Validated HCC-1806 Xenograft Model:
Subcutaneous And Metastatic Xenograft Tumor Model

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Advancing Breast Cancer Research Through Xenograft Models

Breast cancer is one of the most prevalent and aggressive cancers worldwide, representing a leading cause of cancer-related deaths in women. It is a heterogeneous disease, with various subtypes that exhibit distinct biological behaviors, treatment responses, and prognoses. In recent years, xenograft models, particularly patient-derived xenografts (PDXs) and cell line-derived xenografts (CDXs), have emerged as crucial for studying breast cancer biology and testing novel therapies. CDXs are created by implanting established cancer cell lines into immunocompromised mice, providing a reproducible and controlled model for evaluating tumor growth and drug efficacy. In contrast, PDXs are generated by directly implanting tumor tissue from breast cancer patients into mice, preserving the genetic and histological features of the original tumor. This makes PDXs particularly valuable for studying tumor heterogeneity, metastasis, and the personalized response to treatment. Both models have their advantages, with CDXs offering a more standardized approach, while PDXs better replicate the complexity of human breast cancer.

HCC-1806 Cell Line

The HCC-1806 cell line is an epithelial cell line derived from the mammary gland of a 60-year-old Black female patient diagnosed with acantholytic squamous cell carcinoma (ASCC). This tumor was classified as TNM Stage IIB, grade 2. The cell line was initiated in 1995 and took approximately 10 months to fully establish in culture. HCC-1806 cells are often utilized in research focused on understanding breast cancer biology, particularly the molecular mechanisms underlying ASCC. The cell line provides a valuable insight for investigating therapeutic strategies for squamous breast cancer, a rare and aggressive form of the disease. Researchers commonly use HCC-1806 cells in xenograft studies to explore drug responses and to model tumor progression. Its unique characteristics, including high expression of epithelial markers and a distinct histological profile, make it a useful model for studying the heterogeneity of breast cancer subtypes. Additionally, HCC-1806 cells are known for their aggressive growth pattern, which makes them a useful model for studying tumor invasiveness and metastasis. Their utility in preclinical drug testing and their relevance to the study of rare breast cancer subtypes continue to make HCC-1806 an important resource in cancer research.

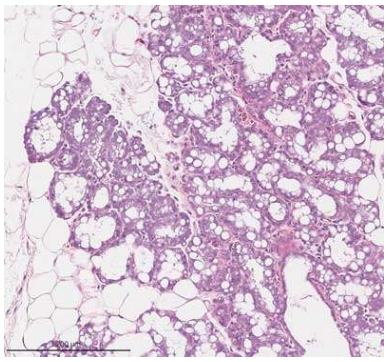

Figure 1. Tumor Histology. H&E stained section of a subcutaneously-implanted HCC-1806 tumor (Altogen Labs).

Altogen Labs Validated HCC-1806 Xenograft Model

Following expansion under aseptic conditions, HCC-1806 cells are harvested and prepared for injection while maintaining a minimum of 98% cell viability, verified by trypan blue exclusion assay. The cell suspension is adjusted to an appropriate density, ensuring that each immunocompromised mouse (e.g., athymic BALB/c or NOD/SCID, 10-12 weeks old) receives a single subcutaneous injection of 1 × 10^6 HCC-1806 cells suspended in 100 µL of a Matrigel-cell mixture. Tumor growth is monitored using digital calipers three times weekly until tumors reach an average size of 75-125 mm^3, at which point treatment administration begins. Animals are randomized into treatment and control cohorts, and test compounds are administered according to a pre-established dosing schedule. Body weights are recorded three times weekly, while tumor volumes are measured daily. The study endpoint is reached when

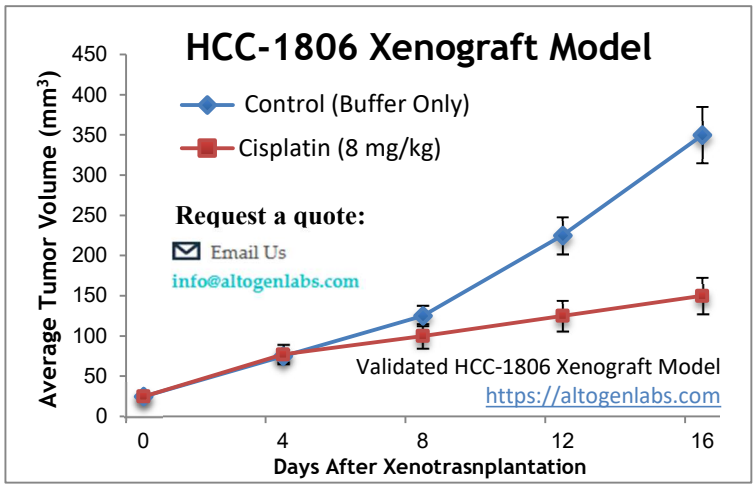

Figure 2. HCC-1806 breast cancer xenografted in immunocompromised mice, mean values +/- SEM (Altogen Labs).

