

2013 Research Grants

Dana Farber Cancer Institute – Dr. Pratiti Bandopadhyay and Dr. Susan Chi

Feasibility of treatment with surgery and chemotherapy only for children with Wnt-positive Medulloblastoma

Medulloblastoma is the most common malignant brain tumor of childhood. The standard of care is maximal surgical resection followed by radiation and chemotherapy. However, radiation therapy has significant long-term side effects including neurocognitive deficits, increased risk of second cancers, the formation of abnormal blood vessels, and the need for hormone replacement therapy and growth deficits. Recently, with increasing sophistication of methods to profile the genomes of tumors, it has been recognized that there are four distinct subgroups of medulloblastoma. One of these subgroups is characterized by up-regulation of a cancer pathway called the Wnt pathway (Wnt-positive medulloblastoma). Children with Wnt-positive medulloblastoma have been shown to have excellent survival with rates of close to 100%. This has raised the question of whether therapy can be safely reduced in these children to minimize long term side effects.

This pilot study will examine the safety of omitting radiation therapy in children with Wnt-positive medulloblastoma. Children who are identified to have Wnt-positive medulloblastomas will be treated with maximal surgical resection followed by chemotherapy but no radiation therapy. The outcomes of children treated without radiation therapy will be carefully monitored and compared. If this study shows that children with Wnt-positive medulloblastoma can be safely treated without radiation therapy it may change the way that these children are treated in future and could spare children the long-term side effects associated with radiation therapy.

City of Hope National Medical Center – Dr. Margarita Gutova

Human Neural Stem Cell-Mediated Drug Delivery for Targeted Treatment of Medulloblastoma

Medulloblastoma is the most common malignant brain tumor of childhood. Current therapies are often severely damaging to brain development and skeletal growth. Therefore, new treatments are critically needed to improve the survival and quality of life of children with medulloblastoma. Major obstacles to successful treatment of pediatric brain tumors include the blood-brain-barrier (BBB), which prevents many anti-cancer agents from entering the central nervous system, and limitations on the amount of chemotherapy that can be given in a dose due to toxicity to normal tissues.

Neural stem cells (NSCs) offer a novel way to overcome these obstacles because they can cross the BBB and migrate to and selectively target tumor cells throughout the brain. NSCs can be genetically modified to act as delivery vehicles for targeted cancer therapy, thereby increasing the tumor-localized concentrations of a drug while minimizing toxicity to normal tissues and the side effects of therapy. The goal of this study is to determine the preclinical effectiveness of an NSC-mediated therapy against two subtypes of medulloblastoma, including Group 3 medulloblastoma, the most aggressive subtype of the disease. We will also investigate a novel, non-invasive route of NSC delivery to the central nervous system - intranasal injection. This study has tremendous potential significance because NSC-based delivery of chemotherapy could improve survival and minimize the serious brain damage caused by current radiation and chemotherapy regimens, thus preserving intellectual function and improving the quality of survivorship of young children with brain tumors.