Patient-Derived Orthotopic Xenograft Models of Pediatric Brain Tumors: In a Mature Phase or Still in Its Infancy?

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In recent years, molecular profiling has led to the discovery of an increasing number of brain tumor subtypes, and associated therapeutic targets. These molecular features have been incorporated in the 2016 new World Health Organization (WHO) Classification of Tumors of the Central Nervous System (CNS), which now distinguishes tumor subgroups not only histologically, but also based on molecular characteristics. Despite an improved diagnosis of (pediatric) tumors in the CNS however, the survival of children with malignant brain tumors still is far worse than for those suffering from other types of malignancies. Therefore, new treatments need to be developed, based on subgroup-specific genetic aberrations. Here, we provide an overview of the currently available orthotopic xenograft models for pediatric brain tumor subtypes as defined by the 2016 WHO classification, to facilitate the choice of appropriate animal models for the preclinical testing of novel treatment strategies, and to provide insight into the current gaps and challenges.

INTRODUCTION

Whilst over the past few decades there has been an improvement in the survival of patients in multiple domains within pediatric oncology, the prognosis for the majority of children with malignant brain tumors remains grim (1). Their poor survival can be attributed to a lack of efficacious therapies, and a limited understanding of the underlying genetic and biochemical abnormalities associated with this group of diseases, which has hindered the development of more effective and patient-specific treatment. In the past years, a number of recurrent mutations have been identified that allow for the identification of tumor subgroups with distinct biological characteristics (2, 3). Importantly, these molecular features have been incorporated into the new (2016) World Health Organization (WHO) classification, which now distinguishes tumor subgroups not only histologically, but also based on molecular characteristics (4). The new classification has improved the diagnosis of pediatric brain tumors, but this knowledge has not yet led to a better prognosis for pediatric brain tumor patients. In order to increase survival rates whilst decreasing treatment-related side-effects, new targeted treatments must be developed which feature subgroup-specific clinical trials, and are conducted based on the distinct underlying genetic aberrations. However, with an increasing number of tumor subgroups and consequently a decreasing number of eligible patients, it will become ever more important to test novel treatment strategies in preclinical research before proceeding to clinical trials. Representative cell lines and
animal models will therefore have to be developed, representing the broad spectrum of pediatric brain tumors. To facilitate the choice of the appropriate preclinical animal model, and emphasize the need for new models that are still lacking, we here provide an overview of the currently available orthotopic xenograft models for pediatric brain tumors, divided by specific subtypes as defined by the 2016 WHO classification (4). Although multiple types of animal models are currently available for the investigation of new treatments for pediatric brain tumors in vivo, we will focus on patient-derived xenografts (PDXs) rather than Genetically Engineered Mouse Models (GEMMs) within which tumor-specific genetic aberrations are introduced. PDXs have been shown to have an increased reliability when reproducing the heterogeneity of the human disease, which may better reflect the therapy response in patients than GEMMs (5, 6). In addition, we will focus on the models that have been established by xenografting fresh patient-derived material rather than established human cancer cell lines that have adapted to growth under artificial culture conditions, and are generally considered less relevant for clinical translation due to a more homogeneous, undifferentiated histology (7–9). Finally, we will only consider intracranial/orthotopic models, as these models retain the tumor-host microenvironment which may play a role in tumor response (10), and tumor growth (11). Moreover, such orthotopic models closely mimic human metastasis and allow to study drug delivery past the blood-brain barrier (5, 7, 12, 13).

**PDX MODELS**

Currently available pediatric brain tumor PDXs are established by xenografting fresh tissue, freshly isolated cell suspensions, or shortly cultured neurospheres in immunosuppressed rats (14), or immunodeficient mice (7, 15–17). Various immunocompromised mouse strains are available, with different rates of engraftment, lifespan, and sensitivity for chemotherapy or radiation (5, 9, 18). Not all strains have been fully characterized, and it is therefore essential to understand these differences when choosing the most appropriate animal model. BALB/c mice, for example, are particularly sensitive to the effects of radiation due to an unknown autosomal recessive genetic locus (19). Therefore, immunodeficient mice on a BALB/c genetic background should not be used for studies involving radiotherapy. Similarly, SCID (severe combined immunodeficient) animals are very sensitive to γ-irradiation, as they harbor a mutation in the Prkdc gene, which is involved in the repair of double strand DNA breaks (20). In contrast, other strains—such as Rag1-deficient (recombination activating gene 1) mice—have been reported to survive radiation doses up to 8.5 Gray, and are considered radioresistant (21). Working with mice on defined genetic backgrounds is therefore advisable for irradiation studies. The same holds true for experiments aimed at testing therapy response when DNA damaging agents are used. The response to cisplatin, doxorubicin, 5-fluoroacil, and oxaliplatin was shown to depend on PRKDC function (22), and should therefore not be tested in SCID mice. For more targeted compounds no clear guidelines exist for the choice of mouse strain, although some differences have been reported on drug sensitivity depending on drug transporters and metabolism (23). In those cases, the choice of the most appropriate PDX model should be based on the molecular subtype of the tumor.

Aside from different responses to therapy, there are also significant differences in tumor engraftment between various strains. Generally, it is believed that the level of immunodeficiency correlates with the tumor take rate (8, 9); as such, the more immunocompromised mouse strains, NOD/SCID/IL2γ-receptor null (NSG) and NOS/Rag/IL2γ-receptor null (NRG), would be most suitable strains for the implantation of primary cancerous cells, stem cells or tissue (9, 19, 24). It has been reported that these models support more robust post-engraftment tumor growth compared to double-mutant mice (25, 26), whilst maintaining the characteristics of the original primary patient tumor (27). However, studies confirming this view have only been performed with specific PDX models for hematological forms of cancer or using subcutaneous injections of tumor cells, and no convincing assessment regarding the preferred mouse strain for pediatric brain tumors has been carried out (24, 28–30).

One major limitation of the use of immunocompromised mice is that the interaction between the tumor and the immune microenvironment is partially or completely lost to ensure tumor engraftment is successful (5, 9). Consequently, the current PDX models cannot be used to study the (tumor) immune microenvironment, or to test novel immunotherapeutic treatment strategies (9). One solution to this problem has been found in the use of humanized-xenograft models (5, 9, 12, 18), in which the peripheral blood or bone marrow of the patient is co-engrafted with the tumor material into mouse strains lacking mouse natural killer cell activity (for example NSG or NRG mice) (9). Although this is a promising strategy for the testing of immunotherapy in the future, no humanized-xenograft models for pediatric brain tumors have yet been described.

Besides the choice of animal strain, other factors may influence the success rate of tumor engraftment. For instance, patient tissue can be collected either at time of diagnosis (biopsy), as part of treatment (surgical resection), or post-mortem. The moment of tissue collection may affect the characteristics of the PDX model, as treatment can change the molecular features of the tumor (31). As such, PDX models established from samples that are retrieved before treatment may be more suitable to test new therapies that can be implemented in the initial treatment schedules, while PDX models from autopsy samples, representing the late stage of disease, may be more appropriate to study resistance mechanisms and treatment effects (32).

In addition, various methods are used for the processing of the tumor cells before injection. Although occasionally whole tumor pieces have been used for implantation (33, 34), the most used method to establish pediatric brain tumor PDX models, is the preparation of cell suspensions either by dissociation of neurospheres or directly from surgical specimen (Table A1). Alternatively, tumor cells can be enriched for brain tumor-initiating cells (BTICs) by sorting for CD133+ cells (35), grown as an adherent layer (31, 36–44), transplanted in the thalamus or subcutaneously to expand the tumor cells (32, 40,
45, 46), or injected intracranially after serial transplantation (16, 35, 40, 46–55).

Although subcutaneous propagation has been shown to retain tumor characteristics and to decrease the time required for the PDX model procedure (7), no significant differences appear to exist between the direct- and indirect xenografting of tumor cells. In a head to head comparison of tumor models, generated by the injection of tumor cells derived directly from the patient and implantation of cultured cells, no variance was observed in tumorigenicity or histopathology of the xenograft (32). The authors did however find a discrepancy in survival time, with xenograft models obtained from cells in culture living longer (see Table A1), correlating to a greater degree with patient survival. This discrepancy between the direct- and indirect method could originate from inequivalent numbers of injected tumor cells, or the presence of stroma and microenvironment in direct implantation.

