THE HARTWELL FOUNDATION

2013 Individual Biomedical Research Award

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High-Resolution Imaging Methods for Neuroblastoma: Improving Tumor Detection and Guiding Therapy Decisions

Neuroblastoma is an early childhood cancer with an average age at diagnosis of 18 months. In 70% of cases, neuroblastoma is not detected before it has spread to multiple sites. Even with exhaustive treatment including surgery, chemotherapy, radiation, and bone marrow transplant, the 5-year survival rate of children with widespread disease is only ~40%. Most patients die as a consequence of small therapy-resistant tumors that are not detectable with current imaging methods. Currently, the only effective method to detect neuroblastoma and assess tumor response to therapy is a combination of structural imaging with x-rays to show tumor location and functional imaging with a radioactive drug (called a radiotracer) injected into the patient to show tumor biology. The radiotracer accumulates in tumor more than in normal tissue and is detected with a medical imaging device called a gamma camera. Unfortunately, this method does not reliably detect small tumors (less than 1 centimeter) nor provide accurate measurement of tumor response during therapy. Moreover, the current clinical radiotracer, meta-iodobenzylguanidine, stays in the patient's blood for hours after injection leading to safety concerns and delaying imaging for 24 hours after injection. A more rapid, sensitive and accurate tumor detection is critical to patient survival. To address this need, Scott will utilize positron emission tomography (PET), an advanced functional imaging technology that provides at least 2-fold better detection of small tumors and allows precise measurement of therapy response. Improved imaging will directly benefit children diagnosed with this deadly disease by improving treatment decisions and facilitating new therapy development. The limitation of this technology is that it requires special radiotracers that are not currently available for neuroblastoma. One such radiotracer, fluorodopamine, dramatically improved detection of a neuroblastoma-related adult cancer. However, due to problematic chemistry, fluorodopamine has never been approved for evaluation in neuroblastoma. Using novel chemistry developed in his laboratory, Scott will synthesize fluorodopamine and evaluate its utility for neuroblastoma imaging. He will verify that it accumulates in neuroblastoma and that the tumors can be visualized by PET imaging. He will then compare the safety of his improved fluorodopamine with meta-iodobenzylguanidine and with fluorodopamine prepared by traditional methods. Finally he will test whether fluorodopamine imaging can measure changes in tumors in response to therapy. If Scott is successful, he will be able to provide the data needed for FDA regulatory approval to quickly move fluorodopamine into clinical testing and ultimately, make fluorodopamine readily available to other pediatric hospitals.