Breast Cancer Xenograft Models:

Subcutaneous, Orthotopic, And Metastatic Xenograft Tumor Models

By Altogen Labs, 11200 Menchaca Road, Suite 203, Austin, TX 78748
Phone: (512) 433-6177 | Email: info@altogenlabs.com

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Introduction

Characterization and Preclinical Application of Xenograft and Allograft Models in Breast Cancer Research

Bridging Tumor Complexity and Therapeutic Discovery with Xenograft Models

Breast cancer is a biologically diverse and clinically complex disease that continues to present major challenges in oncology, particularly in the context of therapeutic resistance and the management of aggressive subtypes. *In vivo* models play a critical role in bridging the gap between *in vitro* experimentation and clinical application by enabling the study of tumor progression, drug response, and resistance mechanisms within a physiological environment. Xenograft and allograft models are among the most widely used in breast cancer research. Xenografts involve the transplantation of human tumor cells or tissues into immunodeficient mice and are further categorized into cell-derived xenografts (CDX), which offer experimental consistency, and patient-derived xenografts (PDX), which maintain the heterogeneity and genetic complexity of primary tumors. Allografts, in contrast, involve the implantation of murine tumor cells into immunocompetent mice of the same genetic background, allowing the preservation of functional immune responses and enabling immuno-oncology studies. Each model system offers distinct advantages and limitations. Xenografts better recapitulate human tumor biology but lack immune interactions, while allografts provide immune-competent contexts but are limited by species-specific tumor characteristics. The integration of both model types within breast cancer research enhances the ability to evaluate therapeutic efficacy, investigate resistance pathways, and explore immune dynamics. These models collectively contribute to the advancement of precision medicine by supporting the development of more effective and biologically informed treatment strategies.

Subcutaneous Breast Cancer Xenograft Model

Subcutaneous xenograft transplantation remains a foundational technique in preclinical breast cancer research, offering a reproducible and accessible platform for *in vivo* evaluation of tumor growth kinetics, drug efficacy, and resistance mechanisms. This approach involves the injection of human or murine cancer cells into the subcutaneous tissue, typically in the flank region of immunodeficient mice, where tumor formation and progression can be readily monitored through caliper measurements or imaging modalities. The simplicity of the procedure, combined with its capacity to support high-throughput therapeutic screening, has contributed to its widespread adoption across a broad range of breast cancer cell lines representing diverse molecular subtypes.

Luminal A and B phenotypes are commonly modeled using cell lines such as MCF7, T47D, ZR75, and BT474, which are estrogen receptor positive and generally exhibit slower tumor growth *in vivo*. These models have been instrumental in elucidating hormone responsiveness and resistance pathways. HER2-positive tumors are effectively represented by BT474, SK-BR-3, JIMT-1, and HCC1954 xenografts, which are frequently utilized in studies investigating HER2-targeted therapies and associated resistance mechanisms. Basal-like and triple-negative breast cancer (TNBC) subtypes, characterized by their aggressive behavior and poor clinical prognosis, are modeled through subcutaneous implantation of cell lines including MDA-MB-231, MDA-MB-468, MDA-MB-157, HCC1806, Hs578T, CAL51, MX1, and SUM185PE. These models have proven particularly valuable in exploring the molecular underpinnings of metastasis and identifying therapeutic vulnerabilities. Notably, the murine 4T1 and EMT6 cell lines, although not of human origin, are widely employed in syngeneic subcutaneous models to investigate immune modulation and immunotherapy efficacy due to their compatibility with immunocompetent hosts.

Recent research underscores the importance of tumor microenvironmental context in modulating therapeutic response, and while subcutaneous models may lack the orthotopic tissue-specific architecture, they remain indispensable for initial *in vivo* drug assessment and mechanistic studies. Variations in tumor take rate, vascularization, and stromal interaction across different cell lines highlight the necessity of selecting models aligned with the biological question under investigation. For instance, MDA-MB-231 and HCC1806 generate rapidly growing tumors with invasive properties, whereas MCF7 and T47D often require exogenous estrogen supplementation and exhibit slower progression. Subcutaneous transplantation also facilitates longitudinal sampling, enabling molecular analyses of treatment-induced changes in tumor composition. As such, it continues to serve as a critical experimental system in the development and refinement of therapeutic strategies in breast cancer research, particularly when used in conjunction with complementary models that capture immune or metastatic dynamics.

Orthotopic Breast Cancer Xenograft Model

Orthotopic xenograft transplantation has emerged as a critical methodology in breast cancer research, offering enhanced biological relevance over subcutaneous models by enabling tumor growth within the native anatomical context of the mammary fat pad. This approach preserves organ-specific microenvironmental cues, including extracellular matrix composition, local vascularization, and stromal and immune cell interactions, which are essential for accurately modeling tumor behavior, metastatic dissemination, and therapeutic response. Orthotopic models have shown superior predictive value for clinical outcomes and are increasingly utilized to study the dynamic interplay between tumor cells and their host milieu.

A broad spectrum of breast cancer cell lines has been adapted for orthotopic transplantation, reflecting the heterogeneity of the disease. Luminal subtypes, including MCF7, T47D, ZR75, and BT474, have been employed to study hormone receptor signaling and endocrine resistance, although some of these lines require estrogen supplementation to support *in vivo* tumorigenesis. HER2-positive models such as SK-BR-3, JIMT-1, HCC1954, and KPL-4 have facilitated investigations into HER2-targeted therapies and mechanisms of resistance. Orthotopic implantation of triple-negative breast cancer (TNBC) cell lines, including MDA-MB-231, MDA-MB-468, HCC1806, CAL51, SUM185PE, Hs578T, and MDA-MB-453, has provided valuable insights into tumor invasion, angiogenesis, and the early steps of metastasis, particularly to the lungs, brain, and lymph nodes. These models recapitulate the aggressive phenotypes observed in TNBC patients and are widely used to evaluate novel therapeutic agents, including immunotherapies and small-molecule inhibitors. The murine 4T1 line, when orthotopically transplanted into immunocompetent mice, closely mirrors the complete metastatic cascade and is considered a gold standard for studying immune modulation and metastatic progression in a syngeneic setting.

Contemporary studies have demonstrated that orthotopic models yield higher fidelity in replicating the tumor microenvironment, including paracrine signaling networks and hypoxic gradients, which are critical determinants of treatment outcome. Additionally, these models support the evaluation of drug distribution and pharmacodynamics within anatomically relevant tissues, which is essential for translating preclinical findings to the clinic. While technically more demanding than subcutaneous transplantation, the increased physiological relevance of orthotopic xenografts justifies their use in studies requiring nuanced assessment of tumor biology and therapeutic efficacy. The integration of orthotopic models with molecular imaging, lineage tracing, and transcriptomic profiling continues to refine their utility, advancing our understanding of breast cancer pathophysiology and informing the development of targeted treatment strategies.

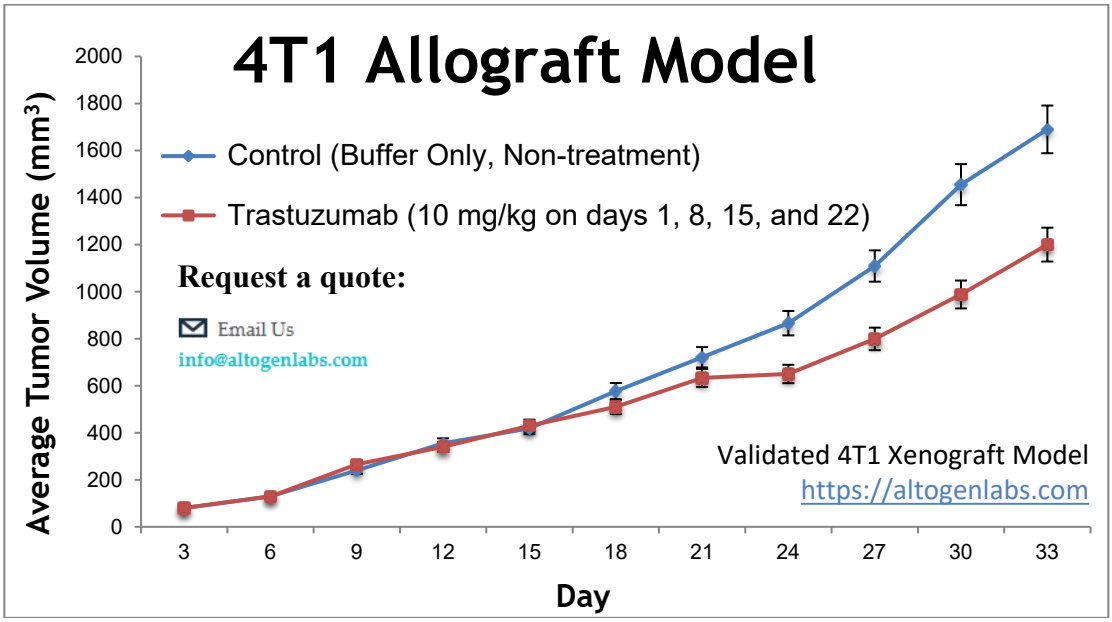
Metastatic Breast Cancer Xenograft Model

Metastatic xenograft and allograft transplantation models are essential for studying the processes driving tumor dissemination and colonization at distant sites, which represent the most lethal phase of breast cancer progression. These models simulate key stages of metastasis, including intravasation, circulation, and secondary organ colonization, thereby offering critical insights into disease biology and therapeutic resistance. Subtypes of breast cancer exhibit distinct metastatic behaviors that are recapitulated through the use of diverse cell lines and implantation methods, such as orthotopic, intravenous, intracardiac, and intraosseous injections.

MDA-MB-231 remains the most extensively characterized model due to its high metastatic efficiency to lung, bone, liver, and brain. Other triple-negative lines, including HCC1806, MDA-MB-453, and MX1, have demonstrated metastatic potential with varying patterns, while HER2-positive lines such as HCC1954 and JIMT-1 are frequently used to investigate resistance to HER2-targeted agents in metastatic contexts. BT474 and ZR75, representing luminal phenotypes, show more limited dissemination but contribute to studies of endocrine therapy resistance and bone metastasis. EMT6 and 4T1, both murine allograft models, are particularly valuable in immunocompetent settings; 4T1 is widely recognized for its ability to spontaneously metastasize from the mammary fat pad to distant organs, mimicking human disease progression.

Recent developments in site-specific metastatic models, such as intracranial and intra-tibial injections, have refined our understanding of organotropism and the tumor microenvironment. Techniques like bioluminescence imaging and molecular tagging now allow real-time monitoring of metastatic spread. Although technically demanding, metastatic transplantation models remain indispensable for evaluating anti-metastatic agents, characterizing mechanisms of resistance, and translating preclinical findings into therapeutic strategies that address advanced-stage breast cancer.

Characterization and Preclinical Application of the 4T1 Allograft Model in Breast Cancer Research



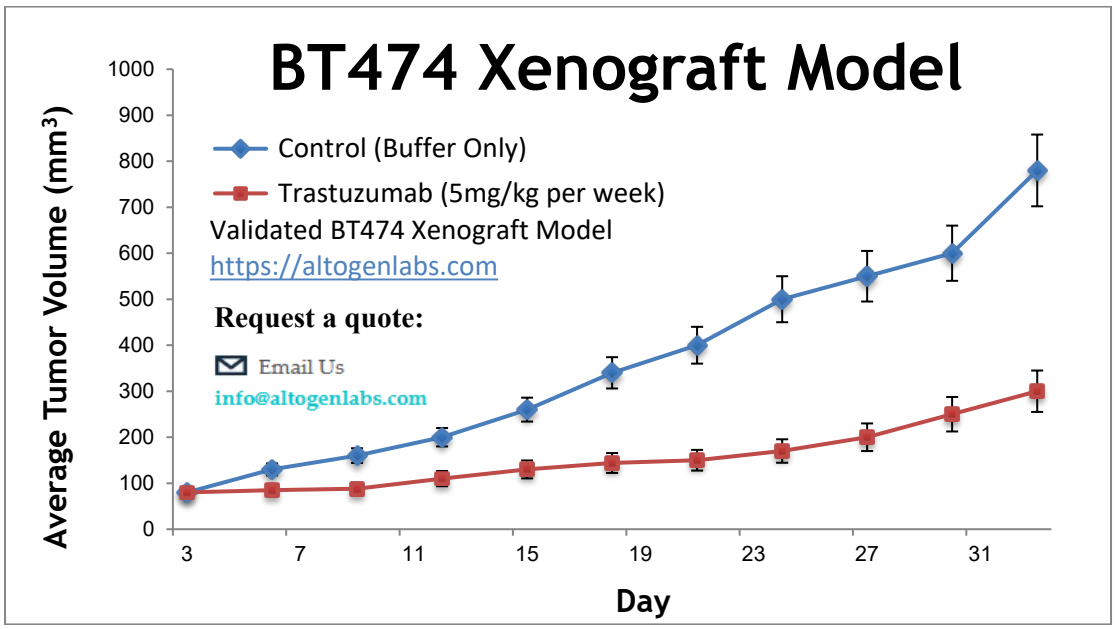
The 4T1 allograft model is a widely utilized murine system for preclinical investigation of metastatic breast cancer, particularly triple negative subtypes. Derived from a spontaneously arising mammary tumor in BALB/c mice, 4T1 cells exhibit aggressive tumor growth, immune evasion, and spontaneous metastasis to the lungs, liver, lymph nodes, and bone marrow. This model closely recapitulates stage IV human breast cancer in terms of progression and metastatic behavior. The 4T1 model is syngeneic, allowing for studies in immunocompetent mice and enabling the evaluation of immunotherapies in a fully functional host immune system. Its reproducibility, metastatic potential, and compatibility with a range of therapeutic approaches make it a cornerstone in translational cancer research.