Besides a better correlation with patient survival, indirect xenografting, encompassing a cell culture step before intracranial implantation, additionally allows for the introduction of the *Firefly luciferase* gene by lentiviral transduction, facilitating non-invasive monitoring of tumor growth by bioluminescent imaging (BLI) in preclinical therapeutic studies (56). Although a temporary culture step as an adherent monolayer may be needed for effective transduction (57), cells are generally grown as neurospheres, since spheroid cultures have been shown to have a greater degree of genetic stability compared to cells grown in attachment (58). Independent of the culture conditions or method of implantation, PDXs should always be compared to the original tumor to validate the models. Preferably this is done both histologically and by molecular analyses, e.g., by confirmation of copy number variations/tumor-specific mutations or DNA methylation profiling. Such validation is extremely important, as some studies even suggest that the presence of stroma cells in post-mortem tissue may generate murine tumors rather than human xenografts (59, 60).

The large variety of available methods and mouse strains indicates that, until recently, no clear consensus existed in the field regarding the best model set-up. However, in the past decade multiple consortia have been founded, such as the Pediatric Preclinical Testing Consortium, the Childhood Solid Tumor Network, the Children’s Oncology Group (COG), and the European EuroPDX resource, that collect and validate PDX models to increase the reproducibility of PDX studies (16). Although currently only few pediatric PDX models are included in the abovementioned databases, these initiatives emphasize the importance of a validated set-up. Furthermore, in order to assure the quality of newly established PDX models, a PDX models Minimal Information standard (PDX-MI) has been developed that defines the minimal information regarding the clinical characteristics and the procedures of implantation in a host mouse strain (31). For all these models it will be important to validate to which extent the xenograft tumor diverges from the donor tumor, both molecularly and histologically (8). However, the provision of such data, as well as peruse of the clinical patient information, might be challenging due to patient privacy or data inaccessibility (31).

### FUTURE PERSPECTIVES

Whilst the number of available orthotopic xenograft models for pediatric brain tumor research is growing, some tumor types are still underrepresented. Models for craniopharyngioma, germinoma, embryonal tumors with multilayered rosettes (ETMR), pineoblastoma, diffuse astrocytoma, oligodendroglioma, and cancers belonging to the “other astrocytic tumors/gliomas” are scarce, and no models have currently been described for e.g., choroid plexus tumors. This paucity may be attributed to a minimal research interest into certain tumor types, the limited availability of tumor material, or a low tumor take-rate (17). Failure of tumor engraftment often occurs with the less aggressively growing (low-grade) tumors, such as pilocytic astrocytoma (61). For some of these tumor types, the use of more invading cells from a metastatic site (62), or samples from recurrent tumors might be an interesting alternative, as more aggressive tumor cells are thought to have a higher take rate *in vivo* (18). Care however needs to be taken to assure the practical use of such models, as recurrences and metastatic clones may differ from the primary tumor at diagnosis. Alternatively, more effective tumor-specific protocols may have to be developed. So far, only few comparative studies have been performed to determine the most optimal protocols per tumor type, with regard to sample size, sample processing, and mouse strain (17). In addition, the choice of animal model and experimental set-up may vary, depending on the research question; for low-grade tumors, for example, studies may be aimed at diminishing treatment-related side-effects, while survival studies will be more relevant for tumor subtypes with a poor prognosis.

Whilst appropriate PDX models for some tumor types are still missing, other pediatric brain tumor types seem to be more strongly represented. This especially holds true for models of glioblastoma, diffuse midline glioma, ependymoma, and medulloblastoma. Preclinical research in these fields is expanding, partly due to the raised interest in these tumor types, and to the increased availability of tumor material. For example, the development of autopsy protocols and the reintroduction of surgical biopsies for diffuse midline gliomas (63) has boosted preclinical research for these tumors, leading to the development of several animal models (16). Yet, more PDX models may be required for these tumor types as well, to cover different subgroups, stages, and heterogeneity of the disease. Full tumor dynamics may be captured by the collection of paired tumor samples at the time of diagnosis and at autopsy, while intratumoral heterogeneity may be covered by the sampling of multiple lesions from the same tumor in rapid autopsy protocols (64). Additional PDX models comprising the complete spectrum of the disease are needed to confirm the reproducibility of preclinical results, and to ensure clinical relevance of laboratory findings.

Despite the presence of a relatively high number of pediatric glioma models, PDXs covering *IDH1* mutations are lacking. Moreover, many described PDX models for pediatric glioma have not been molecularly characterized (16, 35, 38, 48, 65), even though mutation analysis could classify them as belonging
to specific biological subgroups (66). The same holds true for ependymoma (14, 38, 45, 46, 67) and, to a lesser extent, medulloblastoma models (38, 42–44, 68). For other tumor types, such as pineoblastoma, or germ cell tumors no molecular subgroups have yet been identified. Proper model validation and characterization of the available PDXs will be essential to test new therapies, especially when targeted therapy is applied. Many of the currently available PDX models without molecular designation have been established in the early 2000s, and these models may still be useful, provided that molecular profiling is performed. This might be an option for tumor types for which less PDXs are currently available, such as the atypical teratoid rhabdoid tumors (AT/RTs), a relatively rare, but highly aggressive pediatric brain tumor with a poor survival (69), which would benefit from preclinical in vivo studies to ameliorate prognosis and diminish long-term sequelae. One should however keep in mind that validation of those models by comparing the molecular features of the PDX with the original tumor will often not be possible. In such cases, models may be validated by comparing RNAseq-, whole genome sequencing-, and DNA methylation profiles with cohorts of patient data to ensure their representability of the human disease.

In order to translate preclinical findings to the clinic, the proper choice of animal model and experimental set-up will be paramount. Improved PDX models may be used for personalized medicine purposes, where the predictive value of therapy for a certain patient is determined based on a personal panel of mouse tumors. However, such a personalized approach is currently hampered by the time that is needed to develop these models, costs, and the variable rate of engraftment. Alternatively, multiple tumor-specific animal models may be used to conduct so-called Mouse Clinical Trials (MCTs). MCTs use small numbers of mice per treatment arm across a large number of PDX models, resembling human clinical trials more closely than preclinical trials in which large numbers of a specific PDX model are used (70). MCTs will help researchers to understand the correlation of specific genetic factors to therapy response, and may allow to predict patient response, as well as correct patient stratification. For this reason, additional, fully characterized models need to be developed with a special focus on the poorly represented subtypes. These models may be used to determine the best therapeutic regimes for each tumor subtype to implement in standard protocols.

In summary, although progress has been made in the development of orthotopic xenograft models for pediatric brain tumors, there is a clear imbalance in the number of PDX models for different tumor types, and a high variability in methodology and animal strains used. Combined efforts of neurosurgeons, pathologists, pediatric oncologists and preclinical researchers will be needed to develop additional animal models for the design of effective therapeutic strategies.

