Brain Cancer Xenograft Models:

Subcutaneous, Orthotopic, And Metastatic Xenograft Tumor Models

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Overcoming Translational Challenges in Brain Tumor Research through *In Vivo* Modeling

Brain cancer is among the most aggressive and treatment-resistant forms of malignancy, with glioblastoma constituting the most prevalent and lethal subtype. Characterized by rapid progression, diffuse invasion, and marked molecular heterogeneity, brain tumors present significant clinical challenges and are associated with poor patient outcomes. Although advances in genomic profiling have identified key mutations and signaling pathways involved in tumor initiation and progression, such as alterations in EGFR, IDH1, and TP53, translating these insights into effective therapies remains difficult. A major obstacle is the limited availability of preclinical models that faithfully reproduce the structural, genetic, and microenvironmental complexities of human brain tumors. Xenograft and allograft models serve as essential platforms for studying tumor biology and therapeutic response *in vivo*. Cell line-derived xenografts and patient-derived xenografts preserve crucial aspects of tumor architecture and molecular features, particularly when implanted orthotopically into the brain. Allograft models offer complementary insights by enabling immune-competent evaluations of tumor-immune dynamics. The use of these models is driven by the need for physiologically relevant systems that can support therapeutic testing, biomarker validation, and investigation of resistance mechanisms. Incorporating these models into cancer research strengthens the translational relevance of preclinical data, enhances understanding of tumor behavior, and advances efforts to develop more effective treatment strategies for brain cancer.

Subcutaneous Brain Cancer Xenograft Models

Subcutaneous xenograft transplantation remains a foundational methodology in preclinical cancer research, offering a reproducible and scalable platform for evaluating tumor growth kinetics, therapeutic efficacy, and biomarker dynamics *in vivo*. This approach involves the implantation of human cancer cells into the subcutaneous space of immunodeficient hosts, enabling real-time assessment of tumor progression and treatment response within a controlled microenvironment. Despite its anatomical divergence from orthotopic tumor sites, the subcutaneous model provides significant advantages in terms of tumor accessibility, ease of measurement, and compatibility with high-throughput pharmacological screening. It has been particularly valuable in the early-phase evaluation of novel therapeutic agents and mechanistic studies involving tumor proliferation, angiogenesis, and apoptosis.

A substantial body of literature supports the utility of subcutaneous models for investigating brain cancer biology using established glioblastoma and neuroblastoma cell lines. Glioma-derived lines such as A172, LN229, SF268, SF295, SF539, SNB19, SNB75, U87, U118, and U251 MG have demonstrated robust and consistent tumor formation when implanted subcutaneously, allowing for longitudinal monitoring of tumor volume and response to standard-of-care or experimental therapeutics. These models have facilitated the delineation of key oncogenic pathways, including PI3K/AKT, MAPK/ERK, and p53 signaling, and have been instrumental in identifying candidate compounds with antitumor activity. Although the absence of the blood-brain barrier and brain-specific microenvironment limits their ability to fully replicate intracranial tumor physiology, subcutaneous glioma xenografts provide valuable insight into drug pharmacodynamics and resistance mechanisms, particularly in the context of targeted therapies and radiation sensitization.

Similarly, the SKNAS neuroblastoma line has been widely utilized in subcutaneous xenograft studies due to its high tumorigenic potential and representative genetic features, including MYCN amplification and ALK mutations. These models support investigations into neuroblastoma-specific vulnerabilities and have served as benchmarks for evaluating small molecule inhibitors, immunotherapies, and combination regimens. Comparative analyses across cell lines reveal variability in engraftment rates, tumor latency, and vascularization, emphasizing the importance of cell line selection based on molecular subtype and experimental objective.

Current research continues to refine subcutaneous xenograft models through the incorporation of luciferase reporters for bioluminescent imaging, co-implantation with stromal or immune components, and the use of humanized host systems to better approximate human tumor-immune interactions. These enhancements aim to overcome traditional limitations while preserving the model's strengths in throughput and quantitative assessment. As an integral component of the preclinical research pipeline, subcutaneous transplantation of human brain and neuroblastoma cell lines advances the field by supporting robust, scalable, and mechanistically informative investigations that complement more anatomically and immunologically complex models.

Orthotopic Brain Cancer Xenograft Models

Orthotopic xenograft transplantation represents a critical advancement in preclinical cancer modeling by enabling the implantation of human tumor cells directly into the anatomical site of origin, thereby preserving key microenvironmental and spatial features of native tumor biology. In the context of brain cancer, this approach allows for the engraftment of glioblastoma and neuroblastoma cell lines into the cerebral parenchyma, offering a more physiologically relevant platform for studying tumor progression, invasion, angiogenesis, and response to therapeutic agents. Unlike subcutaneous models, orthotopic xenografts recapitulate the unique characteristics of the central nervous system, including interactions with the blood-brain barrier, local immune modulation, and perivascular invasion, all of which critically influence disease course and treatment outcomes.

Extensive research has demonstrated the utility of orthotopic models using established glioma cell lines such as A172, LN229, SNB-19, U87, U118, and U251 MG. These cell lines exhibit differential growth kinetics, invasive potential, and treatment responsiveness when introduced into the intracranial compartment, reflecting inherent biological diversity and providing a robust framework for comparative analyses. Studies have utilized bioluminescence imaging, magnetic resonance imaging, and histopathological evaluation to monitor tumor progression and assess therapeutic efficacy in these models. For example, U87 and U251 MG have been frequently employed due to their reliable engraftment and predictable growth patterns, while LN229 and A172 have facilitated investigations into specific molecular pathways, such as p53-mediated apoptosis and EGFR signaling. Moreover, orthotopic transplantation of the SK-NA-S neuroblastoma line into the central nervous system has enabled the study of metastatic neuroblastoma and its interaction with neural tissue, further broadening the application of this model.

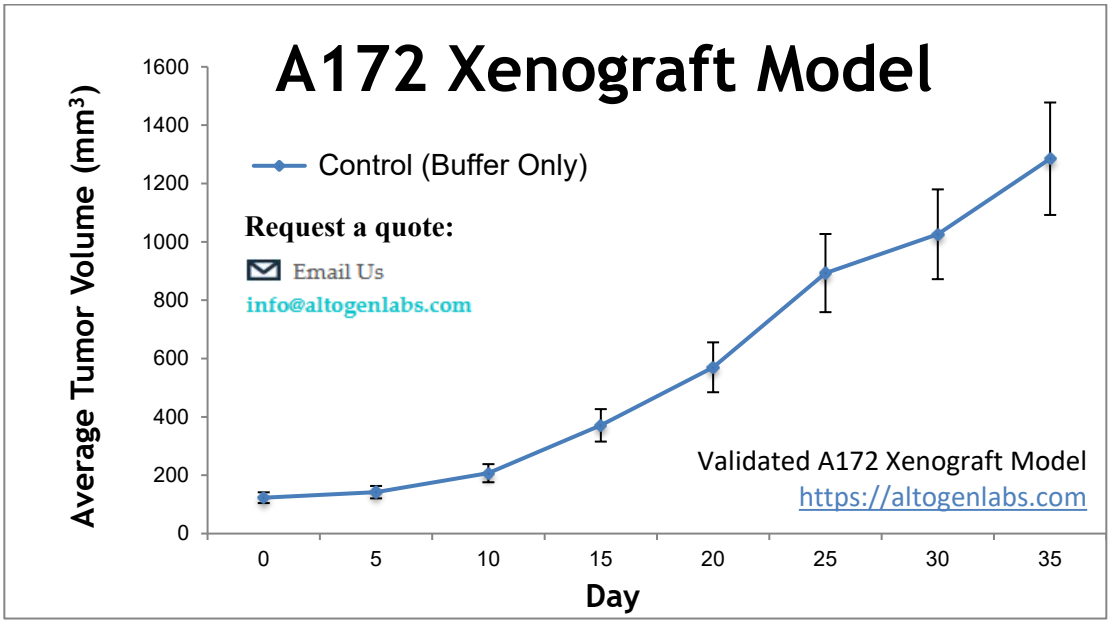
Recent advancements in orthotopic modeling include the use of patient-derived cells, genetically engineered lines with fluorescent or luminescent markers, and co-transplantation strategies incorporating stromal or immune components. These enhancements have improved the fidelity of tumor architecture, enabled real-time monitoring of tumor dynamics, and allowed for more accurate assessments of therapeutic response. Despite the technical complexity of intracranial transplantation and the requirement for specialized surgical techniques and imaging modalities, orthotopic xenografts offer unparalleled advantages in modeling clinically relevant disease features. They provide critical insights into the mechanisms of tumor infiltration, therapeutic resistance, and recurrence, which are often underrepresented in other *in vivo* systems. As such, orthotopic xenograft transplantation remains an indispensable strategy for advancing translational research in neuro-oncology and for developing interventions that more effectively target the biological realities of brain cancer.