tumors reach 2,000 mm³ or the predetermined size limit as per IACUC-approved protocols. At termination, animals are humanely euthanized, and tumors are excised, weighed, and documented using digital imaging. Collected tissues undergo downstream processing, including snap freezing in liquid nitrogen, stabilization in RNAlater, or fixation for histological analysis.

Xenograft models, including cell line-derived xenografts (CDXs) and patient-derived xenografts (PDXs), are critical for assessing the efficacy of novel cancer therapies. The HCC-1806 xenograft model specifically aids in the study of triple-negative breast cancer (TNBC), an aggressive subtype lacking targeted therapies. CDX models provide a highly reproducible system for tumor growth kinetics and drug response evaluations, whereas PDX models preserve the heterogeneity of patient tumors. At Altogen Labs, xenograft studies are conducted under GLP-compliant conditions following IACUC regulations. Mice undergo acclimation and are carefully monitored for tumor progression and clinical signs. We provide comprehensive experimental services, including histopathological evaluation, gene expression analysis (RNA/protein isolation), and customized dosing regimens. Our facilities are also equipped to support specialized diets and water systems for inducible gene expression research, ensuring precise and reliable preclinical data for oncology drug development.

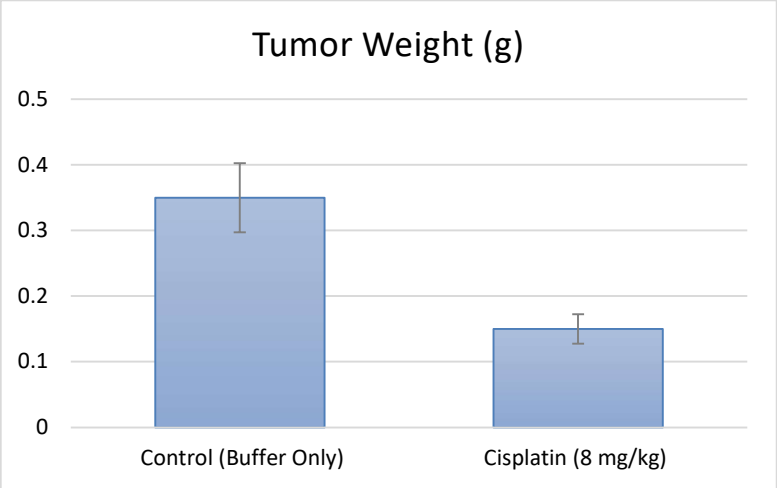

Figure 3. Tumor weight of HCC-1806 cells in control, buffer only mice and cisplatin treated mice at end of the study (Altogen Labs).

Mitochondrial Dysfunction and ROS Generation in GA-Induced HCC-1806 Cell Apoptosis

HCC-1806 is a basal-like triple-negative breast cancer (TNBC) cell line used to investigate the therapeutic effects of gallic acid (GA) on TNBC progression. Research has shown that GA treatment significantly inhibited HCC-1806 cell proliferation and induced apoptosis by modulating key signaling pathways. Specifically, GA suppressed the PI3K/AKT/EGFR pathway, which is known to promote tumor cell survival and resistance to apoptosis. Concurrently, it activated the MAPK signaling cascade, including JNK and p38 pathways, leading to increased pro-apoptotic signaling. GA-induced apoptosis was associated with mitochondrial dysfunction, as evidenced by mitochondrial membrane potential depolarization and increased reactive oxygen species (ROS) generation. Molecular analyses demonstrated that GA upregulated Bax, cleaved caspase-3, and p53 while downregulating anti-apoptotic proteins such as Bcl-2 and phosphorylated EGFR. Additionally, computational molecular docking confirmed GA's strong binding affinity for PI3K, AKT, and EGFR, further supporting its role in inhibiting these oncogenic drivers. These findings highlight the potential of GA as a promising natural compound for TNBC treatment, particularly in patients with elevated PI3K/AKT/EGFR signaling activity.

