Immunotherapy for HCC

Enabling the discovery and development of cancer immunotherapies for HCC with the immune-competent models including syngeneic models and humanized models.

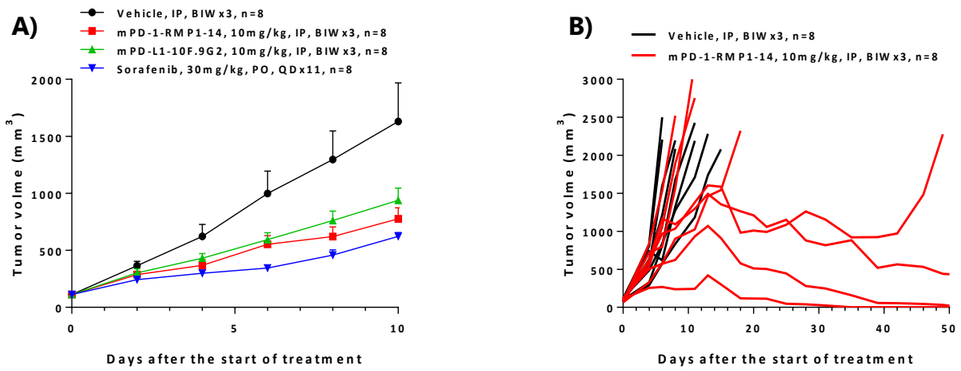

Figure 7. Checkpoint inhibitors in the mouse liver cancer syngeneic models. A) Anti-PD-1 and Anti-PD-L1 treatment in H22 mouse liver cancer syngeneic model in comparison with the stand of care drug Sorafenib. B) Spider plot of MH-22A mouse liver cancer syngeneic model with partial response to the anti-PD-1 treatment.

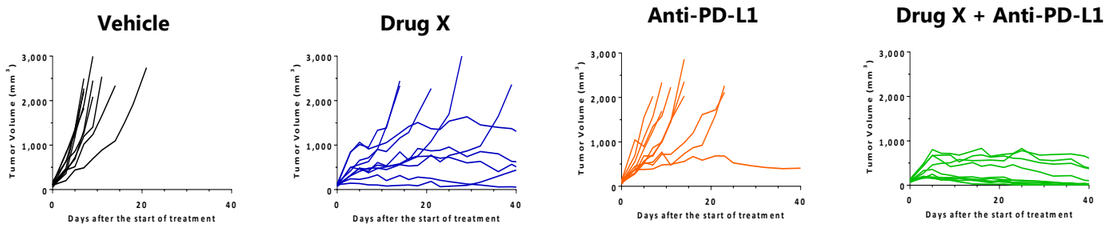

Figure 8. MH-22A mouse liver cancer syngeneic model treated with the combination therapy of small molecule and anti-PD-L1. The combination treatment resulted in a synergistic effect compared to the monotherapies

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Hepatocellular Carcinoma Models

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Hepatocellular Carcinoma Models

Hepatocellular Carcinoma (HCC) is the most common type, accounting for about 80%, of liver cancer. It occurs predominantly in patients with underlying chronic liver disease and cirrhosis.. HCC is the sixth most common cancer worldwide, accounting for approximately 5.7% of all new cancer cases, and is the third leading cause of global cancer death. It is a major health problem in developing countries. In particular, 55% of all HCC cases are reported from China. Approved treatment for HCC contains surgery, radiation therapy, chemotherapy and targeted therapy at the current stage. Immunotherapies for HCC, including check-point inhibitors, immune modulators, adoptive cell therapy and oncolytic virus therapy are now in clinical trials.

WuXi AppTec Oncology & Immunology Unit provides pre-clinical oncology research services for HCC and liver cancer. A range of preclinical platforms have been established to support drug discovery and translational research around HCC and other liver cancers, including cell-line derived xenograft (CDX) models, patient-derived xenograft (PDX) models, NGS and bioinformatics pipelines and histopathology, etc.

Subcutaneous CDX models for HCC

WuXi has 9 CDX models established in mice, with 4 of them validated with standard of care including Cisplatin, Doxorubicin, Sorafenib and etc.

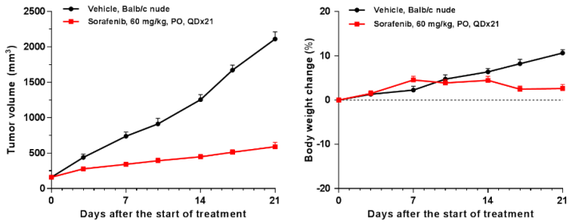

Figure 1 Efficacy study of Sorafenib – targeted therapy for HCC in WuXi CDX model BEL7404.

Table 1. A list of SOC validation WuXi subcutaneous CDX models for HCC:

Model	SOC validation
BEL-7404	Bevacizumab, Cisplatin, Doxorubicin, Sorafenib
Hep3B	BLU9931, Docetaxel, Sorafenib
Huh7	Bevacizumab, BLU9931, Cisplatin, Doxorubicin, Palbociclib, Sorafenib
MHCC97H	Tepotinib

(Hep G2, JHH-7, QGY-7703, SNU-182, SNU-398 are also in-house but not validated with SOC)

Orthotopic CDX models for HCC

WuXi has 2 luciferase labelled liver cancer cell-lines (Hep3B-luc and BEL-7404-luc) which are injected intrahepatically and developed in the primary organ, or spread to the metastasis sites, which could be monitored in real time by IVIS imaging system.

