Validated H1155 Xenograft Model:
Subcutaneous And Orthotopic Xenograft Tumor Model

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Lung Cancer Research and The Role of Xenograft Models

Lung cancer is the leading cause of cancer-related mortality worldwide, with non-small cell lung cancer (NSCLC) accounting for a majority of lung cancer cases. NSCLC is a heterogeneous disease comprising subtypes such as adenocarcinoma, squamous cell carcinoma, and large cell carcinoma, each with distinct molecular and histological features. Despite advancements in targeted therapies and immunotherapies, NSCLC often develops resistance to treatment, requiring ongoing research into different treatments in preclinical settings. Xenograft models, in which human lung cancer cells are implanted into immunodeficient mice, serve as important preclinical tools for studying tumor biology and drug response in a physiologically relevant tumor environment. These models allow researchers to evaluate tumor growth dynamics, test the efficacy of new therapeutic agents, and explore molecular mechanisms of metastasis and drug resistance. By bridging the gap between *in vitro* studies and clinical trials, xenografts contribute significantly to the development of precision medicine approaches for NSCLC treatment.

NCI-H1155 Cell Line

The NCI-H1155 (H1155) cell line is a non-small cell lung cancer (NSCLC) model derived from the lung tissue of a 36-year-old White male diagnosed with poorly differentiated carcinoma. Developed and maintained by the National Cancer Institute (NCI), this cell line exhibits an epithelial morphology and is widely used in cancer research. Researchers utilize NCI-H1155 cells to investigate key aspects of lung cancer biology, including tumor initiation, progression, and response to therapeutic agents. The cell line serves as a valuable tool for studying the molecular mechanisms underlying carcinogenesis and drug resistance. Due to its poorly differentiated nature, NCI-H1155 provides insights into aggressive lung cancer phenotypes. It has been instrumental in preclinical studies aimed at identifying novel treatment strategies for NSCLC. Additionally, this cell line is used to explore genetic and epigenetic alterations associated with lung cancer development. Its applications extend to biomarker discovery and personalized medicine approaches in oncology.

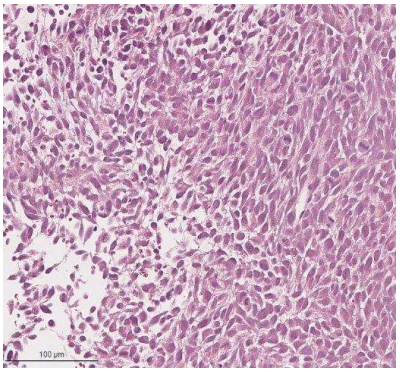

Figure 1. Tumor Histology. H&E stained section of subcutaneously-implanted H1155 tumor (Altogen Labs).

Altogen Labs Validated H1155 Xenograft Model

At Altogen Labs, preclinical xenograft begins by maintaining H1155 cell growth under exponential conditions before injection. Cells are harvested via trypsinization, and viability is assessed using a trypan blue exclusion test, requiring a minimum of 99% viability before proceeding. The cell suspension is then adjusted to the appropriate concentration. NOD/SCID or athymic BALB/C mice, aged 11-12 weeks, receive a single subcutaneous injection in the flank of the hind leg, containing one million H1155 cells mixed with Matrigel in a 120-160 µL volume. Tumor establishment is monitored through palpation up to three times a week, and once detectable, tumors are measured using digital calipers until they reach a volume of 50-150 mm³. Mice are then randomized into predetermined treatment cohorts, and the compound of interest is administered according to the study's treatment schedule. Tumors are measured daily, and mouse