AUTHOR CONTRIBUTIONS

EHe wrote the first draft of the manuscript, while EHu revised the manuscript. Both authors contributed to the conception, design, and approved the submitted version.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## APPENDIX

### TABLE A1 | Overview of available orthotopic xenograft models per tumor entity, based on the 2016 WHO classification of tumors of the central nervous system.

| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/ euthanasia | Source | References |
|------------|----------------------|----------------|--------------------------|---------------------------|---------------------------------------------|---------------------|----------------------------------|---------------|-----|-----------------------------|--------|------------|
| **DIFFUSE ASTROCYTIC AND OLIGODENDROGLIAL TUMORS** |
| bGB1       | Giant cell glioblastoma | Cerebrum (frontal lobe) | ND | Surgical resection | 3.6 y | ND | Short-term adherent cell culture | Right cerebral hemisphere (ML +2 mm, AP +2 mm) | ND | University of Birmingham (38) |
| CCH/MC-DIPG-1 | Diffuse midline glioma, H3K27M mutant | ND | H3.3K27M | ND | ND | NSG, postnatal day 2 | Short-term cell culture in spheroids | 4th ventricle (AP -3 mm, DV -3 mm) | 16–19 days | On request (Dr. Drissi, Cincinnati Children’s Hospital) (71) |
| DIPG-PBTR3 | Diffuse midline glioma, H3K27M mutant | Ventral pons | H3.3K27M | Autopsy | 5 y | NSG, postnatal day 2 | Short-term cell culture in spheroids | 4th ventricle (AP -3 mm, DV -3 mm) | 6 months to clinical symptoms | On request (71) |
| GBM-311FH | Glioblastoma, IDH wild-type | Cortex (left temporal lobe) | Hypermutator | Surgical resection | 10.8 y | NSG | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV -2 mm) | 77–85 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) (72) |
| GBM-611FH | Glioblastoma, IDH wild-type | Cortex (left temporal lobe) | Hypermutator | Autopsy (recurrence) | 11.3 y | NSG | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV -2 mm) | 79–128 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) (72) |
| GU-pBT-7 | Diffuse midline glioma, H3K27M mutant | Right hemisphere (thalamus) | H3.1K27M, EGFR/KRAS amplification, CCND deletion | Surgical resection (primary tumor) | 4.2 y | NOD/SCID, 6–8 weeks | Short-term adherent cell culture | Frontal cortex (ML +2 mm, AP +1 mm, DV -2.5 mm) | 120–125 days | On request (37) |
| GU-pBT-10 | Glioblastoma NOS | Right hemisphere (relapse) | CDKN2A/B deletion | Surgical resection (recurrence) | 10.4 y | NOD/SCID, 6–8 weeks | Short-term adherent cell culture | Frontal cortex (ML +2 mm, AP +1 mm, DV -2.5 mm) | 215–330 days | On request (36) |

(Continued)
| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/ euthanasia | Source | References |
|------------|----------------------|---------------|--------------------------|----------------------------|------------------------------------------|---------------------|-----------------------------------|---------------|-----|---------------------------------|---------|------------|
| GU-pBT-15  | Diffuse midline glioma, H3K27M mutant | Brain stem | H3.3K27M | Surgical resection (primary tumor) | 12.5 y ♀ | NOD/SCID, 6–8 weeks | Short-term adherent cell culture | Frontal cortex – ML +2 mm, AP +1 mm, DV –2.5 mm | – 310–400 days | On request | (36) |
| GU-pBT-19  | Diffuse midline glioma, H3K27M mutant | Right hemisphere (thalamus) | H3.3K27M, RB deletion | Surgical resection (primary tumor) | 6.2 y ♂ | NOD/SCID, 6–8 weeks | Short-term adherent cell culture | Frontal cortex – ML +2 mm, AP +1 mm, DV –2.5 mm | – 285–350 days | On request | (36) |
| GU-pBT-23  | Glioblastoma NOS | Left hemisphere (temporal) | PDGFR/CDK4/MDM2 amplification | Surgical resection (primary tumor) | 2.9 y ♀ | NOD/SCID, 6–8 weeks | Short-term adherent cell culture | Frontal cortex – ML +2 mm, AP +1 mm, DV –2.5 mm | – 70–75 days | On request | (37) |
| GU-pBT-28  | Glioblastoma NOS (cerebellopontine angle) | Pons | EGFR amplification, NF1/CDKN2A/B deletion | Surgical resection (primary tumor) | 11.1 y ♀ | NOD/SCID, 6–8 weeks | Short-term adherent cell culture | Frontal cortex – ML +2 mm, AP +1 mm, DV –2.5 mm | – 130–155 days | On request | (37) |
| HSJD-DIPG-07 | Diffuse midline glioma, H3K27M mutant | Pons | H3.3K27M, ACVR1 R206H | Autopsy | 9.9 y ♂ | Athymic nude Foxn1nu, 6 weeks | Short-term cell culture in spheroids | Pons (ML) +1 mm, AP +1 mm, DV –4.5 mm | – 38–74 days | On request (Dr. Montero-Carcaboso, Barcelona) | (73) |
| Ibs-W0128DIPG/Li-F | Glioblastoma, IDH wild-type | Pons | H3 WT, ACVR1 G328V, PIK3CA Q546K | Autopsy | 8.5 y ♂ | NOD/SCID | Cell suspension from surgical specimen | Pons (DV) –5.2 mm | – 37–70 days | On request (Dr. Li, Houston) | (47) |
| IC-1128GBM | Glioblastoma NOS | Cerebrum | ND | Surgical resection (recurrence) | 8.6 y ♀ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV –3 mm) | – 150–180 days | On request | (16) |
| IC-1406 GBM | Glioblastoma NOS | Cerebrum | ND | Surgical resection | 5 y ♀ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV –3 mm) | – 67–79 days | On request | (48) |

(Continued)
### Table A1 (Continued)

| Model name | Tumor classification | Tumor location | Molecular classification (primary) | Moment of tumor collection | Age in years (y) or months (mo) and sex | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumorgrowth/euthanasia | Source | References |
|------------|----------------------|----------------|-----------------------------------|---------------------------|----------------------------------------|---------------------|-----------------------------------|-----------------|-----|-------------------------------|-------|-----------|
| IC-1502    | GBM Giant cell glioblastoma | Cerebrum | ND | Surgical resection | 4.6 y ♀ | Rag2/SCID, 6–8 weeks | Cellsuspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | – 77–96 days | On request | (48) | |
| IC-1621    | GBM Glioblastoma NOS | Cerebrum | ND | Surgical resection | 6 y ♂ | Rag2/SCID, 6–8 weeks | Cellsuspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | – 125–160 days | On request | (48) | |
| IC-2305    | GBM Glioblastoma NOS | Cerebrum | ND | Surgical resection | 9 y ♂ | Rag2/SCID, 6–8 weeks | Cellsuspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | – ND | On request | (48) | |
| IC-3704    | GBM Glioblastoma NOS | Cerebrum | ND | Surgical resection | 12 y ♂ | Rag2/SCID, 6–8 weeks | Cellsuspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | – ND | On request | (35) | |
| IC-3752    | GBM Glioblastoma NOS | Left hemisphere (frontal) | ND | Surgical resection (atrecurrence) | 4 y ♀ | Rag2/SCID, 6–8 weeks | Cellsuspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | – ND | On request | (35) | |
| IC-4687    | GBM Glioblastoma NOS | Right hemisphere (thalamus) | H3 WT | Surgical resection (atdiagnosis) | 7 y ♀ | NOD/SCID, 6–8 weeks | Cellsuspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | – 40–117 days | On request | (74) | |
| IC-R0315   | GBM Glioblastoma NOS | Left hemisphere (parietal) | H3 WT | Autopsy | 9 y ♀ | NOD/SCID, 6–8 weeks | Cellsuspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | – 35–47 days | On request | (74) | |
| ICb-1227   | Anaplastic astrocytoma NOS (secondary) | Cerebellum | ND | Surgical resection | 16.9 y ♀ | Rag2/SCID, 6–8 weeks | Cellsuspension from surgical specimen | Cerebellum (ML +1 mm, AP −1 mm, DV −3 mm) | – 62–80 days | On request | (16) | |
| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor $^a$ | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/euthanasia | Source | References |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| JHH-DIPG-01 | Diffuse midline glioma, H3K27M mutant | Pons | H3.3K27M | Autopsy | 8 y ♀ | Athymic nu/hu | Short-term cell culture in spheroids | Brainstem (ML +1 mm, AP −5 mm, DV −3.5 mm) | − | 230–245 days | On request | (75) |
| NEM273 | Diffuse midline glioma, H3K27M mutant | Pons | H3.1K27M, ACVR1 G328E | Biopsy | 4.6 y ♀ | Athymic nude, 4–6 weeks | Short-term adherent cell culture | Pons (ML +1 mm, AP −1 mm, DV −5 mm) | + | 220–258 days | On request | (32) |
| NEM285 | Diffuse midline glioma, H3K27M mutant | Pons | H3.3K27M, TP53 A159V | Biopsy | 7.1 y ♀ | Athymic nude, 4–6 weeks | Short-term adherent cell culture | Pons (ML +1 mm, AP −1 mm, DV −5 mm) | + | 174–224 days | On request | (32) |
| NEM289 | Diffuse midline glioma, H3K27M mutant | Pons | H3.2K27M, TP53 W146* | Biopsy | 4.7 y ♀ | Athymic nude, 4–6 weeks | Short-term adherent cell culture | Cell suspension from surgical specimen | Thalamus/Pons– (ML +2 mm, AP −3 mm, DV −3.5 mm/ML +1 mm, AP −1 mm, DV −5 mm) | 117–129 days | On request | |

