR9519	Colorectal	1st: FOLFOX+ Avastin 2nd: XELIRI + Avastin	KRAS G12S	--
CR9524	Colorectal	1st: Fluorouracil + Oxaliplatin + Bevacizumab 2nd: Triflurindine-Tipiracil 3rd: FOLFIRI + Ziv-aflibercept 4th: Investigational 5th: Investigational 6th: Investigational + Pembroluzimab	KRAS G12D, Complete Responses to Investigational + Pembrolizumab – Became Resistant 2 Years Later	--
CR9527	Colorectal	1st: FOLFOX, FOLFIRI + 2nd: Bevacizumab	KRAS G12D	--
CR9528	Colorectal	1st: FOLFOX 2nd: FOLFIRI 3rd: Investigational	KRAS G12C; G12 Inhibitor Responder	Yes
CR9537	Colorectal	1st: FOLFOX 2nd: FOLFIRI 3rd: Investigational	G12 Inhibitor Responder; Became Resistant, KRAS G12C and Q61H	Yes
CR9548	Rectal	1st: FOLFOX 2nd: FOLFIRI + Avastin 3rd: Lonsurf 4th: Investigational	KRAS G13D	--
CR9549	Colorectal	1st: FOLFOX + Avastin 2nd: FOLFIRI + Avastin 3rd: Investigational	KRAS A59T	--
CR9555	Colorectal	1st: FOLFOX + Bevacizumab 2nd: FOLFOX + Avastin 3rd: Irinotecan 4th: Panitumumab, Lonsurf	KRAS p.Q61H	--
CR9560	Colorectal	1st: FOLFOX + Bevacizumab 2nd: FOLFOX + Avastin 3rd: Irinotecan + Panitumumab 4th: Lonsurf 5th: Investigational	KRAS p.Q61H	--

Pretreated PDX Models of Drug Resistance (Immune Checkpoint Inhibitors)

Crown Bioscience offers models derived from patients treated with immune checkpoint inhibitors. Evaluate human-specific immunotherapeutics in these models with our HSC or Mi**Xeno™** (PBMC) humanized model platforms.

Model ID	Cancer Type	Patient Treatment History	Comments
CR9524	Colorectal	1st: Fluorouracil + Oxaliplatin + Bevacizumab 2nd: Triflurindine-Tipiracil 3rd: FOLFIRI + Ziv-aflibercept 4th: Investigational 5th: Investigational 6th: Investigational + Pembroluzimab	Complete Responses to Investigational + Pembrolizumab – Became Resistant 2 Years Later
LU9559	NSCLC	1st: Keytruda + Pemetrexed + Carboplatin 2nd: Keytruda + Pemetrexed	PD-L1 Positive; Resistant to Pembrolizumab
CR9520*	Anus	1st: Fluorouracil + Cisplatin 2nd: Carboplatin + Paclitaxel 3rd: Fluorouracil + Mitomycin + XRT 4th: Nivolumab 5th: Fluorouracil + Oxaliplatin	PD-L1 Expression; Non-responder to Nivolumab
LU9536*	NSCLC	1st: Opdivo 2nd: Investigational + Durvalumab 3rd: Investigational 4th: Investigational	PD-L1 Positive; Non-responder to Nivolumab
CR9551*	Rectal	1st: Fluorouracil + Cisplatin 2nd: Carboplatin + Paclitaxel 3rd: Fluorouracil + Mitomycin 4th: Nivolumab 5th: Fluorouracil + Oxaliplatin 6th: Investigational x2	PD-L1 Expression; Non-responder to Nivolumab
UT9567*	Endometrial	1st: Carboplatin + Taxol 2nd: Lenvima + Pembroluzimab 3rd: Doxil	FBXO16-NRG1 Chromosomal Rearrangement; PD-L1 Expression

*Models are in validation.

Pretreated PDX Models of Advanced Metastatic Disease

Crown Bioscience has 75+ metastatic pretreated PDX models covering a range of cancer types collected from various patient biopsies sites. The table below highlights a selection of pretreated metastatic PDX models.