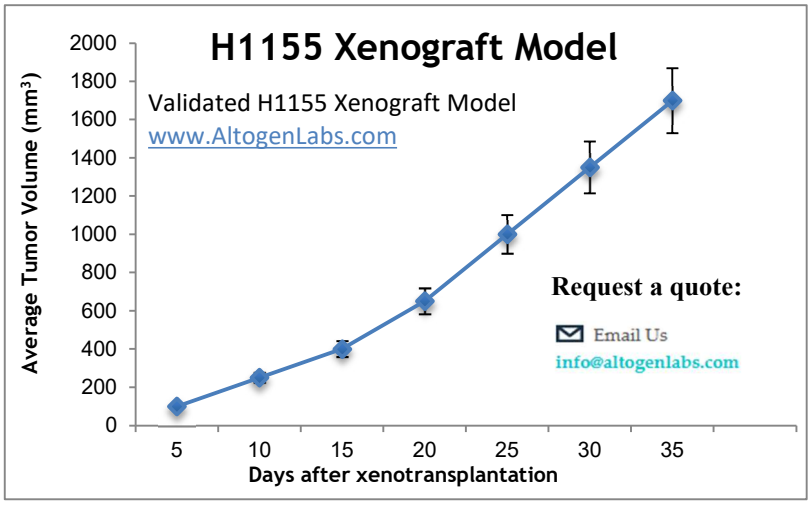

Figure 2. Tumor growth of H1155 carcinoma xenografted *in vivo*, mean values +/- SEM (Altogen Labs).

weights are recorded at least three times per week. When tumors reach a maximum size of 2,000 mm³ or another predetermined limit set by the approved IACUC protocol, animals are euthanized. Tissue collection and necropsy procedures are carried out as outlined in the study's termination protocol. Tumors are excised, weighed, and digitally imaged, followed by a standard gross necropsy with designated tissue collection. Altogen Labs offers additional processing options, including snap-freezing tumors, preserving them in RNA-later reagent, preparing samples for histological analysis, or isolating nucleic acids for genetic studies.

Preclinical NSCLC Research Using Subcutaneous H1155 Xenografts

The subcutaneous H1155 xenograft model involves the implantation of H1155 cancer cells, derived from human non-small cell lung cancer (NSCLC), into immunocompromised mice to study tumor biology and therapeutic responses. These models are established by injecting a suspension of H1155 cells mixed with Matrigel under the skin, allowing for consistent and reproducible tumor growth. The subcutaneous location enables easy monitoring of tumor volume, making it an ideal platform for preclinical longitudinal drug efficacy studies. Additionally, this model provides valuable insights into the molecular mechanisms of NSCLC progression, including tumor heterogeneity and resistance to therapy. Widely used in preclinical research, the H1155 xenograft model supports the evaluation of novel anticancer agents.

Studying NSCLC Progression and Therapy in an Orthotopic Model

The orthotopic H1155 xenograft model involves the implantation of H1155 tumor cells directly into the lungs of immunocompromised mice, providing a physiologically relevant environment for studying non-small cell lung cancer (NSCLC). This model closely mimics the tumor microenvironment, allowing researchers to investigate key aspects of tumor progression, invasion, and metastasis. Unlike subcutaneous models, orthotopic implantation enables the evaluation of lung-specific interactions, including responses to targeted therapies and immunotherapies. Advanced imaging techniques, such as bioluminescence or PET-CT, are often used to monitor tumor growth non-invasively. The model is particularly useful for studying mechanisms of metastasis and drug resistance in NSCLC, offering valuable insights into disease progression.

H1155 Gene Expression and Tumor Biology Insights

H1155 belongs to a group of NSCLC cell lines that do not induce lymphatic vessel formation, distinguishing it from lymphangiogenic counterparts, such as HCC827 or H1993. Genome-wide mRNA expression analysis also revealed significant differences in gene expression between lymphangiogenic and non-lymphangiogenic NSCLC cell lines, with vascular endothelial growth factor C (VEGF-C) identified as a key regulator of lymphangiogenesis. Notably, VEGF-C expression was approximately 50-fold lower in the non-lymphangiogenic group, which includes the H1155 cell, which has researchers suggesting that the H1155 cell line may exhibit distinct tumor progression and possible metastatic behaviors.

Case Study: CXCR4-Targeted Imaging and Therapy

In a study conducted by Azad BB, *et al*., published by *Oncotarget* Journal, researchers investigated the role of the fully human anti-CXCR4 monoclonal antibody (CXCR4-mAb), a protein that helps regulate cell growth, migration, and survival; as both a diagnostic imaging agent and a therapeutic agent in solid tumor models, particularly non-small cell lung cancer (NSCLC) and triple-negative breast cancer (TNBC). The study demonstrated that CXCR4-expressing tumors can be effectively identified using PET imaging. Along with this, researcher found that *in vivo* therapeutic experiments confirmed that CXCR4-mAb significantly reduced tumor growth in CXCR4-overexpressing H1155 xenografts, while low-CXCR4 tumors showed minimal response. The results of this research emphasize the potential of CXCR4-directed precision medicine, offering a non-invasive method to select patients who are most likely to benefit from CXCR4-mAb therapy while mitigating off-target toxicities.