Figure 2. WuXi IVIS system

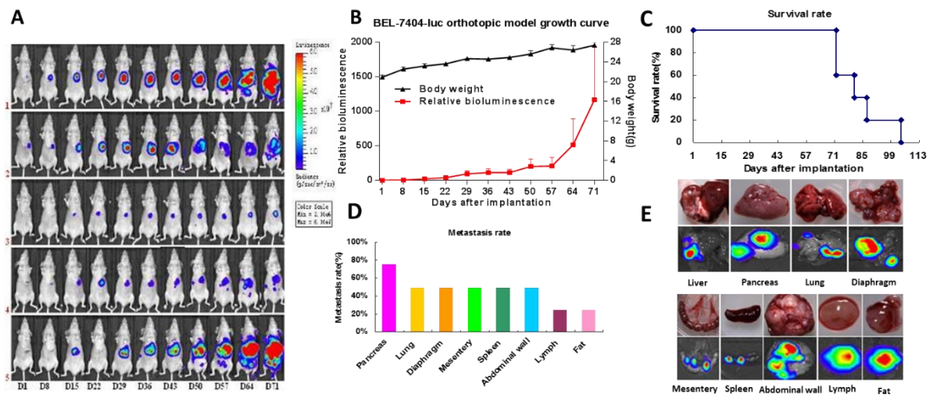

Figure 3. BEL-7404-luc hepatoma orthotopic model. A) Bioluminescent imaging of mice over 71 days (n=5). B) Body weight and bioluminescence measurements. (C) Survival curve during the period. (D) The metastasis rate. (E) Bioluminescent imaging of the primary and metastatic tumor.

PDX models

About 300 HCC PDX models have been established, partially profiled with SOC (25 models), pathology, and genetic profiling (103 models) including WES, SNP6.0 and RNAseq.

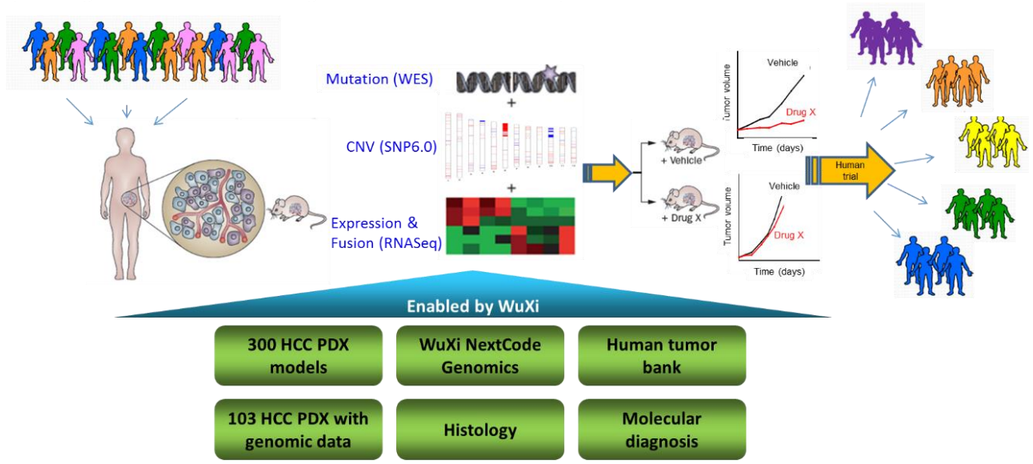

Figure 4. WuXi PDX models are enabling precision medicine for treatment of HCC patients.

Targeted therapy with PDX model

A show case of evaluating MET inhibitors with WuXi HCC PDX models.

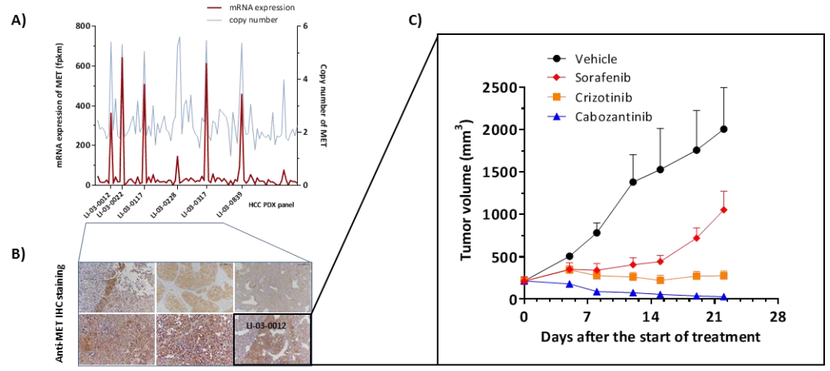

Figure 5. Showcase of METi evaluation with PDX models: A) Genomic profiling of MET by RNA-seq and SNP6.0. B) Model validation based on IHC staining. C) Efficacy study with the selected model.

Orthotopic HCC PDX models

WuXi carries out surgery, that the tumor fragments of PDX can be seeded into the liver lobe for orthotopic PDX modeling. Tumor weight is measured at the end-point as an assessment of the tumor growth rate.

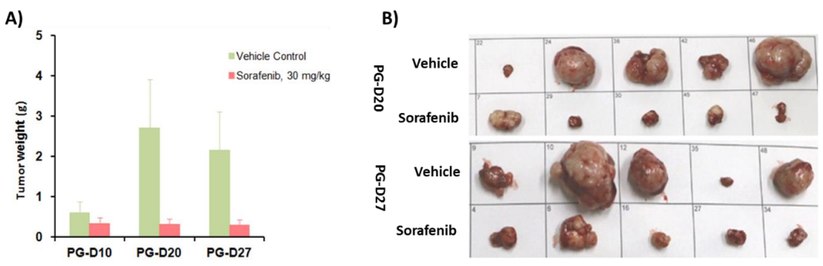

Figure 6. Efficacy study of Sorafenib in the orthotopic HCC PDX model LI-03-0254. A) Tumor weight records at different end-point after the start of treatment. B) Picture of resected tumors.