Metastatic Brain Cancer Xenograft Models

Metastatic xenograft and allograft transplantation models are essential in cancer research for investigating the mechanisms that drive tumor dissemination, organ-specific colonization, and resistance to therapy. These models simulate the metastatic process *in vivo*, allowing researchers to evaluate potential therapeutics and identify molecular targets that contribute to disease progression. In glioblastoma studies, the LN229 cell line has been used in experimental metastasis models via intravenous or intracardiac injection to assess the formation of secondary lesions in distant organs. Although extracranial metastasis is rare in glioblastoma patients, these models help uncover mechanisms of invasion and systemic spread. The SK-NA-S neuroblastoma cell line has been extensively applied in both spontaneous and experimental metastasis models, particularly through orthotopic implantation into adrenal or paraspinal regions, which results in dissemination to the liver, bone marrow, and brain, closely reflecting the clinical patterns of metastatic neuroblastoma.

Recent advances have improved the utility of metastatic models by incorporating bioluminescent imaging, patient-derived xenografts, and genetically engineered tumor cells. These enhancements allow for precise tracking of tumor cell migration, early detection of micrometastases, and real-time evaluation of treatment efficacy. Additionally, allograft models in immunocompetent hosts offer important insights into the role of immune responses in metastasis and support the preclinical assessment of immunotherapies. Although technically demanding and often variable in metastatic efficiency, these models remain critical for understanding the biology of advanced disease and for guiding the development of therapies aimed at preventing or eliminating metastatic cancer.

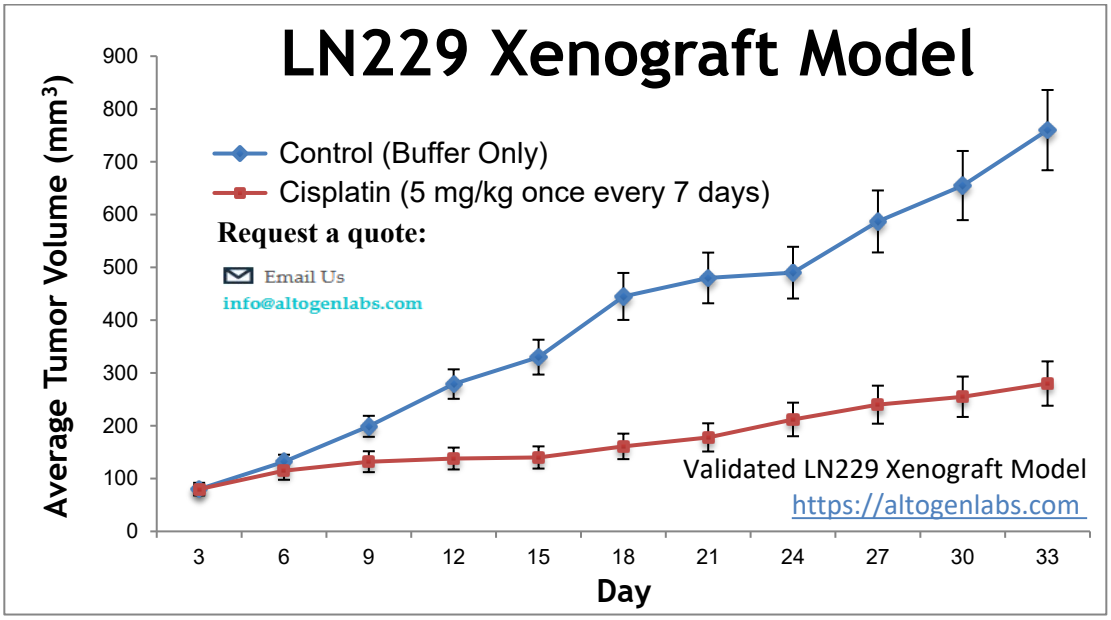
Characterization and Preclinical Application of the A172 Xenograft Model in Brain Cancer Research



The A172 glioblastoma xenograft model, validated and provided by Altogen Labs, serves as a robust and reproducible system for preclinical evaluation of novel therapeutic agents targeting glioblastoma multiforme (GBM), an aggressive and highly treatment-resistant brain cancer. Derived from the brain tissue of a 53-year-old male patient, A172 cells exhibit a mesenchymal gene expression profile and secrete pro-angiogenic factors such as VEGF, FGF2(b), and TGF-β1, contributing to tumor vascularization and progression. These characteristics, along with the expression of CD90, CD105, and tenascin C, make the A172 model highly relevant for studying tumor invasiveness, angiogenesis, and therapeutic resistance. Altogen Labs supports both subcutaneous and orthotopic A172 xenograft models. The subcutaneous model enables accessible monitoring of tumor growth and therapeutic response, while the orthotopic model more accurately replicates the native brain microenvironment, facilitating translational studies that assess blood-brain barrier penetration, immune infiltration, and tumor progression.

Altogen Labs implements rigorous quality control in xenograft studies using athymic BALB/c nude mice. Cells are cultured under aseptic conditions and prepared for injection following viability assessments. Tumor growth is tracked with precision, and experimental endpoints such as Tumor Growth Inhibition (TGI) and Tumor Growth Delay (TGD) are systematically evaluated. Advanced endpoints including histopathology, bioluminescence imaging, immunohistochemistry, and molecular profiling enable a comprehensive understanding of tumor biology and treatment efficacy. Recent studies have demonstrated the utility of the A172 model in evaluating agents such as PSPD3R, which induces autophagy and inhibits tumor proliferation via the miR-20b-5p/Atg7 pathway, and bortezomib, whose efficacy is enhanced by PLK4 inhibition through modulation of the PTEN/PI3K/AKT/mTOR pathway. Additionally, investigations into HSF1-mediated therapy resistance and 3D chromatin architecture, including EGFR amplification and neo-TAD formation, have further established the value of this model for glioblastoma research.

The A172 xenograft model enables flexible therapeutic evaluations through multiple dosing strategies, including intraperitoneal, intravenous, and intracranial administration. It also supports the assessment of pharmacokinetics, systemic toxicity, and molecular markers associated with glioblastoma progression. This model is particularly valuable in early- to mid-stage drug development, offering a clinically relevant system for assessing both cytostatic and cytotoxic responses. Altogen Labs offers this validated model as part of its comprehensive suite of preclinical oncology services. For detailed information, the A172 xenograft model can be accessed on the Altogen Labs website at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/brain-cancer-xenograft/a172-xenograft-model/. The complete technical PDF describing the A172 model is available at https://altogenlabs.com/A172XenograftModel.pdf.