(Continued)
| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/euthanasia | Source | References |
|------------|---------------------|---------------|--------------------------|---------------------------|--------------------------------------------|----------------------------------|---------------|-----|-------------------------------|--------|-------------|
| NEM290     | Diffuse midline glioma, H3K27M mutant | Pons | H3.3K27M, TP53 R175H | Biopsy | 11.6 y ♀ | Short-term adherent cell culture | Pons (ML +1 mm, AP −1 mm, DV −5 mm) | Thalamus/Pons (ML +2 mm, AP −3 mm, DV −3.5 mm/ML +1 mm, AP −1 mm, DV −5 mm) | 131–139 days | On request | (32) |
| NEM292     | Diffuse midline glioma, H3K27M mutant | Pons | H3.3K27M, TP53 P151T | Biopsy | 5.2 y ♀ | Short-term adherent cell culture | Pons (ML +1 mm, AP −1 mm, DV −5 mm) | Thalamus/Pons (ML +2 mm, AP −3 mm, DV −3.5 mm/ML +1 mm, AP −1 mm, DV −5 mm) | 61–73 days | On request | (32) |
| NEM325     | Diffuse midline glioma, H3K27M mutant | Pons | H3.3K27M | Biopsy | 5.5 y ♀ | Cell suspension from surgical specimen | Thalamus/Pons (ML +2 mm, AP −3 mm, DV −3.5 mm/ML +1 mm, AP −1 mm, DV −5 mm) | 87–111 days | On request | (32) |
| NEM328     | Diffuse midline glioma, H3K27M mutant | Pons | H3.1K27M, ACVR1 G328V | Biopsy | 3.5 y ♀ | Short-term adherent cell culture | Pons (ML +1 mm, AP −1 mm, DV −5 mm) | Thalamus/Pons (ML +2 mm, AP −3 mm, DV −3.5 mm/ML +1 mm, AP −1 mm, DV −5 mm) | 239–295 days | On request | (32) |
|            |                     |               |                         |                           |                                           |                                   |               |     |                               |        |             |

(Continued)
| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor ♀♂ | Mouse strain and age | Tumor preparation before injection | Injection site | BLI Time to tumor growth/euthanasia | Source | References |
|------------|----------------------|----------------|--------------------------|---------------------------|-----------------------------------------------|----------------------|----------------------------------|----------------|-----------------------------------|--------|------------|
| NEM335     | Diffuse midline glioma, H3K27M mutant | Pons | H3.3K27M, TP53 R248Q | Biopsy | 6.2 y ♀ | Athymic nude, 4–6 weeks | Cell suspension from surgical specimen | Thalamus/Pons– (ML +2 mm, AP −3 mm, DV –3.5 mm/ML +1 mm, AP −1 mm, DV −5 mm) | 126–134 days | On request (32) |
| NEM347     | Diffuse midline glioma, H3K27M mutant | Pons | H3.3K27M, TP53 R273C | Biopsy | 9.1 y ♀ | Athymic nude, 4–6 weeks | Cell suspension from surgical specimen | Thalamus/Pons– (ML +2 mm, AP −3 mm, DV −3.5 mm/ML +1 mm, AP −1 mm, DV −5 mm) | 117–125 days | On request (32) |
| NEM353     | Diffuse midline glioma, H3K27M mutant | Pons | H3.3K27M | Biopsy | 6.5 y ♀ | Athymic nude, 4–6 weeks | Cell suspension from surgical specimen | Thalamus/Pons– (ML +2 mm, AP −3 mm, DV −3.5 mm/ML +1 mm, AP −1 mm, DV −5 mm) | 81 days | On request (32) |
| nOLG1      | Oligodendroglioma NOS | Cerebrum (right fronto temporo-parietal) | ND | Surgical resection | 6.5 y ND | Short-term adherent cell culture | Right cerebral hemisphere (ML +2 mm, AP +2 mm) | ND | Children’s Brain Tumour Research Centre, Nottingham (38) | (Continued) |
| Model name   | Tumor classification                     | Tumor location                  | Molecular classification       | Moment of tumor collection | Age in years (y) or months (mo) and sex donor | Mouse strain and age | Tumor preparation before injection | Injection site          | BLI | Time to tumor growth/ euthanasia | Source | References |
|--------------|-----------------------------------------|----------------------------------|--------------------------------|---------------------------|----------------------------------------------|---------------------|-----------------------------------|------------------------|-----|-------------------------------|---------|------------|
| PBT-01FH     | Diffuse midline glioma, H3K27M mutant   | Cortex, bilateral thalamic       | H3.1K27M                        | Autopsy (recurrence)      | 5 y ♀                                       | NSG                 | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −2 mm) |     | 89–116 days                  | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |
| PBT-02FH     | Anaplastic astrocytoma, NOS             | Cortex                           | CDK4 amplification, FGFR1 mutation | Autopsy (recurrence)      | 14.8 y ♂                                     | NSG                 | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −2 mm) |     | 52–121 days                  | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |
| PBT-05FH     | Glioblastoma, IDH wild-type             | Cortex, right frontal            | Myc amplification               | Surgical resection (recurrence) | 9.1 y ♀                                    | NSG                 | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −2 mm) |     | 37–42 days                   | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |
| PBT-06FH     | Glioblastoma, IDH wild-type             | Cortex, right frontoparietal     | p 53 mutation, CDK4 amplification | Autopsy (recurrence)      | 15.9 y ♀                                    | NSG                 | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −2 mm) |     | 131–326 days                 | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |
| QCTB-R059    | Diffuse midline glioma, H3K27M mutant   | Thalamus                         | H3.3K27M                        | Surgical resection        | 10.4 y ♀, postnatal day 35                  | NSG                 | Short-term cell culture in spheroids | Thalamus (ML +0.8 mm, AP −1 mm, DV −3.5 mm) |     | 12–14 days                   | Queensland Children’s Medical Research Institute, Brisbane | (76) |
| SF7761       | Diffuse midline glioma, H3K27M mutant   | Pons                             | H3.3K27M (hTERT modified)       | Biopsy                    | 6 y ♀                                        | Athymic nu/nu, 6 weeks | Short-term cell culture in spheroids | Pontine tegmentum (ML +1.5 mm, DV −5 mm) |     | 106–130 days                 | On request | (77) |
| SF8628       | Diffuse midline glioma, H3K27M mutant   | Pons                             | H3.3K27M, p53 mutation          | Biopsy                    | 3 y ♀                                        | Athymic nu/nu, 5 weeks | Short-term adherent cell culture | Pontine tegmentum (ML +1.5 mm, DV −5 mm) |     | 66–70 days                   | On request | (39) |

