MuScreen™

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Fast-track your *in vivo* immunotherapy development with large-scale syngeneic and tumor homograft screening

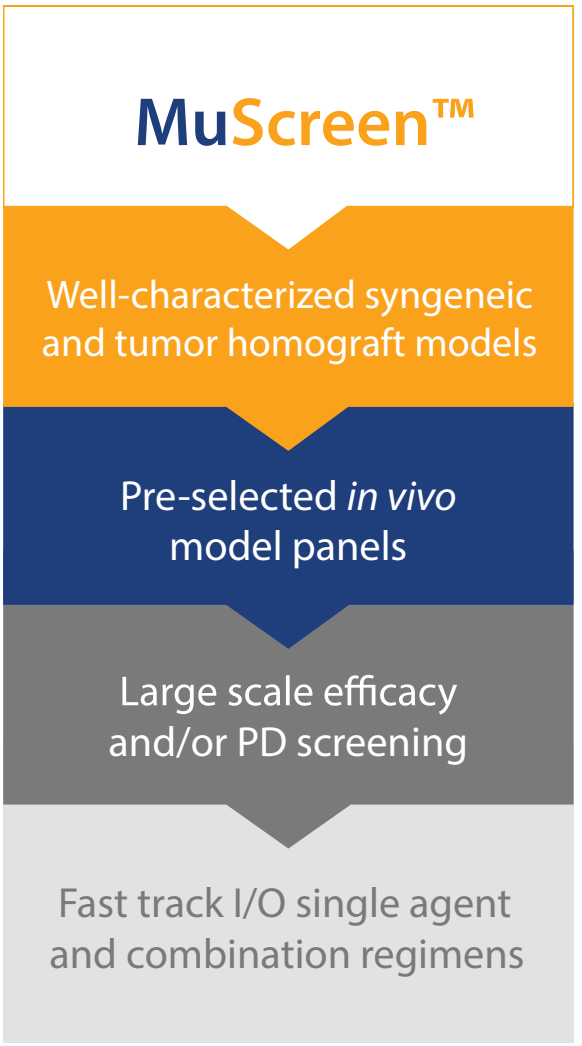
Discover the benefits of running a MuScreen to accelerate your single agent or combination regimen immunotherapy development programs.

For standard oncology agents such as chemotherapies, an *in vitro* screen can quickly and inexpensively identify cells and models for further study. However, for therapeutics targeting the complex host immune system *in vitro* assays often fail, and *in vivo* studies are usually cost prohibitive.

CrownBio has developed MuScreen, a cost-effective *in vivo* screening platform to fast-track preclinical immunotherapy development.

Choose MuScreen To:

- Interrogate well-characterized and validated syngeneic or tumor homograft models.
- Quickly identify responder models or PD markers saving time, and improving efficiency.
- Effectively evaluate combination strategies.
- Accurately investigate PD effects.
- Benefit from CrownBio covering the cost of the vehicle group for all models.



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MuScreen Key Facts

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MuScreen is the most experienced large-scale, *in vivo* screening platform to fast-track single agent and combination immunotherapeutics:

- Built upon our collections of validated and well-characterized syngeneic and unique tumor homograft models.
- Leveraging detailed model checkpoint inhibitor benchmarking data, as well as RNAseq and offering optional FACS/IHC analysis information.
- Performed on a global platform across the US and China.
- Comprising of predesignated syngeneic and tumor homograft panels across a range of cancer types.
- Evaluate TGI on 6 or 12 preset syngeneic models or 8 tumor homograft models.
- Evaluate PD effects (FACS analysis of TIL/TAM) with a panel of 12 syngeneic models.
- Models run on a large scale, preset schedule, with shared vehicle and common groups to improve efficiency, reproducibility, and cost-effectiveness.

Preclinical Immunotherapy Screening Challenges

Immunotherapy represents the most promising new cancer treatment approach since the first development of chemotherapies in the late 1940s. However, advances in the field have inevitably uncovered subsequent challenges and barriers to further development including the need to rapidly establish optimal approaches for preclinical immunotherapy evaluation.