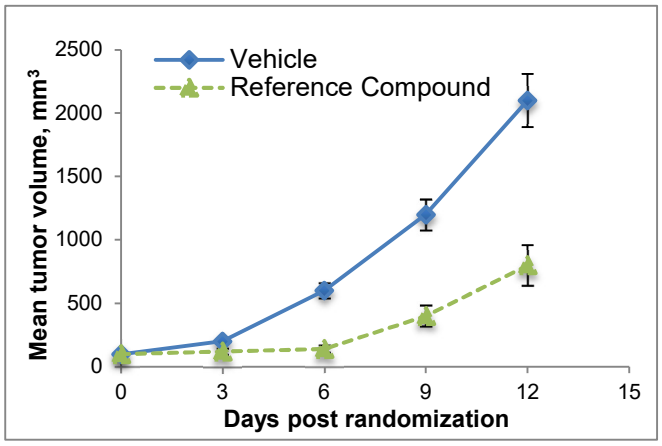

Figure 3. H1155 tumor growth was suppressed when treated with CXCR4-mAb (10 mg/kg).

Taxol Resistance in H1155 Lung Cancer Cells

The H1155 cell line has been extensively studied for its response to taxol, a chemotherapeutic agent that targets microtubules. Research has identified several taxol-sensitizer genes that enhance the cytotoxic effects of taxol when silenced in H1155 cells. These genes were shown to mediate resistance mechanisms, as their knockdown led to a significant decrease in cell viability following taxol treatment. However, further investigation revealed that these sensitization effects were largely specific to H1155 and did not translate to other NSCLC or cancer cell lines, highlighting the unique genetic dependencies of this model.

HCC1155 Subculturing Protocols and Handling Procedures

To ensure optimal cell viability, researchers thaw the H1155 cell vial and initiate culture as soon as it is received. If immediate culture initiation is not possible, the frozen culture is stored in the liquid nitrogen vapor phase, as storage at -70°C would have compromised cell viability. Thawing was carried out by gently agitating the vial in a 37°C water bath for approximately 2 minutes, while taking care to avoid contact between the O-ring and cap with the water to prevent contamination. Once thawed, the vial was removed from the water bath and decontaminated with a 70% ethanol solution. All subsequent procedures were performed under strict aseptic conditions. The thawed cell suspension is transferred into a centrifuge tube containing 9.0 mL of complete culture medium and centrifuged at 125 x g for 5 to 7 minutes. After centrifugation, the cell pellet is resuspended in the recommended culture medium, with careful attention to avoid excessive alkalinity. The suspension is then dispensed into a 25 cm² culture flask, which had been pre-warmed in the incubator for at least 15 minutes to ensure the medium reached a pH of 7.0 to 7.6. Finally, the culture is incubated at 37°C in a 5% CO2 atmosphere to support optimal cell growth.

Researchers maintain cultures by adding fresh medium or replacing the existing medium as needed. When necessary, the cell suspension is centrifuged and resuspended it in fresh medium to establish or propagate cultures. As cell density increases, additional medium was added to support optimal growth. Medium was renewed every 2 to 3 days to ensure the cells had adequate nutrients for sustained culture.

The H1155 xenograft model offers a range of experimental options for cancer research. At Altogen Labs, researchers can assess tumor growth delay (TGD) and tumor growth inhibition (TGI) to evaluate tumor progression and treatment efficacy. Various dosing parameters can be customized, including frequency, duration, and route of administration, with options such as intravenous, intratracheal, continuous infusion, intraperitoneal, intratumoral, oral gavage, topical, intramuscular, subcutaneous, intranasal, and advanced micro-injection or pump-controlled IV techniques. Tumor immunohistochemistry can be performed to analyze molecular markers, while alternative cell engraftment site, such as orthotopic transplantation, tail vein injection, left ventricular injection (for metastasis studies), mammary fat pad, or intraperitoneal injection can expand the scope of research. Additionally, safety toxicology, ADME (absorption, distribution, metabolism, and excretion) analysis, blood chemistry, and survival studies can be conducted, with the option of a comprehensive health observation program. Further evaluations include gross necropsies, histopathology, and toxicity assessments, along with a positive control group treated with cyclophosphamide (30–50 mg/kg) for comparative analysis. Researchers are also able to use fluorescence-based whole-body imaging to visualize tumor dynamics and treatment responses in real time.

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