(Continued)
### TABLE A1 | Continued

| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/euthanasia | Source | References |
|------------|----------------------|----------------|--------------------------|----------------------------|---------------------------------------------|---------------------|-----------------------------------|---------------|-----|-----------------------------|--------|------------|
| SU-pcGBM1  | Glioblastoma NOS    | Cortex         | ND                       | ND                         | NOD/SCID, 6–8 weeks                      | Left hemisphere (ML − 2 mm, AP − 2 mm, DV − 3.5 mm) | + ND               | ND            | On request (Dr. Monje, Stanford) | (65)  |
| SU-pcGBM2  | Glioblastoma, IDH wild-type | Frontal lobe | P53 mutation, Biopsy EGFR amplification | 15 y ♂                   | NSG, postnatal day 35                     | Right hemisphere (ML +0.5 mm, AP +1 mm, DV −1.75 mm) | + 126–163 days | On request | (11) |
| SU-DIPG-I  | Anaplastic astrocytoma, IDH wild-type | Pons | H3 WT, p53 mutation | Autopsy                  | 5 y ♀                                   | 4th ventricle/lateral ventricles (ML +1 mm, AP −3 mm, DV −3 mm/ML +1 mm, AP +2 mm, DV −2 mm) | − 26 weeks to clinical symptoms | On request (Dr. Monje, Stanford) | (78) |
| SU-DIPG-VI | Diffuse midline glioma, H3K27M mutant | Pons | H3.3K27M, p53 mutation | Autopsy                  | 7 y ♀                                   | 4th ventricle/pons (AP −3 mm, DV −3 mm) | ≤ 2 months (BLI) | On request | (47) |
| SU-DIPG-XIIIP* | Diffuse midline glioma, H3K27M mutant | Pons | H3.3K27M | Autopsy | 6 y ♀ | 4th ventricle/pons (ML +0.8 mm, AP −0.5 mm, DV −5 mm) | 19–28 days | On request | (79) |
| SU-DIPG-XIIIFL | Diffuse midline glioma, H3K27M mutant | Frontal lobe metastasis | H3.3K27M | Autopsy | 6 y ♀ | 4th ventricle/pons (ML +0.8 mm, AP −0.5 mm, DV −5 mm) | ND | On request | (79) |

(Continued)
TABLE A1 | Continued

| Model name   | Tumor classification          | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor ♀♂ | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/euthanasia | Source                  | References |
|--------------|------------------------------|----------------|--------------------------|----------------------------|-----------------------------------------------|----------------------|------------------------------------|-----------------|-----|---------------------------------|------------------------|------------|
| SU-DIPG-XIX  | Diffuse midline glioma, H3K27M mutant | Pons           | H3.3K27M                 | Autopsy                    | 2 y ♀                                       | NSG, postnatal day 35 | Short-term cell culture in spheroids | Pons (ML +1 mm, AP −0.8 mm, DV −5 mm) | +   | ND                              | On request           | (80)       |
| SU-pSCG-1    | Diffuse midline glioma, H3K27M mutant | spinal cord    | H3.3K27M                 | Autopsy                    | 12 y ♀                                     | NSG, postnatal day 35 | Short-term cell culture in spheroids | Medulla (ML +0.7 mm, AP −3.5 mm, DV −4.5 mm) | +   | ND                              | On request           | (76)       |
| TT10603      | Diffuse midline glioma, H3K27M mutant | Pons           | H3.3K27M, TPS3 R141C     | Surgical resection         | 7 y ♀                                      | NSG                  | Short-term adherent cell culture    | Brainstem (ML +1 mm, AP −1.5 mm, DV −4.5 mm) | –   | 172 days to onset (MRI)       | On request           | (40)       |
| TT10630      | Diffuse midline glioma, H3K27M mutant | Pons           | H3.3K27M, PPM1D S16E     | Biopsy                     | 4 y ♀                                      | NSG                  | Short-term adherent cell culture    | Brainstem (ML +1 mm, AP −1.5 mm, DV −4.5 mm) | –   | 186 days to onset (MRI)       | On request           | (40)       |
| TT10714      | Diffuse midline glioma, H3K27M mutant | Pons           | H3.3K27M, PPM1D C478X    | Surgical resection         | 6 y ♀                                      | NSG                  | Short-term adherent cell culture    | Brainstem (ML +1 mm, AP −1.5 mm, DV −4.5 mm) | –   | 155 days to onset (MRI)       | On request           | (40)       |
| VUMC-DIPG-F  | Diffuse midline glioma, H3K27M mutant | Pons           | H3.3K27M                 | Biopsy                     | 7 y ♀                                      | FVB athymic, 6–8 weeks | Short-term cell culture in spheroids | Pons (ML +0.8 mm, AP −1 mm, DV −4.5 mm) | +   | 120–179 days                    | On request           | (81)       |

OTHER ASTROCYTIC TUMORS

| Model name   | Tumor classification          | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor ♀♂ | Mouse strain and age | Tumor preparation from surgical specimen | Injection site | BLI | Time to tumor growth/euthanasia | Source                  | References |
|--------------|------------------------------|----------------|--------------------------|----------------------------|-----------------------------------------------|----------------------|------------------------------------------|-----------------|-----|---------------------------------|------------------------|------------|
| IC-3635 PXA  | Pleomorphic xanthoastrocytoma (grade II) | Left temporal lobe | BRAF V600E, CDKN2A deletion | Surgical resection       | 10 y ♀                                      | NOD/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | –   | 175–255 days                    | On request           | (82)       |
### TABLE A1  |  Continued

| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor ♀♂ | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/euthanasia | Source | References |
|------------|----------------------|----------------|--------------------------|---------------------------|-------------------------------------------------|---------------------|-----------------------------------|----------------|-----|-------------------------------|--------|------------|
| **EPENDYMAL TUMORS** | | | | | | | | | | | | |
| BT-44 | Anaplastic ependymoma | Posterior fossa | ND | ND | 2 y ♀ | Athymic nu/nu, 5–6 weeks | Caudate nucleus | – | 100–155 days | On request | (46) |
| BT-57 | Anaplastic ependymoma | Posterior fossa (focal) | ND | ND | 10 mo ♂ | Athymic nu/nu, 5–6 weeks | Caudate nucleus | – | 100–155 days | On request | (46) |
| D528 EP-X | Ependymoma | Posterior fossa | ND | Biopsy | 2.5 y ♀ | BALB/c nu/nu, 3–4 weeks | Right cerebral hemisphere | – | ± 85 days | On request | (67) |
| D612 EP-X | Ependymoma | Posterior fossa | ND | Biopsy | 1.1 y ♀ | BALB/c nu/nu, 3–4 weeks | Right cerebral hemisphere | – | ± 72.5 days | On request | (67) |
| E520-PF1 | Ependymoma | Infratentorial | A/CIMP (+) | Surgical resection | ND | NSG 8–12 weeks | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | + | 30–59 days | On request | (41) |
| EPD-210FH | Anaplastic ependymoma | Posterior fossa | PFA | Autopsy (recurrence) | 10 y ♂ | NSG | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −2 mm) | – | 75–103 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |
| EPD-613FH | Ependymoma, RELA fusion positive (grade III) | ND | RELA | Surgical resection (recurrence) | 16 y ♂ | NSG | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −2 mm) | – | 137–223 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |

(Continued)
| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/ euthanasia | Source | References |
|------------|----------------------|---------------|--------------------------|---------------------------|----------------------------------|------------------|-----------------------------------|---------------|-----|-------------------------------|--------|------------|
| EPD-710FH  | Anaplastic ependymoma| Posterior fossa| PFA | Surgical resection | 2.8 y♂ | NSG | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −2 mm) | – | 115–326 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |
| EPN1       | Anaplastic ependymoma| Posterior fossa| ND | Surgical resection | ND | Wistar Rat, treated with immunosuppressant drugs | Short-term adherent cell culture | 3rd ventricle (ML+1.4 mm, AP +0.8 mm, DV −3.8 mm) | FL | ≤45 days (X-ray/fluorescent imaging) | On request | (14) |
| EPN2       | Anaplastic ependymoma| Posterior fossa| ND | Surgical resection | ND | Wistar Rat, treated with immunosuppressant drugs | Short-term adherent cell culture | 3rd ventricle (ML+1.4 mm, AP +0.8 mm, DV −3.8 mm) | FL | ≤45 days (X-ray/fluorescent imaging) | On request | (14) |
| EPN3       | Anaplastic ependymoma| Posterior fossa| ND | Surgical resection | ND | Wistar Rat, treated with immunosuppressant drugs | Short-term adherent cell culture | 3rd ventricle (ML+1.4 mm, AP +0.8 mm, DV −3.8 mm) | FL | ≤45 days (X-ray/fluorescent imaging) | On request | (14) |
| EPN4       | Anaplastic ependymoma| Posterior fossa| ND | Surgical resection | ND | Wistar Rat, treated with immunosuppressant drugs | Short-term adherent cell culture | 3rd ventricle (ML+1.4 mm, AP +0.8 mm, DV −3.8 mm) | FL | ≤45 days (X-ray/fluorescent imaging) | On request | (14) |
| EPN5       | Anaplastic ependymoma| Posterior fossa| ND | Surgical resection | ND | Wistar Rat, treated with immunosuppressant drugs | Short-term adherent cell culture | 3rd ventricle (ML+1.4 mm, AP +0.8 mm, DV −3.8 mm) | FL | ≤45 days (X-ray/fluorescent imaging) | On request | (14) |
| EPP        | Ependymoma | 4th ventricle | SEC61G-EGFR gene fusion (subclone) | Surgical resection (recurrence) | 3.2 y♂ | CD1 nu/nu, 5 weeks | Short-term cell culture in spheroids | 4th ventricle (ML +0.2 mm, AP −6 mm, DV −4 mm) | – | 70–104 days | On request | (45) |
| EPV        | Ependymoma | Posterior fossa | ND | Surgical resection (recurrence) | 1.9 y♂ | CD1 nu/nu, 5 weeks | Short-term cell culture in spheroids | 4th ventricle (ML +0.2 mm, AP −6 mm, DV −4 mm) | – | 68–149 days | On request | (45) |

