

Immuno-Oncology and Oncology Platform for Screening Discovery Small & Larger Molecules

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Introduction and Background

Immuno-oncology (IO) and oncology platforms are state-of-the-art technology for screening anticancer drugs. IO is most significant research areas in immunotherapy and revolutionized cancer treatment, through the stimulation of the body's own immune system to kill cancer cells. IO agents are rapidly changing the standard of care for people with cancer. More recently, combining IO agents with conventional therapies has been evaluated with some significant improvements in patient outcomes. Adgyl Lifesciences has successfully established these screening platforms to cater client needs.

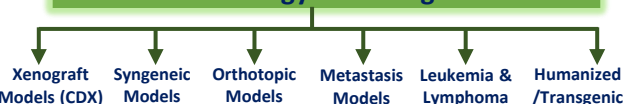
Materials and Methods

Subcutaneous, orthotopic and metastatic model establishment: A appropriate number tumor cells were inoculated to immunocompetent or immunocompromised mice. After tumor induction, treatments were initiated.

Endpoints:

- Tumor volume, Tumor growth inhibition and growth delay
- Body weight, Clinical signs & Survival
- TIL analysis (blood, tumor & spleen),
- Cytokine analysis
- Biomarker – Proximal & distal
- Immunohistochemistry (IHC)

In Vivo Oncology Screening Platform



Syngeneic Models

Breast – 4T1
Bladder – NBT-II
Colon – CT26, MC38
Melanoma – B16F10
Myeloma – J558
Fibrosarcoma – MCA205
Lung – LLC
Liver – Hepa 1-6
Renal – Renca

Orthotopic Models

Breast – MDAMB-231
Bladder – NBT-II, T24
Brain – U87MG
Colon – DLD-1, HCT-116
Liver – HepG2
Lung – A549
Pancreas – BX-PC3, MIAPaCa2
Ovary – SKOV-3

Metastasis Models

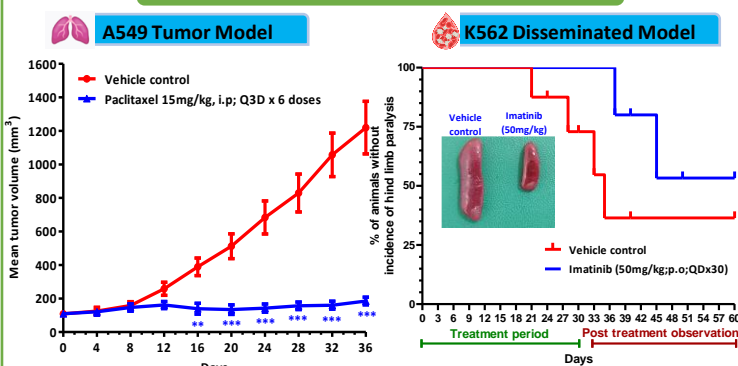
Lung – A549, LLC
Melanoma – B16F10
Fibrosarcoma – MCA205

45+ established CDX Models

Brain – U87MG, A172
Breast – MCF-7, MDAMB-231, MDA-MB-453, MDA-MB-468, HCC1395, BT474
Bladder – T24, HT-1376
Colon – HT29, HCT116, DLD1, COLO-205
Epidermoid – A431
Gastric – N87
Lung – A549, H1975
Liver – HepG2, JHH7
Kidney – ACHN
Melanoma – A375, SK-MEL-28
Prostate – PC3
Pancreas – BxPC-3, MIA PaCa-2
Ovary – SKOV-3
Medulloblastoma – D283
Tongue – CAL27

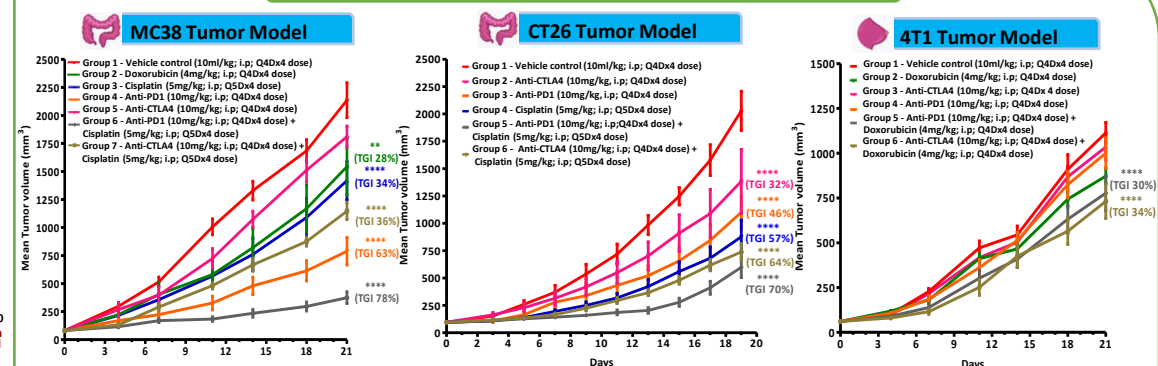
❖ Cell lines are routinely screened for authentication using STR based DNA profiling and mycoplasma test