Altogen Labs has validated subcutaneous, orthotopic, and metastatic 4T1 allograft models. In the subcutaneous model, tumor cells are injected into the hind flank, allowing for non-invasive monitoring of tumor growth. The orthotopic model, involving injection into the mammary fat pad, more accurately mimics the tumor microenvironment and supports spontaneous metastasis. The metastatic model is used to evaluate colonization and dissemination to secondary sites, enabling detailed investigation of metastatic mechanisms and therapeutic strategies targeting tumor spread. All studies follow rigorous protocols for cell preparation, tumor implantation, measurement, treatment administration, and endpoint tissue collection under IACUC-approved procedures.

Recent studies using the 4T1 model have advanced the understanding of tumor-immune dynamics and therapeutic resistance. A hydrogel-based platform, PEIGel, incorporating polyethylenimine and anti-PD-L1 antibodies, demonstrated enhanced immune activation and checkpoint blockade efficacy in 4T1 tumors. Additionally, obesity was shown to exacerbate metastatic spread and immune suppression in this model, providing insights into the interplay between metabolic dysfunction and tumor progression. A separate investigation combined an oncolytic Orf virus with a PAK4 inhibitor, resulting in G2/M arrest, apoptosis, and immune modulation *in vivo*, underscoring the utility of the 4T1 system for evaluating innovative therapeutic combinations.

The oncogenic landscape of 4T1 tumors includes mutations in Trp53 and Pik3g and elevated expression of markers associated with proliferation, metastasis, and immune escape. The presence of murine mammary tumor virus elements and high expression of gastrointestinal antigens such as Gpa33 and Epcam contribute to its aggressive phenotype. This molecular complexity, combined with its metastatic behavior and syngeneic compatibility, makes the 4T1 model highly suitable for evaluating immunotherapies, targeted treatments, and combination regimens.

Learn more about this model on the Altogen Labs website at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/4t1-xenograft-model/. The complete technical PDF describing the 4T1 model is available at https://altogenlabs.com/4T1XenograftModel.pdf.



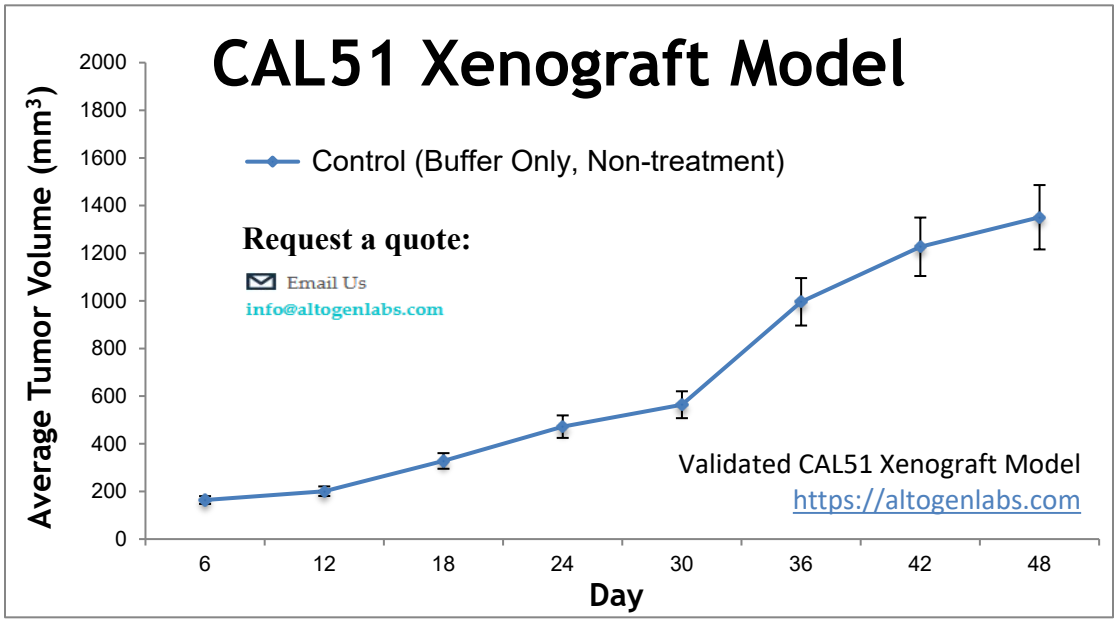
The BT474 xenograft model is a validated preclinical system for studying HER2-positive and hormone receptor-positive breast cancer, offering a clinically relevant platform for investigating tumor growth, drug response, and metastatic progression. Derived from an invasive ductal carcinoma, the BT474 cell line co-expresses HER2, estrogen receptor (ER), and progesterone receptor (PR), making it a critical model for evaluating targeted therapies such as trastuzumab and endocrine treatments. When implanted in immunocompromised mice, BT474 cells form tumors that retain key molecular features of human breast cancer, enabling the analysis of therapeutic efficacy and resistance mechanisms *in vivo*.

Altogen Labs has developed subcutaneous, orthotopic, and metastatic BT474 xenograft models for translational oncology research. In the subcutaneous model, BT474 cells are injected into the flank of immunodeficient mice, facilitating straightforward measurement of tumor growth using calipers. The orthotopic model involves injection into the mammary fat pad, offering a more physiologically relevant environment that mirrors human tumor-stroma interactions and metastatic behavior. For metastasis studies, BT474 cells can also be introduced intravenously to simulate hematogenous dissemination, allowing evaluation of drug efficacy in controlling secondary tumor formation in organs such as the lungs and liver.

The BT474 model has been pivotal in assessing HER2-targeted therapies. Notably, a Fleximer-based antibody-drug conjugate demonstrated enhanced tumor regression and antigen-specific targeting, while maintaining pharmacokinetic stability. Another study utilizing IBL-302, a dual PIM and PI3K/mTOR inhibitor, showed marked tumor suppression in both trastuzumab-sensitive and -resistant BT474 xenografts. These findings underscore the utility of BT474 models for evaluating both monotherapies and combination strategies aimed at overcoming resistance. Additionally, BT474 tumors exhibit characteristic mutations such as PIK3CA and high expression of proliferative markers, and are capable of forming lymphatic and pulmonary micrometastases, further validating their translational relevance.

Altogen Labs offers comprehensive services around BT474 xenograft models, including customizable dosing schedules, multiple administration routes, advanced imaging for tumor tracking, and detailed molecular analyses. Services encompass tumor growth delay, inhibition studies, histopathology, gene and protein expression profiling, and toxicological evaluations. Researchers can select from various endpoints and injection methods to align with specific study goals. Information about this model is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/bt474-xenograft-model/. The complete technical PDF describing the BT474 model is available at https://altogenlabs.com/BT474XenograftModel.pdf.

Characterization and Preclinical Application of the CAL51 Xenograft Model in Breast Cancer Research



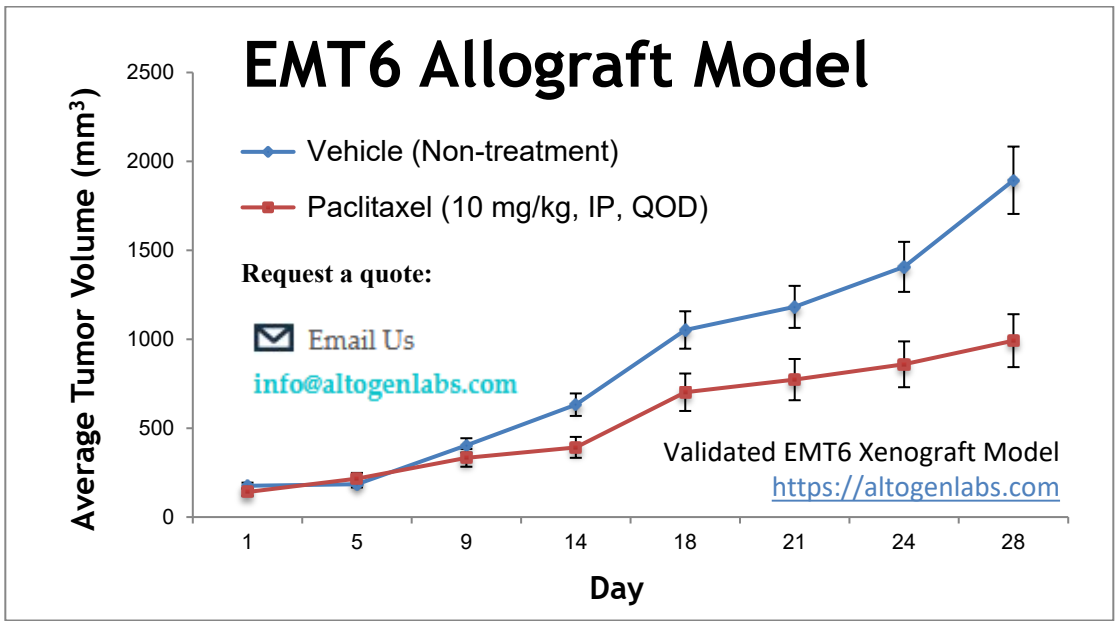
The CAL51 xenograft model is a preclinical *in vivo* platform developed to investigate triple negative breast cancer (TNBC), a clinically aggressive and treatment-resistant subtype of breast malignancies. CAL51 cells, originally derived from a malignant pleural effusion, lack expression of estrogen receptor (ER), progesterone receptor (PR), and HER2, and exhibit features of the basal-like molecular subtype. Unique among TNBC models, CAL51 possesses a stable diploid karyotype, enabling investigation into tumorigenic mechanisms driven by subtle genetic or epigenetic alterations rather than large-scale chromosomal instability. Despite this stability, the cell line demonstrates robust tumorigenicity, rapid proliferation, invasiveness, and resistance to conventional therapies, making it particularly valuable for evaluating mechanisms of therapeutic failure and metastatic progression.

Altogen Labs has developed and validated both subcutaneous and orthotopic xenograft models using CAL51 cells. In the subcutaneous model, cells are injected into the right flank of immunocompromised mice, allowing for consistent tumor volume monitoring and drug efficacy assessment. The orthotopic model involves injection into the mammary fat pad, more closely replicating the tumor's natural microenvironment and supporting studies of local invasion, microenvironmental interactions, and distant metastasis. These models have been widely applied in preclinical studies of chemotherapy, molecularly targeted agents, and immunotherapeutic strategies.

Studies utilizing CAL51 xenografts have provided key insights into resistance pathways and combination therapy development. Inhibition of Aurora kinase A (AurA) with alisertib was shown to induce apoptosis in CAL51 tumors, contingent on the presence of functional p53 and p73. In the absence of these tumor suppressors, cells shifted toward a senescent phenotype, revealing a mechanism of resistance to AurA inhibition. Additional studies demonstrated the efficacy of a novel antibody-drug conjugate consisting of cetuximab linked to a CDK inhibitor. This targeted approach, exploiting EGFR overexpression and cell cycle dysregulation in CAL51, achieved selective cytotoxicity and bystander effects against EGFR-low tumor cells, offering a potential solution to tumor heterogeneity and treatment resistance.

Altogen Labs, a contract research organization based in Austin, Texas, offers CAL51 as part of its comprehensive *in vivo* oncology research services. Learn more about this model on the Altogen Labs website at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/cal-51-xenograft-model/. The complete technical PDF describing the CAL51 model is available at https://altogenlabs.com/CAL51XenograftModel.pdf.