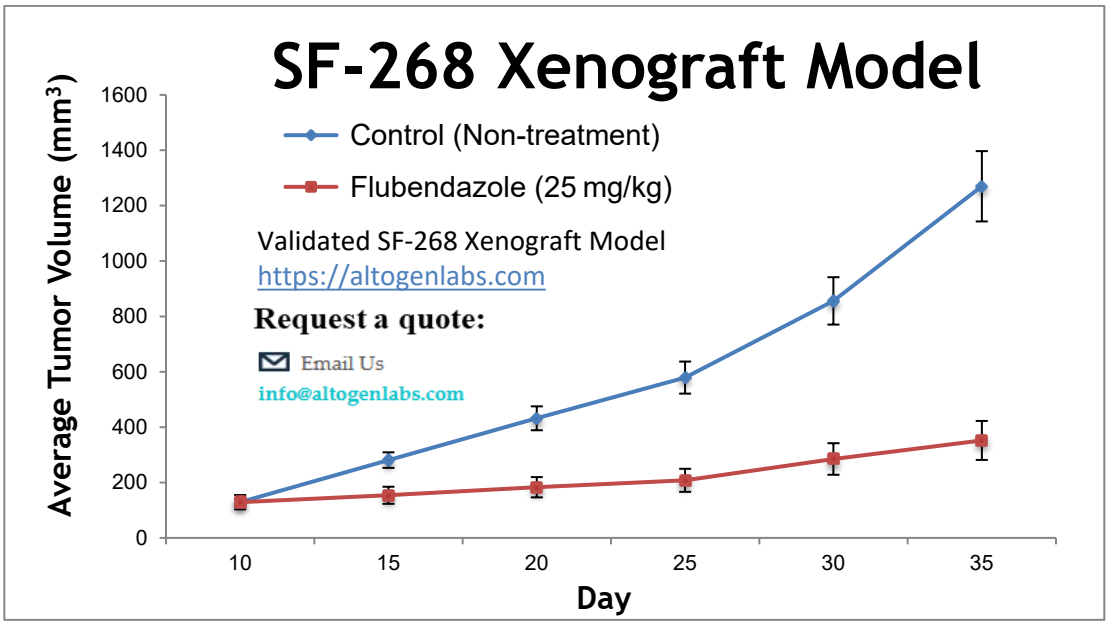
The LN229 glioblastoma xenograft model, validated and provided by Altogen Labs, serves as a clinically relevant and adaptable platform for preclinical evaluation of therapeutic agents targeting brain cancer. Derived from the frontal parieto-occipital cortex of a 60-year-old female glioblastoma patient, the LN229 cell line exhibits epithelial-like morphology and retains key genetic and phenotypic characteristics of the original tumor. This cell line has been extensively utilized in oncology research to investigate glioblastoma progression, therapy resistance, and tumor microenvironment interactions. The LN229 model is available in subcutaneous, orthotopic, and metastatic formats, allowing researchers to assess a wide range of tumor behaviors, including localized growth, brain infiltration, and systemic dissemination.

At Altogen Labs, xenograft studies are conducted using immunodeficient NOD.CB17-Prkdc or BALB/C nude mice. For subcutaneous studies, one million viable LN229 cells suspended in a 50 percent Matrigel solution are injected into the hind leg. Tumors are monitored until they reach a predefined size range, after which animals are randomized into treatment cohorts. Therapeutic interventions are administered according to client-specified dosing schedules. Upon study completion, tumors are excised, weighed, and subjected to downstream analyses such as histology, RNA preservation, and protein expression profiling. The orthotopic model involves intracranial implantation of LN229 cells, allowing researchers to evaluate drug efficacy in the context of the blood-brain barrier and brain-specific tumor microenvironment. The metastatic model involves intravenous injection to study the dissemination of glioblastoma cells to secondary organs, thereby providing insights into metastatic progression and therapeutic response.

This model has demonstrated utility in evaluating novel therapeutic compounds. For example, Prodigiosin has shown efficacy in reducing tumor growth by modulating the KIAA1524 and PP2A signaling pathway, leading to p53-mediated cell cycle arrest. Biguanides such as phenformin and metformin have induced mitochondrial oxidative stress, impaired migration, and inhibited tumor growth in LN229 xenograft models. Additional studies have explored the effects of tumor microenvironment conditions such as extracellular acidity and CXCR4-STAT3 signaling on tumor invasiveness, highlighting the importance of LN229 for modeling glioblastoma adaptation and therapeutic resistance. These investigations underscore the relevance of the LN229 model for testing agents that target both tumor-intrinsic and microenvironmental factors.

Altogen Labs offers comprehensive *in vivo* research services utilizing the LN229 xenograft model, including quantitative gene and protein expression analysis, imaging, toxicity studies, survival tracking, and alternative engraftment strategies. With over 90 CDX and 30 PDX models available, Altogen Labs provides flexible study designs that accommodate a broad spectrum of therapeutic evaluations. Further information on this model can view at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/brain-cancer-xenograft/ln-229-xenograft-model/. The complete technical PDF describing the A172 model is available at https://altogenlabs.com/LN229XenograftModel.pdf.

Characterization and Preclinical Application of the SF268 Xenograft Model in Brain Cancer Research



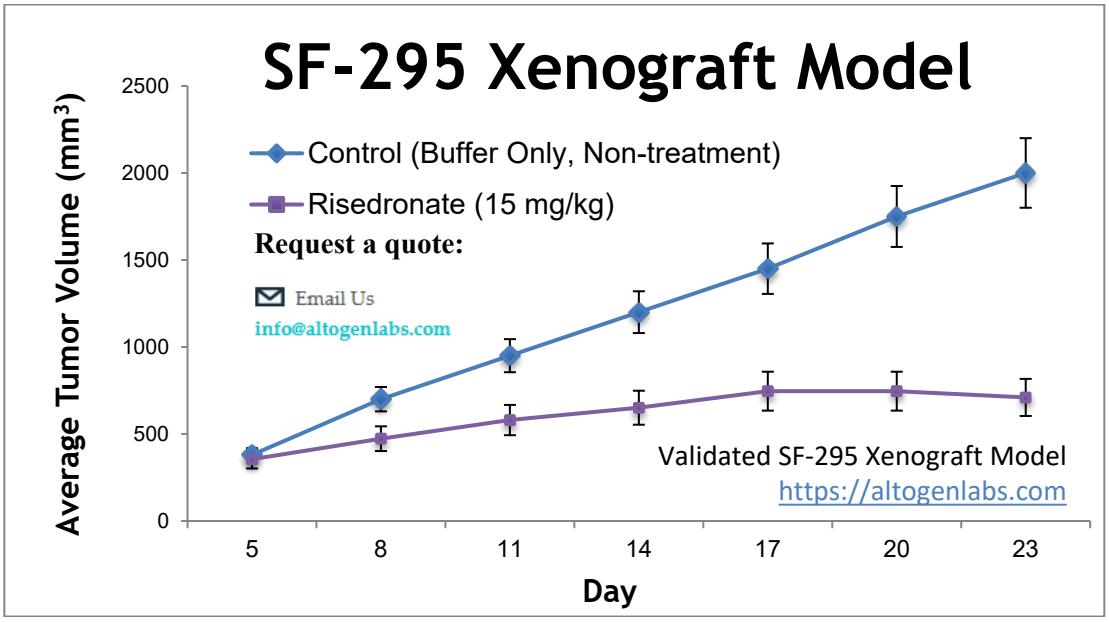
The SF268 glioma xenograft model, developed and validated by Altogen Labs, offers a highly relevant platform for preclinical research in brain oncology. Derived from a human glioma originally misattributed to a female patient but later found to contain a Y chromosome, the SF268 cell line is characterized by anaplastic morphology, rapid proliferation, and poor differentiation. These attributes make it particularly valuable for modeling aggressive gliomas and evaluating therapeutic responses. The model is most commonly employed in subcutaneous formats, where SF268 cells are suspended in a 50 percent Matrigel solution and injected into immunodeficient mice. Tumor progression is tracked through caliper measurements, with treatment groups initiated once tumor volume reaches 100 to 150 mm³. Study endpoints include tumor growth inhibition and delay, pharmacokinetic profiling, toxicity evaluation, and histopathological analyses.

At Altogen Labs, the SF268 model has been used extensively to evaluate both monotherapies and combinatorial treatments. Investigational agents such as flubendazole have shown marked efficacy in reducing tumor growth by inducing G2/M cell cycle arrest and promoting apoptosis through p53 upregulation and suppression of cyclin B1 and p-cdc2. The model has also been instrumental in demonstrating the antitumor effects of repurposed neurological drugs like fingolimod and levomepromazine, as well as their synergistic interactions with temozolomide. Additional studies using SF268 have elucidated resistance mechanisms, such as the HOTTIP-miR-10b-EMT axis that drives chemoresistance and invasiveness, and have identified actionable targets including PI3K and YAP. Agents like PI-103 and RES529 have disrupted SF268 tumor growth by modulating key oncogenic pathways, offering new avenues for glioma treatment development.

The SF268 xenograft model is particularly suited for testing therapies that must overcome barriers such as MGMT-mediated temozolomide resistance and blood-brain barrier permeability. Its aggressive growth and resistance phenotype facilitate rigorous evaluation of cytotoxic and targeted agents under clinically relevant conditions. Altogen Labs conducts all xenograft studies in accordance with IACUC and GLP standards, ensuring ethical and reproducible data generation. Services include a comprehensive suite of analyses, such as immunohistochemistry, gene and protein expression profiling, imaging, toxicity assessments, and survival studies. Researchers can explore alternative study designs incorporating orthotopic implantation or metastatic models and can integrate metabolic or lipid distribution assays for expanded translational insights.