Human CDX tumor models



All data is represented as Mean \pm SEM n=8-10. In A549 human tumor xenograft model Paclitaxel treatment resulted in significant tumor growth inhibition when compared with vehicle control group. In K562 disseminated model the median days for the incidence of hind limb paralysis in vehicle control group was 35 days, while for the Imatinib treated group was 48 days.

Syngeneic subcutaneous tumor models



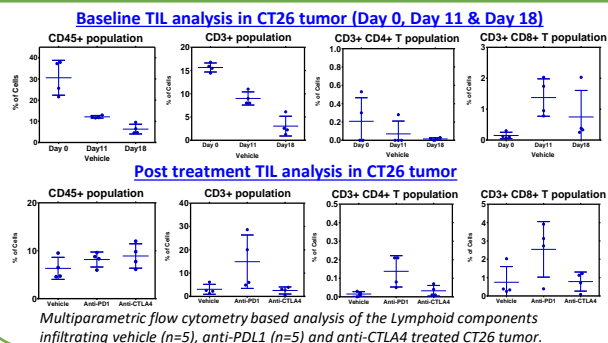
All data is represented as Mean \pm SEM n=8-10. In MC38 syngeneic tumor model standalone treatment of anti-PD1 resulted in moderate tumor growth inhibition. However, combination of Cisplatin with anti-PD1 had improved efficacy outcome when compared with combination of anti-CTLA4. In CT-26 tumor model standalone treatment with anti-PD1 resulted in moderate tumor growth inhibition. Combination of cisplatin with anti-PD1 & anti-CTLA4 showed better tumor growth inhibition. In 4T1 breast tumor model combination of Doxorubicin with anti-CTLA4 and anti-PD1 showed minimal tumor growth inhibition.

Orthotopic Animal Models

Breast cancer Species : SCID mice Cell line : MDA MB-231 	Bladder cancer Species : Wistar rats Cell line : NBT-II 	Brain cancer Species : SCID mice Cell line : U87-MG 	Colon cancer Species : SCID mice Cell line : DLD1 	Liver cancer Species : SCID mice Cell line : HepG2 	Ovarian cancer Species : SCID mice Cell line : SKOV-3
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Note: Other orthotopic model(s) are available or extensive panel of orthotopic models can be customized and validated upon client request

Tumor immunoprofiling



Multiparametric flow cytometry based analysis of the Lymphoid components infiltrating vehicle (n=5), anti-PD1 (n=5) and anti-CTLA4 treated CT26 tumor.

Immune-Profiling, IHC & Cytokine analysis

Sample	Immune Profile (Tumor & Blood)	IHC (Tumor)	Cytokine (Plasma)
Tumor Blood Plasma	T cell: CD45, CD3, CD4, CD8 Treg: CD4+ CD25+ FOXP3+ B cell: CD19, CD20 NK cell: CD16, CD56 TAM: CD33, CD11b, F4/80, Ly6C MDSC: CD33, CD11b, Ly6G DC: CD11c+ CD103+ CD204+	CD4 CD8 CD25 FOXP3	IFN- α , IFN- γ IL-1 beta IL-2, IL-10 IL-12/IL-23p4 IL-4, IL-5 IL-6, IL-8 (CXCL8) TNF- α , GM-CSF IL-13, TNF beta

Access to mice - Athymic nude, SCID, NOD/NOG, SCID Beige, NSG mice, APC Min mice. On request - Humanized mice (huNOG-EX1), hPD1 x hCTLA4 from authorised international source

Lung Metastatic Models

B16F10 Normal Lung Vehicle control Doxorubicin 	MCA205 Normal Lung Vehicle control mAnti-PD1
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All data is represented as Mean \pm SEM n=10

❖ ADGYL is a leading CRO with global presence to cater FFS & FTE discovery programs in Oncology, Immuno-oncology and other disease models

❖ 60+ Oncology models on board with team of 20+ years experienced scientists

❖ First CRO in India to cater efficacy studies in GLP

❖ The *in vivo* models for any specific cancer cell line can be customized and validated based on project needs.

