On behalf of the National Brain Tumor Society and the community we serve, thank you for your generous philanthropic support to advance oligodendroglioma research and treatment.

In this report, we are pleased to share highlights of the progress made, as well as promising new work underway aimed at advancing cutting-edge, treatments-focused research with the potential to change the future for brain tumor patients and families.
About
National Brain Tumor Society

VISION
Conquering and curing brain tumors - once and for all.

MISSION
National Brain Tumor Society unrelentingly invests in, mobilizes, and unites our community to discover a cure, deliver effective treatments, and advocate for patients and care partners.
Gliomas are one of the most common types of primary brain tumors and make up approximately 80% of all malignant primary brain tumors. This group includes oligodendroglioma. Low-grade glioma patients are severely underserved due to the historic lack of research and treatment development in these rare cancer types.

From 2013 to today, NBTS has funded a total of $2 million in grants to 11 researchers across nine different institutions, all focused on oligodendroglial and related low-grade glioma research. During this period, NBTS’ strategy to address the problem has focused on funding research projects that revealed genetic risk factors, established models capable of testing potential treatments, built scientific infrastructure to predict if treatments will work, launched novel therapeutic approaches and helped propel a groundbreaking treatment toward a pivotal clinical trial lead by a biopharma prepared to bring a new therapy to patients.

This report focuses specifically on NBTS funded research related to oligodendroglialoma. It describes results over a seven year time span and exciting next steps to drive research forward aimed at novel treatments and ultimately, cures.
Dr. Anders Persson’s (University of California San Francisco) 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 can also be used for screening potential new treatments.
Drs. Mario Suva and David Louis at Massachusetts General Hospital 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. As a result, their research illustrated the importance of treatment strategies directed at eliminating stem-like tumor cells in order to kill oligodendroglioma.
Dr. Ingo Mellinghoff and his team at Memorial Sloan Kettering Cancer Center led pioneering work funded by NBTS that resulted in new strategies for drug targeting glioma patients with the IDH mutation that has now resulted in a phase III clinical trial now seeking FDA approval for a new medicine.
Drs. Robert Jenkins and Daniel Lachance of the Mayo Clinic 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. NBTS funding has laid the foundation for continuing work 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 tumors could eventually help develop early detection and intervention strategies. This project received further funding in 2016 that has led to a major grant award from the National Institutes of Health.
A team from Yale University led by Dr. Elizabeth Claus created The International Low-Grade Glioma Registry, a web-based tool that is designed to collect biological data from patients to study multiple aspects of the low-grade glioma patient experience, including risk factors associated with developing these tumors. To date, the team has collected pilot data from more than 350 patients, with an ultimate goal of 2,000. The Yale/team will also use biological data collected from patients to predict how low-grade glioma patients will respond to treatment and compare outcomes across different patient subsets. Already, the efforts have identified differences in low-grade gliomas in males and females.
Drs. Jenkins, Lachance, Song, and their collaborators have linked an inherited genetic mutation (a single nucleotide polymorphism, or SNP, rs55705857) to a higher risk of an individual developing glioma tumors with mutations in their IDH genes, including oligodendroglioma. They developed a genetic risk model to predict which inherited genetic variants (including rs55705857 and several others) are most likely to lead to the development of oligodendroglioma and other glioma brain tumors and also began to elucidate how SNPs interact with other key parts of a person’s genetic machinery to lead to tumor growth.
Researchers Dan Brat and Lee Cooper at Emory and Northwestern University have established state-of-the-art Artificial Intelligence (AI) and Machine Learning platforms that can take patient data at diagnosis and more accurately predict, based on the mutations found in the tumor, how aggressive the tumor will behave, and how it might respond to certain treatments. These tools could eventually allow doctors to make better, more informed decisions about how to plan treatment for oligodendroglioma patients and if they need more aggressive treatments like chemotherapy following surgery. These tools will be tested in clinical trials in the near future and eventually brought into standard clinical practice, if validated.
The Jackson Laboratory team led by Dr. Roel Verhaak — which launched a large, international collaboration called The Glioma Longitudinal AnalySiS (GLASS) Consortium to collect and make available a major open dataset of how low-grade gliomas change over time — has begun to identify molecular changes that occur in recurrent low-grade glioma tumors, like oligodendroglial, following initial treatment. These molecular changes could potentially be exploited as new drug targets leading to the development of new treatments.
Dr. Samuel Cheshier and his team while at Stanford defined the role of a specific protein expressed on cancer cells that prevents immune cells from attacking the tumor. They nick-named the protein ‘do not eat me’. More importantly, they established very difficult-to-build pre-clinical models to demonstrate what is called ‘experimental proof of principle’ that blocking this protein with an antibody drug could be a valid immunotherapy approach. This is an example where NBTS laid the groundwork for drug discovery by funding model-building work.
NBTS is now poised to leverage the collective knowledge of these initiatives toward promising new research aimed at rapidly identifying and developing treatments that exploit the unique characteristics of low-grade gliomas. Philanthropic support remains critical for this next phase of discovery and progress.

In particular, we feel that advancing development of drugs such as DNA Damage Response inhibitors (DDRi) and Isocitrate dehydrogenase (IDH) inhibitors could lead to a paradigm changing therapies for glioma patients. We describe these new strategies that are being considered for future funding in more detail on the next page.
Systematic Identification, Prioritization and Advancement of Revolutionary New Class of Cancer Drugs

Drugs that target the DNA Damage Response (DDR) may offer a new way of treating cancer, selectively killing cancer cells by inhibiting the DDR mechanisms that cancer cells require or are “addicted” to but sparing normal healthy cells that do not rely on these pathways, in essence targeting the Achilles heal of cancers. These new drugs called DNA Damage Repair inhibitors (DDRi’s) have potential both as stand alone therapies in subsets of brain tumors where specific mutations, such as those seen in oligodendroglioma, can be targeted that would benefit from a DDRi and in combination with radiation and chemotherapies. The NBTS Defeat Brain Tumors program will rapidly test out these potential treatments against astrocytomas and oligodendrogliomas through a consortium of world-class institutions, sharing data and conducting experiments and clinical trials to either fail fast or to graduate the best DNA damage repair inhibitors to more mature clinical trials capable of getting approval for patients. There is also great potential to combine this class of treatments with immunotherapy and innovative surgical approaches to achieve even greater benefit.

Targeting the IDH Mutation in Brain Tumors

Isocitrate dehydrogenase (IDH) is a key rate-limiting enzyme found in oligodendrogliomas and is a potential therapeutic target for drug therapy. NBTS Defeat Brain Tumors program will fund projects aimed at identifying and evaluating promising treatments that target IDH through systemic approaches including immunotherapy and as well as precision medicine drug targeting approaches and projects that combine investigational and standard of care treatments.
THANK YOU

The power of your philanthropy

Thanks to your generous support, we are now poised to advance promising therapies to the next stage of evaluation. At this pivotal time, continued philanthropic support will allow NBTS to bring forward a new class of promising approaches to be evaluated by leading brain tumor researchers, with the potential to change the landscape for patients living with oligodendroglioma.

Should you wish to learn more about the promising research underway, including opportunities for support, we would welcome a conversation at anytime.