Validated NCI-H226 Xenograft Model:
Subcutaneous Xenograft Tumor Model

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Xenograft Models in Lung Cancer Therapy Development

Lung cancer remains a critical global health concern, ranking among the foremost causes of cancer-related mortality worldwide. The disease's complexity, characterized by diverse subtypes and substantial molecular heterogeneity, poses significant challenges to the development of effective therapeutic strategies. Lung cancer xenograft models, which involve implanting human lung cancer cells into immunocompromised mice, serve as an essential *in vivo* system for investigating tumor biology and therapeutic responses. These models enable researchers to explore the molecular pathways driving tumor progression and metastasis while assessing the efficacy of novel treatment modalities. By closely replicating human disease conditions, xenograft models facilitate the identification and preclinical evaluation of promising drug candidates, as well as bridging the gap between laboratory research and clinical application.

NCI-H226 Cell Line

The NCI-H226 cell line is derived from the pleural effusion of a patient with mesothelioma. This epithelial cell line is extensively employed in oncological research to investigate tumorigenic processes and assess the cytotoxicity of emerging therapeutic agents. NCI-H226 serves as a critical model for elucidating mechanisms of tumor progression, drug resistance, and evaluating targeted treatment strategies; allowing the model to contribute to the development of more effective therapies for mesothelioma and related lung cancers.

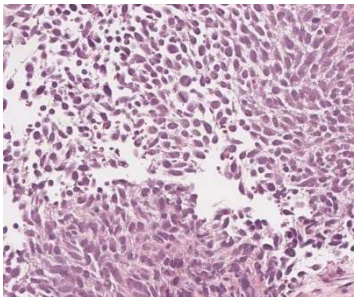

Figure 1. H&E stained section of subcutaneously-implanted NCI-H226 tumor (Altogen Labs).

Altogen Labs Validated NCI-H226 Xenograft Model

At Altogen Labs, in the preclinical xenograft study, NCI-H226 cells are cultured under exponential growth conditions before preparation for injection. Cells are harvested using trypsin-EDTA, assessed for viability, and resuspended at a concentration of 1 × 10^6 cells in 150 µL of a 50% Matrigel solution. Athymic BALB/c immunocompromised mice (10–12 weeks old) receive subcutaneous injections of the cell suspension into the flank of one hind leg. Tumor growth is monitored until tumors reach an average volume of 100–150 mm^3, after which mice are randomized into designated treatment groups and administered the test compound according to the experimental schedule. Tumor size is measured daily, and body weights are recorded 2–3 times per week. The study concludes when tumors reach 2,000 mm^3, followed by necropsy, tumor excision, weighing, digital imaging, and sample preservation via snap freezing or fixation in 10% neutral-buffered formalin for histological analysis.

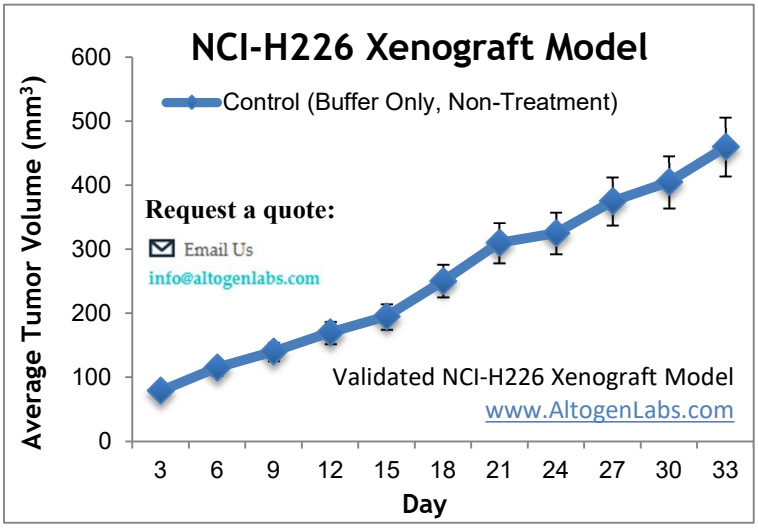

Figure 2. Tumor growth of NCI-H226 cells as subcutaneous xenograft *in vivo*, tumor volume, mean values +/- SEM (Altogen Labs).

Subcutaneous NCI-H226 Lung Cancer Xenograft Model

The subcutaneous NCI-H226 lung cancer xenograft model is a widely utilized preclinical platform for studying tumor biology and evaluating therapeutic interventions in thoracic malignancies. In this model, NCI-H226 cells are implanted subcutaneously into immunodeficient mice, enabling the formation of solid tumors that mimic key aspects of human disease. This model facilitates the investigation of tumor growth kinetics, angiogenesis, and metastatic potential while providing a controlled environment to assess the efficacy and toxicity of novel anticancer agents. Additionally, the subcutaneous implantation allows for easy tumor monitoring and measurement, making it a valuable tool for preclinical drug screening and mechanistic studies.

Case Study: Tastin Promotes NSCLC Progression via ErbB4-Mediated PI3K/AKT and ERK1/2 Activation

In a study by Yue A. *et al*., published by *Experimental Biology and Medicine* journal, researchers investigated the role of tastin in non-small-cell lung cancer (NSCLC) progression using NCI-H226 cells. Tastin was found to be significantly overexpressed in NSCLC tissues, correlating with poor patient prognosis. Silencing tastin in NCI-H226 cells led to reduced proliferation, migration, and invasion capabilities. Mechanistically, tastin interacts with ErbB4, activating the PI3K/AKT and ERK1/2 signaling pathways that drive tumor growth. *In vivo* experiments with xenograft models confirmed that tastin knockdown suppressed tumor development. These findings highlight tastin as a potential therapeutic target for NSCLC. Overall, the study emphasizes the critical role of tastin in enhancing the malignancy of NCI-H226 lung cancer cells.

