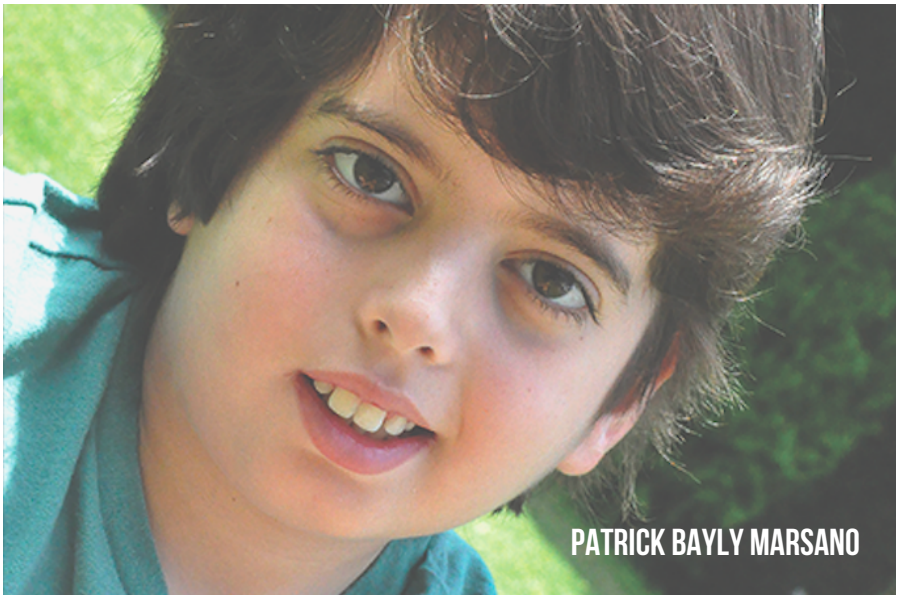
Children's Brain Tumor Project
powered by families

Weill Cornell Medicine

# PRECISION MEDICINE PROGRAM FOR CHILDREN WITH BRAIN TUMORS

*Children's Brain Tumor Project, Weill Cornell Medicine*




One of the major roadblocks to discovering promising new treatments for children with rare brain tumors like gliomatosis cerebri, thalamic glioma, DIPG, and choroid plexus carcinoma, is the lack of tumor tissue and genetic data available. Researchers need to study samples from brain tumors to learn more about them, and more importantly, the scientific findings may quickly inform the child's oncology team on potential therapeutic treatment options based on those findings.

Thanks to the generosity of the Patrick Bayly Marsano Foundation, the Children's Brain Tumor Project at Weill Cornell Medicine now has the tools to collect tumor tissue from a patient and to analyze that tissue through genetic sequencing, bioinformatics, targeted therapy, drug screening and immunophenotyping at no cost to the patient family. In other words, this enables the research team to study the genetics of the tumor, seek targets based on the presence or absence of genetic mutations, test different drugs against the tumor, and discover unique ways in which the oncology team might be able to treat a child's brain tumor more effectively. This option wasn't available to most children in recent years, and it is one that may lead to new treatments or alternative approaches for children suffering from rare, refractory or recurrent brain tumors, *today*.

This practice of tailoring the prevention, diagnosis, and treatment of an individual patient based on the molecular characteristics of that patient's disease is known as *precision medicine*, and it is a highly innovative option for families faced with the devastating diagnosis of a rare pediatric brain tumor. Participating in the analysis of the disease at a molecular level is an approach that works simultaneously with standard treatment protocols already in place, while providing the clinical team with a wealth of information specific to the patient that may enable them to make customized adjustments to that treatment protocol along the way.

# TUMOR TISSUE COLLECTION TO INFORM SCIENCE

The lab at the Children's Brain Tumor Project Weill Cornell Medicine is made up of a diversified team of neuroscientists who combine their areas of expertise in order to enable the most thorough processing of tumor tissue donations, examining the genetics and behavior of these tumors from all angles. The roadmap depicted below illustrates the many variables in science that one donation can contribute to.