Nitroxidative Stress and Mitochondrial Dysfunction in HCC-1806 Cold Plasma Therapy

Research has used the HCC-1806 cell line used to evaluate the therapeutic potential of cold atmospheric plasma (CAP) in breast cancer treatment and found that CAP exposure significantly reduced HCC-1806 cell viability by inducing apoptosis and necrosis, with mitochondrial membrane potential loss being a key early event in cell death. The treatment also led to an increased BAX/BCL2 ratio and decreased procaspase-3 expression, confirming apoptotic pathway activation. Additionally, HCC-1806 cells exhibited unique nitroxidative stress responses, including elevated intracellular nitric oxide (NO) levels and reduced superoxide concentrations, suggesting an intrinsic ability to metabolize plasma-derived reactive nitrogen species. Inhibition of cytochrome c oxidase further enhanced CAP-induced cytotoxicity, indicating that oxidative stress modulation could potentiate plasma therapy. CAP also induced cell cycle arrest in the G2/M phase, impairing HCC-1806 proliferation and long-term survival. These findings highlight CAP's potential as an innovative non-invasive therapeutic strategy for TNBC, particularly in tumors resistant to conventional therapies.

HCC-1806 Subcutaneous Xenografts

The subcutaneous HCC-1806 xenograft model is a well-established preclinical system for studying triple-negative breast cancer (TNBC). In this model, HCC-1806 cells are injected subcutaneously into immunocompromised mice, typically in the right flank, allowing for efficient tumor establishment and monitoring. Tumor growth is assessed using digital calipers, providing a reproducible and measurable system for evaluating therapeutic responses. This model is widely used to test novel anti-cancer compounds, including small molecules, biologics, and combination therapies. The subcutaneous approach offers a controlled tumor microenvironment, making it ideal for pharmacokinetic and pharmacodynamic studies. While it does not fully replicate the tumor's natural site, it remains essential for drug efficacy screening. Study endpoints are determined based on tumor volume limits, with tissue collection enabling histological, molecular, and genomic analyses. The HCC-1806 subcutaneous model provides a reliable platform for investigating tumor biology and treatment responses in TNBC research.

Modeling Triple-Negative Breast Cancer Metastasis with HCC-1806

The metastatic HCC-1806 model is a valuable preclinical system for studying the dissemination and progression of triple-negative breast cancer (TNBC). This model is typically established through orthotopic implantation of HCC-1806 cells into the mammary fat pad of immunocompromised mice, allowing for spontaneous metastasis to distant organs such as the lungs, liver, and lymph nodes. It provides a clinically relevant platform for investigating metastatic mechanisms, tumor microenvironment interactions, and potential therapeutic interventions targeting metastatic TNBC. Researchers utilize this model to study gene expression changes associated with metastasis, evaluate novel anti-metastatic agents, and assess drug resistance in disseminated tumors. Imaging techniques such as bioluminescence or fluorescence tracking can be employed to monitor metastatic progression *in vivo*. The metastatic HCC-1806 model enables detailed histological and molecular analyses of metastatic lesions, facilitating the identification of new biomarkers and therapeutic targets. By mimicking key aspects of human TNBC metastasis, this model plays a critical role in advancing treatment strategies for aggressive and treatment-resistant breast cancer subtypes.

Chemotherapy: Mithramycin A as a Potential Therapy for KLF5-Driven Triple-Negative Breast Cancer

Another study by Liu R, *et al.*, published by *Scientific Reports* journal, examines the anti-cancer effects of Mithramycin A (MIT) in triple-negative breast cancer (TNBC), with a particular focus on HCC-1806, a basal-like TNBC cell line characterized by high expression of the oncogenic transcription factor Krüppel-like factor 5 (KLF5). The findings demonstrate that MIT suppresses HCC-1806 cell proliferation and survival in a dose-dependent manner by inhibiting Sp1-mediated transcription of KLF5. Downregulation of KLF5 by MIT leads to impaired DNA synthesis, G1/S cell cycle arrest, and apoptosis, as confirmed by increased Annexin V staining and cleaved PARP levels. Overexpression of KLF5 partially rescues MIT-induced apoptosis and loss of cell viability, confirming the central role of KLF5 suppression in MIT's mechanism of action. Furthermore, in an HCC-1806 xenograft model, MIT significantly inhibits tumor growth without causing systemic toxicity. ChIP assays reveal that MIT disrupts Sp1 binding to the KLF5 promoter, further validating its transcriptional inhibitory effect. The study underscores the potential of MIT as a therapeutic agent for basal-like TNBC, particularly in patients with high KLF5 expression. Given the lack of effective targeted therapies for TNBC, MIT's ability to suppress tumor growth through the Sp1/KLF5 axis presents a promising avenue for further clinical investigation.