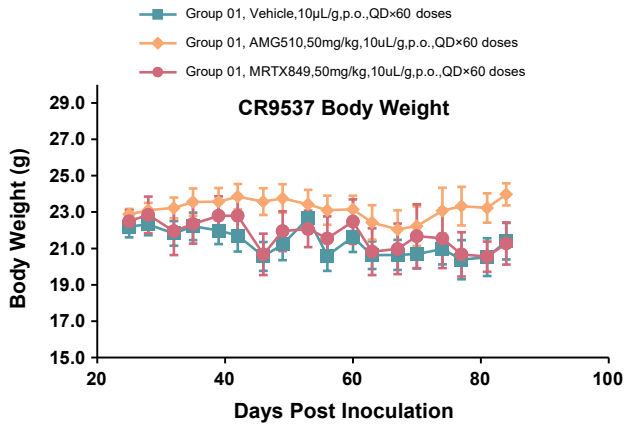
Model ID	Cancer Type	Biopsy Site	Patient Treatment History	Comments
BR9480	Breast Cancer (TNBC)	Skin Metastasis	16-0017348 AC-T, 3-2014- 9-2015, Xgeva 9-15 - 6-2016, Olaparib 9-2015-4-2016, add Carboplatin 1-2016-4-2016, 4-2016 PD1 Inhibitor Trial, Xeloda 6-2016, Progressive Disease	IHC (P5): HER2(0.5+), ER(-), PR(-); Primary-met Pair with BR9479; Slow Growth Rate, Slight Ulceration. Clinical Metastasis, Brain, Lung, and Bone.
CR11486	Colorectal Cancer (ADC)	Liver	Oxaliplatin, Leucovorin, 5FU, and Avastin	Classified as Colorectal Cancer by Molecular Pathology (RNAseq Clustering) and IHC, Might Be Due to the Metastasic Liver Cancer.
ES9500	Esophageal Cancer (EAC)	Skin and Subcutaneous Lesion	1st: Cisplatin + Fluorouracil, 2nd: Epirubicin + Cisplatin + Fluorouracil, 3rd: Docetaxel, 4th: Pembrolizumab	Smoker (1 Pack/Day for 20 years, Quit 22 years Ago), Slight Ulceration. Metastatic Adenocarcinoma.
HN9501	Head and Neck Cancer (HNSCC)	Left Neck Mass	1st: Carboplatin + Paclitaxel, 2nd: Nivolumab, 3rd: Fluorouracil + Carboplatin + Cetuximab	Previous Smoker, Slight Ulceration. Metastatic Nonkeratinizing SCC.
OV9522	Ovarian Cancer (Serous Carcinoma)	Right Inguinal Lymph Node	1st: Carboplatin + Taxol + Avastin, 2nd: Doxil + Avastin	Metastatic Adenocarcinoma Consistent with Serous Ovarian Primary. From Same Patient as OV9502.
UT9517	Uterine Cancer (Serous Carcinoma)	Ascites Fluid	1st: Taxol + Carboplatin + Avastin, 2nd: Avastin, 3rd: Doxil	Metastatic Adenocarinoma Consistent with a High Grade Serous Carcinoma. Ulceration

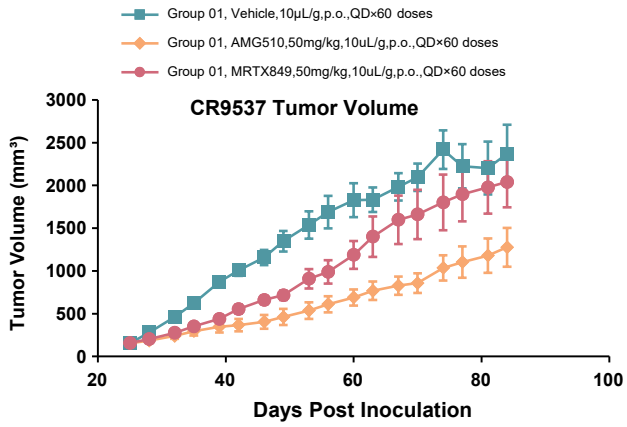
Model Validations

Crown Bioscience validates pretreated models by performing efficacy studies that mirror the patients' treatment history and confirm drug resistance or responsiveness in the PDX models, increasing the predictive value of using these models for developing next-generation therapeutics. Interactive versions of standard of care (SOC) efficacy plots are available in our online PDX database (**HuBase**).

