Validated HCC827 Xenograft Model:
Subcutaneous And Metastatic Xenograft Tumor Model

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Lung Cancer and Non-Small Cell Lung Cancer (NSCLC) Xenograft Models in Cancer Research

Lung cancer remains one of the leading causes of cancer-related deaths worldwide, and despite advancements in early detection and treatment, the prognosis for NSCLC patients remains poor, primarily due to late-stage diagnoses and the development of resistance to therapies. Xenograft models, in which human cancer cells are implanted into immunocompromised mice, have become invaluable tools in the study of NSCLC. These models allow for the evaluation of tumor growth, metastasis, and response to novel therapeutic agents in a more biologically relevant context. Specifically, NSCLC xenografts provide a platform to investigate the molecular underpinnings of the disease, including the role of key mutations and signaling pathways that drive tumorigenesis. As these models closely replicate human disease, they are critical for preclinical testing of potential treatments and for developing personalized cancer therapies. Consequently, NSCLC xenografts are essential in advancing the understanding and treatment of lung cancer.

HCC827 Cell Line

The HCC827 cell line is an epithelial-derived culture established from a lung adenocarcinoma tumor of a 39-year-old female patient. This cell line is characterized by its epithelial morphology and is widely used as an *in vitro* model for studying the molecular mechanisms driving lung cancer, specifically adenocarcinoma. HCC827 cells harbor an EGFR exon 19 deletion mutation, making them particularly sensitive to EGFR-targeted therapies, and they exhibit high levels of EGFR expression. The cell line is commonly utilized in drug screening, resistance studies, and therapeutic research, offering valuable insights into the development of targeted treatments for NSCLC. Furthermore, HCC827 cells are frequently employed in preclinical studies to explore EGFR signaling pathways, tumor progression, and potential therapeutic agents. Their strong growth characteristics and clinical relevance make HCC827 cells a crucial resource for advancing lung cancer research.

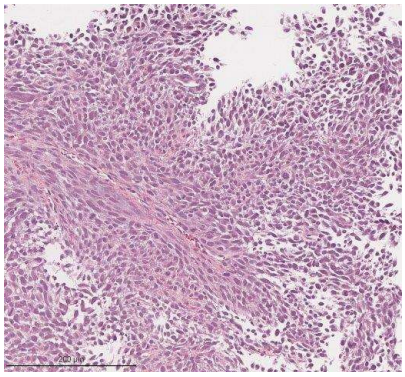

Figure 1. Tumor Histology. H&E stained section of subcutaneously-implanted HCC827 tumor (Altogen Labs).

Altogen Labs Validated HCC827 Xenograft Model

HCC827 cells are harvested during the exponential growth phase, pelleted by centrifugation at 10 minutes, and resuspended in sterile serum-free medium with 50% Matrigel. A 100 µL suspension containing 2 to 5 × 10^6 cells is subcutaneously implanted into the back left flank of immunocompromised mice. Tumors are allowed to grow to 150–200 mm^3 before treatment. Tumor growth is monitored biweekly using digital calipers. Mice are randomized into control and treatment groups, and tumor volume, body weight, and general health are recorded. Treatment response is assessed by tumor size reduction, imaging analyses, and post-mortem histological evaluations of tumor architecture, cell viability, and molecular markers. Statistical analysis is performed to compare tumor growth and response between treatment and control groups. All experimental procedures adhere to institutional animal care and use guidelines to ensure ethical conduct and animal welfare in accordance with IACUC.

