

NOVEL DRUG DEVELOPMENT AT ANTICANCER IN SOI (MetaMouse ®) MODELS

1. The metalloproteinase inhibitor Batimastat: Active against a SOI human-patient colon tumor model ¹ including:
 - a. Inhibition of primary tumor growth
 - b. Inhibition of metastatic events
 - c. Extension of survival.
2. The metalloproteinase inhibitor CT1746: Active against a SOI human colon tumor xenograft model ² :
 - a. Arrest of primary tumor growth
 - b. Inhibition of metastatic events, and
 - c. A large increase in survival.
3. IFN- γ : Active against a patient pleural cancer SOI model ³:
 - a. Elimination of metastatic events
 - b. Decrease in cachexia, and
 - c. Extension of survival.
4. Angiogenesis inhibitor TNP-470: Active in patient colon and stomach tumor SOI models ⁴⁻⁸:
 - a. Inhibition of liver metastasis in colon cancer
 - b. Minimal or no effect on primary tumor.
5. Anti-VEGF antibody: Active in SOI model of colon and stomach cancer ^{7, 9, 10}:
 - a. Inhibition of liver metastasis in colon cancer
 - b. Minimal or no effect on primary tumor.
6. Antisense phosphorothionate oligonucleotide specific for VEGF-receptor active in SOI model of stomach cancer ¹¹:
 - a. Inhibition of peritoneal tumor dissemination
 - b. Increased tumor cell apoptosis
 - c. Microvessel density (MVD) in tumor nodules.
7. New platinum analogs {Pt(cis-dach)(DPPE)-2NO₃} and {Pt(trans-dach)(DPPE)-2NO₃} active in SOI model of bladder and stomach cancer ^{12, 13}:
 - a. No metastases in either of the high- or low-dose platinum-analog-treated groups in SOI model of bladder cancer.
 - b. No mesenteric lymph node metastases in the groups treated with the high or low doses of both new platinum analogs with SOI model of colon cancer.
8. Liposomal doxorubicin (Doxil) ¹⁴.
 - a. Inhibition of MDA-MB-231 human breast tumor xenografts, which were resistant to free doxorubicin.
9. Camptothecin analog DX-8951f: Active in SOI models of pancreatic cancer ¹⁵.
 - a. DX-8951f showed efficacy against two human pancreatic tumor cell lines in the SOI-GFP model. DX-8951f 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.
10. Cytosine analog, CS-682: Active in SOI model of pancreatic cancer ^{16,17,34}.
 - a. CS-682 showed efficacy on inhibiting pancreatic cancer growth and metastasis in a RFP orthotopic nude mouse model of human pancreatic model.
 - b. CS-682 showed efficacy in an adjuvant treatment orthotopic model of human pancreatic cancer suggesting possibility of chronic use of CS-682 to control pancreatic cancer.
11. Estrogen analog 2-methoxyoestradiol-bis-sulphamate: active in MDA-MB-435 SOI model of breast cancer ¹⁸.
12. Truncated galectin-3 (galectin-3C) was found active in an orthotopic breast cancer xenograft nude mouse model imaged with green fluorescent protein ¹⁹.

13. The agonistic anti-LTBR monoclonal antibody (mAb) CBE11 inhibited tumor growth in xenograft models and potentiated tumor responses to chemotherapeutic agents³⁵.
14. Additive effects of glufosfamide and gemcitabine in fluorescent orthotopic mouse models of human pancreatic cancer^{36,37}.
15. A monoclonal antibody to the chemokine receptor CXCR2 was effective against pancreatic cancer in the SOI model³⁸.
16. TSU68 prevents liver metastasis of colon cancer xenografts by modulating the premetastatic niche³⁹.
17. Type II PDGFR β /B-RAF inhibitor disrupts angiogenesis and tumor growth⁴⁰.
18. A small molecule inhibitor of SDF-1/CXCR4 inhibits vasculogenesis, but not angiogenesis, and prevents the recurrence of glioblastoma following irradiation in mice⁴¹.
19. HER-2 therapy inhibits metastasis of esophageal cancer⁴².
20. Metronomic gemcitabine therapy greatly inhibits metastasis of pancreatic cancer⁴³.
21. Bisphosphonate olpadronate inhibits bone metastasis in prostate cancer⁴⁴.
22. Knockdown of the β_1 integrin subunit reduces primary tumor growth and inhibits pancreatic cancer metastasis⁴⁵.
23. High antimetastatic efficacy of MEN4901/T-0128, a novel camptothecin carboxymethyl-dextran conjugate⁴⁶.
24. Imaging the inhibition by anti- β_1 integrin antibody on lung seeding of single cells in live mice⁴⁷.
25. Traditional Medicinal Herb *Celastrus orbiculatus* Thunb on human hepatocellular carcinoma in an orthotopic fluorescent nude mouse model⁴⁸.
26. Real-time imaging of induction of apoptosis of human breast cancer cells by the traditional Chinese medicine herb *Tubeimu*⁴⁹.
27. Paclitaxel nanosuspensions for targeted chemotherapy – nanosuspension preparation, characterization, and use⁵⁰.
28. Therapeutic effect of 1 M tegafur-0.4 M 5-chloro-2,4-dihydropyridine-1 M potassium oxonate (S-1) on liver metastasis of xenotransplanted human colon carcinoma.³²
29. Efficacy comparison of traditional Chinese medicine LQ versus gemcitabine in a mouse model of pancreatic cancer.⁵³
30. Comparison of efficacy and toxicity of Traditional Chinese Medicine (TCM) herbal mixture LQ and conventional chemotherapy on lung cancer metastasis and survival in mouse models.⁵⁴
31. Traditional Chinese medicine herbal mixture LQ arrests Fucci-expressing HeLa cells in G0/G1 phase in 2D plastic, 2.5D Matrigel®, and 3D Gelfoam® culture visualized with Fucci imaging.⁵⁵
32. Photoimmunotherapy lowers recurrence after pancreatic cancer surgery.⁵⁸
33. Nanoparticle albumin-bound-paclitaxel: a limited improvement under the current therapeutic paradigm of pancreatic cancer.⁵⁹

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-response, differential sensitivity of primary and metastatic tumors, reproducibility, and correlation to historical clinical activity of the drugs including 5-FU, CDDP, mitomycin-C as well as the new agents listed above ^{1, 4-8, 11-13, 20-33,51,52,56,57}.

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