

# GEMM-Derived Allografts

In the modern genetically engineered mouse models (GEMMs), oncogenes are activated and/or tumour-suppressor genes are inactivated somatically, generally through temporally controlled and tissue-specific expression of CRE recombinase. Animals then develop tumours in the tissue of interest.

However, with long latency periods, mice developing disease at different stages, and 100% penetrance not achievable, this rapidly becomes complex and costly. To overcome this, the mouse derived allograft model has been developed. It is comprised of allografts of spontaneous tumors from GEMM, engrafted in syngeneic mice with complete immunocompetency.

GEMM-derived allograft models enable characterisation of genomic drivers and treatment responses by modelling immune and micro-environmental changes more accurately than xenografts. Greater use of such models in target validation, assessment of tumour response, investigation of pharmacodynamic markers of drug action, modelling resistance and understanding toxicity has the potential to markedly improve the success of cancer drug development.

## Case 1: KPC mice Derived Allograft



Fig1. The spontaneous pancreatic tumor of KPC mouse model with large volume, uneven surface and multiple nodular projections.

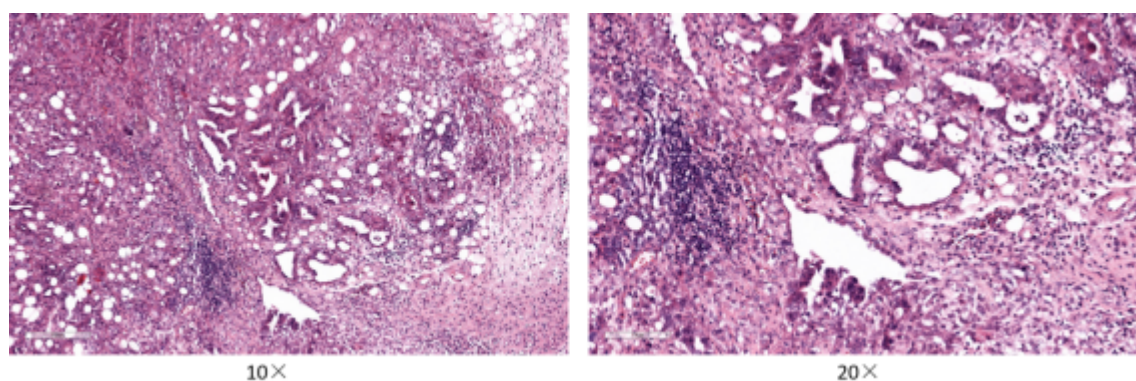


Fig2. HE staining of pancreatic tumor from KPC mouse model.

The tumor cells from KPC mouse model demonstrated disorderly arranged pancreatic cells, irregular tissue structure, dilated pancreatic ducts, inflammatory cells infiltration and stromal fibrosis as was seen in pancreas adenocarcinoma.

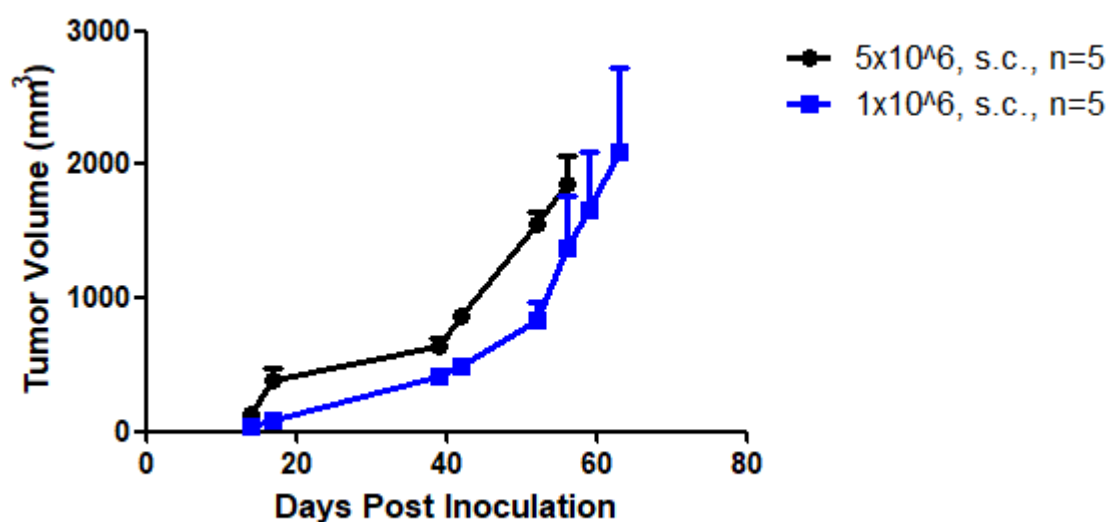


Fig3. Changes in pancreatic tumor volume of tumor-burdened mice.