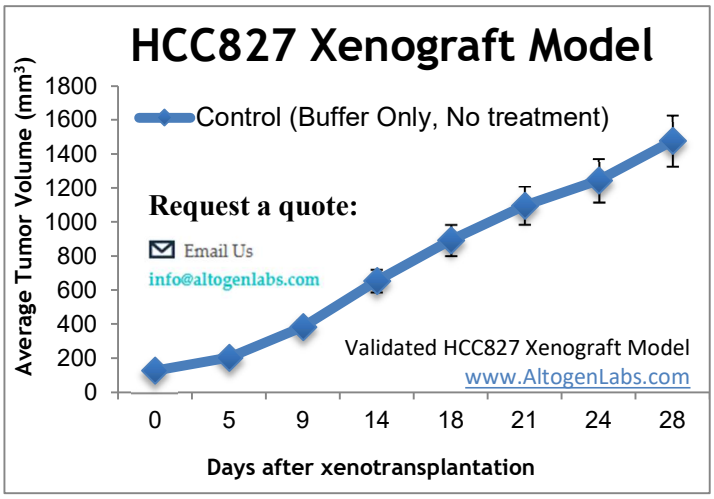

Figure 2. HCC827 adenocarcinoma xenografted in immunocompromised mice, mean values +/- SEM.

Case Study: Oxymatrine Targets EGFR Signaling to Suppress NSCLC Growth in HCC827 Cells

A study conducted by Li W. et al., published in *Cancer Medicine* journal, examines the antitumor potential of oxymatrine, focusing on its effects on non-small cell lung cancer (NSCLC) and its suppression of the epidermal growth factor receptor (EGFR) signaling pathway. Oxymatrine was shown to inhibit EGFR activation and its downstream targets, including Akt and cyclin D1, leading to significant G0/G1 cell cycle arrest in HCC827 cells. *In vivo* experiments with HCC827 xenograft mouse models demonstrated that oxymatrine substantially suppressed tumor growth without observable toxicity. Mechanistically, oxymatrine's inhibition of Akt signaling was critical, as exogenous Akt expression rescued cyclin D1 levels and reversed the cell cycle arrest. This study highlights HCC827 as a model for understanding EGFR-targeted therapies and underscores oxymatrine's potential as a novel therapeutic agent for NSCLC.

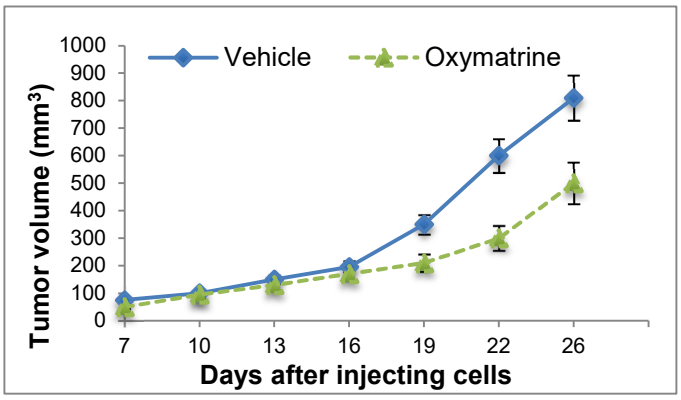

Figure 3. Treatment with oxymatrine (30 μmol/L) resulted in a significant inhibition in the growth of HCC827 xenograft tumors.

Additional Case Study: Targeting HER3 to Enhance EGFR Inhibitor Efficacy in HCC827 NSCLC Models

Another study by Wu Y, *et al.*, published by *Molecular Cancer Therapeutics* journal explores the use of EZN-3920, a locked nucleic acid-based antisense oligonucleotide, to downregulate HER3 and enhance the effectiveness of EGFR and HER2 inhibitors in cancer treatment. EZN-3920 specifically inhibited HER3 mRNA and protein expression, resulting in reduced phosphorylation of HER3 and AKT, which are key drivers of tumor growth and survival. In xenograft models using HCC827 cells, a model for EGFR-overexpressing non-small cell lung cancer (NSCLC), EZN-3920 significantly suppressed tumor growth both alone and in combination with EGFR inhibitors like gefitinib. Notably, EZN-3920 also showed efficacy in gefitinib-resistant HCC827 cells, demonstrating its potential to overcome resistance mechanisms involving HER3. These findings underscore the importance of HER3 in NSCLC and highlight EZN-3920 as a promising therapeutic strategy for cancers reliant on HER3-mediated signaling pathways.

