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MetaMouse®  AngioMouse®  OncoBrite®  StromaMouse®
CONTRACT RESEARCH AND LICENSING
www.anticancer.com
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Pre-Clinical Oncology Services
World leader in metastatic mouse tumor models and GFP imaging
AntiCancer Inc., is a leading cancer research company providing contract drug discovery and evaluation services to pharmaceutical and biotechnology companies and cancer researchers since 1984.

AntiCancer Inc., has developed numerous novel technologies including MetaMouse® and AngioMouse® – the leading mouse models of cancer as well as Oncobrite, the most powerful de vivo imaging method.

AntiCancer Inc., holds approximately 150 patents for cancer-related products and has published more than 600 scientific papers including in such journals as Cell, Cancer Cell, PNAS.

AntiCancer Inc., provides customized contract services for in vivo drug evaluation including developing cancer models, design of individual protocols, performing entire research programs as well as expertise data analysis and reports. Ongoing data feedback maximizes the flow of information, allowing optimum study flexibility and the development of the best possible solutions, with the overall process being facilitated by a dedicated Project Co-ordinator.

IN VIVO RESEARCH AND DEVELOPMENT

AntiCancer’s patented MetaMouse® is the most clinically accurate mouse cancer model. MetaMouse® represents clinical cancer, especially with regard to metastasis and drug sensitivity. Combined with GFP imaging, primary tumor growth and metastases can be tracked with real-time non-invasive whole body imaging. Effective drugs can be rapidly discovered and evaluated in the MetaMouse® models utilizing human tumor cell lines and patient tumors. These unique MetaMouse® models have been used for innovative drug discovery and mechanism studies in over 300 contract studies for more than 20 years and serve as a bridge linking pre-clinical and clinical research and drug development.

Subcutaneous xenograft models

Subcutaneous xenograft tumor models are a convenient means to test novel potential anticancer drugs in vivo. A large variety of human and murine cell lines are available for implantation.

MetaMouse®

In MetaMouse orthotopic models, the primary tumor develops in the organ corresponding to its origin and metastasizes to mimic the complexity of tumor behavior in patients. Transfection of cancer cells with fluorescent protein genes allows real-time in vivo visualization of tumor growth, metastasis, angiogenesis and gene expression. Orthotopic models have been proven to be highly valuable in elucidating pathogenesis of tumor growth and metastasis and drug discovery and evaluation.

AngioMouse®

We have utilized multicolored fluorescent proteins to develop imaging models of tumor angiogenesis. Intra-vital and non-invasive imaging can visualize angiogenic capillaries at both primary and metastatic sites. Color-coded imaging allows visualization of cancer cells expressing one color fluorescent protein interacting with their blood vessels expressing another color fluorescent protein. This model is highly valuable for discovery and evaluation of anti-angiogenic agents.

StromaMouse™

StromaMouse models express one or more color of fluorescent protein in stromal cells and cancer cells express another color fluorescent protein. The model enables study of the tumor micro-environment (TME) and is ideal for discovery and evaluation of anti-stromal therapeutics.

Introduction


AntiCancer’s publication on novel drug discovery and evaluation using MetaMouse®
AntiCancer’s publications on novel drug discovery and evaluation using MetaMouse®


Selective Comparison of the inhibitory effect of the angiogenesis inhibitor, TNP
VEGF receptor antisense therapy inhibits angiogenesis and peritoneal dissemination of human gastric cancer in nude mice.

Activity of the new platinum analog \(\text{Pt}((\text{Cyano})_{2}\text{dach})_{2}\text{Cl})\) in live, non-metastatic model.

Antimetastatic Glioma U87 RFP tumor in GFP mouse

High DsRed2 and AntiCancer’s fluorescent protein-expressing cancer cell line collection available for purchase and contract studies

Dual-color cancer cell line

(a) HT-1080 cells expressing cytoplasmic DsRed2 and nuclear histone-2B-EGFP before and after SDS-PAGE under native conditions. The square boxes indicate the regions where the spectra were taken from. (b) 2-photon excitation spectra of EGFP, DsRed2, and Alexa Fluor 660. The solid lines represent the isolated protein in SDS-PAGE or soluble Alexa Fluor 660 and the dashed lines living dual-color cells. The calculated efficiency to excite DsRed2 at 1100 nm was 20-fold higher compared with excitation at 760 nm. (c) Simultaneous excitation of EGFP at 830 nm and DsRed2 at 1100 nm in live, non-fixed HT-1080 dual-color cells. Bars, 20 μm. (Andresen V, et al. Curr Opin Biotechnol 20, 54-62, 2009). (d) HT1080 cells expressing cytoplasm EGFP and nuclear DsRed2.