Immuno-oncology needs to target the complex host immune system and *in vitro* screens fail to meet this need, while standard *in vivo* screens tend to be cost prohibitive. Instead, a large-scale, *in vivo* screening platform of syngeneic and tumor homograft models enables cost effective preclinical immunotherapy research, for both single agents and combination therapies.

CrownBio's Unique MuScreen Platform to Fast-Track Immunotherapeutic Development

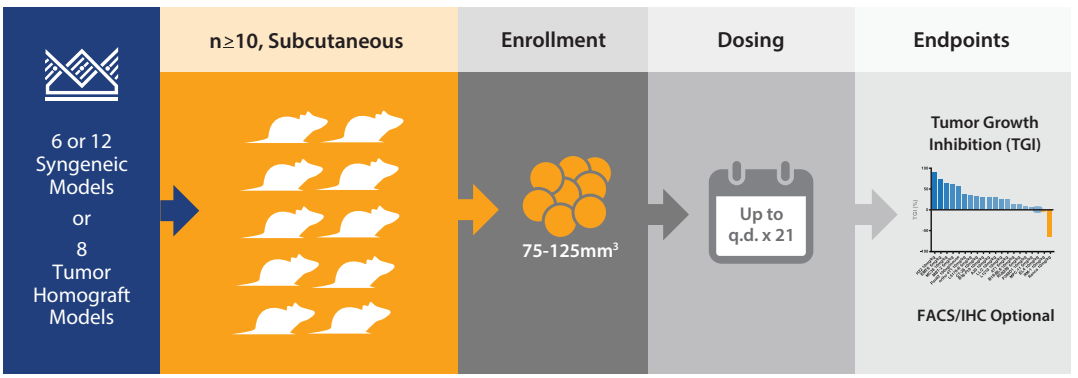
Panels of our syngeneic and tumor homograft models are utilized within MuScreen, the most experienced large-scale, *in vivo* screening platform for cancer immunotherapeutics. MuScreen can be used to rapidly focus immuno-oncology research efforts such as screening for efficacy, identifying PD markers, evaluating combination therapies, and qualifying drug resistance.

The platform is designed to fast-track the *in vivo* screening of immunotherapy compounds either as single agents or combination regimens. MuScreen leverages detailed profiling data on our syngeneic and tumor homograft models, including efficacy benchmarking with anti-PD-1, PD-L1, and CTLA-4 antibodies, RNAseq data, and FACS analysis on both baseline and treated tumor samples, which aids in the discovery of biomarkers to predict response.

Screen for I/O Compound Efficacy

MuScreen Efficacy Mode is run following a preset schedule across our syngeneic and tumor homograft models along with a shared vehicle group. **Figure 1** shows an overview of the study design. The main endpoint is TGI (with optional FACS and IHC) and frozen or fixed tumors are available on request.

Figure 1: Efficacy Mode Study Design



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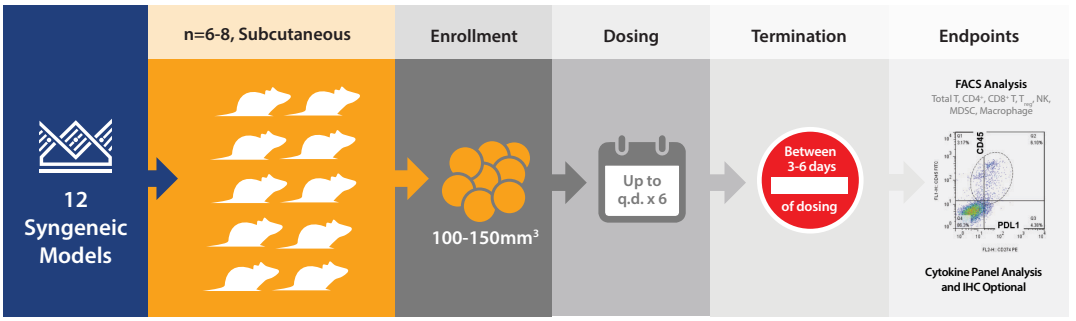
Screen for I/O Compound PD Effects

MuScreen PD Mode is run on a preset schedule and is currently only available with our syngeneic 12 model panel, with a shared vehicle group. **Figure 2** shows an overview of a pooled screen study design. The MuScreen PD Mode can also be run as an individualized screen, with the study design and dosing customized to fit a given client compound's mechanism of action. Our main study endpoint is FACS analysis of tumor infiltrating lymphocytes and tumor associated macrophages. Additional endpoints can also include cytokine panel profiling in blood and tumor, IHC for bio-marker analysis (on tumor tissues, blood cells, lymph nodes, and spleen cells), and frozen or fixed tumors are available on request.