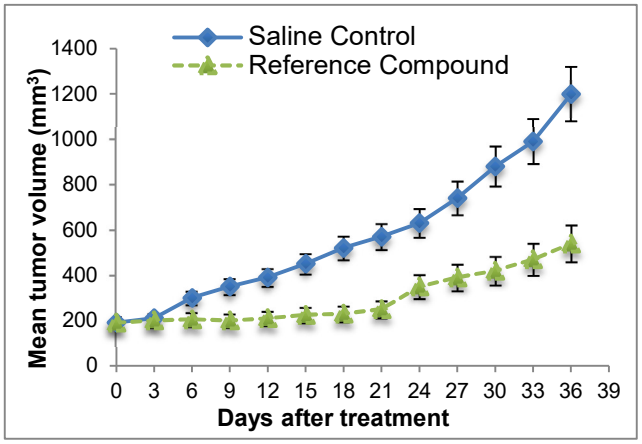

Figure 4. Treatment with a reference compound (30 mg/kg) led to a suppression of the growth of HCC827 xenograft tumors.

HCC827 Subculturing Protocols and Handling Procedures

In the protocols for HCC827, the volumes specified are for a 75 cm² culture flask, and adjustments to the dissociation medium volume are made accordingly for other culture vessel sizes. Researchers begin by removing and discarding the culture medium, then briefly rinsing the cell layer with either a 0.25% (w/v) Trypsin-0.53 mM EDTA solution or Dulbecco's Phosphate Buffered Saline (D-PBS) to eliminate any serum traces containing trypsin inhibitor. Next, 1.0 to 3.0 mL of Trypsin-EDTA solution is added to the flask, and cells are monitored under an inverted microscope until the cell layer disperses, typically within 5 to 15 minutes. To prevent clumping, the flask is not agitated by shaking or tapping during this process, and if cells are difficult to detach, the flask is placed at 37°C to facilitate detachment. Following cell dissociation, 6.0 to 8.0 mL of complete growth medium is added, and cells are gently aspirated using a pipette. The cell suspension is then transferred to a centrifuge tube and spun at approximately 125 x g for 5 to 10 minutes. After discarding the supernatant, the cell pellet is resuspended in fresh growth medium and aliquots of the suspension are transferred to new culture vessels. A recommended inoculum of 5 x 10^3 to 7 x 10^3 viable cells/cm² is used, and the cultures are incubated at 37°C, maintaining a cell concentration between 3 x 10^4 and 5 x 10^4 cells/cm². A sub-cultivation ratio of 1:4 to 1:6 is suggested, with medium renewal every 2 to 3 days. It is essential to carefully monitor cell growth to ensure that the cultures remain healthy and at the desired confluence. Any signs of contamination should be addressed immediately to maintain optimal culture conditions.

To maintain the highest HCC827 cell viability, researchers thawed the vial and initiated culture as soon as the cells were received. If continued storage was necessary, the frozen culture was stored in the liquid nitrogen vapor phase, as storage at -70°C would compromise cell viability. The vial was thawed rapidly (within approximately 2 minutes) by gentle agitation in a 37°C water bath, ensuring that the O-ring and cap remained above the water to minimize the risk of contamination. After thawing, the vial was removed from the water bath and decontaminated with 70% ethanol, with all subsequent steps performed under strict aseptic conditions. The vial contents were transferred to a centrifuge tube containing 9.0 mL of complete culture medium and centrifuged at 125 x g for 5 to 10 minutes. The cell pellet was then resuspended in the recommended complete medium and dispensed into a 25 cm^2 or 75 cm^2 culture flask. To prevent excessive alkalinity during recovery, the culture vessel containing the complete growth medium was pre-incubated for at least 15 minutes, allowing the medium to equilibrate to the optimal pH range of 7.0 to 7.6 before adding the cells. After plating, the cells were carefully monitored for confluency and any signs of contamination. The cultures were then incubated at 37°C in a suitable incubator with a 5% CO2 atmosphere, as recommended for the specific growth medium. This careful procedure ensures that the cells recover efficiently and retain their viability for experimental use.