Altogen Labs offers this validated SF268 model as part of its extensive catalog of over 90 CDX and 30 PDX models for oncology research. Detailed information about the SF268 xenograft model is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/brain-cancer-xenograft/SF268-xenograft-model/. The complete technical PDF describing the LN229 model is available at https://altogenlabs.com/SF268XenograftModel.pdf.

Characterization and Preclinical Application of the SF295 Xenograft Model in Brain Cancer Research



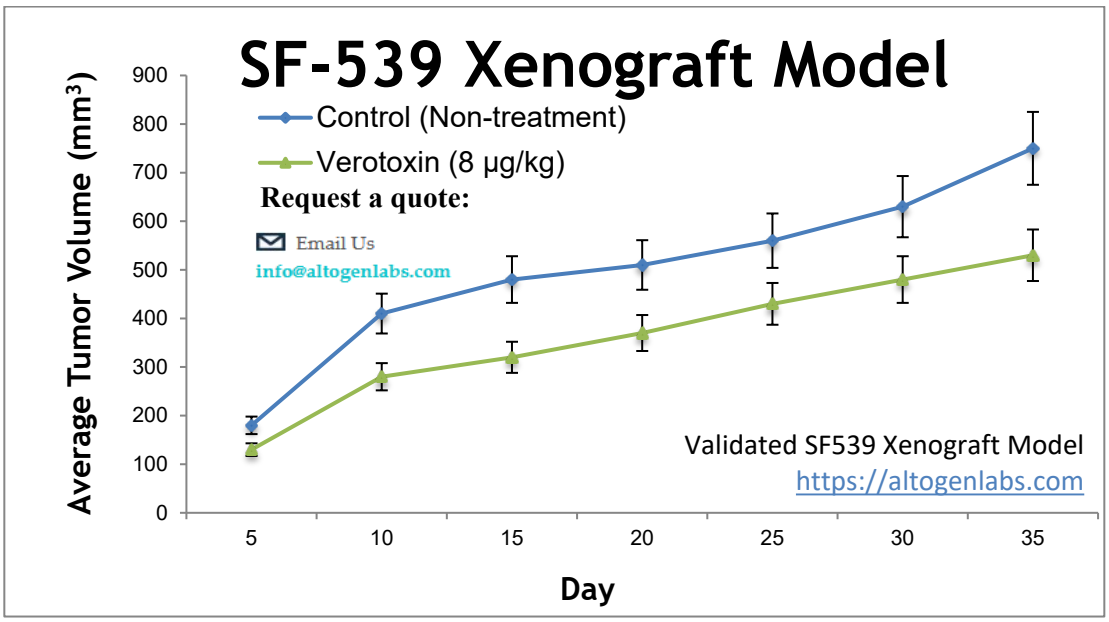
The SF295 glioblastoma xenograft model, developed and validated by Altogen Labs, provides a clinically relevant platform for investigating therapeutic strategies targeting advanced brain malignancies. The SF295 cell line originates from a 67-year-old female patient with glioblastoma and is characterized by homozygous mutations in PTEN and TP53, two commonly dysregulated genes in glioblastoma. These genetic alterations contribute to the cell line's aggressive phenotype and resistance to conventional therapies. As a late-stage glioma model, SF295 is frequently used to study the mechanisms underlying tumor progression, chemoresistance, and the impact of targeted therapeutics.

In preclinical studies conducted at Altogen Labs, SF295 cells are cultured to exponential growth and injected subcutaneously into immunodeficient mice (typically BALB/C or NOD/SCID strains). One million cells suspended in a 50 percent Matrigel solution are delivered into the hind leg flank. Tumor volume is monitored daily using digital calipers, and animals are weighed regularly to assess systemic effects of treatment. Experimental compounds are administered following protocol-defined dosing schedules once tumors reach approximately 100 mm³ in volume. Upon study termination, tumors are excised and subjected to downstream analyses including histology, gene expression profiling, and protein quantification. All procedures are performed in compliance with IACUC and GLP regulations, ensuring scientific rigor and ethical standards.

This model has been used to assess numerous therapeutic modalities. Risedronate has demonstrated antitumor activity *in vivo* by significantly reducing SF295 tumor mass. Investigations into resistance mechanisms have shown that SF295 cells downregulate topoisomerase I, conferring resistance to camptothecin and its analogs. However, these cells remain sensitive to topoisomerase II inhibitors such as etoposide, indicating therapeutic alternatives. Studies have also evaluated novel drug combinations, such as BACPTDP with gemcitabine, and NAD+ precursors with PARG inhibitors to overcome temozolomide resistance. The metabolic vulnerabilities of SF295 cells have been explored using schweinfurthin compounds, which disrupt central metabolic pathways and signaling networks.

Altogen Labs offers the SF295 xenograft model as part of a broader platform of over 90 CDX and more than 30 PDX models. Services include tumor growth inhibition and delay studies, advanced dosing strategies, imaging, immunohistochemistry, toxicity profiling, and molecular characterization. The SF295 model is especially well suited for evaluating agents that target therapy-resistant glioblastoma and for identifying molecular biomarkers of treatment response. More information is available at www.altogenlabs.com, and at https://altogenlabs.com/xenograft-models/brain-cancer-xenograft/sf-295-xenograft-model/.

Characterization and Preclinical Application of the SF539 Xenograft Model in Brain Cancer Research



The SF539 xenograft model is a robust and extensively validated preclinical platform used to investigate glioblastoma multiforme (GBM), particularly gliosarcoma subtypes exhibiting both mesenchymal and glial characteristics. Derived from a recurrent GBM tumor of a 34-year-old female patient, the SF539 cell line expresses elevated levels of extracellular matrix proteins including collagen IV, fibronectin, and laminin, and displays high expression of low-density lipoprotein receptor-related protein (LRP), indicative of enhanced lipid metabolism and tumor aggressiveness. This model is characterized by its notable sensitivity to temozolomide, attributable to MGMT promoter methylation and low MGMT protein expression, making it informative for studying DNA-damaging agents and mechanisms of drug resistance.

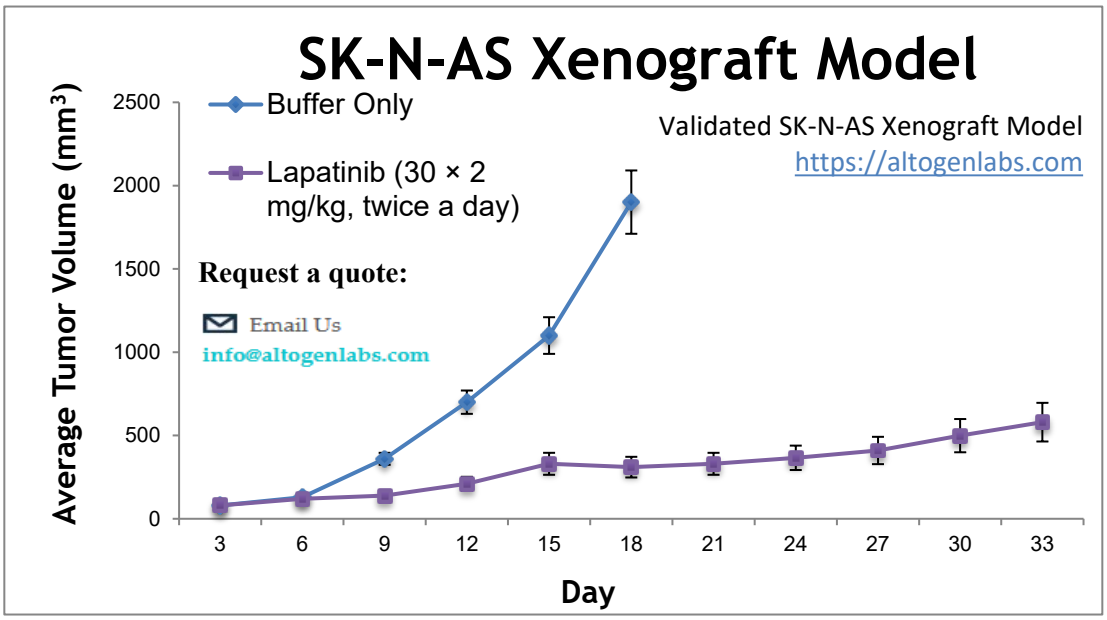
Altogen Labs has established a subcutaneous xenograft model using SF539 cells for the *in vivo* evaluation of novel therapeutic agents. Tumors are initiated by injecting one million cells suspended in Matrigel into the flank of immunocompromised mice. Tumor volumes are monitored regularly with digital calipers, and animals are randomized into treatment groups when tumors reach approximately 100 mm³. At study endpoints, tumors are excised, weighed, and analyzed for gene and protein expression, histopathology, and molecular profiling. Altogen Labs also offers variable dosing schedules, multiple administration routes, and comprehensive toxicology and pharmacology assessments, all conducted under GLP and IACUC-compliant conditions.

