Overview

National Brain Tumor Society (NBTS) launched the Oligodendroglioma Community Research Fund as a response to a passionate and dedicated patient and care partner community who envisioned the need for better understanding of, and accelerated treatment development for, this rare and underserved brain tumor type. Since its inception, the fund has directly raised, and enabled partnerships that resulted in, millions of dollars for this previously underfunded area of research.

Defining Oligodendroglioma

Following the 2016 updates to the World Health Organizations (WHO) classifications of brain tumors, oligodendroglioma are defined as diffuse glioma tumors that have a mutation to the IDH-family of genes and a complete loss of the chromosome arms 1p and 19q. Both of these two key markers (IDH mutations and 1p/19q co-deletion) were discovered with the help of NBTS funding, and now serve as a critical foundation for virtually all future research efforts.

Due in part to their relative rarity, both preclinical and clinical research efforts on oligodendroglioma lag behind the more prevalent forms of brain tumors. Therefore, critical investment in this area of research is required to accelerate the development of new, effective treatments for oligodendroglioma patients. The recent WHO update, which called for diagnoses to be based both on histology (how a tumor looks under a microscope) and molecular characteristics, along with advances in pathology, make it an especially opportune time to drive research forward toward treatments.

Making an Impact

Through the commitment and leadership of families impacted by this disease, the fund has been able to launch three rounds of grant-making for eight separate projects totaling nearly $2.2 million to 10 researchers across eight different institutions; all highly-focused on oligodendrogliomas and related low-grade gliomas.

These grants have led to the development of much needed models to better study this disease, as well as scientific discoveries that have increased the field’s understanding of what drives oligodendroglioma growth, and pointed toward novel approaches that could be developed into new treatments for oligodendroglioma patients.

1 Following the 2016 WHO update to brain tumor classification, oligoastrocytoma is no longer a defined diagnostic entity and in the future will be classified as either oligodendroglioma or astrocytoma.
Background

The Oligodendroglioma Community Research Fund was launched in June of 2011 through the leadership of the family of Spencer and Zach Greene, along with the support of many additional donors, including NBTS fundraising teams, Team Oligo, Well Wishes for Jeffrey, Let’s Get Physical, Team Sparky, as well as the Claeys, Fager, Greg, Leonard, Long, Moragne, Neidorf, Reller, Rosen, and Souki families. Because of their efforts and others, NBTS established the Organization’s first Community Research Fund, with a goal of raising $300,000 earmarked for oligodendroglioma research projects.

The fund then grew with the generosity and partnership of the family of Ashley Dabbiere, who wanted to direct fundraising specifically for oligodendroglioma research. And, today, thanks to the Greene and Dabbiere families and the broader oligodendroglioma community, the fund has far exceeded its original fundraising goal and, more importantly, catalyzed and expedited innovative research.

Through three phases of grants – the fund and its partners have worked to: dramatically increase scientific understanding of how oligodendrogliomas grow and evolve; identify potential early intervention approaches; determine how different sub-types of low-grade gliomas, including oligodendrogliomas, progress; engage patients and gather data to better understand the disease over time; and to study a novel therapeutic approach. All told, the Oligodendroglioma Community Research Fund has advanced the knowledge necessary to ultimately generate better treatments and cures for patients with oligodendroglioma and related tumors.

Research Funding & Accomplishments

Phase I Research Grants

In 2013, the first grants through the Oligodendroglioma Community Research Fund were made to Dr. David Louis and his colleague, Dr. Mario Suva, at Massachusetts General Hospital, as well as Dr. Anders Persson at the University of California, San Francisco. Each grant was for $300,000 over two years.

- **Drs. Louis & Suva (Massachusetts General Hospital)** – Drs. Louis and Suva directly applied cutting-edge scientific technology to study oligodendroglioma tumors cells, which allowed them to gain unprecedented insight into the diversity of cell types and the genetic mechanisms driving tumor growth. For the first time, they were able to precisely map the cellular construction of patient tumors, which has led to a new understanding of how these tumors grow. As a result, this research has illustrated the importance of treatment strategies directed at eliminating stem-like tumor cells in order to eliminate oligodendroglioma. This work garnered a major paper in the top scientific and medical journal, Nature, and was selected for three presentations at the 2015 Society for Neuro-Oncology Annual Meeting, while also receiving an award for basic research at the conference.