Studying Lung Cancer with HCC827 Subcutaneous Models

Subcutaneous HCC827 models are commonly used in preclinical studies to evaluate the efficacy of targeted therapies for non-small cell lung cancer (NSCLC). In this model, HCC827 cells, which harbor an EGFR exon 19 deletion mutation, are implanted subcutaneously into immunocompromised mice, typically in the flank area. The subcutaneous HCC827 model also provides valuable insights into the effectiveness of therapies targeting EGFR-driven tumors, given the cell line's sensitivity to EGFR inhibitors like erlotinib. Tumor progression is monitored regularly using digital calipers, and treatment effects are evaluated based on tumor volume reduction, changes in body weight, and general health of the mice. This model can also be utilized to study resistance mechanisms that may emerge with long-term therapy, helping to guide the development of next-generation therapies. In addition to tumor size, post-mortem histological analysis is conducted to examine tumor architecture, cellular viability, and molecular markers associated with therapy response. The tumor microenvironment is also analyzed to assess immune cell infiltration and vascular changes induced by treatment.

NSCLC Metastasis with HCC827 Preclinical Models

Metastatic HCC827 models are crucial for investigating the spread and progression of non-small cell lung cancer (NSCLC) driven by EGFR mutations, particularly exon 19 deletions. These models are typically established by injecting HCC827 cells intravenously, allowing the tumor cells to circulate and establish secondary growths in distant organs, such as the lungs, liver, or lymph nodes. Metastatic HCC827 models are valuable for understanding the mechanisms of tumor invasion and organ-specific metastasis in EGFR-mutant lung adenocarcinoma. They also serve as powerful tools for evaluating therapies targeting metastatic spread, including EGFR inhibitors, combination therapies, and potential novel agents. The models closely replicate the metastatic progression seen in advanced-stage NSCLC and provide insights into how tumors adapt to treatment. Advanced imaging techniques like bioluminescence and MRI are often employed to track metastatic lesions in real-time, offering a non-invasive approach for monitoring tumor burden. Histopathological analysis of metastatic sites enables the identification of cellular and molecular changes, shedding light on how therapies impact tumor progression. These models are particularly useful for preclinical studies focused on identifying novel treatment strategies and understanding the underlying biology of metastatic NSCLC.

Targeting EGFR in Lung Cancer with HCC827 Cells

The HCC827 cell line, derived from a lung adenocarcinoma, is characterized by its oncogene addiction to the epidermal growth factor receptor (EGFR). Specifically, it harbors a deletion mutation in exon 19 (Del E746-A750), a common sensitizing mutation associated with non-small cell lung cancer (NSCLC). This mutation leads to constitutive activation of the EGFR tyrosine kinase domain, driving uncontrolled proliferation and survival signaling. HCC827 cells are particularly sensitive to EGFR tyrosine kinase inhibitors (TKIs) like gefitinib, making them a widely used model for studying TKI efficacy and resistance mechanisms. The development of acquired resistance in this cell line is often linked to secondary mutations, such as T790M in exon 20, or alternative pathway activations, such as MET amplification. This cell line has been instrumental in exploring combination therapies and innovative strategies to overcome TKI resistance, including RNA-mediated and multitargeted approaches.

The HCC827 xenograft model offers a valuable platform for preclinical studies aimed at evaluating therapeutic agents targeting EGFR-driven lung adenocarcinoma. At Altogen Labs, researchers examine key experimental endpoints, such as Tumor Growth Delay (TGD) and Tumor Growth Inhibition (TGI), which can provide crucial insights into the efficacy of treatment regimens. The HCC827 cell line also supports a variety of dosing methods, including intraperitoneal, intravenous, and oral gavage administration, allowing for flexible and tailored therapeutic protocols. For more detailed

investigation, additional techniques such as imaging and tumor site-specific injections can be employed. Comprehensive analyses, including tumor immunohistochemistry, molecular profiling, survival assessments, and histopathological evaluations, ensure a thorough assessment of therapeutic responses. The model also enables the evaluation of immune cell infiltration, angiogenesis, and changes in the tumor microenvironment. The HCC827 model is especially effective in studying the impact of EGFR-targeted therapies and exploring mechanisms of resistance, making it an essential tool in lung cancer research.

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Keywords: HCC827, xenograft, *in vivo*, cancer, preclinical, research, *in vivo* pharmacology, metastatic

Other Available Validated Altogen Labs 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/

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