Abstract

Although effective chemotherapies are available for patients with chronic lymphocytic leukemia (CLL), the disease currently remains incurable. For this reason, investigators are seeking alternative treatment approaches to fully eradicate these tumor cells in patients. The immune system refers to the coordinated defense mechanisms used by the body to protect itself from infections and diseased cells. Generally speaking, the immune system is composed of both immune cells capable of recognizing and killing bacteria and cells infected by viruses, as well as proteins, called antibodies, which bind to, and thereby target for destruction, bacteria, viruses, and virally infected cells. Unfortunately, most cancer cells are not effectively recognized by the immune system and are therefore not killed by the patient's immune system. Immunotherapy is a broad term used to describe treatments wherein aspects of this immune system are manipulated in such a way as to allow for the recognition, and subsequent killing, of cancer cells. To date, investigators have already made great strides in the clinical setting using antibodies such as rituximab and alemtuzumab to target and kill CLL tumor cells. However, the use of cells from the immune system to target and kill CLL cells is currently largely restricted to pre-clinical laboratory studies. We have used gene therapy technologies to alter a type of immune cell called a T cell, in such a way that these cells can subsequently recognize and directly kill CLL tumor cells. We have previously conducted experiments in the laboratory that suggest such an approach may be a promising new therapy for patients with CLL. To this end, we are currently in the process obtaining government approval for a study wherein we will isolate T cells from patients with CLL, genetically alter these cells in the laboratory to recognize CLL tumor cells, and subsequently inject these cells back into the patient. However, what remains unclear at this time is whether T cells obtained from patients with CLL will function as well as T cell obtained from healthy donors. In fact, multiple prior studies on T cells obtained from CLL patients suggest that these immune cells may be impaired in their ability to kill diseased cells as a result of an adverse influence of CLL tumor cells on these cells. The overall goals of our proposal are to better clarify these defects in T cell function, assess the impact of prior chemotherapy on patient T cell function, and ultimately to determine whether we can overcome these defects in the laboratory in order to allow us to effectively use this treatment approach in patients with CLL. We believe that these studies, generously supported by the CLL foundation, will ultimately allow us to design more effective means of using this promising novel technology to treat patients with CLL.