2008 Research Grants

Memorial Sloan Kettering Cancer Center - Drs. Oren Becker and Rosandra Kaplan

Stromal Contribution of Bone Marrow Progenitors in Medulloblastoma.

Medulloblastomas are brain tumors that arise in the cerebellum of children. Using animal models, this study examines whether medulloblastomas contain cells that originate from the bone marrow. Recently, it has been observed that in adults, bone marrow derived cells contribute to the formation of tumor blood vessels and assist tumor cells to invade normal tissue. These researchers hypothesize that these bone marrow derived cells act the same way in children’s brain tumors. Medulloblastoma cancer stem cells reside near blood vessels and are more resistant to treatment with radiation and cisplatin. Cells derived from the bone marrow may also be more resistant to such treatment and may play a role in supporting the cancer stem cells. In this study the researchers will use drugs that inhibit bone marrow derived cells of medulloblastoma-bearing mice to assess if medulloblastoma tumor growth will be affected. They will use these inhibitors to determine if they increase the effectiveness of radiation and chemotherapy. They will also study the number of bone marrow derived cells in the blood and cerebrospinal fluid of children with brain tumors to determine if the number of these cells correlates with the stage or tumor recurrence. They hypothesize that drugs that can block bone marrow derived cells are potential novel treatments for children with brain tumors.

Dana-Farber Cancer Institute Dr. Mark Kieran

Phase I Study of AdV-tk+ Prodrug Therapy in Combination with Radiation Therapy for Pediatric Brain Tumors

Childhood brain tumors called gliomas – those that arise in the glial cells – typically have a poor outcome. Patients suffering from this disease usually survive for only a short number of months, so innovative approaches to treatment are critical. This study is a Phase I clinical trial in which pediatric patients’ gliomas will be removed surgically, and a gene therapy vector, AdV-tk, will be injected directly into the tumor site. In the days that follow, patients will receive prodrug and standard radiotherapy; standard chemotherapy may be used as well. This approach will allow simultaneous targeting of the tumor with multiple methods. This multiple method therapy has been tested using animal models and has been successfully used in adults with brain tumors and other cancers. This combination therapy shows great promise as an improved form of treatment for children with brain tumors.
Immunotherapeutic Targeting of Stem Cells in Pediatric Brain Tumors

Although surgery, chemotherapy, and radiation therapy work in some cases of childhood gliomas and medulloblastomas, the devastating side effects of these therapies and relative lack of efficacy necessitate the development of novel, targeted therapies for the developing brain. In this study, the research looks to harness the power of a person's own immune system to fight these tumors. The researchers will attempt to identify immunogenic proteins expressed by the brain tumor stem cell population. The genes, Bmi-1, SOX2, MELK, and FoxM1 have been shown to play critical roles in cancer growth. T-cells which are capable of proliferating and activating in response to these proteins will then be tested against cell lines generated from pediatric tumor samples and in animal models. The results will be used to develop individualized vaccines for pediatric patients with brain tumors.