In recent years, engineered T cell immunotherapies have emerged as powerful treatments first for acute lymphoblastic leukemia (ALL), and now for a rapidly growing variety of lymphoid malignancies. The University of Washington and the Fred Hutchinson Cancer Center pioneered early developments in this field. The central innovation was the development of a chimeric antigen receptor, or CAR. CAR proteins, are encoded in a lentivirus capable of delivering instructions to a patient’s own immune cells and instructing the immune cells to attack cancer. CAR modification leads a patient’s T cells to become reinvigorated. This approach results in complete remissions in more than 90% of ALL patients, including those that have become resistant to chemotherapy. Yet, when applied to patients with AML, the responses have been rare and transient. The goal of this research is to start to uncover reasons why AML is less responsive to CAR T cell therapy and how this resistance could be overcome.

The fund provided support for two key aspects of my research. First was a search to identify characteristics of patients who may be best served by enrolling on trials of novel AML-directed CAR T cell therapy and to define characteristics of success using past outcomes of AML patients as benchmarks. Prior projects funded by the Lee Endowed Memorial Fund have similarly leveraged our institutional database to define expected outcomes. I reviewed the course of over 1200 patients. These data helped broaden our inclusion criteria for an upcoming trial. In addition, discussion of these data at national meetings has met with positive review. A manuscript has been prepared and will be submitted for publication in the coming month, recognizing the support of the James Chung Yam Lee Endowed Memorial Fund for Leukemia.

A second area of support was to acquire blood samples from AML patients to pilot CAR manufacture. As you can imagine, blood cells from AML patients may respond to laboratory manipulation in a manner much different from cells obtained from volunteer healthy donors. These critical samples enable our team to develop T cell culture techniques on the ‘real’ material we are likely to receive from patients in the future.

These samples will not be just for ‘practice.’ Research has recently emerged showing that AML cells suppress immune responses, and that T cell immune suppression in particular may be one mechanism of AML therapeutic evasion. As part of this work, I am comparing therapeutic CAR T cell products manufactured from healthy donors and from AML patients. Funds from the Lee Endowed Memorial Fund were used to purchase cell samples and reagents for this work. I am happy to report that CAR T cell lots from 4 healthy donors and 10 AML patients have been manufactured, and that comparisons among these samples are ongoing. Should we find differences, these data may direct future strategies to enhance the potency of CAR T cell therapies manufactured for AML immunotherapy.