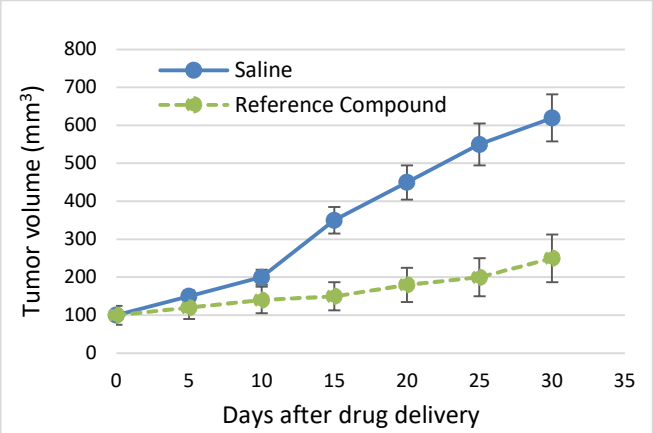

Figure 4. HCC-1806 tumor growth was suppressed when treated with the reference compound (0.3 mg/kg).

Case Study: Synergistic Inhibition of HCC-1806 TNBC Growth by FTY720 and EGFR Blockade

A study by Martin JL, *et al.,* published by *Breast Cancer Research* journal, investigates the combined therapeutic effect of FTY720 (Fingolimod), a sphingosine kinase (SphK) inhibitor, and gefitinib, an EGFR tyrosine kinase inhibitor, in basal-like triple-negative breast cancer (TNBC). HCC-1806, a basal-like TNBC cell line with high EGFR expression, was a primary model for evaluating treatment efficacy. The combination of FTY720 and gefitinib showed synergistic inhibition of cell proliferation in HCC-1806, as demonstrated by live-cell imaging. In an orthotopic xenograft model using HCC-1806 tumors, this combination therapy significantly suppressed tumor growth and extended survival compared to monotherapy or control treatments. Mechanistically, the treatment downregulated phosphorylated EGFR (pEGFR) and decreased Ki67 expression, indicating reduced proliferation. The combination therapy also enhanced cleaved caspase-3 levels, signifying increased apoptosis in HCC-1806 tumors. Notably, the synergistic effect was dependent on IGFBP-3, a key tumorigenic mediator in TNBC, suggesting that IGFBP-3 could serve as a biomarker for predicting therapeutic response. The study further demonstrated that immune-competent mice responded better to the treatment compared to immune-deficient models, underscoring the potential role of the immune system in enhancing drug efficacy. These findings support the potential clinical application of FTY720-gefitinib combination therapy for basal-like TNBC, particularly in patients with high IGFBP-3 expression.

Oncogenic Drivers of HCC-1806: EMT, ECM Degradation, and Epigenetic Dysregulation

HCC-1806 is a basal-like triple-negative breast cancer (TNBC) cell line characterized by aggressive tumorigenic properties and genomic instability. A key oncogenic feature of HCC-1806 is the dysregulation of epithelial-to-mesenchymal transition (EMT) pathways, which enhance its invasive potential. This cell line exhibits high matrix metalloproteinase (MMP) activity, particularly MMP-2 and MMP-9, which degrade the extracellular matrix (ECM) and facilitate metastasis. Additionally, HCC-1806 harbors mutations in TP53, a tumor suppressor gene frequently altered in TNBC, leading to defects in apoptosis and genomic maintenance. Epigenetic alterations, including EZH2 overexpression, contribute to transcriptional silencing of key tumor suppressor genes, further driving malignancy. The PI3K/AKT and JAK/STAT signaling pathways are hyperactivated in HCC-1806, supporting its survival, proliferation, and resistance to therapy. Recent studies highlight the role of long non-coding RNAs (lncRNAs) and microRNAs (miRNAs) in modulating HCC-1806 oncogenesis, with miR-200 family members being notably downregulated, promoting EMT and stemness. Understanding these oncogenic drivers provides insights into potential therapeutic targets for basal-like TNBC.