SF539 xenografts have been instrumental in evaluating novel therapies for glioma. Studies have demonstrated that the dinuclear platinum compound Pt2ad exhibits superior cytotoxicity compared to cisplatin and temozolomide, with selective activity against SF539 cells. Additional investigations have shown that osimertinib induces paraptosis through endoplasmic reticulum stress and the PERK–eIF2α–CHOP signaling pathway in SF539 cells, while TRIP13 modulates resistance to this cytotoxic response. FKBP9, another oncogenic factor, has been shown to promote SF539 tumor growth and confer resistance to ER stress inducers via activation of p38 MAPK signaling. The model has also been used to explore structure–activity relationships of hybrid compounds containing thiazolidinone scaffolds, revealing high selectivity and potency against SF539 gliomas.

From a molecular perspective, SF539 exhibits a low basal expression of MYC and mitochondrial topoisomerase TOP1MT, suggesting a unique metabolic profile that differs from more MYC-driven cancers. This regulatory axis may represent a potential vulnerability, particularly for therapies targeting mitochondrial function and bioenergetics. As such, SF539 serves as a critical model for evaluating therapies targeting both canonical oncogenic pathways and non-apoptotic cell death mechanisms in glioblastoma.

More information about this model is available on the Altogen Labs website at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/brain-cancer-xenograft/SF268-xenograft-model/. The complete technical PDF describing the LN229 model is available at https://altogenlabs.com/SF268XenograftModel.pdf.

Characterization and Preclinical Application of the SK-N-AS Xenograft Model in Brain Cancer Research



The SK-N-AS xenograft model is a well-characterized preclinical platform for investigating high-risk, non-MYCN-amplified neuroblastoma, a pediatric malignancy noted for its aggressive clinical behavior and poor prognosis. Derived from a metastatic bone marrow lesion, the SK-N-AS cell line exhibits 1p and 11q chromosomal loss, wild-type p53, and inherent resistance to chemotherapeutic agents such as vincristine and doxorubicin. These characteristics, combined with its reproducible tumor formation and biological relevance, make the model highly valuable for studying mechanisms of drug resistance, tumor progression, and therapeutic response.

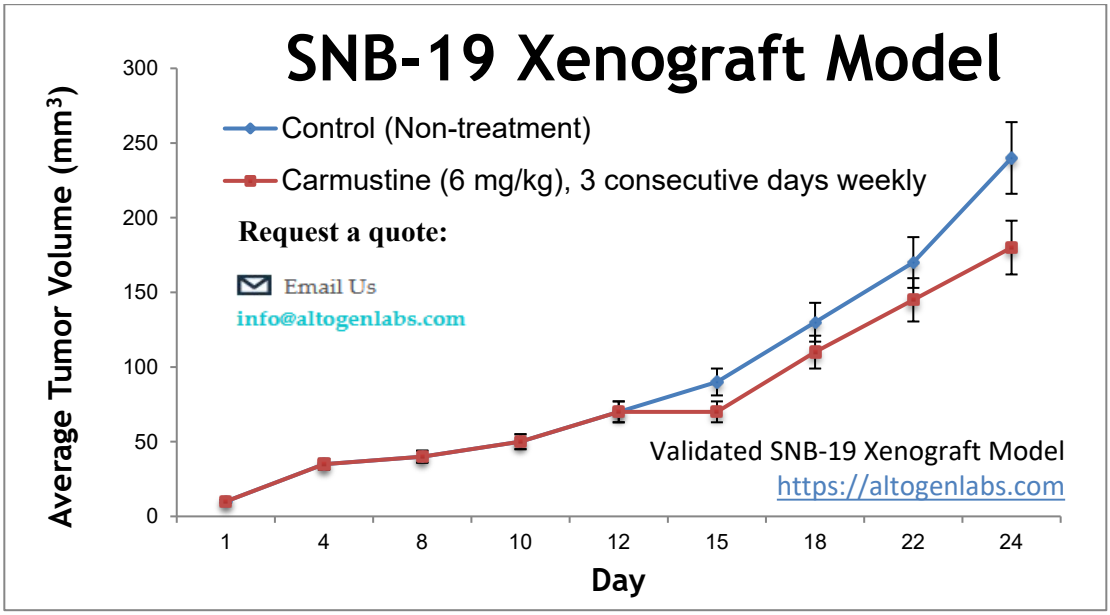
Altogen Labs offers validated subcutaneous, orthotopic, and metastatic xenograft models using SK-N-AS cells. In the subcutaneous model, one million viable cells are injected into the hind limb of immunodeficient mice, and tumor growth is monitored via caliper measurements. Orthotopic models, involving adrenal or paraspinal implantation, replicate the tumor's native microenvironment, allowing for in-depth evaluation of tumor-stromal interaction, angiogenesis, and localized invasion. Metastasis models utilize intravenous or intracardiac routes to study systemic disease progression and organ-specific colonization, including bone, liver, and lung metastases.

Preclinical investigations using SK-N-AS xenografts have yielded significant findings. For example, the model has been used to evaluate Polo-like kinase 1 (PLK1) inhibitors such as BI 2536, which significantly reduced tumor volume *in vivo*. Epigenetic modulation with KDM1A inhibitors like NCL-1 induced differentiation, suppressed angiogenesis, and led to durable tumor regression without overt toxicity. Metabolic vulnerabilities have also been explored, including the role of glutamine metabolism in drug resistance, revealing that SK-N-AS cells display cytostatic responses to glutamine antagonists unless co-treated with Bcl-2 inhibitors or modified to overexpress Myc. Furthermore, COX-2 expression in SK-N-AS mediates osteolytic lesion formation in bone metastasis models, and its inhibition reduces tumor-induced bone degradation, angiogenesis, and osteoclast recruitment.

The SK-N-AS model has also facilitated the study of reprogrammed cancer stem cell populations. Treatment with DNA methylation inhibitors induces expression of stemness markers such as SOX2 and CD133, yielding a tumor-initiating phenotype with high engraftment potential and increased sensitivity to Hsp90 inhibition. Additionally, Wnt signaling via Frizzled2 (FZD2) has been identified as a key oncogenic driver, integrating canonical and non-canonical pathways to regulate MYC expression, ERK activation, and β-catenin signaling. Targeting FZD2 markedly reduces proliferation, migration, and angiogenesis in SK-N-AS tumors, providing a compelling rationale for therapeutic intervention.

Additional details about the SK-N-AS xenograft model can be found at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/brain-cancer-xenograft/sk-n-as-xenograft-model/.

Characterization and Preclinical Application of the SNB-19 Xenograft Model in Brain Cancer Research



The SNB-19 xenograft model is a well-established and extensively characterized preclinical system used to investigate glioblastoma multiforme (GBM), particularly in the context of therapeutic resistance, tumor metabolism, and epigenetic regulation. Derived from a human GBM tumor, SNB-19 cells display key molecular alterations commonly observed in primary glioblastomas, including PTEN loss, p53 dysfunction, and moderate EGFR expression. These cells exhibit aggressive growth, resistance to standard therapies such as temozolomide and radiation, and have been widely used to study nanoparticle-based drug delivery, RNA interference, and epigenetic modifiers. Despite lacking the invasive phenotype of more aggressive GBM lines, SNB-19 offers a robust and reproducible model for translational research.

