

The Sontag Foundation

THE SONTAG FOUNDATION

Our Mission

The Sontag Foundation is dedicated to **advancing brain cancer research** by investing in brilliant scientists who are committed to the pursuit of bold, innovative, and transformative ideas.

\$100M+ to support brain cancer research and provide services to brain cancer patients through the Sontag Foundation and its founders.

Priorities



\$65 million has been invested since 2003 to launch the careers of extraordinary scientists with the potential to make a significant impact in the field of brain cancer research.

\$25.5 million directly related to glioblastoma.

SONTAG INNOVATION FUND

A venture-philanthropy fund with a mission to accelerate solutions to diagnose, treat, prevent and cure brain cancer.

\$3.5 million has been deployed since 2021 by the Sontag Innovation Fund.

Brain Tumor Network

Founded in 2014, BTN provides free individualized navigation to help brain tumor patients facilitate access to quality healthcare.

\$20 million from the Sontag Foundation and its founders to support the efforts of BTN.

Special Initiatives

An additional **\$4.55 million** in research related to glioblastoma funded by the Sontag Foundation through the Brain Tumor Funders Collaborative, Distinguished Scientist alumni awards, and other projects.

Portfolio Priorities

THE SONTAG FOUNDATION



Distinguished Scientist Award

\$750K

career development
award distributed
over 5 years

Applicant's career track
and proposed research
should demonstrate
outstanding promise as
contributors to science
relevant to brain cancer
research.



The Sontag Innovation Fund

\$250K - 1M

per investment

The Fund focuses on
providing investments to
companies developing
therapeutics, medical
devices, and other
technologies that can
impact brain cancer
patient treatment and/or
quality of life.



Young Investigator Awards

ASCO

*Conquer Cancer Sontag Foundation
Young Investigator Award*

\$50K

one-year grant

AACR

*Sontag Foundation Brain Cancer
Research Fellowship*

\$120K

two-year grant



Collaborative Funding

Co-Funder Model

Addresses a Critical
Topic in the Field

Examples

*The Brain Tumor Funders
Collaborative; NBTS & Sontag
Foundation imaging end-point
study; Sontag Foundation &
Focused Ultrasound workshop;
and Mark Foundation & Sontag
Foundation GBM workshop*

**Previous Projects: Basic
Research, Clinical Trials,
Team Science**

Gaps in the Research or Clinical Pipeline

We must reach newly diagnosed patients at the time of diagnosis in order to properly educate about the need for tissue storage, molecular profiling, and clinical trials.

- **Enrollment in clinical trials is poor** across oncology, including neuro-oncology, despite the limited benefit of available standard of care therapies.
- If we do not get patients **enrolled in the right trial** for them, we are going to continue to run on a hamster wheel in terms of progress.



Recommendation

Fund a study to develop uniform educational handouts and materials designed for newly diagnosed GBM patients, neurosurgeons, and oncologists.

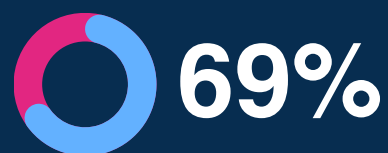
Why is this important?

Ensuring optimal care for patients, helping to guide personalized treatment decisions, better informing the research community, and ultimately working to close the gaps in access to quality healthcare.

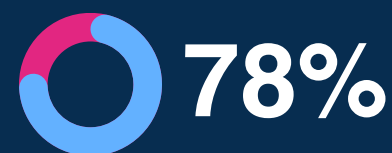


Brain Tumor Network

○ Data Collected from Our Brain Bank
○ Data Collected from BTN Survey



of GBM patients were not informed about **tissue storage**.



of GBM patients did not have their **tissue stored**.



of GBM patients were not offered **enrollment** in any clinical trial.



of GBM patients reported no discussion of the option for a **second opinion**.



of GBM patients did not have their tumor tested beyond initial **diagnosis**.



of GBM patients were not informed of **tumor testing**.



of GBM patients did not have their **molecular profiling** explained to them in terms of potential treatment.

Gaps in the Research or Clinical Pipeline

The brain tumor community needs preclinical models that properly recapitulate human disease and predict successful translation of therapies.

COMMON CHALLENGES WITH EXISTING MODELS:

In Vitro

- Lack of tumor heterogeneity
- Lack tumor invasiveness
- No Tumor Microenvironment
- No vascularization

Small Animal

- Immunocompromised host, or host lacking human immune system
- Lack of tumor heterogeneity
- Lack tumor invasiveness
- Major anatomical and physiological host differences
- Tumors often immunogenic
- Underlying genetics of tumor differ

Large Animal

- Time and Cost prohibitive
- Limited number of animals
- Dog patients vs. controlled experiments
- Require specialized infrastructure/expertise
- Anatomical and physiological host differences



Recommendation

Use funds for programs that:

1. Establish novel preclinical models.
2. Compare and contrast commonly used models.
3. Establish standards for models that will help the community select the most promising preclinical programs for clinical translation.

Why is this important?

This is critical to help gain a better understanding of human brain tumors, determine which current models are ideal for translational programs, generate new models that contribute to successful translation of therapies, and establish appropriately strict standards for which programs should be advanced into the clinic. This would ultimately save time, money and help ensure that patients are getting the absolute best care possible.