Characterization and Preclinical Application of the EMT6 Allograft Model in Breast Cancer Research



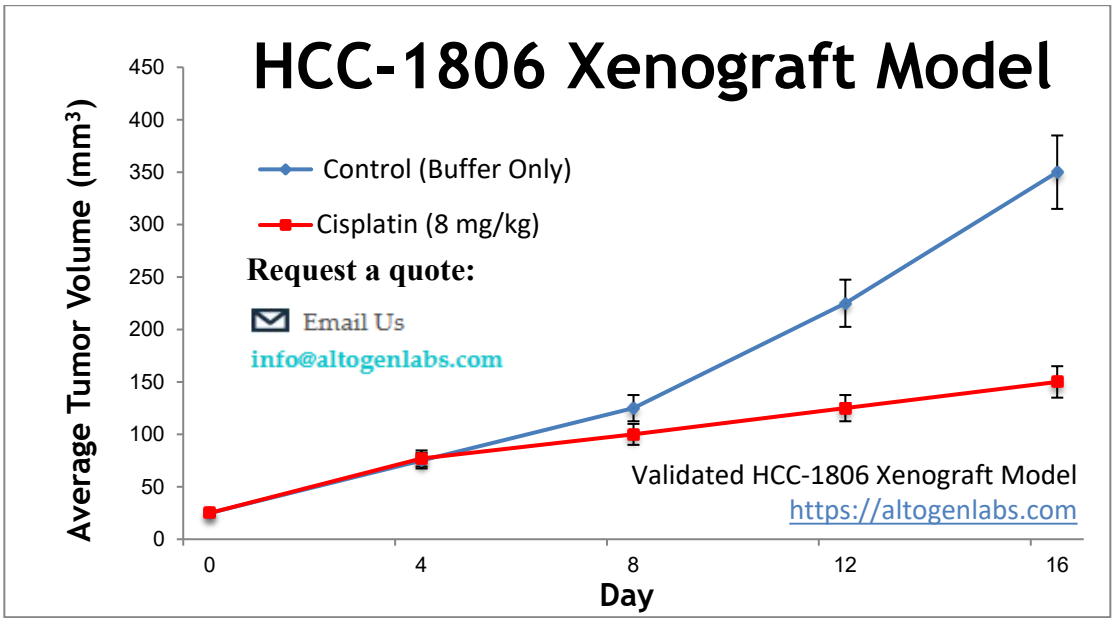
The EMT6 allograft model is a robust and widely used syngeneic mouse model for studying breast cancer in immunocompetent hosts. Derived from a spontaneous murine mammary carcinoma in BALB/c mice, EMT6 cells exhibit aggressive tumor growth, spontaneous metastasis, and the ability to generate immunologically active tumors. These features make EMT6 an ideal system for evaluating immunotherapies, investigating tumor microenvironment dynamics, and assessing combination strategies involving chemotherapy, radiation, or immune modulation.

Altogen Labs has validated subcutaneous and metastatic EMT6 tumor models for preclinical research. In the subcutaneous model, EMT6 cells are injected into the mammary fat pad or flank of BALB/c mice. Tumor growth is monitored using calipers, and once tumors reach a measurable size, animals may undergo surgical resection followed by treatment allocation. Post-treatment evaluations include histological analysis, digital imaging, and downstream molecular assessments such as RNA, protein, or tissue profiling. The metastatic model enables spontaneous or experimental metastasis to the lungs and liver, supporting studies on tumor dissemination and therapeutic response to systemic disease.

Several studies have demonstrated the utility of EMT6 models in advancing immunotherapy research. For instance, combining oncolytic reovirus with PD-1 blockade enhanced anti-tumor immunity, increased CD8+ T cell infiltration, and prolonged survival. In another study, overexpression of chemerin led to enhanced recruitment of natural killer and cytotoxic T cells, suppressing tumor growth through immune activation. Moreover, EMT6 tumors are responsive to conventional agents such as paclitaxel, and studies have revealed that tumor progression can be accelerated by hyperglycemia, mediated by miR-467-driven suppression of thrombospondin-1 and increased tumor-associated macrophages. These findings support the model's relevance for investigating metabolic influences on cancer progression.
The EMT6 system supports flexible inoculation methods, including modified subcutaneous injection into the fourth mammary fat pad for consistent tumor formation. It is also compatible with advanced imaging and molecular analyses. Researchers can assess therapeutic efficacy through endpoints such as tumor growth delay and inhibition, while monitoring immune infiltration, cytokine profiles, and resistance mechanisms. Because EMT6 cells are syngeneic to BALB/c mice, the model enables exploration of immune checkpoint inhibitors, cytokine modulation, and combination regimens in a physiologically relevant immune context.

More information about the EMT6 allograft model can be found at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/emt6-allograft-model/. The complete technical PDF describing the EMT6 model is available at https://altogenlabs.com/EMT6AllograftModel.pdf.

Characterization and Preclinical Application of the HCC1806 Xenograft Model in Breast Cancer Research



The HCC1806 xenograft model is a validated preclinical platform used to study triple-negative breast cancer (TNBC), particularly basal-like subtypes characterized by high aggressiveness and lack of targeted therapies. Derived from a mammary gland tumor of a 60-year-old Black female patient diagnosed with acantholytic squamous cell carcinoma, HCC1806 cells exhibit rapid tumorigenicity, epithelial marker expression, and invasive potential. These attributes make HCC1806 a representative model for evaluating tumor progression, therapeutic resistance, and the efficacy of anti-cancer compounds targeting molecular drivers of TNBC.

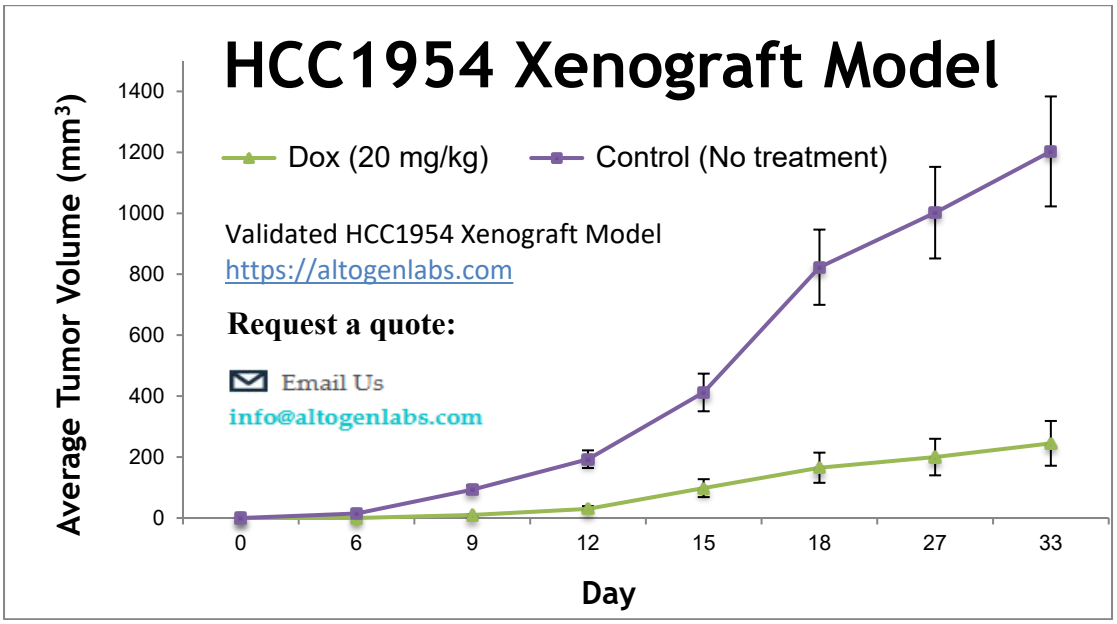
Altogen Labs offers a comprehensive HCC1806 xenograft model system, including both subcutaneous and metastatic tumor models. In the subcutaneous model, one million HCC1806 cells suspended in Matrigel are injected into the flank of immunocompromised mice. Tumor development is monitored using calipers, and treatment begins when tumors reach 75 to 125 mm³. At study endpoints, tumors are excised and evaluated via histology, protein and RNA analyses, or imaging. The metastatic model is established through orthotopic implantation into the mammary fat pad, enabling spontaneous dissemination to organs such as the lungs and lymph nodes. These models facilitate in-depth investigation of metastatic progression, drug resistance, and gene expression changes associated with disseminated disease.

Recent studies using the HCC1806 model have elucidated key oncogenic mechanisms and evaluated promising therapeutic strategies. Gallic acid induced apoptosis by modulating PI3K/AKT/EGFR and MAPK signaling pathways, leading to mitochondrial dysfunction and ROS generation. Cold atmospheric plasma therapy triggered nitroxidative stress, cell cycle arrest, and enhanced apoptosis through altered mitochondrial membrane potential. Mithramycin A demonstrated efficacy by downregulating KLF5 transcription, inhibiting DNA synthesis, and suppressing tumor growth both *in vitro* and *in vivo*. A synergistic regimen of FTY720 and gefitinib inhibited HCC1806 tumor proliferation, reduced EGFR activation, and increased apoptosis, particularly in models with high IGFBP-3 expression. Collectively, these findings support HCC1806 as an effective system for testing both monotherapies and combination regimens targeting TNBC.

On a molecular level, HCC1806 is defined by high EGFR expression, TP53 mutation, MMP-driven extracellular matrix degradation, and dysregulation of EMT pathways. Epigenetic alterations, such as EZH2 overexpression, and suppression of tumor-suppressive miRNAs further contribute to its malignancy. These features align with the biology of aggressive basal-like TNBC and allow the model to become reliable for investigating mechanisms of tumor growth, metastasis, and therapy resistance.

Learn more about this model on the Altogen Labs website at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/hcc-1806-xenograft-model/. The complete technical PDF describing the HCC1806 model is available at https://altogenlabs.com/HCC1806XenograftModel.pdf.

Characterization and Preclinical Application of the HCC1954 Xenograft Model in Breast Cancer Research



The HCC1954 xenograft model is a validated preclinical system for investigating HER2-positive breast cancer, particularly in the context of drug resistance and tumor heterogeneity. Derived from a stage IIA, grade 3 invasive ductal carcinoma of a 61-year-old Asian female, the HCC1954 cell line exhibits HER2 overexpression, TP53 and PIK3CA mutations, and anchorage-independent growth. These features support its utility in modeling aggressive tumor phenotypes and evaluating the efficacy of novel therapeutic strategies, especially for HER2-targeted interventions.

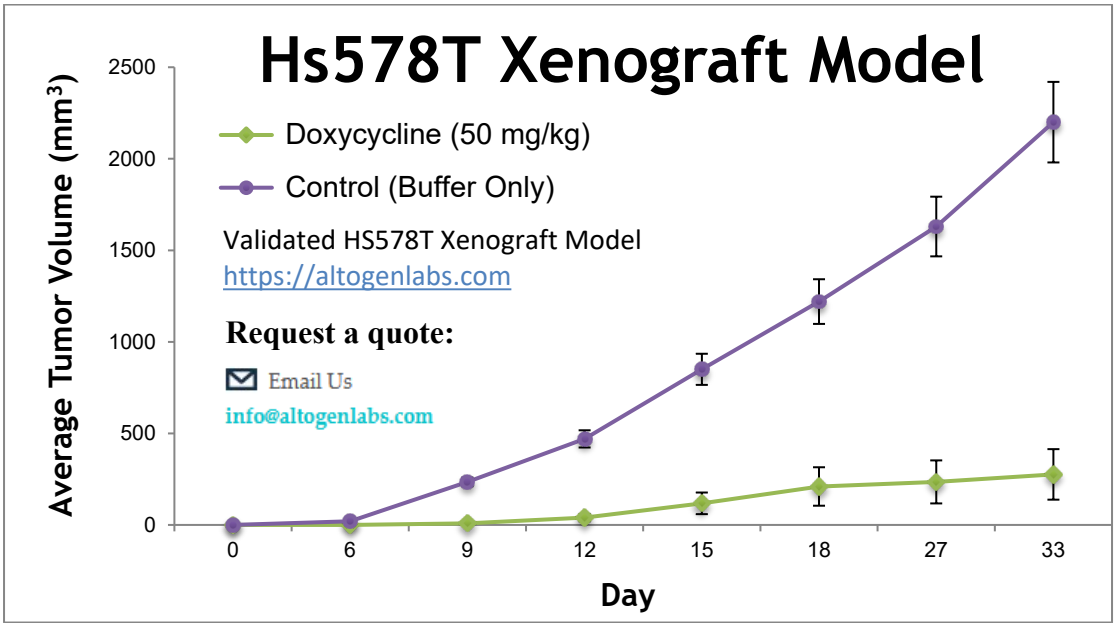
Altogen Labs offers validated subcutaneous, orthotopic, and metastatic HCC1954 xenograft models to support comprehensive preclinical drug development. In the subcutaneous model, highly viable HCC1954 cells are injected into the flank of immunodeficient mice, where tumor growth is measured using calipers and monitored until endpoint criteria are met. Orthotopic implantation into the mammary fat pad enables tumor development within the native microenvironment, while the metastatic model allows the study of spontaneous dissemination, particularly to the brain. Tissue collection, histology, RNA and protein analyses, and tumor imaging are all incorporated into these study designs, conducted under GLP and IACUC-compliant conditions.

The HCC1954 model has proven valuable for testing therapeutic combinations to overcome trastuzumab resistance. Studies have shown that agents such as tucatinib enhance radiosensitivity, and that co-treatment with PI3K inhibitors may improve responses in PIK3CA-mutant contexts. Lovastatin has also been demonstrated to sensitize HCC1954 tumors to lapatinib by disrupting ErbB2 membrane localization. Other strategies include using anti-HER2 CAR-T cells in combination with PD1 blockade, which significantly reduces tumor growth and enhances T cell activity. Additionally, FISH and spectral karyotyping have revealed extensive chromosomal rearrangements, including disruptions in MRE11A and NSD1, further supporting its role as a model of high genomic instability.