- **Dr. Persson (University of California San Francisco)** – Dr. Persson’s research specifically focused on the development of oligodendroglioma tumors that harbor a commonly found mutation, called the “IDH1-R132H” mutation. Dr. Persson sought to create both cellular and animal models that mimic these tumors in humans, to study how they grow, develop, and progress. Through this work, Dr. Persson not only provided new insight into the first transforming steps that cause oligodendroglial cells to become cancerous, but also created new, much needed models that can be used to better study oligodendrogliomas with the IDH1-R132H mutation—which could also be used for screening potential new treatments.

“We are very excited to continue our work, particularly to explore how this new knowledge could enable [therapeutic] targeting of the actual cells responsible for oligodendroglioma growth.”

– Dr. Mario Suva
Phase II Research Grants

In 2014, NBTS issued a second round of funding from the Oligodendroglioma Community Research Fund for a grant to a research project led by Drs. Robert Jenkins and Daniel Lachance of the Mayo Clinic. They hypothesized that inherited variants of certain genes (called “germline alterations” or “SNPs”) interact with the brain environment to initiate and/or facilitate the growth and progression of oligodendroglioma tumors.

This initial funding has laid the foundation for continuing work (see below), into how SNPs – which Dr. Jenkins has been able to identify a number of – contribute to the development of oligodendroglioma. Understanding how these SNPs can cause cancer, could eventually help develop early detection and intervention strategies. Another important benefit of their research is the development of model cell lines that closely mirror oligodendroglioma, which could be used to discover and test therapeutic approaches for patients, complementary to Dr. Persson’s model work.

Phase III Research Grants

In 2016, NBTS partnered with the Dabbiere family who had recently launched a new oligodendroglioma research network called LOGLIO, and OligoNation, a nonprofit organization founded by the Greene’s—to combine with previously raised NBTS Community Research Fund donations—and successfully award $1.25 million for five new, important research projects.

NBTS-Dabbiere LOGLIO Related Award Projects

$1 million dollars was allocated from a major fundraising event hosted by the Dabbiere’s to benefit NBTS – in addition to other dollars from the Oligodendroglioma Community Research Fund – in order to invest in four new research projects (each for $250,000 over two years) within the LOGLIO network studying low-grade gliomas, and specifically oligodendrogliomas.

• The Glioma Longitudinal AnalySiS (GLASS) Consortium
  Led by Dr. Roel Verhaak, The Jackson Laboratory for Genomic Medicine
  
  Overview: This grant provided seed funding to start the GLASS Consortium, which aims to create a large, international open dataset of how low-grade gliomas develop over time and during treatment. This project will include a comprehensive molecular analysis of tumors (and blood samples) obtained at time of diagnosis and at disease recurrence. This dataset will provide an important foundation to improve understanding of potential critical weaknesses in these tumors, and how these cancer vulnerabilities can be exploited with medicines to help patients live longer. The database will eventually be open and available for all brain tumor researchers to access, use, and reference in future low-grade glioma research.
  
  Progress Update: The Consortium has been able to enlist more than 50 participating researchers from 17 different countries, including the US, UK, Australia, Canada, China, Germany, Italy, the Netherlands, and Norway. The team is currently aggregating existing data from the individual participating institutions and has already generated 1,600 data profiles and collected data from more than 350 patients. Additionally, Dr. Verhaak just published a paper proposing a model of how gliomas form and develop. They hope their model will lead to additional studies that will help identify convincing therapeutic vulnerabilities.

• Functional Characterization of Germline Risk Variants in Oligodendroglioma
  Led by Dr. Robert Jenkins, Mayo Clinic, with Dr. Jun Song, University of Illinois
  
  Overview: This project is a continuation of Dr. Jenkins work (see previous page) to determine how inherited genetic variants (called SNPs) contribute to the development of oligodendroglioma.
  
  Progress Update: Dr. Jenkins and Dr. Song are analyzing how these SNPs contribute to the transformation of healthy to cancerous cells. They now believe they may contribute to disease-risk by interacting with, and changing how, certain other genes get turned on or off in the cell. They have analyzed four of the seven inherited genetic variants they want to study and have identified several associated target genes whose expression may be altered by these SNPs.
• **Identification of Molecular Triggers of Aggressive Growth in Oligodendroglioma**  
  *Led by Dr. Daniel Brat, Northwestern University*
  
  **Overview:** Dr. Brat and his collaborators are using traditional scientific techniques, combined with cutting-edge computational models and machine-learning tools, to identify the molecular triggers that make some oligodendroglioma-like tumors become more aggressive than others. Ultimately, this information could be used to stratify oligodendroglioma patients based on the molecular characteristics of their tumor into high, low, and moderate risk groups that could guide more precision treatments.