It is best to give consent for sharing tumor tissue in advance of a surgical procedure (tumor resection or biopsy) to ensure the tissue goes from the OR directly to the lab for immediate processing and advanced preservation. If the surgery cannot take place at the same facility as the lab, it is important for the patient family to share the specific requirements of tissue preservation with the surgical team to ensure the recovery agents used at the receiving lab are compatible.

## SEQUENCING

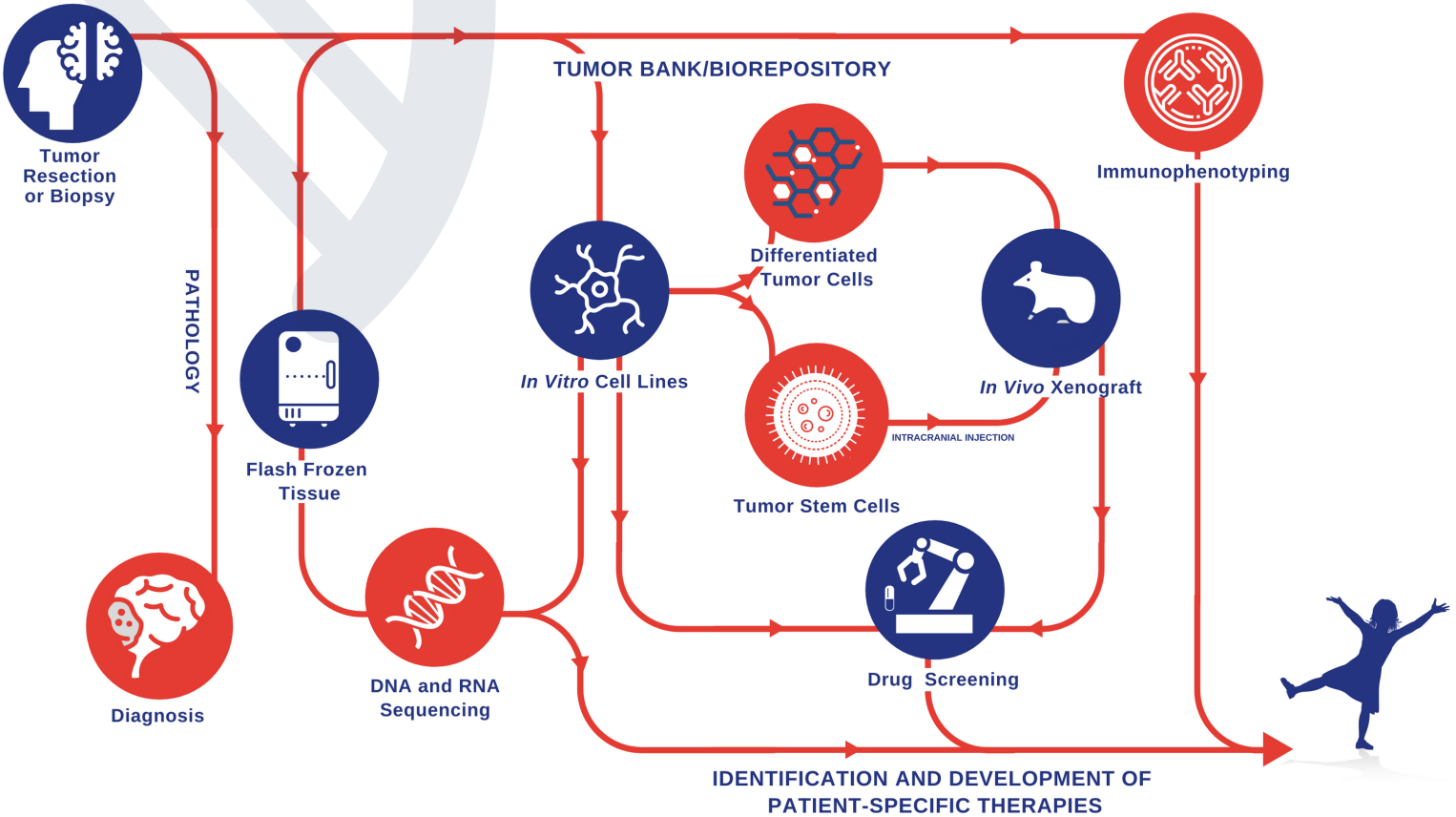
Genomic sequencing of both DNA and RNA enables our team to identify mutations and/or gene expression alterations, which are the foundation to cancer. Not only is the identification of gene alterations essential to making an accurate diagnosis, but genetic subtypes identified within a particular diagnosis are known to affect an individual's response to treatment. Ideally, adjustments to treatment can be made accordingly. Information derived from sequencing also enables the scientific team to use targeted drugs when actionable mutations are discovered.