HCC1954 xenografts also offer insight into tumor microenvironment interactions and immune modulation. NK cell depletion has been shown to promote metastatic outgrowth, while β1 integrin and CD166 contribute to invasiveness and therapeutic resistance. The expression of E-cadherin suggests a hybrid epithelial–mesenchymal state that supports both adhesion and motility. These features make the model particularly relevant for exploring mechanisms of immune escape and metastasis in HER2-amplified tumors.

For more information, the HCC1954 model page is accessible at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/hcc1954-xenograft-model/. The complete technical PDF describing the HCC1954 model is available at https://altogenlabs.com/HCC1954XenograftModel.pdf.

Characterization and Preclinical Application of the HS578T Xenograft Model in Breast Cancer Research



The HS578T xenograft model is a validated and widely employed preclinical platform for investigating triple-negative breast cancer (TNBC), a highly aggressive subtype characterized by the absence of estrogen receptor, progesterone receptor, and HER2 amplification. Derived from the pleural effusion of a 44-year-old woman with metastatic breast cancer, HS578T cells exhibit high invasiveness, rapid proliferation, and metastatic capability. These properties make the model ideal for evaluating drug resistance mechanisms, identifying therapeutic targets, and studying metastasis in TNBC.

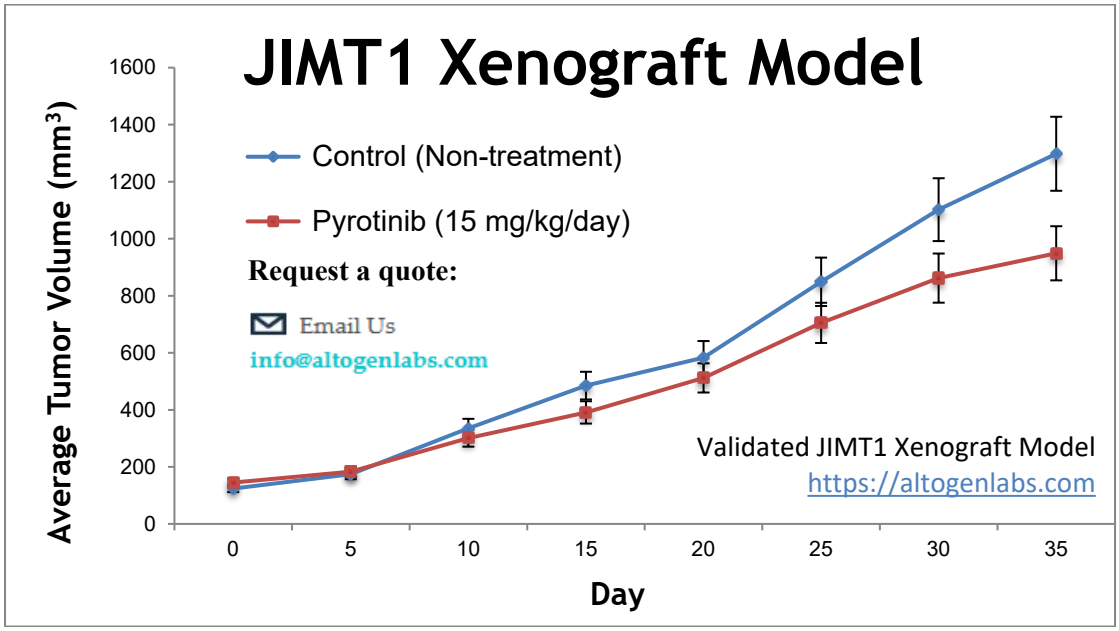
Altogen Labs offers both subcutaneous and orthotopic HS578T xenograft models. In the subcutaneous model, one million viable cells suspended in Matrigel are injected into the rear flank of immunodeficient mice, where tumor volume is tracked using calipers. This method provides a highly reproducible and straightforward system for assessing tumor growth inhibition and therapeutic efficacy. The orthotopic model, which involves injection into the mammary fat pad, more closely mimics the native tumor microenvironment and supports investigation of local invasion, distant metastasis, and immune-tumor interactions. Upon reaching endpoint criteria, tumors are excised and processed for histology, nucleic acid isolation, and digital imaging, enabling a wide range of molecular and cellular analyses.

The HS578T model has contributed significantly to the understanding of oncogenic pathways and therapeutic vulnerabilities in TNBC. Overexpression of Nischarin has been shown to suppress epithelial-mesenchymal transition (EMT) by downregulating mesenchymal markers and EMT-associated transcription factors, thereby reducing invasiveness. Other studies have demonstrated that TrkC enhances metastatic potential by stabilizing JAK2 and activating the JAK2/STAT3/Twist1 axis. Additionally, Contactin-1 (CNTN1) was identified as a driver of cell cycle progression, migration, and invasion in this model. From a metabolic perspective, HS578T tumors exhibit elevated PHGDH expression, and loss of Parkin was found to promote tumor growth through dysregulated serine synthesis, revealing a potential metabolic vulnerability.

The model is also well-suited for immuno-oncology applications. Altogen Labs utilizes humanized mice engrafted with CD34+ hematopoietic stem cells to replicate human immune responses, enabling the evaluation of CAR-T cells, checkpoint inhibitors, and other immunotherapies. Tumor monitoring is supported by fluorescence-based imaging, MRI, histopathology, and blood chemistry analysis. Toxicity and survival endpoints can be incorporated to provide comprehensive therapeutic assessment.

Additional information on the HS578T xenograft model is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/hs578t-xenograft-model/. The complete technical PDF describing the HS578T model is available at https://altogenlabs.com/HS578TXenograftModel.pdf.

Characterization and Preclinical Application of the JIMT1 Xenograft Model in Breast Cancer Research



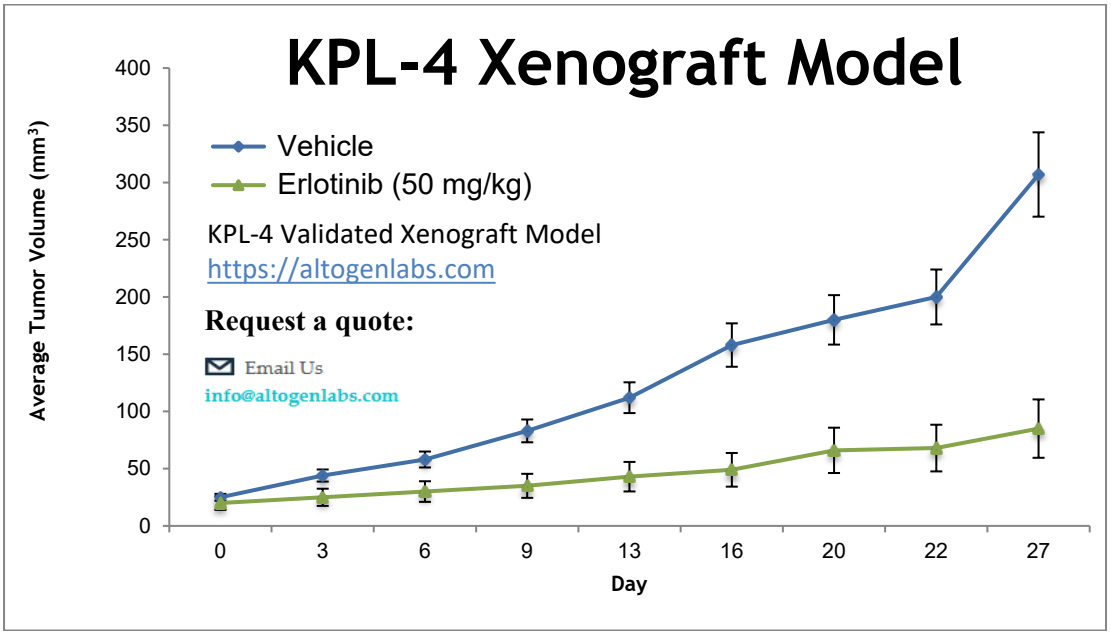
The JIMT1 xenograft model is a preclinical platform specifically designed to investigate HER2-positive breast cancer that is resistant to trastuzumab. Derived from a patient with HER2-amplified ductal carcinoma who exhibited clinical resistance to trastuzumab, the JIMT1 cell line maintains high HER2 expression but is intrinsically resistant to anti-HER2 monoclonal antibody therapies. This resistance is attributed to epitope masking, PIK3CA mutations, and activation of alternate survival pathways. Due to these properties, JIMT1 xenografts provide a clinically relevant model for studying resistance mechanisms, evaluating next-generation HER2-targeted agents, and developing effective combination strategies.

Altogen Labs offers validated subcutaneous, orthotopic, and metastatic JIMT1 xenograft models. In the subcutaneous model, one million JIMT1 cells are injected into the flanks of immunocompromised mice using a Matrigel-cell suspension, and tumor growth is monitored regularly until reaching 75 to 150 mm^3. Animals are then randomized into treatment groups for evaluation of therapeutic efficacy. The orthotopic model involves injection into the mammary fat pad, allowing tumor development in a native microenvironment. This approach enhances interactions with stromal and vascular components and provides insights into local tumor progression and drug responses. The metastatic model, established through intracardiac injection, enables dissemination to distant organs such as the lungs and brain, mimicking hematogenous spread. Tumor burden in metastatic sites can be tracked through bioluminescent imaging, MRI, or histopathology.

JIMT1 xenografts have been instrumental in elucidating mechanisms of trastuzumab resistance and testing novel anti-HER2 agents. Studies have demonstrated that monoclonal antibodies targeting alternative HER2 epitopes, such as Erb-hRNase and Erb-hcAb, suppress tumor growth by inhibiting MAPK and Akt pathways. These agents bypass trastuzumab resistance and show reduced cardiotoxicity. Furthermore, inetetamab, a trastuzumab analog, demonstrated enhanced efficacy when combined with tyrosine kinase inhibitors such as pyrotinib or chemotherapeutic agents like cyclophosphamide. These combinations resulted in superior tumor suppression compared to standard trastuzumab-pertuzumab therapy. *In vivo* data also suggest that trastuzumab, although ineffective directly against JIMT1 cells, may delay tumor progression through antibody-dependent cellular cytotoxicity (ADCC), implicating immune effector mechanisms in therapeutic response.

The JIMT1 model is also compatible with advanced immuno-oncology approaches when paired with humanized mouse models. Learn more about this model on the Altogen Labs website at www.altogenlabs.com.

Characterization and Preclinical Application of the KPL-4 Xenograft Model in Breast Cancer Research



The KPL-4 xenograft model is an established preclinical system for studying HER2-positive breast cancer, particularly in the context of targeted therapy evaluation and resistance mechanisms. Derived from a human metastatic tumor in the axillary lymph node, KPL-4 cells express estrogen receptor, progesterone receptor, and HER2, and demonstrate aggressive growth, invasiveness, and metastatic potential. These features make KPL-4 a clinically relevant model for investigating oncogenic signaling pathways, therapeutic resistance, and the development of next-generation targeted agents.

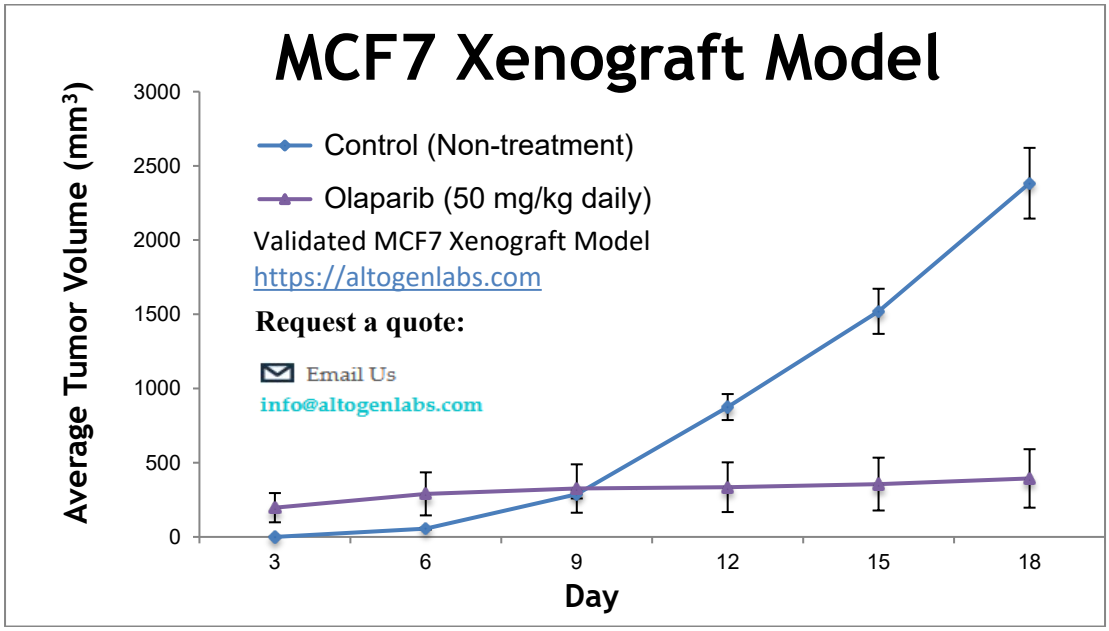
Altogen Labs offers both subcutaneous and orthotopic xenograft models utilizing KPL-4 cells. In the subcutaneous model, one million viable cells suspended in a Matrigel mixture are injected into the hind flank of immunodeficient mice. Tumor volumes are monitored via caliper measurement, and treatment begins once tumors reach 50 to 150 mm^3. In orthotopic models, KPL-4 cells are implanted into the mammary fat pad, allowing tumor growth within a biologically relevant microenvironment that better mimics primary breast cancer. These models facilitate evaluation of drug efficacy, resistance development, tumor microenvironmental influences, and metastatic progression. Post-treatment assessments include necropsy, tumor excision, immunohistochemistry, RNA and protein profiling, and histological analysis.