(Continued)
### TABLE A1 | Continued

| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex | Mouse strain and age | Tumor preparation before injection | Injection site | BLI Time to tumor growth/ euthanasia | Source | References |
|------------|----------------------|----------------|--------------------------|---------------------------|----------------------------------------|---------------------|-----------------------------------|---------------|-----------------------------------|--------|------------|
| IC-1425EPN | Ependymoma, RELA fusion positive (grade III) | supratentorial | C11orf95-RELA fusion | Surgical resection (recurrence) | 9 y ♂ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | 85–180 days | On request [50] |
| nEPN1 | Ependymoma RELA fusion positive (grade II) | supratentorial (right parietal) | C11orf95-RELA fusion | Surgical resection (recurrence) | 13.5 y ♂ | ND | Short-term adherent cell culture | Right cerebral hemisphere (ML +2 mm, AP +2 mm) | ND | Children’s Brain Tumour Research Centre, Nottingham [38] |
| nEPN2 | Ependymoma | 4th ventricle | ND | Surgical resection | 3.4 y ND | ND | Short-term adherent cell culture | Right cerebral hemisphere (ML +2 mm, AP +2 mm) | ND | Children’s Brain Tumour Research Centre, Nottingham [38] |

### TUMORS OF THE PINEAL REGION

| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex | Mouse strain and age | Tumor preparation before injection | Injection site | BLI Time to tumor growth/ euthanasia | Source | References |
|------------|----------------------|----------------|--------------------------|---------------------------|----------------------------------------|---------------------|-----------------------------------|---------------|-----------------------------------|--------|------------|
| PBT-08FH | Pineoblastoma | Pineal region | Drosha (splice site and splice site mutation) | Surgical resection | 11.2 y ♀ | NSG | Cell suspension from surgical specimen | Right cerebellum (ML +2 mm, AP −2 mm, DV −2 mm) | 245 days | BTRL (Brain Tumor Resource Lab—https://research.fnrc.org) [72] |
| Pineo-113FH | Pineoblastoma | ND | ND | Surgical resection | 8 y ♂ | NSG | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −2 mm) | 162–301 days | BTRL (Brain Tumor Resource Lab—https://research.fnrc.org) [72] |

### EMBRYONAL TUMORS—MEDULLOBLASTOMA

| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex | Mouse strain and age | Tumor preparation before injection | Injection site | BLI Time to tumor growth/ euthanasia | Source | References |
|------------|----------------------|----------------|--------------------------|---------------------------|----------------------------------------|---------------------|-----------------------------------|---------------|-----------------------------------|--------|------------|
| BO-101 | Medulloblastoma, NOS | Cerebellum | ND | Surgical resection | 9 y ♂ | Athymic nu/nu, 3–4 weeks | Short-term adherent cell culture | Right cerebral hemisphere | ND | On request [42] |
| CHLA-01-MED = CRL-3021 | Medulloblastoma | Posterior fossa | Non WNT/non SHH Group 4, Myc amp | Surgical resection (at diagnosis) | 8 y ♂ | NOD/SCID 4–6 weeks | Short-term cell culture in spheroids | Right – caudate/putamen (ML +2 mm, AP +0.5 mm, DV −3.3 mm) | 44 days to onset | ATCC (www.ATCC.org) [83] |

(Continued)
| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex | Mouse strain and age | Tumor preparation before injection | Injection site BLI | Time to tumor growth/ euthanasia | Source | References |
|------------|----------------------|----------------|--------------------------|---------------------------|--------------------------------------|---------------------|------------------------------------|-----------------|----------------------------------|--------|------------|
| CHLA-259   | Medulloblastoma, large cell/anaplastic | Posterior fossa (4th ventricle) | ND | Surgical resection (at diagnosis) | 14 y♂ | NOD/SCID 4–6 weeks | Short-term adherent cell culture | Right caudate/putamen (ML +2 mm, AP +0.5 mm, DV −3.3 mm) | Cerebellum | 39–77 days | CCR (children cell line repository—www.cells.org) | (43) |
| DMB006     | Medulloblastoma | ND | Non WNT/non SHH Group 4 | Surgical resection | ND | NSG | Cell suspension from surgical specimen | Left cerebellar hemisphere (ML −1.5 mm, AP −7 mm, DV −2 mm) | Cerebellum | <9 days (MRI) | On request | (52) |
| DMB012     | Medulloblastoma, desmoplastic | ND | SHH | ND | 3 y♀ | NSG | Cell suspension from surgical specimen | Left cerebellar hemisphere (ML −1.5 mm, AP −7 mm, DV −2 mm) | Cerebellum | 61–69 days | On request | (52) |
| HD-MB03    | Medulloblastoma, large cell/anaplastic | 4th ventricle | Non WNT/non SHH Group 3, Myc amp | Surgical resection | 3 y♂ | CB17-SCID | Short-term semi-adherent cell culture | Right cerebellum (ML +1 mm, AP −1 mm, DV −3 mm) | Cerebellum | 65–93 days | On request | (16) |
| ICb-984MB  | Medulloblastoma, anaplastic | Cerebellum | SHH | Surgical resection | 7.8 y♀ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebellum (ML +1 mm, AP −1 mm, DV −3 mm) | Cerebellum | ND | On request | (85) |
| ICb-1078MB | Medulloblastoma, anaplastic | Cerebellum | Non WNT/non SHH Group 4 | Surgical resection | 11.7 y♂ | Rag2/SCID, 5–7 weeks | Cell suspension from surgical specimen | Cerebellum | ND | On request | (49) |
| ICb-1140MB | Medulloblastoma, anaplastic | Cerebellum | WNT | Surgical resection | 6 y♂ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Cerebellum | ND | On request | (16) |
| ICb-1192MB | Medulloblastoma, classic | Cerebellum | WNT | Surgical resection | 12.4 y♂ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebellum (ML +1 mm, AP −1 mm, DV −3 mm) | Cerebellum | 75–95 days | On request | (16) |
| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor ♀♂ | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/euthanasia | Source | References |
|------------|----------------------|----------------|--------------------------|-----------------------------|-----------------------------------------------|---------------------|-----------------------------------|----------------|------------------|----------------------------------|--------|------------|
| ICB-1197MB | Medulloblastoma, nodular | Cerebellum | Non WNT/non SHH Group 3 | Surgical resection | 5 y ♀ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebellum (ML +1 mm, AP −1 mm, DV −3 mm) | – | 272–305 days | On request | (16) |
| ICB-1299MB | Medulloblastoma, anaplastic | Cerebellum | Non WNT/non SHH Group 3 | Surgical resection | 2.8 y ♀ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebellum (ML +1 mm, AP −1 mm, DV −3 mm) | – | 108–125 days | On request | (16) |
| ICB-1338MB | Medulloblastoma, nodular | Cerebellum | SHH | Surgical resection | 0.5 y ♂ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebellum (ML +1 mm, AP −1 mm, DV −3 mm) | – | 140–203 days | On request | (16) |
| ICB-1487MB | Medulloblastoma, classic | Cerebellum | Non WNT/non SHH Group 4 | Surgical resection | 6.9 y ♂ | Rag2/SCID, 5–7 weeks | Cell suspension from surgical specimen | Cerebellum | – | ND | On request | (85) |
| ICB-1494MB | Medulloblastoma, anaplastic | Cerebellum | Non WNT/non SHH Group 3 | Surgical resection | 5.2 y ♀ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebellum (ML +1 mm, AP −1 mm, DV −3 mm) | – | 55–105 days | On request | (16) |
| ICB-1572MB | Medulloblastoma, large cell | Cerebellum | Non WNT/non SHH Group 3 | Surgical resection | 14.8 y ♂ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebellum (ML +1 mm, AP −1 mm, DV −3 mm) | – | 40–82 days | On request | (16) |
| ICB-1595MB | Medulloblastoma, anaplastic | Cerebellum | Non WNT/non SHH Group 3 | Surgical resection | 1.2 y ♀ | Rag2/SCID, 5–7 weeks | Cell suspension from surgical specimen | Cerebellum | – | ND | On request | (85) |
| ICB-Z01109MB | Medulloblastoma, anaplastic | Cerebellum | ND | Surgical resection | 7 y ♀ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebellum (ML +1 mm, AP −1 mm, DV −3 mm) | – | ND | On request | (68) |