Additional Case Study: Inhibition of FGF/FGFR Pathway in NCI-H226 Mesothelioma Cells

Another study conducted by Blackwell C. *et* al, published by *Oncotarget* journal, researchers explored the efficacy of GSK3052230, an FGF ligand trap, in inhibiting tumor growth in mesothelioma models. NCI-H226 mesothelioma cells, characterized by high FGF2 and FGFR1 expression, exhibited significant sensitivity to GSK3052230 treatment. *In vivo*, GSK3052230 notably suppressed tumor growth in NCI-H226 xenograft models, demonstrating dose-dependent tumor growth inhibition. The treatment effectively reduced MAPK pathway signaling, as evidenced by decreased phospho-ERK and phospho-S6 levels in both *in vitro* and *in vivo* settings. Additionally, GSK3052230 led to a significant reduction in tumor vessel density, indicating its impact on angiogenesis. The observed antitumor effects highlight the dependency of NCI-H226 xenografts on FGF/FGFR autocrine signaling. These findings support further clinical evaluation of GSK3052230 as a promising therapeutic strategy for mesothelioma.

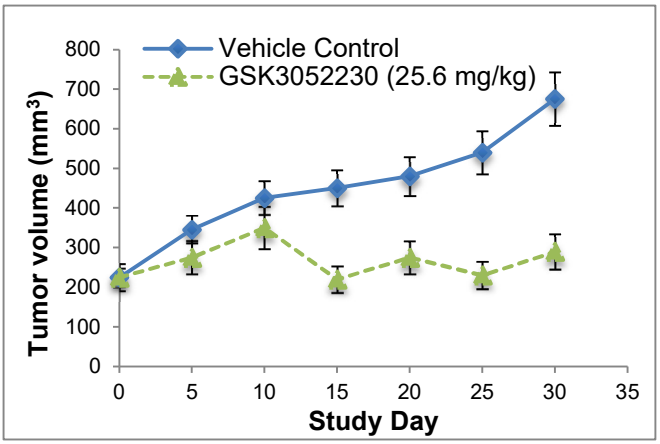

Figure 3. Administering GSK3052230 (25.6 mg/kg) to NCI-H226 xenograft tumors led to reduced tumor size.

EIF4G1 Regulates NCI-H226 Growth

EIF4G1 was found to be highly expressed in LSCC tissues and cell lines, including NCI-H226, and its overexpression correlated with poor patient prognosis. Functional assays demonstrated that silencing EIF4G1 in NCI-H226 cells significantly inhibited proliferation, colony formation, and cell cycle progression by inducing G1 phase arrest. Western blot analysis revealed that EIF4G1 regulates LSCC cell growth through the AKT/mTOR and Cyclin D1 pathways. *In vivo*, EIF4G1 knockdown suppressed tumor growth in xenograft models, supporting its role in LSCC tumorigenesis. This suggest that EIF4G1 acts as a key regulator of LSCC progression and could serve as a prognostic marker and therapeutic target, particularly in NCI-H226 cells. Further research is needed to explore the clinical potential of targeting EIF4G1 in LSCC treatment.

The NCI-H226 xenograft model offers a versatile platform for comprehensive preclinical evaluation of therapeutic agents targeting lung cancer. At Altogen Labs, key experiments include Tumor Growth Delay (TGD) and Tumor Growth Inhibition (TGI), allowing precise assessment of treatment efficacy. Flexible dosing regimens can be tailored in terms of frequency, duration, and administration routes, including intravenous, intratracheal, continuous infusion, intraperitoneal, intratumoral, oral gavage, and advanced micro-injection techniques. The model supports alternative cell engraftment sites, such as orthotopic transplantation, tail vein, or left ventricular injections for metastasis studies, enhancing its applicability to diverse research objectives. Additional analyses encompass tumor immunohistochemistry, blood chemistry, toxicity and survival assessments, gross necropsy, and histopathology. Positive control groups using cyclophosphamide (50 mg/kg,

intramuscularly) can be incorporated to benchmark therapeutic responses. Moreover, lipid distribution, metabolic profiling, and fluorescence-based whole-body imaging further expand the model's capacity for detailed mechanistic and efficacy studies. The flexibility of the NCI-H226 xenograft model allows for the exploration of combination therapies, testing multiple drugs or treatment regimens simultaneously. This approach enhances the potential for identifying synergistic effects that could improve treatment outcomes in lung cancer.

References:

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NCI-H226 Xenograft Model. https://altogenlabs.com/xenograft-models/lung-cancer-xenograft/nci-h226-xenograft-model/

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Keywords: NCI-H226, H226, xenograft, *in vivo*, cancer, preclinical, research, *in vivo* pharmacology

Other Available Altogen Labs Validated Xenograft Models:

A549 Xenograft Model: https://altogenlabs.com/xenograft-models/lung-cancer-xenograft/a549-xenograft-model/

Calu-3 Xenograft Model: https://altogenlabs.com/xenograft-models/lung-cancer-xenograft/calu-3-xenograft-model/

Calu-6 Xenograft Model: https://altogenlabs.com/xenograft-models/lung-cancer-xenograft/calu-6-xenograft-model/

NCI-H460 Xenograft Model: https://altogenlabs.com/xenograft-models/lung-cancer-xenograft/h460-xenograft-model/

NCI-H1975 Xenograft Model: https://altogenlabs.com/xenograft-models/lung-cancer-xenograft/nci-h1975-xenograft-model/

NCI-H1155 Xenograft Model: https://altogenlabs.com/xenograft-models/lung-cancer-xenograft/h1155-xenograft-model/