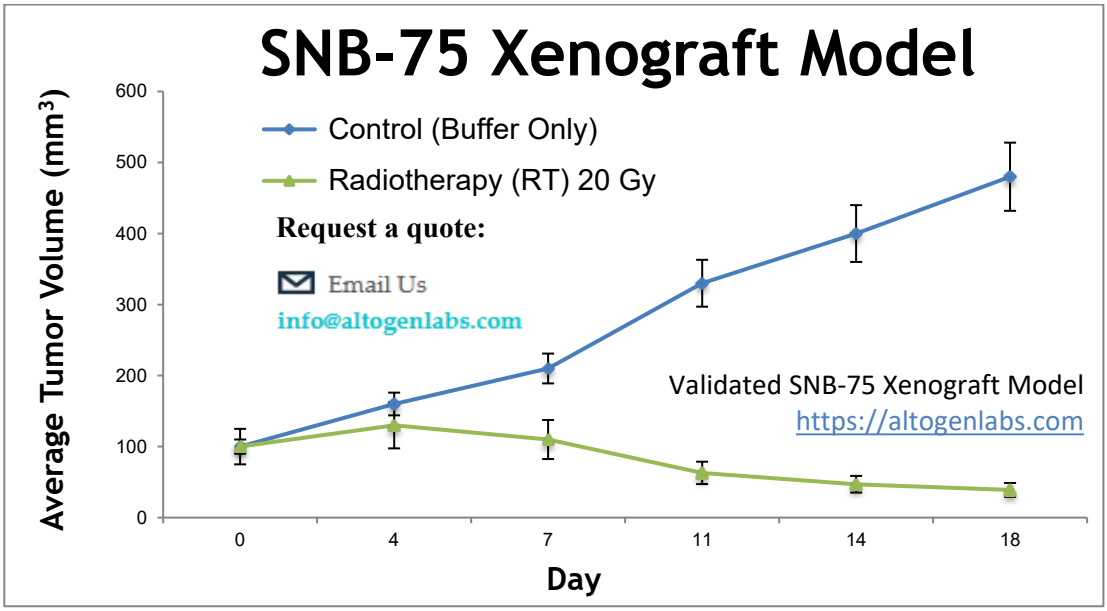
Altogen Labs offers both subcutaneous and orthotopic SNB-19 xenograft models. In the subcutaneous model, one million viable cells are implanted in the flanks of immunodeficient mice, and tumor volume is monitored via digital calipers. Tumors are excised at endpoint for histopathology, molecular profiling, and tissue banking. In the orthotopic model, cells are stereotactically injected into the murine striatum to replicate the anatomical and microenvironmental conditions of human GBM. This approach enables investigation of tumor cell infiltration, therapy resistance, and blood-brain barrier penetration. Studies using orthotopic SNB-19 models have elucidated critical molecular mechanisms driving glioma pathogenesis and resistance, including the role of circular RNAs, hormone-sensitive lipase, and the miR-195-5p regulatory axis.

Recent investigations have also used SNB-19 to define treatment-resistant tumor-initiating cell populations that express pluripotency markers such as SOX2 and OCT4 and exhibit neural lineage plasticity. These resistant cells have been shown to survive conventional therapies and initiate tumor recurrence. Moreover, the SNB-19 model has proven responsive to mTOR pathway inhibitors such as RES529, which induces apoptosis, inhibits proliferation, and suppresses angiogenesis. Additionally, RNA interference targeting Cathepsin B and uPAR in SNB-19 cells has demonstrated strong apoptotic induction and reduced invasiveness, highlighting the therapeutic potential of dual gene silencing strategies.

Altogen Labs conducts all SNB-19 xenograft studies in IACUC-accredited, GLP-compliant facilities. Services include tumor growth inhibition studies, toxicology, pharmacokinetics, gene expression analysis, immunohistochemistry, and *in vivo* imaging. Genetically engineered SNB-19 lines with gene overexpression or silencing are available to support mechanistic studies and target validation. The SNB-19 model offers a valuable and flexible platform for evaluating therapeutic response, resistance mechanisms, and glioblastoma biology in a clinically relevant context.

More information about the SNB-19 xenograft model is available at www.altogenlabs.com, specifically at https://altogenlabs.com/xenograft-models/brain-cancer-xenograft/snb-19-xenograft-model/.

Characterization and Preclinical Application of the SNB-75 Xenograft Model in Brain Cancer Research



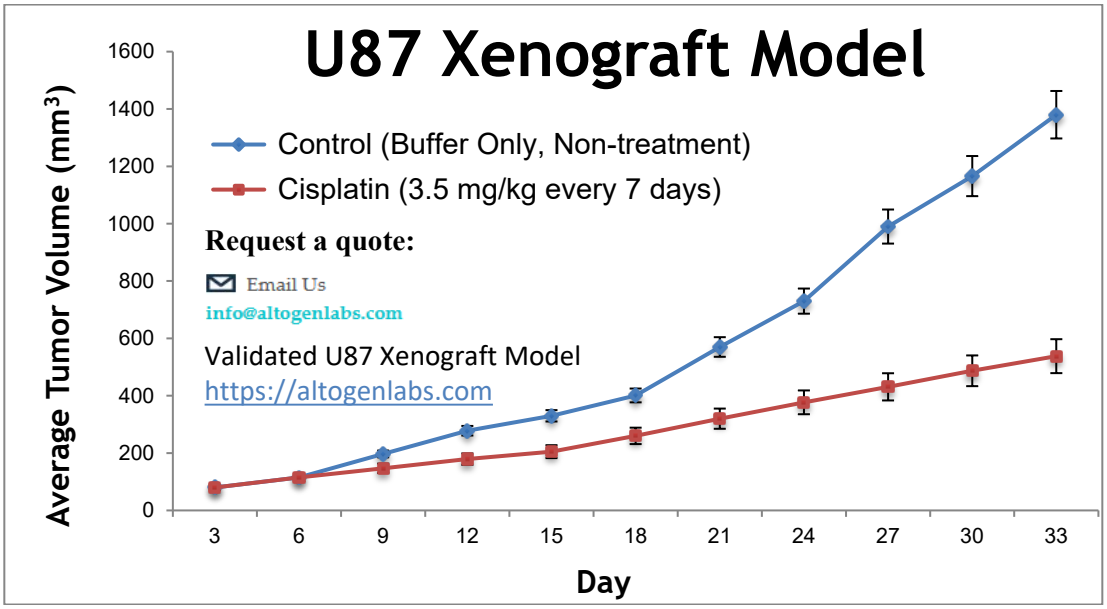
The SNB-75 xenograft model is a validated and versatile preclinical platform developed to support glioblastoma multiforme (GBM) research, particularly in the evaluation of tumor biology, therapeutic resistance, and mitochondrial regulation. Derived from a human primary GBM tumor and included in the NCI-60 cell line panel, SNB-75 retains clinically relevant mutations such as TP53 alteration, EGFR amplification, and deregulated PTEN expression. While less characterized than other GBM models like U87 or U251, SNB-75 exhibits moderate invasiveness, resistance to alkylating agents such as temozolomide, and a distinct mitochondrial phenotype, making it an important system for exploring underrepresented aspects of GBM pathogenesis and treatment.

Altogen Labs has developed a subcutaneous xenograft model using SNB-75 cells for drug efficacy and toxicity screening. Tumors are established by injecting one million cells in 50 percent Matrigel into the flanks of immunodeficient BALB/c or NOD/SCID mice. Tumor progression is monitored with digital calipers, and treatment initiation occurs when tumors reach volumes of 120 to 150 mm³. At endpoint, tumors are excised, weighed, and processed for histopathology, gene expression, and molecular analyses. Optional endpoints include immunohistochemistry, RNA and protein extraction, blood chemistry, and advanced imaging modalities such as MRI or whole-body fluorescence. All procedures are conducted in GLP-compliant and IACUC-approved facilities, with comprehensive reporting and client-specific customization.

SNB-75 xenografts have been utilized in several mechanistic and therapeutic studies. Investigations into the role of Guanylate-Binding Protein 1 (GBP-1) revealed that SNB-75 maintains a fission-resistant mitochondrial network, characterized by elongated morphology and low Drp1 recruitment despite high GBP-1 expression. This phenotype contrasts with other GBM models and underscores SNB-75's utility in studying fission-independent mitochondrial regulation. Moreover, depletion of Casein Kinase 1 epsilon (CK1ε) via shRNA or small-molecule inhibitors induced β-catenin-mediated apoptosis in SNB-75 cells, identifying CK1ε as a potential therapeutic target. Additional studies demonstrated hypoxia-induced epithelial-to-mesenchymal transition (EMT) via the HIF1α–ZEB1 signaling axis, further emphasizing SNB-75's responsiveness to tumor microenvironmental conditions. The model has also been used to evaluate antineoplastic compounds such as compound 6h, a tubulin-interacting agent that demonstrated promising cytotoxic activity against SNB-75 cells. Furthermore, transcriptomic analyses have identified genes such as MDM2, DDB2, and MAFF as negative prognostic indicators in SNB-75 and other GBM models, while CTBP2 expression correlated with enhanced CD8+ T-cell infiltration and improved survival, supporting its role in immune surveillance and potential for immunotherapeutic targeting.

