Systems Biology Approaches to Brain Tumor Research Research Grant

Grantor: National Brain Tumor Society
Closes: 12/17/2010
Maximum: $100,000.00

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Deadline: December 17, 2010

Grant awards will range from $40k to $100k for the year depending upon the needs presented in the application. Funds may be used for travel, meetings and other appropriate expenses associated with non-laboratory planning requirements and collaborations, as well as for traditional (e.g. salary, etc.) appropriations.

National Brain Tumor Society seeks grant applications that embrace a systems biology approach for scientific research to benefit brain tumor patients.

Beyond the complication of the existence of a large number of types of brain tumors lies the dynamic biological complexity of tumors at a number of levels ranging from genomic, biochemical, cellular and micro-environmental. These levels of complexity characterize both differences between individual tumors of the same histopathological type as well as within and between the different cells that make up individual tumors. Much laboratory and clinical research, as well as standard of care therapy experience (surgery, radio- and chemotherapy), has demonstrated the enormous resilience of brain tumors such as glioblastoma (GBM) and their capacity to adapt to and overcome a variety of standard and experimental therapeutic approaches. Targeted therapies that hold the promise of being more effective than standard therapies have thus far been largely ineffective in trials that focus on single targets.

While it is generally accepted that combination therapies may be required, which combinations will be most effective is not known. Furthermore, the complexity of tumor signal transduction circuitry and adaptive alterations, heterogeneity of cells within tumors, and their enhanced mutational rate coupled with extreme cellular phenotypic plasticity makes these types of tumors dynamic moving targets even for combination therapies.

The tenet of modern approaches to cancer research involves the identification and validation of new targets, and the subsequent identification of therapeutic agents directed against those targets. For tumors such as GBM, a number of targets have been identified presenting a sizeable number of therapeutic combinations to be evaluated in clinical trials. While the identification of more new targets may be valuable, and the “rational” evaluation of therapeutics directed against targets based on current knowledge is valuable, the field has reached a tipping point. In thinking of future therapies, it will be necessary to move away from treatment modalities intended to alter a target(s) without taking into account the adaptive response of targeted cells or other nontargeted cells. Research needs to go beyond looking at targets in isolation and needs to addresses a higher-level biological order presented by tumor complexity, adaptability and the emergence of a complex adaptive system. National Brain Tumor Society seeks to do just that, to encourage systems biology research approaches through this RFA.

For more information on this viewpoint on the support of systems biology brain tumor please read the NBTS perspective paper at: www.braintumor.org/Perspectives.

SYSTEM BIOLOGY AND BRAIN TUMOR RESEARCH:
Systems biology research involves the evaluation of complex biological systems as a whole, comprised of interconnecting networks of multiple layers of component systems.

Understanding the higher-level properties of brain tumors as interactive complex biological systems rather than collections of individual component parts (e.g. genes, proteins, etc.) or immediate interactive component partners offers the promise of finding therapeutic approaches that include effective ways to prevent compensatory and adaptive tumor mechanisms that allow for their development of resistance and for their recurrence.

Systems biology is frequently described as a field at the intersection of biology, applied mathematics, engineering and the physical sciences. A brain tumor systems biology research program that incorporates all of these components might be considered a “top down” program due to the nature of its inclusive approach. These are exemplified by programs in the comprehensive genomic/molecular profiling of GBMs, and the characterization of individual cells of single brain tumors using nanotechnology and microfluidics. These types of typically large research programs are important for the progression of the field and need to be encouraged.

It is the goal of NBTS to encourage research programs that although they may be less expansive, they incorporate the essence of a systems biology perspective. The essential core of this perspective is that to understand the biological complexity of brain tumors in order to find approaches that tumors cannot survive or adapt to, it is critical to know the broader biological consequences, interconnections and interactions that result from the inhibition of any particular target or targets. The broader therapeutic consequences of targeting a particular pathway cannot be understood by only studying the effect that has occurred on the intended target, but rather the effect on the entire system and how it seeks homeostasis has to be evaluated. Such a strategy that emanates from the study of even a single target might be thought of as a “bottom up” systems biology research approach.

NBTS RESEARCH GRANTS IN BRAIN TUMOR SYSTEMS BIOLOGY:
National Brain Tumor Society believes in the potential positive impact of brain tumor research that embraces a systems biology perspective at all levels, from a bottom up approach to a top down approach. NBTS looks to encourage a systems biology perspective in any area of brain tumor research ranging from signal transduction to immunotherapeutics to mathematical algorithms for high throughput testing of therapeutic hypotheses.

NBTS recognizes the challenges in developing creative and innovative research programs from this perspective, particularly for the bottom up approach. As such, NBTS will employ a two-stage grant process.

The ultimate goal at the end of the two-stage process is the development of testable therapeutic approaches in brain tumor patients that takes into account the various levels of tumor complexity and that has the potential to eradicate or manage

brain tumors in a way that prevents them from utilizing adaptive mechanisms that enable them to survive and/or recur.

The purpose of large multi-year Stage 2 Advanced grants is to support the research required to understand areas of research from a systems biology perspective and to apply that understanding into the development of an actionable translational plan.

The purpose of the smaller one-year Stage 1 Standard grants is to provide the time and support required to effectively develop a comprehensive strategy and team for Stage 2 research. Stage 1 grants are intended to support the feasibility/planning studies needed to develop that strategy. As such, Stage 1 applications should envision and describe an overview of what Stage 2 research would look like and articulate the roadmap and plans for getting there.

Proposed studies that would result in the accumulation of larger sets of data (e.g. –omic analyses) without etermining an understanding of biological context and effects will not be considered for support.

Eligibility for applying for a Stage 2 grant is contingent on going through the Stage 1 process. NBTS looks to award from seven to ten Stage 1 grants to high quality applications and about three Stage 2 grants.

Stage 1:
NBTS seeks creative systems biology feasibility/planning study grant applications. These Standard Grants will be awarded for 1 year of study/planning.

During this stage support will be provided for either (1) laboratory research that establishes the basis of a larger systems biology brain tumor research program (potentially funded in stage two); and/or (2) the development of a research plan that transforms your particular area of research into a systems biology research approach that incorporates a broader biological context and that will serve as the basis of a larger research program (potentially funded in stage two). Laboratory research is not required for the planning studies. It is the goal of NBTS to fund both types of feasibility/planning studies in this stage. The expected deliverable of both feasibility/planning types of study is a detailed research proposal for the stage two grant applications.

For either type of project, applications should clearly describe the plans and timeline for accomplishing the goals of year one studies. Collaboration in creative and innovative ways and/or with partners not traditionally considered is highly encouraged. Plans for creating integrated teams of collaborators should be described.

Keeping in mind that the intent of Stage 2 research is translational application, specific plans for incorporating that translational goal should be built into Stage 1 studies and application, such as the inclusion of clinical scientist(s) into the research team.

A description for your plan for bioinformatics analyses (e.g. the right analytical tools and bioinformatics experts) should be included as needed.

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Stage 2:
This research grant application stage will be built upon the first year Stage 1 grants. These grants will be awarded for 3 years at a level of $500k/year or greater. Only projects supported in Stage 1 will be considered for funding in Stage 2.

Both “top down” and “bottom up” brain tumor systems biology research will be considered for funding. This applies to any area of brain tumor research. The goal is the identification and development of effective interventional approaches based upon an understanding of the broader biological interconnections and complexities that characterize brain tumors.

The expected deliverable at the end of the 3 years is the elucidation and description of an implementable plan for translation of research into a therapeutic approach and clinical trial. Details about the application for Stage 2 grants will be issued at a later date.

National Brain Tumor Society

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