(Continued)
| Model name     | Tumor classification | Tumor location   | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor ♀♂ | Mouse strain and sex donor | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/euthanasia | Source | References |
|----------------|----------------------|------------------|--------------------------|---------------------------|--------------------------------------------------|---------------------------|----------------------------------|----------------|-----|-----------------------------|--------|------------|
| ICB-J1017MB    | Medulloblastoma, anaplastic | Cerebellum | Non WNT/non SHH Group 3 | Surgical resection | 9 y ♂ | Cell suspension from surgical specimen | Right cerebellum (ML +1 mm, AP −1 mm, DV −3 mm) | ND | On request | (68) |
| MB3W1          | Medulloblastoma, anaplastic | 4th ventricle | Non WNT/non SHH Group 3, Myc amplification | Surgical resection | 1.8 y ♀ | Short-term cell culture in spheroids | Right cerebellum | 28–55 days | On request | (86) |
| MB-LU-181      | Medulloblastoma | ND | Non WNT/non SHH Group 3 | Surgical resection | 4 y ♀ | Short-term cell culture in spheroids | Right cerebellum (ML +1 mm, AP −2 mm, DV −2.5 mm) | 70–126 days | On request | (87) |
| Med-113FH      | Medulloblastoma, large cell/anaplastic | Cerebelum | SHH | Surgical resection | 9.9 y ♀ | Cell suspension from surgical specimen | Right cerebellum (ML +2 mm, AP −2 mm, DV −2 mm) | 72–112 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |
| Med-114FH      | Medulloblastoma, large cell/anaplastic | Cerebelum | Non WNT/non SHH Group 3, Myc amplification | Surgical resection | 6.6 y ♀ | Cell suspension from surgical specimen | Right cerebellum (ML +2 mm, AP −2 mm, DV −2 mm) | 31–60 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |
| Med-1512FH     | Medulloblastoma, desmoplastic | Cerebelum | Non WNT/non SHH Group 4 | Surgical resection | 6 y ♀ | Cell suspension from surgical specimen | Right cerebellum (ML +2 mm, AP −2 mm, DV −2 mm) | 124–226 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |
| Med-1712FH     | Medulloblastoma, desmoplastic | Cerebelum | SHH | Surgical resection | 4.9 y ♀ | Cell suspension from surgical specimen | Right cerebellum (ML +2 mm, AP −2 mm, DV −2 mm) | 86–157 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (53) |

(Continued)
| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age (y/ mo) and sex donor | Mouse strain and age | Tumor preparation before injection | Injection site | BLI Time to tumor growth/euthanasia | Source References |
|------------|----------------------|---------------|-------------------------|-----------------------------|-----------------------------|------------------------|-----------------------------|--------------|----------------------------------|------------------|
| Med-191FH  | Medulloblastoma, large cell/anaplastic | Cerebellum | Non-WNT/non-SHH Group 3 | Surgical resection | 3.5 y ♀ | NSG Cell suspension from surgical specimen | - | Right cerebellum (ML + 2 mm, AP − 2 mm, DV − 2 mm) | 52–91 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) |
| Med-210FH  | Medulloblastoma | Cerebellum | Non-WNT/non-SHH Group 3 | Surgical resection | 5.2 y ♀ | NSG Cell suspension from surgical specimen | - | Right cerebellum (ML + 2 mm, AP − 2 mm, DV − 2 mm) | 18–224 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) |
| Med-211FH  | Medulloblastoma, classic | Cerebellum | Non-WNT/non-SHH Group 3 | Surgical resection | 2.8 y ♂ | NSG 6–8 weeks Cell suspension from surgical specimen (serial transplantation) | - | Right cerebellum (ML + 2 mm, AP − 2 mm, DV − 3 mm) | 42–64 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) |
| Med-2112FH | Medulloblastoma, large cell/anaplastic | Cerebellum | Non-WNT/non-SHH Group 3 | Surgical resection | 7 y ♂ | NSG Cell suspension from surgical specimen | - | Right cerebellum (ML + 2 mm, AP − 2 mm, DV − 2 mm) | 56–77 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) |
| Med-314FH  | Medulloblastoma, classic | Cerebellum | SHH Group | Surgical resection (recurrence) | 10 y ♀ | NSG Cell suspension from surgical specimen | - | Right cerebellum (ML + 2 mm, AP − 2 mm, DV − 2 mm) | 95–133 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) |
| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/ euthanasia | Source | References |
|------------|----------------------|----------------|--------------------------|--------------------------|-----------------------------------------------|---------------------|----------------------------------|----------------|-----|-------------------------------|--------|-----------|
| Med-411FH  | Medulloblastoma, large cell/anaplastic | Cerebellum | Surgical resection | 3 y♂ | NSG, 6–10 week | Cell suspension from surgical specimen | Right cerebellum (ML +2 mm, AP −2 mm, DV −2 mm) | + | 29–39 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (53) |
| Med-511FH  | Medulloblastoma | Cerebellum | Surgical resection (primary tumor) | ND | CD1 nu/nu | Cell suspension from surgical specimen | Cortex | + | 62–68 days | on request (Dr. Olson, Fred Hutch) | (54) |
| Med-610FH  | Medulloblastoma, large cell/anaplastic | Cerebellum | Surgical resection | 5.3 y♂ | NSG | Cell suspension from surgical specimen | Right cerebellum (ML +2 mm, AP −2 mm, DV −2 mm) | – | 148–187 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |
| Med-813FH  | Medulloblastoma, classic | Cerebellum | Surgical resection | 2.6 y♂ | NSG | Cell suspension from surgical specimen | Right cerebellum (ML +2 mm, AP −2 mm, DV −2 mm) | – | 32–78 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |
| Med-913FH  | Medulloblastoma, classic | Cerebellum | Surgical resection | 7.5 y♀ | NSG | Cell suspension from surgical specimen | Right cerebellum (ML +2 mm, AP −2 mm, DV −2 mm) | – | 175–415 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) | (72) |
| nMED1      | Medulloblastoma, NOS | Cerebellum | Surgical resection | 3.4 y | ND | Short-term adherent cell culture | Right cerebral hemisphere (ML +2 mm, AP +2 mm) | – | ND | Children’s Brain Tumour Research Centre, Nottingham | (38) |