For more information on the SNB-75 xenograft model, please visit www.altogenlabs.com, specifically https://altogenlabs.com/xenograft-models/brain-cancer-xenograft/snb-75-xenograft-model/ for the model.

Characterization and Preclinical Application of the U87 Xenograft Model in Brain Cancer Research



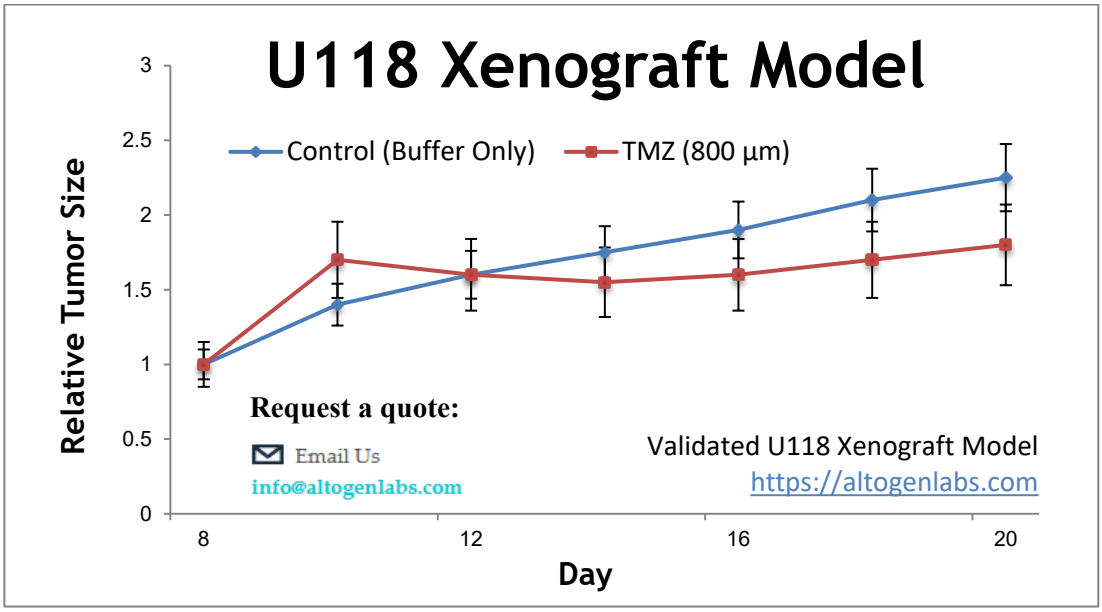
The U87 xenograft model is one of the most widely utilized and well-characterized preclinical systems for glioblastoma multiforme (GBM) research. Derived from a human malignant glioma, U87 cells exhibit rapid proliferation, robust tumorigenicity, and consistent growth in immunodeficient mice. While the model does not fully recapitulate the highly invasive nature or intratumoral heterogeneity of clinical GBM, its reproducibility and defined genetic background make it highly suitable for early-phase therapeutic screening and mechanistic studies. U87 cells express glial markers such as GFAP, display EGFR overexpression, and retain a p53 mutation with wild-type PTEN status, making them a reliable model for studying proliferation, angiogenesis, and resistance pathways. These characteristics have made U87 xenografts foundational in evaluating new chemotherapeutics, targeted agents, and drug delivery systems.

Altogen Labs provides both subcutaneous and orthotopic U87 xenograft models, each offering unique advantages for *in vivo* studies. In the subcutaneous model, U87 cells are injected into the flank of immunodeficient mice where tumors grow in a predictable, vascularized, and measurable fashion. This configuration is ideal for assessing tumor growth inhibition, compound efficacy, and pharmacodynamic endpoints. For more physiologically relevant studies, orthotopic models are established via stereotactic injection into the mouse brain, replicating the native tumor microenvironment and allowing for the assessment of intracranial tumor growth, local invasion, and blood-brain barrier permeability. Altogen Labs supports comprehensive study execution under IACUC and GLP-compliant conditions, including tumor monitoring, survival analysis, histopathology, gene and protein expression, toxicity evaluation, and real-time fluorescence imaging.

Numerous investigations have utilized U87 xenografts to explore both molecular pathways and therapeutic interventions. Inhibition of mGluR1 has been shown to suppress PI3K/Akt/mTOR signaling, leading to decreased proliferation and increased apoptosis. Overexpression of RND1 in U87 cells sensitizes tumors to temozolomide by inhibiting AKT-mediated epithelial-mesenchymal transition, while secreted CD44 from U87 cells has been implicated in promoting tau aggregation, linking glioblastoma to neurodegenerative processes. Studies have also demonstrated that dual-drug nanoparticle therapies, combining paclitaxel and temozolomide, achieve enhanced tumor suppression with reduced systemic toxicity. These findings underscore the utility of the U87 model in advancing translational neuro-oncology.

More information about Altogen Labs' U87 xenograft model is available at www.altogenlabs.com, specifically https://altogenlabs.com/xenograft-models/brain-cancer-xenograft/u87-xenograft-model/ for the model.

Characterization and Preclinical Application of the U118 Xenograft Model in Brain Cancer Research



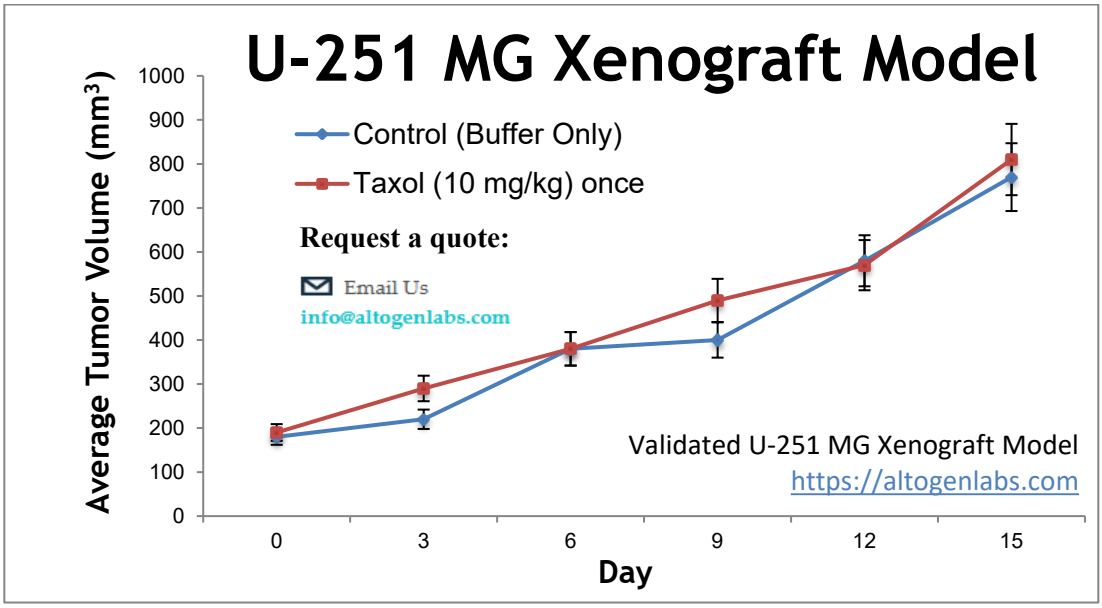
The U118 glioblastoma xenograft model, validated and offered by Altogen Labs, constitutes a clinically relevant preclinical system for investigating the pathobiology and therapeutic response of mesenchymal glioblastoma multiforme (GBM), one of the most aggressive and treatment-resistant forms of brain cancer. Derived from human astrocytoma, U118 cells harbor critical molecular aberrations frequently observed in high-grade gliomas, including PTEN deletion, p53 mutation, and persistent activation of the PI3K/AKT signaling cascade. These features confer a high degree of invasiveness and intrinsic resistance to standard chemotherapeutic agents such as temozolomide (TMZ), making U118 an optimal model for exploring novel therapeutic strategies aimed at overcoming resistance mechanisms. The U118 cell line exhibits a mesenchymal phenotype and expresses biomarkers such as CD44 and YKL-40, further aligning it with aggressive GBM subtypes. Altogen Labs has developed subcutaneous and orthotopic xenograft models utilizing U118 cells, facilitating detailed investigation of tumor progression, angiogenesis, therapeutic resistance, and molecular response under conditions that closely mimic the *in vivo* tumor microenvironment.