KPL-4 xenografts have demonstrated utility in evaluating HER2-targeted therapies. A recent study using a novel dual-variable-domain antibody-drug conjugate (DVD-ADC) revealed potent antitumor activity *in vitro* and significant tumor regression *in vivo*, with greater efficacy than T-DM1. Another investigation utilizing eigenspectra multispectral optoacoustic tomography (eMSOT) imaging illustrated that docetaxel treatment reduced tumor oxygenation and vascular density, leading to hypoxia and vascular disruption. These findings suggest the model's value in monitoring dynamic tumor responses and optimizing treatment regimens.

Mechanistically, KPL-4 tumors are driven by overexpression of ErbB family receptors, particularly HER2, HER3, and EGFR. These receptors engage in autophosphorylation and activate downstream PI3K/AKT and MAPK signaling, which promote tumor proliferation, survival, and therapeutic resistance. The model has shown sensitivity to combinations such as trastuzumab, pertuzumab, and docetaxel, which yield enhanced tumor regression by synergistically inhibiting HER2 signaling and increasing apoptosis and immune infiltration. Additionally, high IL-6 production in KPL-4 tumors is associated with cachexia and immune evasion, and correlates with tumor burden *in vivo*.

For more information, researchers can access the KPL-4 model webpage at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/kpl-4-xenograft-model/. The complete technical PDF describing the KPL-4 model is available at https://altogenlabs.com/KPL4XenograftModel.pdf.

Characterization and Preclinical Application of the MCF7 Xenograft Model in Breast Cancer Research



The MCF7 xenograft model is an extensively validated preclinical platform for studying estrogen receptor-positive (ER-positive) breast cancer, particularly in the context of hormone-responsive tumor growth, therapeutic resistance, and drug development. Originating from a breast adenocarcinoma in a 69-year-old patient, the MCF7 cell line expresses estrogen, progesterone, and glucocorticoid receptors, and retains key features of differentiated mammary epithelium. Its responsiveness to estradiol and ability to form hormone-driven tumors make it a foundational model for exploring endocrine therapies and their mechanisms of action in luminal A breast cancer.

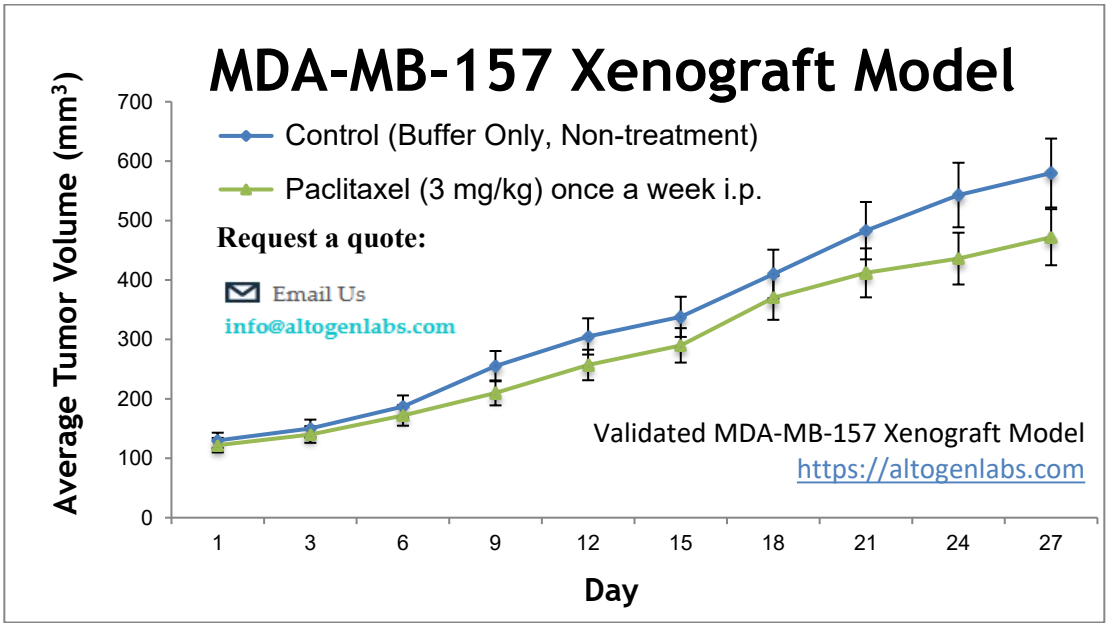
Altogen Labs offers both subcutaneous and orthotopic MCF7 xenograft models, supporting comprehensive tumor biology investigations. In the subcutaneous model, one million viable cells are suspended in a Matrigel mixture and injected into the flank of immunocompromised mice. Tumor growth is measured using digital calipers, and animals are monitored for body weight and treatment-related toxicity. Upon reaching 100 to 150 mm³, tumors are randomized into treatment groups and evaluated for growth inhibition. The orthotopic model involves implantation into the mammary fat pad, providing a more physiologically relevant microenvironment that captures stromal interactions and hormone-dependent growth dynamics. Tissue samples from both models can be preserved for downstream analysis, including histology, RNA preservation, proteomics, and immunohistochemistry.

MCF7 xenografts are well suited for evaluating endocrine therapies and combination regimens. Studies have shown that fulvestrant combined with S-1, an oral fluoropyrimidine, results in enhanced tumor suppression through downregulation of ERα and progesterone receptors. Additionally, the CDK4/6 inhibitor G1T38 demonstrated superior tumor control compared to palbociclib, with fewer hematologic side effects, and showed synergy when combined with fulvestrant or PI3K inhibitors. These findings underscore the utility of the MCF7 model for assessing therapeutic combinations and resistance mechanisms.

The MCF7 cell line also provides a platform to study lipid metabolism in hormone-sensitive breast cancer. Research has revealed that cholesterol levels modulate MCF7 cell proliferation and gene expression, with cholesterol depletion reducing Ki67 and increasing hormone receptor expression. Furthermore, MCF7 cells respond to ethanol exposure with increased oncogenic signaling, and they can form mammospheres, allowing exploration of cancer stem cell biology and recurrence.

Detailed information about the MCF7 xenograft model is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/mcf7-xenograft-model/. The complete technical PDF describing the MCF7 model is available at https://altogenlabs.com/MCF7XenograftModel.pdf.

Characterization and Preclinical Application of the MDA-MB-157 Xenograft Model in Breast Cancer Research



The MDA-MB-157 xenograft model is a validated and widely used preclinical platform for investigating triple negative breast cancer (TNBC), a highly aggressive and therapeutically resistant subtype of breast malignancy. Derived from the pleural effusion of a patient with medullary carcinoma, MDA-MB-157 cells lack estrogen receptor, progesterone receptor, and HER2 expression, making them an ideal system for modeling receptor-independent tumor progression. These cells exhibit mesenchymal characteristics, pronounced invasiveness, and elevated EGFR expression, traits associated with advanced TNBC phenotypes. Their reliance on glycolytic metabolism and tendency toward genomic instability further enhance their utility in studying metastatic behavior, therapeutic resistance, and oncogenic signaling pathways.

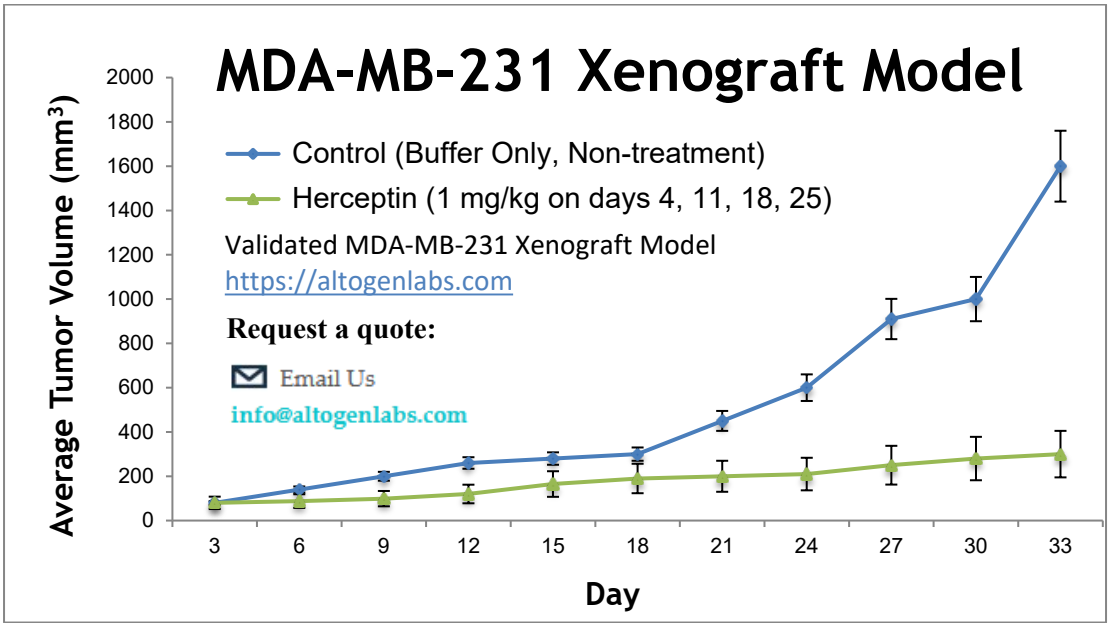
Altogen Labs offers a validated subcutaneous MDA-MB-157 xenograft model in immunodeficient mice. After confirming greater than 98 percent cell viability, one million cells are injected into the flank of BALB/c or NOD/SCID mice in a Matrigel suspension. Tumor development is monitored using digital calipers, and once tumors reach 100 to 150 mm³, animals are randomized into treatment cohorts. Studies are conducted under GLP-compliant and IACUC-approved protocols, with detailed documentation of tumor volume, body weight, and clinical observations. Following the study endpoint, tumors are excised, weighed, and subjected to histopathology, immunohistochemistry, or molecular analysis to evaluate treatment effects.

This model has been employed in studies exploring tumor suppressor pathways and synthetic lethality. DAXX overexpression was shown to suppress RAD51, sensitizing tumors to PARP inhibitors and enhancing apoptosis through homologous recombination disruption. In another study, the histone deacetylase inhibitor panobinostat induced G2/M arrest, apoptosis, and reversal of epithelial-to-mesenchymal transition by upregulating CDH1, indicating therapeutic potential against TNBC. These findings underscore the value of the MDA-MB-157 model for assessing novel epigenetic modulators and DNA repair-targeted agents.

MDA-MB-157 cells also exhibit dysregulated mitosis driven by overexpression of MAD2L2 and defective anaphase-promoting complex activity, contributing to mitotic slippage and chromosomal instability. This karyotypic heterogeneity, alongside hyperactivation of the PI3K/AKT/mTOR, MAPK, and STAT pathways, positions the model as a robust platform for evaluating kinase inhibitors and other targeted therapies. Phytochemicals such as fisetin and quercetin have demonstrated efficacy in reversing mesenchymal phenotypes and inhibiting migration, highlighting the model's utility in metastasis research.

Additional information about the MDA-MB-157 model is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/mda-mb-157-xenograft-model/. The complete technical PDF describing the MDA-MB-157 model is available at https://altogenlabs.com/MDAMB157XenograftModel.pdf.