Altogen Labs offers a comprehensive range of services utilizing the HCC-1806 Cell Line Derived Xenograft (CDX) model, utilized for advancing triple-negative breast cancer (TNBC) research. The HCC-1806 model is derived from a primary acantholytic squamous cell carcinoma (ASCC) and is widely used to study the aggressive nature of TNBC, including its molecular drivers, tumor microenvironment interactions, and resistance mechanisms. This model enables researchers to investigate key oncogenic pathways and tumor suppressor alterations, providing valuable insights into TNBC progression and therapeutic vulnerabilities. The HCC-1806 CDX model is particularly suited for evaluating novel treatment strategies, including small-molecule inhibitors, immunotherapies, and combination regimens aimed at overcoming TNBC's inherent resistance to conventional therapies. In addition, Altogen Labs offers the capability to generate genetically engineered HCC-1806 cell lines with overexpression or RNA interference (RNAi)-mediated gene silencing, allowing precise functional studies of cancer-associated genes.

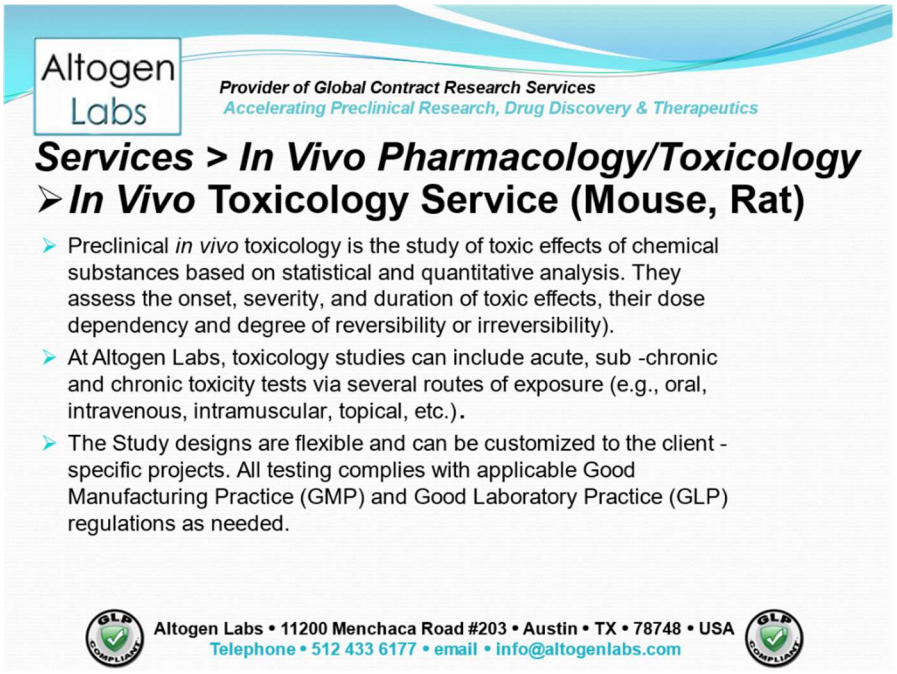

Figure 5. *In vivo* toxicology services available at Altogen Labs for HCC-1806 (Altogen Labs).

Xenograft studies utilizing the HCC-1806 model at Altogen Labs follow a structured, rigorous protocol to ensure reproducibility and high-quality data. Tumor implantation is performed by subcutaneous injection, and once tumors reach a mean volume of 75-125 mm^3, compound dosing is initiated according to customized study designs. Test compounds can be administered through intravenous, intraperitoneal, oral gavage, or intratumoral routes, with treatment schedules tailored to specific research objectives. Tumor growth is closely monitored using digital calipers, and body weight, overall health, and potential adverse effects are systematically recorded throughout the study. Altogen Labs operates under IACUC-approved protocols and maintains full GLP compliance, ensuring ethical animal care and scientific integrity. Additional services include histopathological evaluation, gene expression analysis using RT-PCR, protein biomarker assessments, toxicity profiling, and fluorescence-based imaging for in-depth tumor characterization. This comprehensive approach provides valuable preclinical data to support drug development efforts and enhance our understanding of TNBC biology and therapeutic response.

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Keywords: HCC-1806, breast cancer, xenograft, breast, *in vivo*, cancer, preclinical, research, *in vivo* pharmacology, CDX, PDX, metastatic

Other Available Altogen Labs Validated Xenograft Models:

BT474 Xenograft Model: https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/bt474-xenograft-model/

Hs578T Xenograft Model: https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/hs578t-xenograft-model/

MCF7 Xenograft Model: https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/mcf7-xenograft-model/

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T-47D Xenograft Model: https://altogenlabs.com/xenograft-models/breast-cancer-xenograft/t-47d-xenograft-model/

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