Figure 2: PD Mode Study Design



MuScreen-Syngeneics

Choose between 6 or 12 well-characterized syngeneic models to evaluate your I/O compound efficacy or PD effect.

Syngeneic models are an ideal platform for proof of concept studies and to evaluate your surrogate or cross reactive agent mechanism of action and PD effects.

Key advantages of MuScreen-Syngeneics include:

- Robust and well-established *in vivo* screening platform using well-validated models
- Comprehensive model characterization data including:
  - Immune checkpoint inhibitor benchmarking
  - Baseline tumor immune profile
  - Tumor RNAseq
- Availability of historical model data
- Global screening capabilities

Table 1: Syngeneic Models Available for MuScreen

Cancer Type	Model	Mouse Strain	Immune Cell Profiling	RNAseq
Breast	**EMT-6**	**BALB/c**	**Yes**	**Yes**
Colorectal	**CT-26**	**BALB/c**	**Yes**	**Yes**
	MC38	C57BL/6	Yes	Yes
Kidney	Renca	BALB/c	Yes	Yes
Liver	H22*	BALB/c	Yes	Yes
	Hepa 1-6	C57BL/6	Yes	Ongoing
Lung	LL/2	C57BL/6	Yes	Yes
Lymphoma	**A20**	**BALB/c**	**Yes**	**Yes**
Melanoma*	B16-BL6	C57BL/6	Yes	Yes
	B16-F10	**C57BL/6**	**Yes**	**Yes**
Pancreatic	**Pan02**	**C57BL/6**	**Yes**	**Yes**
Prostate	**RM-1**	**C57BL/6**	**Yes**	**Yes**

Models highlighted in blue are used in the 6 model US MuScreen
* This line is not applicable for FACS

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MuScreen-Tumor Homograft

Test your I/O agent antitumor efficacy *in vivo* on a unique panel of well-characterized tumor homograft models. Tumor homografts are transplants of spontaneous or carcinogen-induced GEMM tumors in immunocompetent syngeneic hosts.

Our tumor homografts combine the predictive power of GEMM with the operational simplicity required for pharmacology studies, providing an ideal model to evaluate your agent's efficacy in a novel I/O model system.

Key advantages of MuScreen-Tumor Homografts include:

- Unique models encompassing disease-specific mutations of human cancers
- Models preserving relevant tumor stroma for a more translatable response to I/O
- Comprehensive model characterization data including:
  - Immune checkpoint inhibitor benchmarking
  - Baseline tumor immune profile
  - Tumor RNAseq

Table 2: Tumor Homograft Models Available for MuScreen

Cancer Type	Model	Mutations/ Carcinogen	Strain Background	Immune Profiling	RNAseq	Growth Curve	SoC Data
Breast	mBR6004	MMTV-PyVT TG	FVB/N	Yes	Yes	Yes	Yes
Lung	mLU6045	$Kras^{(G12D)}$; $P53^{-/-}$	C57BL/6	Yes	Yes	Yes	Yes
	mLU6050	Urethane	BALB/c	Yes	Yes	Yes	Yes
	mLU6054	$Kras^{(G12D)}$; $Pten^{Flox/Flox}$	C57BL/6	Yes	Yes	Yes	Yes
Lymphoma	mLY6043	IgH-Myc TG (Eμ Myc)	C57BL/6	Yes	Yes	Yes	Yes
Pancreatic	mPA6115	$Kras^{(G12D)}$; $P53^{-/-}$; PDx-1 cre	C57BL/6	Yes	Yes	Yes	Yes
Sarcoma	mSA9003	$P53^{-/-}$	C57BL/6	Yes	Yes	Yes	Yes
Skin	mSK6005	$Apc^{Min/+}$	C57BL/6	Yes	Yes	Yes	Yes

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