Characterization and Preclinical Application of the MDA-MB-231 Xenograft Model in Breast Cancer Research



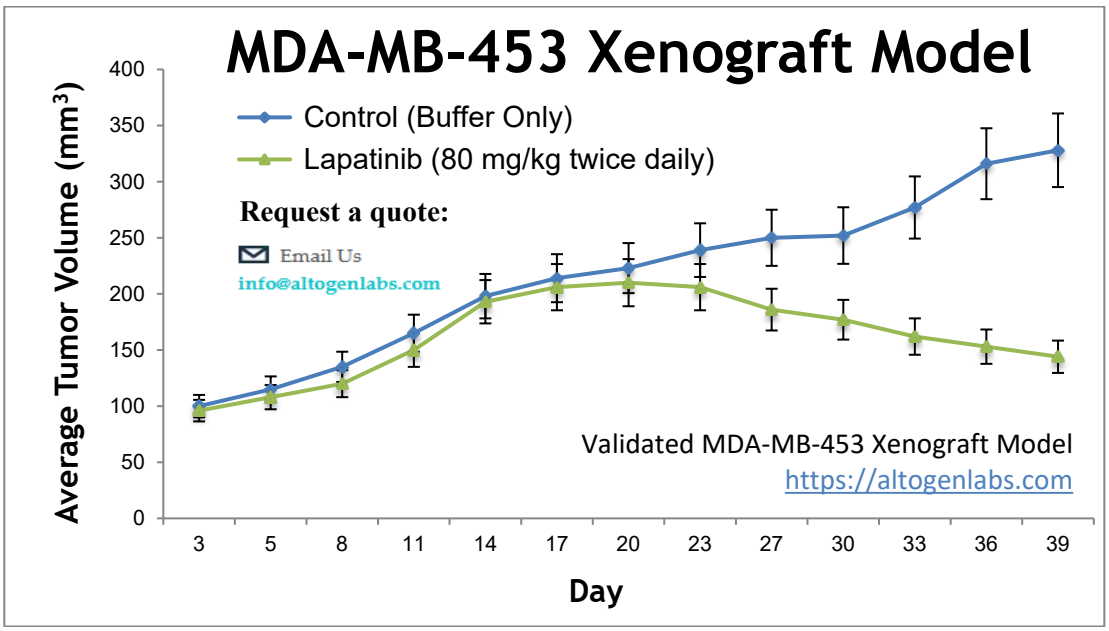
The MDA-MB-231 xenograft model is a widely utilized preclinical system for investigating triple-negative breast cancer (TNBC), a subtype characterized by the absence of estrogen receptor, progesterone receptor, and HER2 expression. Originally derived from a metastatic pleural effusion in a 51-year-old female patient, MDA-MB-231 cells are highly invasive and metastatic, exhibiting mesenchymal-like traits and responsiveness to cytokines and growth factors. Their genetic profile includes mutant TP53 and hyperactivation of the PI3K/AKT and MAPK pathways, making this model an essential platform for evaluating aggressive tumor behavior, therapeutic resistance, and metastasis.

Altogen Labs offers validated subcutaneous, orthotopic, and metastatic xenograft models using MDA-MB-231 cells. In the subcutaneous model, one million cells suspended in Matrigel are injected into the flank of immunocompromised mice. Tumors are monitored with digital calipers and randomized into treatment groups once volumes reach 50 to 150 mm^3. Orthotopic models involve injection into the mammary fat pad to replicate the tumor microenvironment more closely, allowing study of local invasion and distant metastasis. The metastatic model facilitates full evaluation of the metastatic cascade, with tumor dissemination to the lungs, liver, and lymph nodes. These models support comprehensive assessments of tumor growth, pharmacologic intervention, survival, toxicity, and metastatic burden.

MDA-MB-231 xenografts have been extensively used in targeted therapy development. Studies have shown that foretinib, a MET inhibitor, significantly reduces tumor volume and downregulates HGF/MET signaling in this model. Additional work targeting EGFR-expressing cancer stem cells with cetuximab, alone or combined with ixabepilone, demonstrated selective efficacy depending on TNBC subtype. Moreover, antisense mitochondrial RNA knockdown induced cell cycle arrest and apoptosis, reducing tumor burden by suppressing cyclins and CDKs. Other interventions, such as DEK oncogene silencing, decreased cellular redox potential and invasiveness, providing insight into the metabolic reprogramming of TNBC cells.

The model is also valuable for assessing therapeutic resistance. For instance, SPHK inhibition, once thought critical for cancer cell viability, had minimal impact on MDA-MB-231 survival, challenging its utility as a therapeutic target. These results highlight the importance of using well-characterized models to test the biological relevance of proposed targets.

Detailed information about the MDA-MB-231 model is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/mda-mb-231-xenograft-model/. The complete technical PDF describing the MDA-MB-231 model is available at https://altogenlabs.com/MDAMB231XenograftModel.pdf.



The MDA-MB-453 xenograft model is a validated *in vivo* platform for investigating HER2-positive and androgen receptor (AR)-positive breast cancer, particularly in the context of molecular apocrine subtypes. Derived from a metastatic pericardial effusion in a 48-year-old female patient, MDA-MB-453 cells are estrogen receptor-negative, progesterone receptor-negative, and HER2-positive. These tumors exhibit moderate growth kinetics, AR-driven signaling, and a defined histopathological profile, making the model highly suitable for evaluating targeted therapies, hormonal interventions, and novel chemotherapeutic agents.

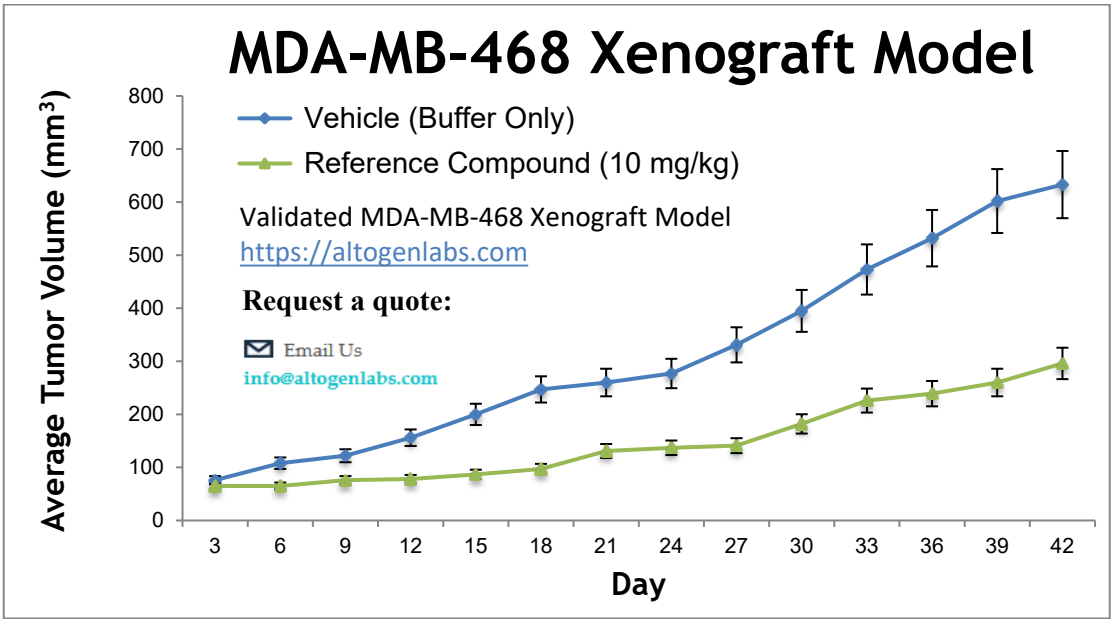
Altogen Labs offers subcutaneous, orthotopic, and metastatic xenograft models using MDA-MB-453 cells. In the subcutaneous model, one million viable cells suspended in Matrigel are injected into the flanks of immunocompromised mice. Tumor volume is measured regularly, and treatment begins once tumors reach 90 to 150 mm³. The orthotopic model involves mammary fat pad injection, replicating the native breast microenvironment and enabling the study of tumor-stroma interactions, therapeutic response, and progression. The metastatic model, established through spontaneous or intravenous injection, allows researchers to investigate lung colonization and systemic dissemination under defined experimental conditions.

MDA-MB-453 xenografts have been used to evaluate the efficacy of targeted therapies. Acetyltanshinone IIA (ATA), for example, has demonstrated significant tumor growth inhibition by inducing S-phase arrest and apoptosis, downregulating HER2 and EGFR signaling, and activating AMPK to suppress lipid and protein biosynthesis. Lapatinib also showed tumor suppression *in vivo* through HER2 pathway inhibition. Additionally, black rice anthocyanins (BRACs) reduced metastatic burden and tumor invasion by inhibiting u-PA and disrupting cellular adhesion and motility, supporting natural compound-based therapies for HER2-driven malignancies.

MDA-MB-453 cells harbor a K-RAS mutation (G13D), resulting in constitutive MAPK signaling, and deletion of p16INK4A, which dysregulates the cell cycle. The model also contains an AR mutation (Q865H) that alters ligand responsiveness, leading to differential activation of androgen-responsive and Wnt-associated gene networks. These molecular features contribute to chemoresistance, endocrine signaling variability, and tumor heterogeneity, making this model highly valuable for dissecting complex oncogenic pathways and AR-targeted strategies in breast cancer.

More information about the MDA-MB-453 model is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/mda-mb-453-xenograft-model/. The complete technical PDF describing the MDA-MB-453 model is available at https://altogenlabs.com/MDAMB453XenograftModel.pdf.

Characterization and Preclinical Application of the MDA-MB-468 Xenograft Model in Breast Cancer Research



The MDA-MB-468 xenograft model is an extensively validated preclinical platform for investigating triple-negative breast cancer (TNBC), an aggressive subtype that lacks expression of estrogen receptor, progesterone receptor, and HER2. Derived from a pleural effusion of a 51-year-old patient with metastatic breast adenocarcinoma, MDA-MB-468 cells exhibit rapid proliferation, PTEN loss, and EGFR overexpression, features that contribute to their high tumorigenic potential and resistance to hormone-targeted therapies. This model is widely employed to study oncogenic signaling, therapeutic resistance, and the efficacy of emerging chemotherapeutic and targeted interventions.

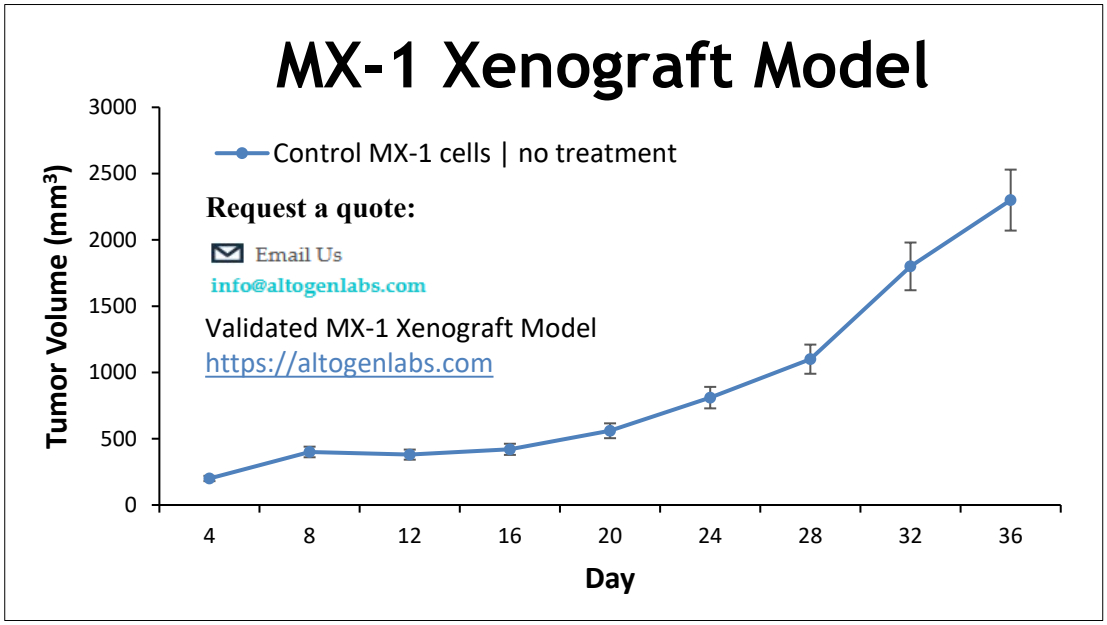
Altogen Labs offers both subcutaneous and orthotopic MDA-MB-468 xenograft models. In the subcutaneous model, one million viable cells are injected into the hind flank of immunocompromised mice using a Matrigel suspension. Tumor growth is measured using calipers until tumors reach 50 to 150 mm³, after which treatment protocols are initiated. The orthotopic model involves implantation into the mammary fat pad, more accurately replicating the tumor microenvironment and supporting studies on invasion, metastasis, and drug response in a physiologically relevant context. Both models allow for tumor excision, histopathological analysis, gene expression profiling, and protein quantification at study endpoints.

The MDA-MB-468 model has proven valuable for studying HER2-low cancers and non-receptor-mediated mechanisms of action. Although HER2 expression is minimal, high doses of trastuzumab deruxtecan (T-DXd) inhibit tumor growth through bystander cytotoxicity, independent of HER2 binding. This supports the model's utility in studying antibody-drug conjugate pharmacokinetics and payload distribution. Additionally, YC-1 has been shown to inhibit tumor growth by inducing degradation of the epigenetic regulator EZH2 via c-Cbl-mediated ubiquitination, while also downregulating polycomb repressive complex components. Another study using anti-EGFR nanobody-conjugated quantum dot micelles demonstrated significantly enhanced drug delivery and tumor regression in MDA-MB-468 xenografts, without systemic toxicity.

MDA-MB-468 cells display dysregulation of the PI3K/AKT and MAPK pathways, with EGFR signaling persistence due to impaired c-Cbl function. The model has been used to elucidate the roles of PEA-15 and other regulators in ERK localization, highlighting their therapeutic relevance. Metabolic profiling reveals distinct differences between MDA-MB-468 *in vitro* conditions and TNBC patient serum, indicating that integration of *in vivo* metabolic studies is necessary for translational insight.

Additional information about the MDA-MB-468 model is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/mda-mb-468-xenograft-model/. The complete technical PDF describing the MDA-MB-468 model is available at https://altogenlabs.com/MDAMB468XenograftModel.pdf.