AntiCancer's fluorescent protein-expressing cancer cell line collection available for purchase and contract studies

AntiCancer’s publication on novel drug discovery and evaluation using MetaMouse®


7. Anti-Cancer’s fluorescent protein-expressing cancer cell line collection available for purchase and contract studies


Feasibility for the drug discovery in the SOI models has been demonstrated with colon, pancreatic, stomach, bladder, and lung cancer where chemotherapy has resulted in dose limiting toxicities such as myelosuppression and clinical phlebothrombosis. The metalloproteinase inhibitor Batimastat: Active against a SOI human colon tumor xenograft model 1, 43 showing minimal or no effect on primary tumor. 

- Inhibition of primary tumor growth
- Inhibition of metastatic events, and
- A large increase in survival,

- IPN-2: Active against a patient pleural cancer SOI model 44, 45 showing minimal or no effect on primary tumor.
- Angiogenesis inhibitor TNP-470: Active in patient colon and stomach tumor SOI models 46, 47 showing minimal or no effect on primary tumor.
- Anti-VEGF antibody: Active in SOI model of colon and stomach cancer 48, 49, 50 showing minimal or no effect on primary tumor.
- Anti-angiogenesis phosphorothioate oligonucleotide specific for VEGF-receptor active in SOI model of stomach cancer 51, 52 showing minimal or no effect on primary tumor.

- Inhibition of peritumoral tissue dissemination
- Increased tumor cell apoptosis
- Microvessel density (MVD) in tumor nodules.

- New platinum analogs (Pt(cis-dach)(DDPE)Zn(2+)) and (Pt(trans-dach)(DDPE)Zn(2+)) active in SOI model of bladder and stomach cancer 1, 4, 37 showing minimal or no effect on primary tumor.

- No metastases in either the high- or low-dose platinum-analog treated groups in SOI model of bladder cancer.

- No mesenteric lymph node metatases in the groups treated with the high or low doses of both new platinum analogs with SOI model of colon cancer.

- Upregulated desmocollin (Dol) 53,

- Inhibition of MDA-MB-231 human breast tumor xenografts, which were resistant to free doxorubicin 54, 55.

- Camptothecin analog DX-8951F: Active in SOI models of pancreatic cancer 56, 57, 58 showing minimal or no effect on primary tumor.

- CX-8451 showed efficacy against two human pancreatic tumor cell lines in the SOI-GFP model. CX-8451 was highly effective against primary and metastatic growth in the two models and showed significantly higher efficacy than gemcitabine, the standard treatment of pancreatic cancer.

- Cytosine analog, CS-682: Active in SOI model of pancreatic cancer 1, 37, 59, 60 showing minimal or no effect on primary tumor.

- CS-682 showed efficacy in an adjacent treatment orthotopic model of human pancreatic cancer suggesting possibility of chronic use of CS-682 to control pancreatic cancer.

- Estrogen analog 2-methoxyestradiol bis-sulfamate: active in MDA-MB-435 SOI model of breast cancer 61, 62, 63, 64 showing minimal or no effect on primary tumor.

- Truncated galectin-1 (galectin-3C) was found active in an orthotopic breast cancer xenograft nude mouse model indicating high therapeutic potential for breast cancer protein 65.

- The agonistic anti-LTBR monoclonal antibody (mAb) CB11 inhibited tumor growth in xenograft models and potentiated tumor responses to chemotherapeutic agents 66, 67, 68.

- Additve effects of gliofosfamide and gemcitabine in fluorescent mouse models of human pancreatic cancer 69, 70 showing minimal or no effect on primary tumor.

- TX886 prevents liver metastasis of colon cancer xenografts by modulating the proinflammatory cytokine 71, 72, 73.

- Type II PDE6B/8B-RAF inhibitor disrupts angiogenesis and tumor growth 74, 75, 76.