(Continued)
| Model name | Tumor classification          | Tumor location           | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/euthanasia | Source | References |
|------------|-------------------------------|--------------------------|--------------------------|---------------------------|-----------------------------------------------|----------------------|------------------------------------|----------------|-----|-------------------------------|--------|------------|
| nMED2      | Medulloblastoma, NOS         | Frontal bilateral (metastasis) | ND                       | Surgical resection (recurrence) | 10.6 y ♀♂ | ND | Short-term adherent cell culture | Right cerebral hemisphere (ML +2 mm, AP +2 mm) | ND | Children’s Brain Tumour Research Centre, Nottingham (38) |
| PBT-07FH   | Medulloblastoma              | ND                       | Non WNT/non SHH Group 3  | Surgical resection | 3.5 y ♀ | NSG | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −2 mm) | 67–169 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) (72) |
| RCMB18     | Medulloblastoma, anaplastic | ND                       | SHH                      | Surgical resection | 7 y ♀♂ | NSG 6–8 weeks | Cell suspension from surgical specimen | Cerebellum + | 34–58 days | on request (Dr. Wechsler-Reya, Sanford-Burnham medical Discovery Institute) (52) |
| RCMB28     | Medulloblastoma              | ND                       | Non WNT/non SHH Group 3  | ND | ND | NSG 6–86–8 weeks | Cell suspension from surgical specimen | Cerebellum − | ND | On request (53) |
| RCMB32     | Medulloblastoma              | ND                       | SHH                      | ND | ND | NSG 6–8 weeks | Cell suspension from surgical specimen | Cerebellum − | ND | On request (53) |
| SU-MB-02   | Medulloblastoma, large cell/anaplastic | ND | Non WNT/non SHH Group 3, Myc amplification | Autopsy (leptomeningial spread) | 3 y ♀♂ | NSG 4–6 weeks | Short-term cell culture in spheroids | Cerebellum + (AP −2 mm, DV −2 mm) | 33–40 days | On request (Dr. Cho, Stanford) (65) |
| SU-MB-09   | Medulloblastoma              | ND                       | Non WNT/non SHH Group 4  | Surgical resection | 9 y ♀ | NSG 4–6 weeks | Short-term cell culture in spheroids | Cerebellum + (AP −2 mm, DV −2 mm) | 83–100 days | On request (Dr. Cho, Stanford) (65) |
| UM-MB1     | Medulloblastoma, NOS         | Posterior fossa          | ND                       | Surgical resection | 4 y ♀ | CD1 nu/nu, 4 weeks | Short-term adherent cell culture | Right cerebral hemisphere (ML +1 mm, AP +2 mm, DV −3.5 mm) | ND | On request (44) |
| Model name | Tumor classification | Tumor location | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/ euthanasia | Source | References |
|------------|----------------------|----------------|--------------------------|---------------------------|---------------------------------------------|----------------------|-----------------------------------|---------------|-----|-------------------------------|--------|------------|
| BT183      | Embryonal tumor with multilayered rosettes, C19MC-altered | ND C19MC amplification ND | 2 y ♂ | NOD/SCID, 6–8 weeks | Short-term cell culture in spheroids | Right striatum (ML +2 mm, AP −1 mm, DV −3 mm) | 8–45 days | On request (88) |
| IC-2864 PNET | CNS embryonal tumor, NOS | ND ND Surgical resection 14 y ♀ | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | 48–76 days | On request (89) |
| NCH3602    | Embryonal tumor with multilayered rosettes, C19MC-altered | Right hemisphere C19MC amplification Surgical resection | 2 y NSG, 6–8 weeks | Short-term cell culture in spheroids | Right striatum (ML +2,5 mm, AP +1 mm, DV −3 mm) | ND | On request (90) |
| ncPNET     | CNS embryonal tumor, NOS | Cerebrum (left frontal) ND Surgical resection | 5 y ND | Short-term adherent cell culture | Right cerebral hemisphere (ML +2 mm, AP +2 mm) | ND | Children’s Brain Tumour Research Centre, Nottingham (38) |
| ATRT-310FH | Atypical teratoid/rhabdoid tumor | Anterior cranial fossa ATRT SHH Surgical resection | 6.1 y ♀ | NSG, 6–8 weeks | Cell suspension from surgical specimen (serial transplantation) | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −2 mm) | 33–143 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) |
| ATRT-312FH | Atypical teratoid/rhabdoid tumor | Cortex (parietal lobe) ATRT MYC ND | 1.8 y ♂ | NSG | Cell suspension from surgical specimen | Right cerebral hemisphere (ML +1 mm, AP +1.5 mm, DV −2 mm) | 40–89 days | BTRL (Brain Tumor Resource Lab—https://research.fhcrc.org) |

(Continued)
| Model name       | Tumor classification          | Tumor location                      | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/euthanasia | Source | References |
|-----------------|-------------------------------|-------------------------------------|--------------------------|---------------------------|-----------------------------------------------|---------------------|-----------------------------------|----------------|-----|-------------------------------|--------|------------|
| CHLA-06-ATRT    | Atypical teratoid/rhabdoid tumor | Posterior fossa                     | INI-1 loss               | Surgical resection (primary tumor) | 3 mo ♀                                  | ND                  | Right striatum – (ML +2 mm, AP −3 mm, DV −3 mm) | 14–20 days |     | On request                    | ATCC   | (55)       |
| CHLA-266        | Atypical teratoid/rhabdoid tumor | posterior fossa                     | INI-1 loss               | Surgical resection (at diagnosis) | 2.5 y ♀                               | NSG 6–8 weeks | Right – caudate/putamen (ML +2 mm, AP +0.5 mm, DV −3.3 mm) | 40–50 days |     | On request                    | CCR    | (43)       |
| SU-ATRT-02      | Atypical teratoid/rhabdoid tumor | Supratentorial                      | ND                       | Surgical resection (primary tumor) | 2 y ♀                                 | NSG 5–6 weeks | Right striatum + (ML +2 mm, AP −2 mm, DV −3.5 mm) | 50–63 days |     | On request                    | On request | (65)       |

**Germ cell tumors**

| Model name       | Tumor classification | Tumor location          | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/euthanasia | Source | References |
|-----------------|---------------------|-------------------------|--------------------------|---------------------------|-----------------------------------------------|---------------------|-----------------------------------|----------------|-----|-------------------------------|--------|------------|
| IC-6999GCT      | Germinoma           | C6 spinal cord          | ND                       | Surgical resection (metastasis-recurrence) | 16 y ♀                                | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebral – hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | 80–242 days |    | On request                    | On request | (62)       |
| IC-9320GCT      | Germinoma           | Supratentorial          | KIT D816H                | Surgical resection (metastasis) | 1.5 y ♀                               | Rag2/SCID, 6–8 weeks | Cell suspension from surgical specimen | Right cerebral – hemisphere (ML +1 mm, AP +1.5 mm, DV −3 mm) | 60–160 days |    | On request                    | On request | (62)       |

**Tumors of the sellar region**

| Model name       | Tumor classification                        | Tumor location                      | Molecular classification | Moment of tumor collection | Age in years (y) or months (mo) and sex donor | Mouse strain and age | Tumor preparation before injection | Injection site | BLI | Time to tumor growth/euthanasia | Source | References |
|-----------------|---------------------------------------------|-------------------------------------|--------------------------|---------------------------|-----------------------------------------------|---------------------|-----------------------------------|----------------|-----|-------------------------------|--------|------------|
| adaCP 1         | Adamantinomatous ND craniopharyngeoma       | CTNNB1 mutation                     | Surgical resection       | 16 y ♀                    | NSG, 5–8 weeks                               | Tumor tissue         | Right cerebral – hemisphere (ML +3 mm) | ND             | On request | ND                           | On request | (33)       |
| ACP1            | Adamantinomatous Sellar region craniopharyngeoma | CTNNB1 mutation                   | Surgical resection       | 9 y ♀                     | NMRI nu/nu, 5 weeks                          | Tumor tissue         | Right cerebral – hemisphere (ML +3 mm) | ND             | On request | ND                           | On request | (34)       |

*Indicated are the location, classification, and moment of collection of the original tumor sample, patient characteristics, mouse/rat strain used, tumor preparation, and injection site. References concern the first manuscripts describing the model only. To facilitate the choice of appropriate models for the preclinical therapeutic studies, this table also indicates whether the model allows for bioluminescence imaging (BLI), time to tumor growth/euthanasia (as estimated from Kaplan-Meier curves, unless otherwise indicated), and source where to obtain cells. “On request” refers to the corresponding author of the reference. FL, Fluorescence (MION-Rh); ND, Not described.*