Characterization and Preclinical Application of the MX-1 Xenograft Model in Breast Cancer Research



The MX-1 xenograft model is a robust and extensively validated preclinical system used for studying triple-negative breast cancer (TNBC), a clinically aggressive subtype lacking expression of estrogen receptor, progesterone receptor, and HER2. Derived from a metastatic tumor of a 29-year-old female patient, MX-1 cells exhibit epithelial morphology, a moderate proliferation rate, and notable sensitivity to various chemotherapeutic agents. Their triple-negative status and reproducible *in vivo* growth characteristics make this model highly suitable for evaluating novel therapeutic strategies and overcoming drug resistance in TNBC.

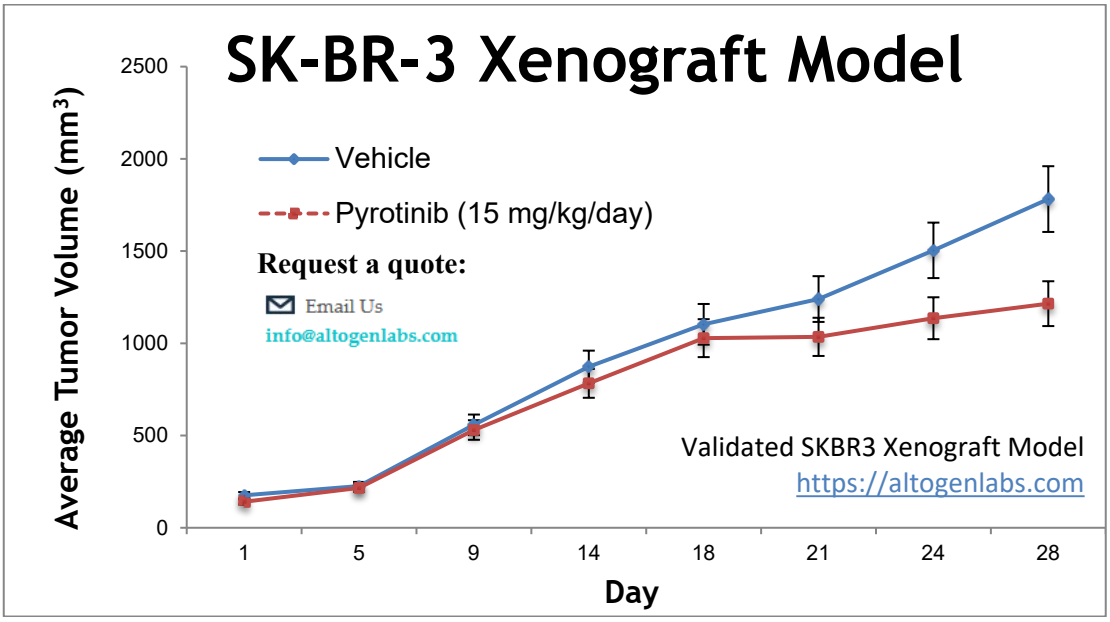
Altogen Labs has developed subcutaneous and metastatic MX-1 xenograft models for preclinical research. In the subcutaneous model, one million viable MX-1 cells suspended in a Matrigel mixture are injected into the flank of immunodeficient mice. Tumor volumes are monitored with calipers until they reach 50 to 150 mm³, at which point treatment begins. The metastatic model enables investigation of tumor dissemination to secondary organs such as lungs and liver, supporting studies on invasion, colonization, and therapeutic inhibition of metastatic progression. Both models are suitable for evaluating chemotherapy, kinase inhibitors, antibody-based therapies, and immunomodulators.

MX-1 xenografts have been employed in studies targeting drug-resistant cancers. The multi-kinase inhibitor T03 has demonstrated potent antitumor activity in Taxol-resistant MX-1 variants by downregulating Raf/MEK/ERK and Akt/mTOR signaling pathways, inducing apoptosis, and reducing tumor volume. Another study highlighted the effectiveness of desoxyepothilones, synthetic microtubule-stabilizing agents, which led to complete tumor regression in MX-1-bearing mice. The doxorubicin analog nemorubicin was shown to be metabolically activated into PNU-159682, a highly cytotoxic metabolite, which produced substantial tumor regression, underscoring the importance of bioactivation in therapeutic efficacy. In parallel, studies with growth hormone-releasing hormone (GHRH) antagonists revealed that compounds such as AVR-352 and AVR-354 effectively suppressed MX-1 tumor growth by modulating inflammatory and cell cycle regulatory pathways. High expression of the MX1 gene has been associated with worse clinical outcomes in breast cancer patients, particularly in TNBC, where it may contribute to metastatic progression and resistance to standard therapies.

Altogen Labs offers comprehensive services for the MX-1 model, including tumor growth delay and inhibition studies, custom dosing schedules, toxicity analysis, necropsy, and histopathology. Advanced imaging techniques such as whole-body fluorescence are available for real-time tracking of tumor dynamics. The model supports a range of administration routes and is compatible with orthotopic and tail vein engraftment for metastasis research. Genetically modified variants and RNAi knockdown systems are also available to study gene function in tumor progression.

Detailed information about the MX-1 xenograft model can be found at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/mx1-xenograft-model/. The complete technical PDF describing the MX-1 model is available at https://altogenlabs.com/MX1XenograftModel.pdf.

Characterization and Preclinical Application of the SK-BR-3 Xenograft Model in Breast Cancer Research



The SK-BR-3 xenograft model is a rigorously validated preclinical system designed to investigate HER2-positive breast cancer. Derived from a metastatic pleural effusion in a female patient, SK-BR-3 cells exhibit high levels of HER2 (ERBB2) amplification, while lacking estrogen and progesterone receptor expression. These cells possess an epithelial morphology and grow as monolayers *in vitro*. Their molecular profile, marked by extensive genomic rearrangements and oncogene amplifications including ERBB2, EGFR, and MYC, renders this model particularly suited for evaluating HER2-targeted therapies, resistance mechanisms, and signaling pathway inhibitors *in vivo*.

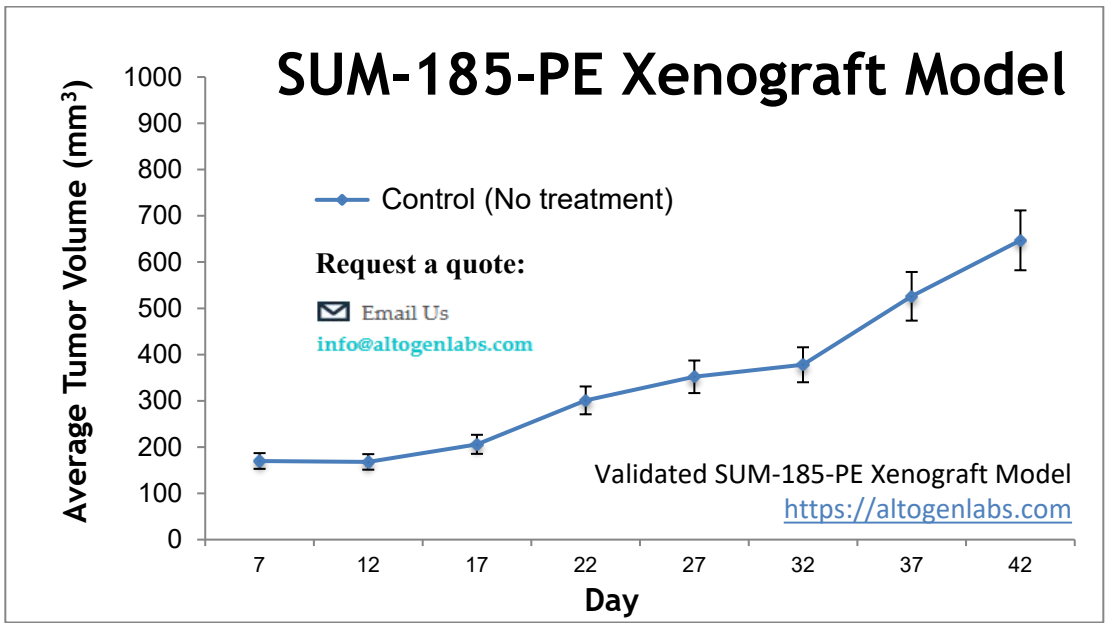
Altogen Labs provides both subcutaneous and orthotopic SK-BR-3 xenograft models. In the subcutaneous model, one million cells are injected into the flank of immunocompromised BALB/c or NOD/SCID mice using a Matrigel suspension. Tumors are measured with digital calipers, and treatment begins once tumor volumes reach 75 to 150 mm³. The orthotopic model involves mammary fat pad implantation, closely recapitulating the native microenvironment and facilitating studies of tumor invasion and metastasis. At study conclusion, tumors are excised, weighed, and processed for histological, molecular, and imaging analyses.

These models have been instrumental in testing HER2-targeted agents including trastuzumab, pyrotinib, and novel therapeutics. Pyrotinib has demonstrated potent tumor suppression in SK-BR-3 xenografts, reducing tumor weight significantly compared to controls. Additional studies revealed that silibinin, a natural flavonoid, inhibits EGFR phosphorylation and downstream oncogenic signaling, suppressing tumor growth and angiogenesis. Tolfenamic acid, a nonsteroidal anti-inflammatory drug, has been shown to reduce ERBB2 expression and inhibit cell cycle progression, further supporting its use in HER2-positive breast cancer treatment strategies.

Mechanistically, SK-BR-3 cells utilize EGFR/ERK/c-fos signaling to activate SIRT1 through G-protein-coupled estrogen receptor (GPER) stimulation. This axis promotes tumor growth and resistance to DNA-damaging agents such as etoposide. Inhibition of SIRT1 or GPER reduces proliferation and induces apoptosis, identifying these pathways as potential therapeutic targets. Long-read sequencing has uncovered structural variations including ERBB2 fusions and nested amplifications, offering additional targets for precision therapy development.

Altogen Labs performs xenograft studies under IACUC and GLP-compliant conditions. Services include tumor growth delay and inhibition studies, customized drug administration regimens (intravenous, subcutaneous, oral), and advanced molecular profiling via RT-PCR and WES protein analysis. Real-time tumor monitoring is supported by fluorescence-based imaging systems. Additional information about the SK-BR-3 model is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/skbr3-xenograft-model/. The complete technical PDF describing the SK-BR-3 model is available at https://altogenlabs.com/SKBR3XenograftModel.pdf.

Characterization and Preclinical Application of the SUM185PE Xenograft Model in Breast Cancer Research



The SUM185PE xenograft model is a validated preclinical platform developed for the study of HER2-positive and luminal androgen receptor (LAR)-positive triple-negative breast cancer (TNBC), a molecular subtype marked by its aggressive behavior and resistance to standard hormone therapies. Derived from a pleural effusion of a patient with anaplastic breast carcinoma, SUM185PE cells lack estrogen and progesterone receptors while overexpressing HER2. These cells also express luminal cytokeratins (KRT8, KRT18, KRT19), indicating a partially differentiated phenotype. Their oncogenic profile includes PIK3CA amplification and AR expression, making them particularly well-suited for evaluating targeted therapies involving PI3K, mTOR, and AR signaling.

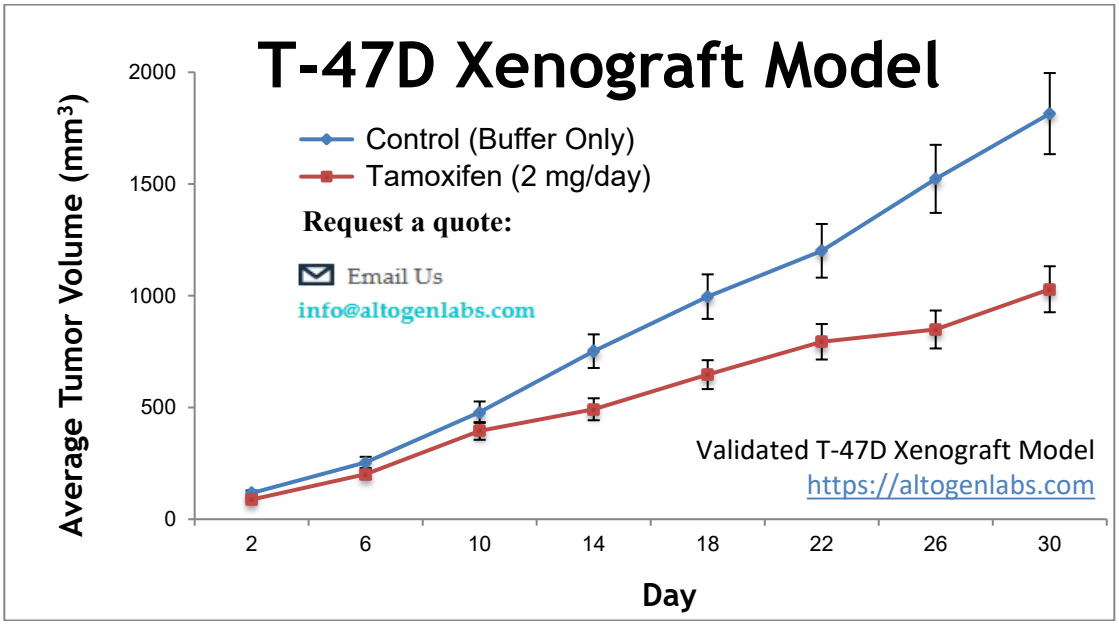
Altogen Labs offers both subcutaneous and orthotopic SUM185PE xenograft models. In the subcutaneous model, one million viable cells are injected into the flanks of immunocompromised mice, suspended in Matrigel to promote tumor engraftment. Tumor progression is monitored using calipers, with mice randomized into treatment cohorts upon reaching 75 to 150 mm³. In the orthotopic model, cells are implanted into the mammary fat pad, providing a more biologically relevant environment for studying local invasion, tumor-stroma interactions, and metastasis. Endpoints include tumor volume analysis, necropsy, histopathology, and molecular profiling.