  **Progress Update:** Dr. Brat and his team have begun analyzing the molecular features of oligodendrogliomas to find which molecules, signaling networks, proteins, and genomic alterations inside these tumors are associated with worse and/or better prognosis. To date, they have identified two molecular alterations involving mutations in the Notch and PI3K signaling pathways – that are particularly predictive in assessing the likelihood that a patient’s tumor will progress more aggressively and rapidly. Additionally, they have just published a study demonstrating that “Deep Learning” via new computational technology is consistently more accurate than humans at classifying gliomas for diagnosis and predicting prognosis.

• **The International Low-Grade Glioma Registry**  
  *Led by Dr. Elizabeth Claus, Yale University and Brigham & Women’s Hospital*
  
  **Overview:** Dr. Claus is collecting real-world data from low-grade glioma patients via smartphone- and web-based applications in order to create the first global low-grade glioma patient “registry.” The registry will allow researchers around the world to generate new research information on 1) risk of low-grade glioma, 2) response of low-grade glioma patients to treatment, and 3) compare outcomes across different patient subsets. These data will also inform appropriate clinical treatment strategies, as well as the conception and design for clinical trials to test potential new medicines for these patients.

  **Progress Update:** To date, Dr. Claus and her team have completed enrollment for more than 200 patients in the registry from 21 states and seven countries which are largely representative of the overall low-grade glioma patient population. Eventually, she hopes to enroll 400-500 patients for this phase of the project, and ultimately 2,000 overall.

**NBTS-OligoNation Grant Project** $250,000 was granted by NBTS and OligoNation (with additional support from the Dabbiere family) for a research project studying a novel type of immunotherapy for oligodendroglioma patients.

• **Anit-CD47 Based Multimodality Immunotherapy Against Malignant Oligodendroglioma**  
  *Led by Dr. Samuel Cheshier, Stanford University*
  
  **Overview:** Dr. Cheshier is seeking to determine if an approach to immunotherapy, using a specific antibody that recognizes a protein called CD47, could work for oligodendroglioma patients. Different cancers use CD47 as a “don’t eat me!” signal to escape being identified and attacked by our bodies’ own immune system.

  **Progress Update:** Before Dr. Cheshier can test this approach in actual oligodendroglioma patients in clinical trials, he has to test it in laboratory models to make sure it appears to be safe and effective. To date, his team has identified six *in vitro* laboratory models consisting of oligodendroglial cells grown in lab dishes – including two cell lines they created themselves – that can be used to test the anti-CD47 immunotherapy. Their analysis confirmed that these cell lines all contained high amounts of CD47 in them. Next, they will test the immunotherapy *in vitro* alone, and also in combination with other drugs and types of immunotherapies that might make the anti-CD47 treatment even more potent at killing oligodendroglioma cells. Dr. Cheshier and his team will then undertake studies *in vivo* in mouse tumor models. If all is successful they will look to move into clinical trials.
Summary & Conclusion

With the exception of the *Phase I Research Grants*, these projects are not yet complete. Yet, already the collective work of NBTS Oligodendroglioma Community Research Fund grantees has:

- Dramatically improved knowledge about the characteristics of oligodendroglioma, allowing researchers and doctors to better understand the ‘enemy’ and its potential vulnerabilities,
- Unveiled new understanding of what drives oligodendroglioma tumor growth, and how it could be slowed, stopped, and/or reversed,
- Launched a groundbreaking global network to study oligodendroglioma development over time,
- Engaged patients to advance oligodendroglioma research through a registry, and
- Initiated a new study to determine if a particular immunotherapy might work for oligodendroglioma patients.

NBTS will continue to provide updates on this program, its overall results and achievements, and the accomplishments and progress of individual projects as they become available moving forward.

Community Research Fund Model – How You Can Get Involved

The Community Research Fund model is a vehicle that allows donors to pool their donations for the study of a particular type of brain tumor they have a collective stake in fighting, while ensuring the research meets strict scientific standards through the expertise of the National Brain Tumor Society’s distinguished Scientific Advisory Council. Donations large and small can be combined and directed to fund research studies. While one individual or family may not be able to fund a research grant in its entirety, combining their donations with others can make a meaningful impact.

For information about contributing to the Oligodendroglioma Research Fund please contact 617-924-9997.