1. Vogelbaum MA, Krivosheya D, Borghei-Razavi H, Sanai N, Weller M, Wick W, Soffietti R, Reardon DA, Agbi MK, Galanis E, Wen PY, van den Bent M, Chang S. Phase 0 and window of opportunity clinical trial design in neuro-oncology: a RANO review. *Neuro Oncol*. 2020 Nov 26;22(11):1568-1579. doi: 10.1093/neuonc/noaa149. PMID: 32598442; PMCID: PMC7690357.

2. Wen PY, Weller M, Lee EQ, Alexander BM, Barnholtz-Sloan JS, Barthel FP, Batchelor TT, Bindra RS, Chang SM, Chiocca EA, Cloughesy TF, DeGroot JF, Galanis E, Gilbert MR, Hegi ME, Horbinski C, Huang RY, Lassman AB, Le Rhun E, Lim M, Mehta MP, Mellingshoff IK, Minniti G, Nathanson D, Platten M, Preusser M, Roth P, Sanson M, Schiff D, Short SC, Taphoorn MJB, Tonn JC, Tsang J, Verhaak RGW, von Deimling A, Wick W, Zadeh G, Reardon DA, Aldape KD, van den Bent MJ. Glioblastoma in adults: a Society for Neuro-Oncology (SNO) and European Society of Neuro-Oncology (EANO) consensus review on current management and future directions. *Neuro Oncol*. 2020 Aug 17;22(8):1073-1113. doi: 10.1093/neuonc/noaa106. PMID: 32328653; PMCID: PMC7594557.

3. Marin BM, Porath KA, Jain S, Kim M, Conage-Pough JE, Oh JH, Miller CL, Talele S, Kitange GJ, Tian S, Burgenske DM, Mladek AC, Gupta SK, Decker PA, McMinn MH, Stopka SA, Regan MS, He L, Carlson BL, Bakken K, Burns TC, Parney IF, Giannini C, Agar NYR, Eckel-Passow JE, Cochran JR, Elmquist WF, Vaubel RA, White FM, Sarkaria JN. Heterogeneous delivery across the blood-brain barrier limits the efficacy of an EGFR-targeting antibody drug conjugate in glioblastoma. *Neuro Oncol*. 2021 Dec 1;23(12):2042-2053. doi: 10.1093/neuonc/noab133. PMID: 34050676; PMCID: PMC8643472.

4. Bagley SJ, Kothari S, Rahman R, Lee EQ, Dunn GP, Galanis E, Chang SM, Nabors LB, Ahluwalia MS, Stupp R, Mehta MP, Reardon DA, Grossman SA, Sulman EP, Sampson JH, Khagi S, Weller M, Cloughesy TF, Wen PY, Khasraw M. Glioblastoma Clinical Trials: Current Landscape and Opportunities for Improvement. *Clin Cancer Res*. 2022 Feb 15;28(4):594-602. doi: 10.1158/1078-0432.CCR-21-2750. PMID: 34561269; PMCID: PMC9044253.

5. Mandel JJ, Yust-Katz S, Patel AJ, Cachia D, Liu D, Park M, Yuan Y, Kent TA, de Groot JF. Inability of positive phase II clinical trials of investigational treatments to subsequently predict positive phase III clinical trials in glioblastoma. *Neuro Oncol*. 2018 Jan 10;20(1):113-122. doi: 10.1093/neuonc/nox144. PMID: 29016865; PMCID: PMC5761583.

6. Ventz S, Lai A, Cloughesy TF, Wen PY, Trippa L, Alexander BM. Design and Evaluation of an External Control Arm Using Prior Clinical Trials and Real-World Data. *Clin Cancer Res*. 2019 Aug 15;25(16):4993-5001. doi: 10.1158/1078-0432.CCR-19-0820. Epub 2019 Jun 7. PMID: 31175098; PMCID: PMC6697596.

Gaps in the Research or Clinical Pipeline

The field needs more early stage clinical trials that can provide insight into the biological effects of novel therapies and generate more reliable evidence of efficacy as early as possible.



Lack of infrastructure and funding for early-stage clinical trials that can determine if and how an agent is working as intended.^[1-2]



Inadequate Phase 2 trial design has contributed to subsequent Phase 3 failures in brain tumor studies.^[3-4]

“

High failure rate of phase III trials demonstrated the urgent need to increase the reliability of phase II trials of treatments for glioblastoma.^[4]



Recommendation

Use funds for:

- **Early-stage clinical trials** that will establish if an agent is working as intended (e.g. Phase 0, WoO).
- **Studies to develop technologies** which could help provide reliable evidence of efficacy during Phase 2 trials in a resource-constrained environment, such as using external/synthetic controls in the brain tumor space.^[5-6]

Why is this important?

Clinical trials that can determine if an agent is working as intended will result in continued testing of only the agents that have a verified biological effect, which will benefit patients. It will also help to determine why an agent did not work in the case of a clinical trial failure. More informative trials will also help avoid costly Phase III failures.

1. Vogelbaum MA, Krivosheya D, Borghei-Razavi H, Sanai N, Weller M, Wick W, Soffietti R, Reardon DA, Aghi MK, Galanis E, Wen PY, van den Bent M, Chang S. Phase 0 and window of opportunity clinical trial design in neuro-oncology: a RANO review. *Neuro Oncol.* 2020 Nov 26;22(11):1568-1579. doi: 10.1093/neuonc/noaa149. PMID: 32598442; PMCID: PMC7690357.

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6. <https://www.3ds.com/newsroom/press-releases/medidata-synthetic-control-arm-supported-us-food-and-drug-administration-use-medicenna-therapeutics-corp-phase-3-registrational-trial-recurrent-glioblastoma>