Orthotopic xenografts are established via stereotactic implantation of luciferase-tagged U118 cells into the brains of immunodeficient models, enabling real-time, noninvasive monitoring of intracranial tumor growth and therapeutic impact. These models have been employed to evaluate the efficacy of targeted agents, radiosensitizers, and combination therapies involving PI3K/mTOR and HDAC inhibitors. In parallel, subcutaneous models allow for reproducible tumor establishment and convenient longitudinal measurement of tumor growth kinetics. Experimental endpoints include tumor volume quantification, survival analysis, and molecular characterization through immunohistochemistry, gene expression profiling, and proteomic assays. Tumor tissue can be processed for downstream analyses via formalin fixation, snap-freezing, or RNAlater stabilization, depending on specific research objectives. Studies at Altogen Labs are conducted in compliance with GLP and IACUC regulations, with all procedures performed in state-of-the-art, accredited *in vivo* facilities. Study customization options include variable dosing regimens, use of positive control compounds, incorporation of imaging modalities such as MRI and bioluminescence, and extended pharmacodynamic or toxicology assessments.

The utility of the U118 model has been substantiated by numerous investigations, including studies identifying miR-181 as a tumor-suppressive regulator through inhibition of Selenoprotein K (SELK), bioprinting-based models of angiogenesis in co-culture with endothelial cells, and combinatorial approaches reversing TMZ resistance via inhibition of the serine biosynthesis enzyme PHGDH. Additional research has demonstrated that activation of the tumor suppressor phosphatase PP2A via small molecule compounds significantly impairs U118 viability and colony formation, offering an alternative strategy to kinase-targeted therapies.

Detailed information about the U118 xenograft model is available at www.altogenlabs.com, specifically https://altogenlabs.com/xenograft-models/brain-cancer-xenograft/u118-brain-cancer-xenograft-model-altogen-labs/ for the model.

Characterization and Preclinical Application of the U-251 MG Xenograft Model in Brain Cancer Research



The U-251 MG glioblastoma xenograft model provided by Altogen Labs is a rigorously validated preclinical system designed to investigate therapeutic efficacy, tumor biology, and resistance mechanisms in glioblastoma multiforme (GBM). U-251 MG cells, originating from a human glioblastoma specimen, harbor hallmark molecular features of aggressive gliomas, including a p53 mutation, PTEN loss, and activated PI3K/Akt signaling. These cells exhibit robust proliferative capacity, resistance to apoptosis, and invasive growth, making them highly representative of treatment-refractory GBM. Altogen Labs has developed both subcutaneous and orthotopic xenograft models using U-251 MG, offering a translational platform for testing chemotherapeutic agents, targeted therapies, and radiation sensitizers under physiologically relevant conditions. The subcutaneous model allows for reproducible tumor formation and convenient longitudinal measurements, while orthotopic implantation enables assessment of tumor behavior within the brain's native microenvironment, including vascularization, hypoxia, and drug penetration through the blood-brain barrier.

All *in vivo* studies are conducted under GLP-compliant and IACUC-approved protocols. U-251 MG cells are cultured in exponential growth, harvested under sterile conditions, and injected into immunodeficient mice using Matrigel suspensions. Tumor growth is monitored by caliper measurements or bioluminescence imaging, and animals are randomized into treatment cohorts upon reaching predetermined tumor volumes. Endpoints include tumor growth inhibition, tumor growth delay, survival analysis, and comprehensive molecular characterization. Tissue specimens may be processed for histology, RNA/protein isolation, and immunohistochemistry, enabling detailed evaluation of drug mechanisms and biomarker modulation. Imaging modalities, including MRI and whole-body fluorescence, are also available to support dynamic tracking of therapeutic response.

Recent investigations employing the U-251 MG model have provided important insights into GBM pathophysiology. These include elucidation of metabolic suppression via the MBNL1/circNTRK2/PAX5 regulatory axis, demonstration of PI3K/mTOR inhibition by the botanical drug PBI-05204, and apoptotic induction through NF-kappaB suppression using Saponin 1. In addition, sulforaphane has been shown to inhibit invasion and promote cell death through modulation of Bcl-2 family proteins and MMP activity, while radiotracer studies using [18F]olaparib have highlighted the influence of compound mass on tumor uptake in PARP-targeted imaging. Collectively, these studies confirm the U-251 MG model's value in addressing glioblastoma stemness, metabolic adaptation, and therapeutic resistance.

Altogen Labs supports the customization of xenograft studies to align with investigator goals, offering flexible dosing regimens, advanced drug delivery techniques, and integration of mechanistic assays. The U-251 MG model remains an indispensable resource for preclinical oncology, enabling detailed exploration of molecular pathways and facilitating the translation of experimental therapeutics into clinical candidates. Additional information about this xenograft model is available on the Altogen Labs website at www.altogenlabs.com, specifically https://altogenlabs.com/xenograft-models/brain-cancer-xenograft/ug-251mg-xenograft-model/ for the model.

Altogen Labs Offers Comprehensive Preclinical Oncology Testing Services

Altogen Labs is a premier preclinical contract research organization that provides comprehensive, high-precision *in vivo* and *in vitro* services to support oncology drug development and translational biomedical research. Leveraging a robust infrastructure and a team of experienced scientists, Altogen Labs offers end-to-end study execution that spans model selection, experimental design, compound administration, data collection, and advanced molecular analysis. With a strong focus on reproducibility, regulatory compliance, and scientific rigor, the laboratory operates in fully GLP-compliant and IACUC-regulated facilities, ensuring that all studies meet the highest ethical and technical standards required for preclinical development.

At the core of Altogen Labs' offerings is an expansive portfolio of over 90 validated cell line-derived xenograft (CDX) models and more than 30 patient-derived xenograft (PDX) models, which collectively provide researchers with flexible and biologically relevant platforms for evaluating a wide spectrum of oncologic therapies. This catalog includes widely used models such as A172, LN229, SF268, SF295, SF539, SK-N-AS, SNB19, SNB75, U87, U118, and U251 MG, among others. These xenograft systems support tumor growth inhibition (TGI) and tumor growth delay (TGD) studies, enabling the assessment of both cytostatic and cytotoxic treatment modalities. Models are available in subcutaneous, orthotopic, and metastatic configurations, with customization options that allow for alignment with specific therapeutic mechanisms, disease states, and clinical objectives.

Altogen Labs offers a wide range of administration routes to suit various study requirements, including intravenous, intraperitoneal, intratumoral, oral gavage, intranasal, subcutaneous, and site-specific orthotopic delivery. Studies are designed to provide rich pharmacodynamic and pharmacokinetic insights and can be adapted to short-term efficacy screening or long-term survival analysis. The laboratory supports extensive downstream data collection and analysis, including tumor imaging, histological evaluation, blood chemistry profiling, and comprehensive molecular analyses such as RT-qPCR, Western blotting, immunohistochemistry (IHC), flow cytometry, and RNA sequencing. Full necropsy and tissue banking services are also available, facilitating retrospective studies and biomarker discovery.

In addition to xenograft research, Altogen Labs offers custom cell line engineering services to generate stable overexpression, knockdown, or CRISPR-modified lines for mechanistic studies. Clients can also utilize Altogen's proprietary liposomal formulation technologies for nucleic acid delivery, including siRNA, mRNA, and plasmid DNA, enabling *in vivo* gene modulation and therapeutic screening. Specialized services such as inducible knockdown systems, *in vivo* RNAi delivery, ELISA assay development, and cell-based assay design further expand the laboratory's capabilities in molecular and cellular biology.

Each study conducted at Altogen Labs is accompanied by a complete reporting package that includes raw datasets, statistical evaluation, graphical data visualization, and expert interpretation of results. Clients receive full transparency throughout the study lifecycle, including access to protocols, in-life updates, health monitoring data, and archived samples upon request. Altogen Labs' collaborative approach ensures that each project is tailored to the sponsor's research goals, whether focused on drug efficacy, biomarker validation, target discovery, or safety evaluation.
With a strong foundation in oncology research and a multidisciplinary service model, Altogen Labs is positioned as a trusted partner for biotechnology companies, academic institutions, and pharmaceutical developers seeking high-quality, translationally relevant preclinical data. The laboratory's extensive model catalog, technical expertise, and commitment to scientific excellence collectively support the development of next-generation cancer therapies. Additional information, including detailed technical PDFs for all available xenograft models, can be accessed through the Altogen Labs website at www.altogenlabs.com.