FOR BUSINESS RELATED QUERIES, PLEASE CONTACT:

✉ bd@advinus.com

IVIS Spectrum (*In Vivo* Imaging System)

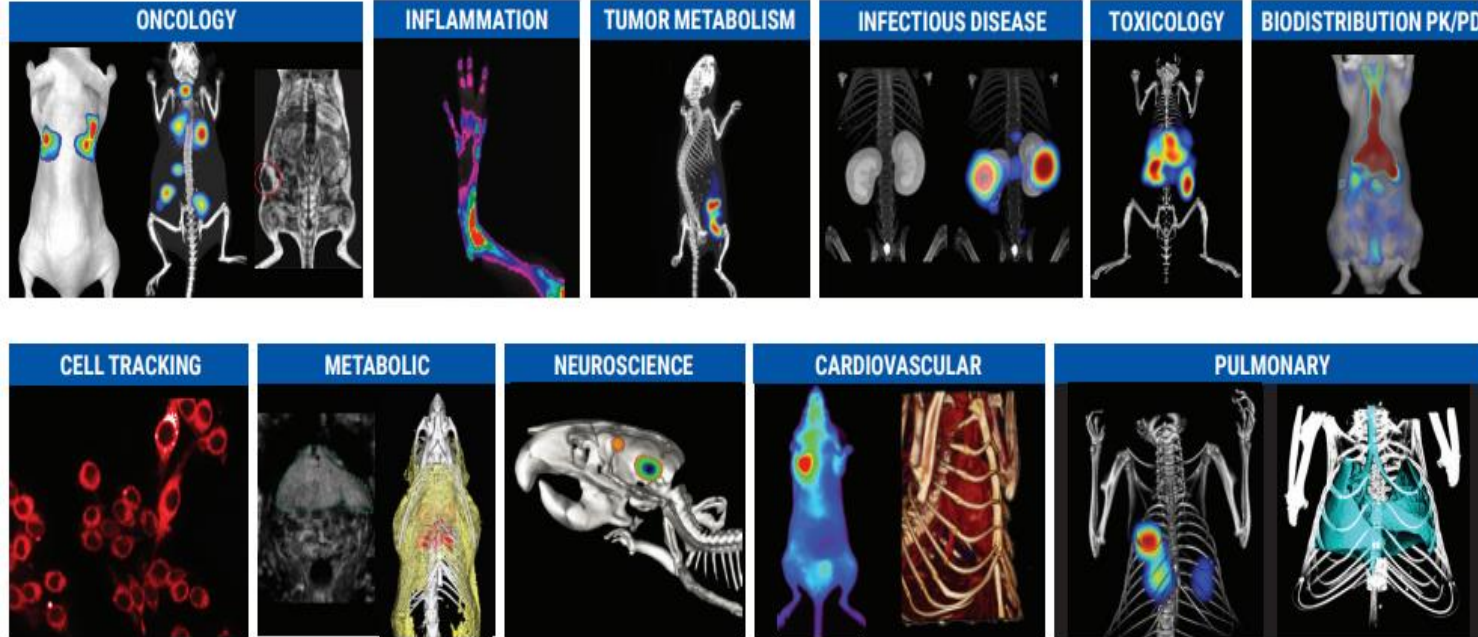
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PerkinElmer IVIS® Spectrum



Research Disease Area



As adapted from IVIS brochure & literature

Our state-of-the-art, preclinical **small animal IVIS imaging system** has **2D & 3D optical tomography** in one platform to offer following services,

- ❖ **Non-invasive longitudinal monitoring of disease progression:** Oncology, Inflammation, CNS, CVD, Metabolic Disorders
- ❖ **Real time monitoring and biodistribution of**
 - Stem cells trafficking
 - Antibodies (mAbs, Bispecific's, CART, T cells, Gamma-delta ($\gamma\delta$) T cells)
 - Target specificity for antibodies

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PerkinElmer IVIS® Spectrum

Whole body 3D
Optical Tomography

Labelling range

- ❖ **Bioluminescent: cell line**
 - BxPC3 Red F-Luc
 - U87MG Red F-Luc
 - PC3 Red F-Luc
 - T24 RFP cell line
- ❖ **Luciferase MC38**
- ❖ **Fluorescent agents**
- ❖ **Dil fluorophore**
- ❖ **RFP - Red to far infra red range**
- ❖ **Gold nanoparticles**