Sequencing isn't just about identifying mutations that are currently treatable, it is a vehicle for scientific discovery. Identifying mutations in advance means that when researchers do discover a treatment option for a particular mutation, they may be able to apply it to treatment protocols for children who present with the same markers in the future.

As depicted below, sequencing is just one of the ways - in addition to drug screening and immunophenotyping, to identify patient-specific therapies.

## BIOINFORMATICS

Bioinformatics is advanced computing and mathematics to analyze data, including gene expression or deletion, protein analysis, advanced imaging, and clinical annotations, to provide insights into the biology of a tumor. The practice of aggregating and sharing research data to inform scientists is particularly important in the case of rare pediatric brain tumors. Powerful computational research technology, sometimes referred to as "big data," enables information on rare diseases to be more easily shared and analyzed, resulting in a better understanding of these diseases and how to treat them.



# TECHNOLOGY AT WORK

## DRUG SCREENING

High throughput drug screening is the ability to use automated equipment to rapidly test thousands of different drug compounds for a biological response from the tumor tissue. This allows scientists to identify drugs or a combination of drugs that may have the highest potential efficacy against the patient's disease. For example, the Children's Brain Tumor Project at Weill Cornell is a member of both the Englander Institute of Precision Medicine and Rockefeller University, which are located in close proximity to the lab and have access to more than 300,000 compounds for rapid testing against patient-derived cells generated in our laboratory. The first step in the process involves *in vitro* high-throughput drug screening. The team uses chemical libraries to identify drugs, including the most current FDA-approved anticancer drugs, that specifically target gene alterations identified in the patient-specific cells. Taking it a step further, the patient's cancer cells may be transplanted into immune-deficient mice to generate an *in vivo* mouse model that imitates the behavior of the patient tumor from which the cells were derived. These models can then be used to validate the drugs identified in the *in vitro* screen for their efficacy *in vivo*. These models will also provide information about the toxicity of the selected drugs or combination of drugs being considered.


# A NEW APPROACH

## IMMUNOPHENOTYPING

Immunophenotyping allows us to understand the immune microenvironment of the tumor, meaning, how the tumor impacts the child's immune system and how his or her body reacts against the tumor. It is helpful to know which immune cells are present in the tumor microenvironment so the team can identify which specific cells should be targeted. Ideally, treatment can be adapted depending on the immune cells present in the tumor, as well, in order to amplify those immune cells that are effectively fighting the disease.

Children's Brain Tumor Project
powered by families

Co-founded by two pediatric neurosurgeons, Dr. Jeffrey Greenfield and Dr. Mark Souweidane, the Children's Brain Tumor Project is a research initiative with a single goal: to bring hope to the hundreds of children each year who have to confront the heartbreaking diagnosis of a pediatric brain tumor.

CHILDRENSBRAINTUMORPROJECT.ORG
@CHILDRENSBRAINTUMORPROJECT
INFO@CHILDRENSBRAINTUMORPROJECT.ORG