# THE HARTWELL FOUNDATION

## 2015 Individual Biomedical Research Award

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### Non-Inflammatory Cancer Vaccines Using Lymph Nodes on a Microfluidic Chip

Pediatric cancer is the second leading cause of death for children under the age of 15, behind only accidental injuries. Survivors often suffer through aggressive therapies of radiation and chemotherapy that severely compromise quality of life and produce long-term health consequences. For example, in 2014, there were over 10,000 new diagnoses of pediatric cancer in this age group in the U.S., with about 1,300 children not expected to survive beyond 2015. Of these cases, 26% represent acute lymphoblastic leukemia, for which survival is >80% with existing therapies. However, the remaining 74% of children with cancer endure a lower expected survival rate and will receive highly toxic therapies; including, about 3000 children with tumors of the brain, central nervous system, or neuroblastoma (tumor of nerve cells outside the brain). With 700 new cases each year in the U.S., neuroblastoma is the most common cancer in infants less than 1-year-old. Half of these cases are designated high-risk, usually with cancer metastasis to the lymph nodes at the time of diagnosis. These children have a 5-year survival rate of only 40% - 50%. Today, new treatments are urgently needed to treat pediatric cancer more efficiently and with fewer side effects. One exciting potential strategy is active immunization; in effect, a cancer vaccine that recruits the child's own immune system to fight the tumor. To achieve this effect requires a particular type of immunity called a killer T-cell response, but it is not known how to design vaccines to produce a protective killer response without undesirable inflammatory side effects. To address this need, Rebecca proposes a new paradigm. Instead of the century-old concept that inflammation is the driving force to acquired immunity, she hypothesizes that soon after vaccination the spatial organization and local behavior of cells inside the lymph node predict the level of protection that the vaccine will provide. To test her hypothesis, she will build a custom "lab-on-a-chip" microfluidic platform to culture live tissue samples from the lymph node and mimic what happens in the body. In this way, she expects to rapidly determine the spatial patterns that predict a protective immune response with minimal inflammation. Following calibration of the lymph node lab-on-a-chip model with a set of well-characterized vaccines with known long-term outcomes, she will use her platform to examine the effectiveness of new vaccines against pediatric cancer, using neuroblastoma as a model system. Once a putative vaccine is identified, she will evaluate it in mouse models of the cancer. If Rebecca is successful, a prototype therapeutic vaccine for neuroblastoma will be identified that can be positioned for clinical translation. If successful, her microfluidic culture platform will also provide a system for creating safe and effective vaccines for other disease conditions, as well.