

NON-TECHNICAL ABSTRACT

Vaccines have been traditionally used to protect individuals against viral and bacterial disease. The success of this approach has led investigators to study its potential for treating cancer patients. It is thought that a cancer vaccine would generate a response that would enable the patient's own immune system to kill tumor cells. A requirement of this approach is the knowledge of cancer-associated, immunogenic proteins. Immunogenic proteins are those that stimulate the patient's immune system to destroy tumor cells but preferentially leave non-cancer cells unharmed.

Recently, a newly identified cancer-associated protein, cytochrome P450 isoenzyme 1B1 (CYP1B1), was described. This protein may have the qualities of an immunogenic protein. Although low levels of CYP1B expression may be detected in normal cells, it is preferentially expressed by cancer cells. To explore the possibility of a CYP1B1 vaccine, it was important to provide evidence that the human immune system can recognize CYP1B1 expressing cells and kill them. Tissue culture experiments performed with human immune cells taken from patients demonstrated that the immune cells recognized and killed tumor cells positive for CYP1B1 expression. Experiments performed in mice have also suggested that the immune system is capable of recognizing and responding to tumor cells expressing CYP1B1. These basic scientific findings support the clinical investigation of a CYP1B1-directed vaccination for the treatment of human cancer.

A plasmid system has been chosen to produce a clinical formulation for use in activating the human immune response to CYP1B1. Plasmids are small circular DNAs that are not associated with virus. They do not contain elements to promote integration into the human genome. For these reasons, plasmids are thought to be one of the safest DNA expression vectors. To facilitate delivery of the CYP1B1 plasmid to the proper human cells, the plasmid is trapped in tiny spheres that are taken up by specialized cells in the human body. These cells activate the human immune system to respond to cancer cells that are positive for CYP1B1. It is thought that this response will result in the death of cancer cells within the patient. Data from toxicity studies performed in animals, as well as from human trials of CYP1B1 in tiny spheres demonstrate that this system induces immune responses specific for CYP1B1. Data from these studies also suggest, but have not yet proven, the safety of the system in humans. It is believed that the immune responses observed following immunization with CYP1B1 in tiny spheres can be enhanced by co-administration with commercially available agents that are known to safely augment the immune response in humans. This protocol is designed to test the feasibility and safety of targeting CYP1B1 B1 as a novel tumor associated immunogenic protein through DNA vaccination in combination with commercially available agents that are known to safely enhance the immune response in humans.