CR9537 Colorectal PDX Model Validation

PDX model CR9537 was derived from a patient treated with combination chemotherapy and investigational treatments and was a KRAS G12C Inhibitor responder, but became resistant. Validation studies evaluating two different KRAS G12C inhibitors in this model show a partial response to AMG510 treatment and resistance to MRTX849 treatment.

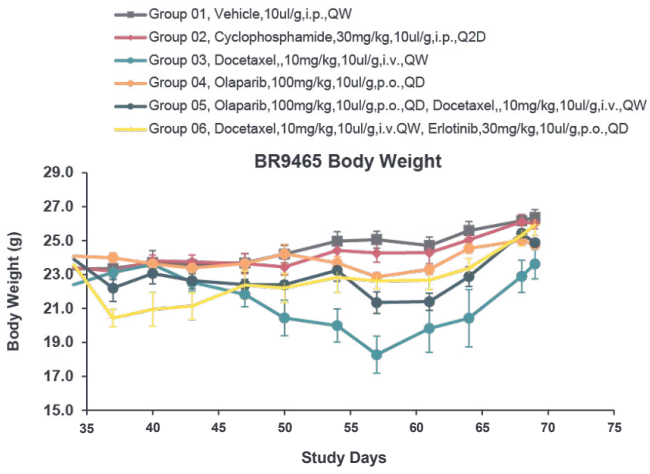


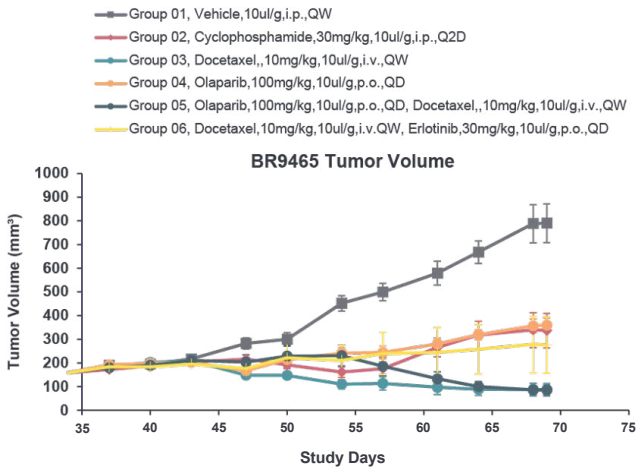


Treatment started on day 25 after tumor inoculation. Mean TV at randomization: 155 mm³, G1, n=8, G2, n=4, G3, n=4
Mice in Group 01 euthanized on days 61, 75, and 78 due to humane end points

BR9465 Triple Negative Breast Cancer PDX Model Validation

PDX model BR9465 was derived from a patient treated with radiotherapy, cyclophosphamide, doxorubicin, paclitaxel, liposomal doxorubicin, zoledronic acid, capecitabine, and docetaxel. This model was developed from pleural effusion, and mutations in BRCA1, RB1, and TP53 were identified. Response to cyclophosphamide, docetaxel, and olaparib single treatment was observed. Response to a combination of olaparib and docetaxel was also observed, but there was no difference from docetaxel single treatment.





Summary

Crown Bioscience has characterized and validated a collection of pretreated PDX models covering a range of indications, treatment types, and mutations that mirrors the patient population and cancer treatments of today, for the development of next generation therapeutics.

To view data for specific pretreated models or browse models, register for or log into **HuBase**, our free PDX database, at https://www.crownbio.com/databases/hubase to view treatment history, available validation (SOC) data, genomic, and proteomic data to help you find the best models for your research needs.

Reference

[1] Gillet *et al*. Redefining the relevance of established cancer cell lines to the study of mechanisms of clinical anti-cancer drug resistance. *Proc Natl Acad Sci USA* 2011;108: 18708-13.

Get in touch

Sales
US: +1 858 622 2900
UK: +44 870 242 2900
busdev@crownbio.com
www.crownbio.com

Science
consultation@crownbio.com