- A small molecule inhibitor of SOD-1/CXCR4 inhibits vasculogenesis, but not angiogenesis, and prevents the recurrence of glioblastoma following radiation in mice 77, 78.

- HER-2 therapy inhibits metastasis of esophageal cancer 79, 80.

- Metronomic gemcitabine therapy greatly inhibits metastasis of pancreatic cancer 81, 82.

- Bisphosphonate clodronate inhibits bone metastasis in prostate cancer xenograft 83, 84 showing minimal or no effect on primary tumor.

- Knockdown of the β1 integrin subunit reduces primary tumor growth and inhibits pancreatic cancer metastasis 85, 86 showing minimal or no effect on primary tumor.

- High antiangiogenic efficacy of MN9409T-T2132, a novel camptothecin carbothemycyanidogen conjugate 87, 88, 89.

- Inhibiting the anti-β1 integrin antibody on lung seeding of single cells in mice 90, 91, 92.

- Efficacy of the Chinese traditional medicinal herb Celastus orbiculatus Thumb on human hepatocellular carcinoma in an orthotopic fluorescent nude mouse model 93, 94 showing minimal or no effect on primary tumor.

- Real-time imaging of induction of metastasis of human breast cancer cells by the traditional Chinese medicine hellebore Tuberbus 95, 96, 97.

**Feasibility of the Drug Discovery in the SOI Models**

- Metastatic renal cell carcinoma xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic prostate cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic breast cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic colon cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic pancreatic cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic stomach cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic bladder cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic lung cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic glioblastoma xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic breast cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic colon cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic pancreatic cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic stomach cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic bladder cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic lung cancer xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
- Metastatic glioblastoma xenografts: Tumor xenografts demonstrating metastases to multiple organ and sites.
Featured Imaging

**Tumor Growth**
- Whole-body imaging of GFP-expressing liver metastases.
- Whole-body imaging of GFP-expressing skull and liver metastases.
- Whole-body imaging of orthotopically-growing RFP-expressing human glioma.

**Metastasis**
- Whole-body imaging of highly disseminated GFP-expressing lymphoma.
- Fluorescence imaging of GFP-expressing tumor metastases in the mouse skeletal system.
- Fluorescence imaging of GFP-expressing mouse melanoma bone metastasis.
- Dual-color imaging of fibrosarcoma lung metastases.

**Anticancer Drug Efficacy**
- **REAL-TIME WHOLE-BODY IMAGING OF DRUG RESPONSE ON GFP-EXPRESSING HUMAN METASTATIC TUMORS GROWING ORTHOTOPICALLY IN MICE**

**Angiogenesis**
- Angiogenesis in GFP-expressing tumors in AngioMouse®
- Dual-color imaging of tumor angiogenesis in AngioMouse®

**Gene Expression**
- Whole-body imaging of GFP gene expression in the liver.
- Whole-body imaging of GFP gene expression in the brain.
- Whole-body imaging of GFP gene expression in the liver.

**Bacterial Infection**
- Whole-body real-time imaging of GFP bacterial infection.

Quantitative Whole-Body Real-Time Imaging Technologies For Drug Discovery and Evaluation*

More than 100 GFP, RFP or dual-color expressing tumor cell lines for MetaMouse®, AngioMouse®, and SromaMouse®.

All types of agents: small molecules, proteins, genes can be evaluated in MetaMouse®, AngioMouse®, and SromaMouse®:

- Dual color models for imaging cancer and stromal cells.
- Quantitative high-throughput drug screening and evaluation in vivo. The Olympus OV100, Indec FluorVivo and UVP iBox small animal imaging systems were developed in partnership with AntiCancer Inc.

Orthotopic metastatic MetaMouse®–AngioMouse®–SromaMouse® models: cell lines and patient tumors of all types. Colored nude mice are available. Customized contract research for all types of drug discovery and evaluation.

Key publications and patents

GFP patents: US 6,232,523; 6,235,967; 6,251,384; 6,649,159; 6,905,831; Japanese patents 3,709,343 and 4,021,197; European patents 979,298 and 1,156,833; Australian patents 749,338 and 2001249297.

MetaMouse® patents: US 5,491,284 and 5,569,812; European patent 437,488; Japanese patent 2,664,261.