SUM185PE xenografts have proven particularly useful for testing therapies that target AR-driven and PI3K-dependent pathways. Ceritinib has demonstrated efficacy by inhibiting both AR-dependent and AR-independent signaling, suppressing downstream FAK-YB1 and WNT/β-catenin pathways, and enhancing the effects of paclitaxel. Similarly, deguelin selectively inhibits SUM185PE growth by destabilizing AR and reducing PI3K/mTOR signaling, revealing vulnerabilities in LAR-positive TNBC. These studies support combination therapies involving PI3K or mTOR inhibitors with antiandrogens as a rational strategy for treatment-resistant TNBC.

Genomic instability in SUM185PE cells includes frequent gains at 8q (MYC), deletions at 17p (TP53), and aberrations affecting chromosome 3q (PIK3CA), driving both proliferative and survival signaling. The cells exhibit high sensitivity to PI3K inhibitors such as wortmannin, but resistance to MEK inhibitors, indicating pathway-specific dependencies. These findings highlight the therapeutic potential of precision medicine strategies targeting PI3K and AR in LAR-TNBC.

Altogen Labs supports a full suite of services including tumor growth delay and inhibition studies, intravenous and oral dosing, fluorescence imaging, gene expression profiling, and histopathological evaluation. More information about the SUM185PE xenograft model is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/sum185pe-xenograft-model/. The complete technical PDF describing the SUM185PE model is available at https://altogenlabs.com/SUM185PEXenograftModel.pdf.

Characterization and Preclinical Application of the T-47D Xenograft Model in Breast Cancer Research



The T-47D xenograft model is a clinically relevant preclinical platform used to evaluate estrogen receptor-positive (ER-positive), luminal A subtype breast cancer. Derived from a pleural effusion of a 54-year-old female patient with infiltrating ductal carcinoma, T-47D cells express estrogen and progesterone receptors, while lacking HER2 amplification. This molecular phenotype makes the model highly suitable for assessing endocrine therapies, hormone receptor signaling, and resistance mechanisms. T-47D cells are also amenable to genetic modification and widely used for transfection-based functional studies in breast cancer research.

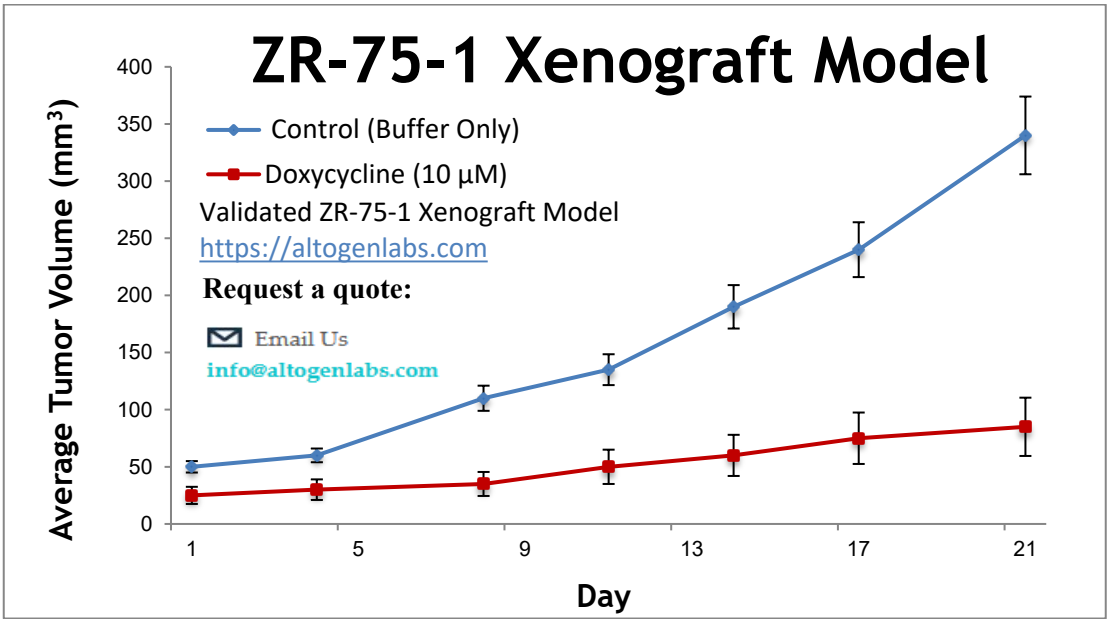
Altogen Labs has validated both subcutaneous and orthotopic xenograft models using T-47D cells. In the subcutaneous model, one million cells suspended in Matrigel are injected into the flanks of NOD/SCID mice, and tumor growth is measured using digital calipers. Since T-47D tumors are estrogen-dependent, exogenous estrogen is administered to support proliferation. Tumors typically reach 75 to 150 mm³ before treatment groups are assigned. The orthotopic model involves implantation into the mammary fat pad, more accurately replicating the tumor microenvironment and enabling studies of invasion, stroma interaction, and metastatic potential. Both models support histological, molecular, and imaging analyses of therapeutic response.

Recent studies using the T-47D xenograft have identified several promising therapeutics. DHW-208, a novel 4-aminoquinazoline derivative, demonstrated strong anti-tumor effects by inhibiting PI3K/AKT/mTOR signaling, inducing apoptosis, and promoting G0/G1 arrest. It outperformed BEZ235 in efficacy and toxicity. Calycosin, a natural isoflavone, inhibited EMT by suppressing BATF and TGFβ1 signaling, resulting in reduced tumor cell migration, increased E-cadherin expression, and diminished MMP activity. Additionally, RHAMM knockdown unexpectedly promoted migration and EMT via AKT/GSK3β/Snail signaling, revealing its unique role as a suppressor of metastasis in luminal A breast cancer.

Cytogenetically, T-47D cells possess a hypotriploid karyotype with 57 to 66 chromosomes, marked by frequent deletions and complex rearrangements involving chromosomes 1, 4, 6, 10, and X. These chromosomal abnormalities contribute to genomic instability, which may influence tumor progression and drug response. Compared to other luminal models like MCF-7 or BT474, T-47D exhibits a distinct cytogenetic profile, making it an important complementary system in hormone receptor-positive breast cancer research.

Altogen Labs conducts xenograft studies under IACUC and GLP-compliant conditions and offers flexible study designs, including various administration routes (oral, intravenous, intratumoral), tumor growth inhibition assessments, and endpoint analyses. Molecular evaluations include mRNA and protein expression, histopathology, and whole-body fluorescence imaging. More information is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/t-47d-xenograft-model/. The complete technical PDF describing the T-47D model is available at https://altogenlabs.com/T47DXenograftModel.pdf.

Characterization and Preclinical Application of the ZR-75-1 Xenograft Model in Breast Cancer Research



The ZR-75-1 xenograft model is a validated *in vivo* platform for studying estrogen receptor-positive (ER-positive) breast cancer, particularly luminal B subtypes characterized by co-expression of progesterone receptor and HER2. Derived from a human ductal adenocarcinoma, ZR-75-1 cells grow as adherent epithelial monolayers and are extensively used to investigate hormonal therapies, targeted agents, and mechanisms of treatment resistance. Their genetic profile includes activation of the PI3K/AKT/mTOR pathway, a critical oncogenic axis frequently implicated in endocrine resistance, making this model highly relevant for preclinical research.

Altogen Labs provides subcutaneous, orthotopic, and metastatic ZR-75-1 xenograft models. In the subcutaneous model, one million cells suspended in Matrigel are injected into the flank of immunocompromised mice, where tumors form in a consistent and measurable manner. Orthotopic implantation into the mammary fat pad replicates the native tumor microenvironment, enabling studies of tumor-stroma interaction, invasion, and localized drug effects. For metastasis studies, tail vein injection facilitates hematogenous spread to distant organs such as the lungs and bones. All models are conducted under IACUC and GLP-compliant conditions with digital tumor volume monitoring, necropsy, and comprehensive tissue analysis.

ZR-75-1 xenografts have contributed significantly to the study of therapeutic resistance and metabolic targeting. A key study demonstrated that CDK4/6 inhibitor-resistant ZR-75-1 tumors retain dependence on PI3K signaling, and the p110α-selective inhibitor alpelisib reversed tumor progression. When used in combination with endocrine therapies or CDK4/6 inhibitors, PI3K blockade proved effective in restoring treatment sensitivity, supporting triplet combination strategies for resistant ER-positive tumors. Additionally, the model was instrumental in elucidating the oncogenic function of DCXR, a glycolysis-regulating enzyme. Silencing DCXR suppressed tumor growth, while 2-deoxy-D-glucose reversed its tumor-promoting effects, highlighting glycolysis as a metabolic vulnerability.

ZR-75-1 tumors have also shown sensitivity to dual metabolic inhibition. A combination of rapamycin and doxycycline disrupted mTOR signaling and mitochondrial function, inducing selective autophagy-dependent cell death without triggering apoptosis or necrosis. This metabolic strategy suppressed tumor growth and required sustained treatment to prevent recurrence. Furthermore, ZR-75-1 cells exhibit sensitivity to glutamate dehydrogenase inhibition, distinguishing their glycolytic profile from more proliferative triple-negative breast cancers and suggesting therapeutic relevance in targeting tumor-specific metabolic pathways.

More information for the ZR-75-1 model is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/zr-75-1-xenograft-model/. The complete technical PDF describing the ZR-75-1 model is available at https://altogenlabs.com/ZR751XenograftModel.pdf.

Comprehensive Xenograft Modeling and Preclinical Oncology Services at Altogen Labs

Altogen Labs offers a broad spectrum of specialized services that support the development and evaluation of oncology therapeutics within a highly controlled and clinically relevant preclinical framework. Central to these services is the laboratory's extensive portfolio of validated xenograft models, encompassing cell line-derived (CDX), patient-derived (PDX), and metastatic systems that represent major molecular subtypes of breast cancer, including luminal A and B, HER2-amplified, and triple-negative phenotypes. These models are complemented by rigorous analytical capabilities and a flexible infrastructure that allows for tailored study designs aligned with client-specific objectives.

In addition to xenograft studies, Altogen Labs provides a comprehensive suite of preclinical services, including tumor growth inhibition and delay assessments, survival analysis, pharmacokinetics, toxicology, and biodistribution studies. The laboratory supports multiple administration routes such as intravenous, subcutaneous, intraperitoneal, oral gavage, and intratumoral injection, with advanced delivery techniques including pump-controlled infusion and microinjection. Fluorescence-based whole-body imaging and digital tumor volume tracking allow for real-time monitoring of treatment effects, while endpoint analyses include necropsy, histology, and molecular profiling of both tumor and normal tissues.

Molecular characterization services include quantitative gene expression analysis via RT-PCR, Western blotting, and protein quantification using the WES capillary-based system. Tumor tissues can be processed for RNA and protein isolation, formalin fixation, or cryopreservation, depending on downstream requirements. Immunohistochemistry and immunofluorescence staining are available to evaluate biomarker expression, tumor architecture, and treatment-induced phenotypic changes. Furthermore, Altogen Labs offers the development of genetically engineered cell lines for overexpression or RNA interference-based gene silencing to enable mechanism-of-action studies and validation of novel targets.

As part of its immuno-oncology research services, Altogen Labs utilizes humanized rodent models engrafted with CD34+ hematopoietic stem cells, peripheral blood mononuclear cells (PBMCs), or induced pluripotent stem cells (iPSCs). These platforms allow for the evaluation of checkpoint inhibitors, CAR-T cells, bispecific antibodies, and tumor-immune interactions within a functional humanized immune system.

Altogen Labs also provides acute and sub-chronic toxicity testing, following OECD-aligned guidelines, to support investigational new drug (IND) applications and other regulatory submissions. The laboratory is fully GLP-aligned and IACUC-compliant, ensuring adherence to ethical and scientific standards throughout the study lifecycle.

Altogen Labs combines technical expertise, regulatory diligence, and scientific innovation to deliver high-quality, translational data that accelerates oncology drug development. By offering integrated capabilities from model selection and study execution to molecular endpoint analysis and comprehensive reporting, Altogen Labs remains a trusted partner for advancing preclinical cancer research. For detailed information about available models, services, and study inquiries, please visit www.altogenlabs.com.