Wild-type mice were inoculated with pancreatic tumor cells from KPC mice, and pancreatic tumors grew in size over time.

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#### **Case2:** Kras-LSL-G12D/+ mice Derived Allograft

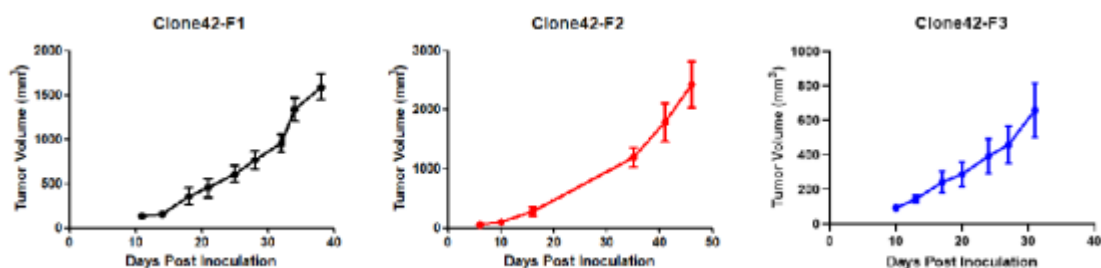


Fig4. Growth of s.c. lung cancer allografts in vivo..

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**Case3:** H11-LSL-Myc/+; Rosa26-LSL-Luc-EGFP/+; Alb-Cre/+ mice Derived Allograft

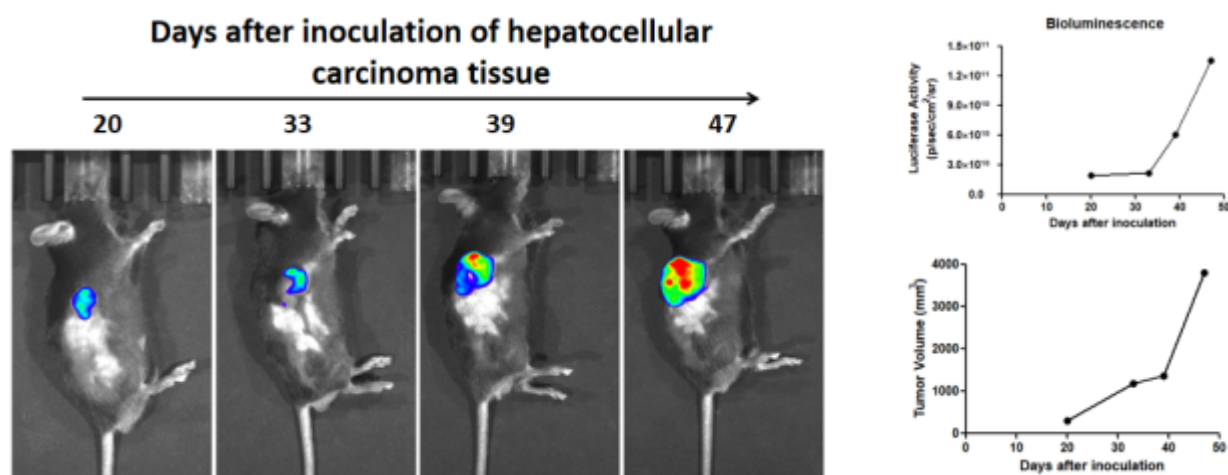


Fig5. Representative *in vivo* bioluminescence imaging showing the growth of tumors in C57BL/6 mice inoculated with hepatocellular carcinoma tissue from H11-LSL-Myc; Rosa26-LSL-Luc-EGFP; Alb-Cre mice.

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