

Non-Technical Abstract

Hemophilia A is a severe inherited bleeding disorder resulting from a deficiency of factor VIII, a protein required for normal blood clotting. Current treatment is limited to the administration of the factor VIII protein at the time of a bleeding episode. Presently it is not possible to prevent the bleeding episodes.

Transkaryotic Therapy for hemophilia A represents a fundamental change in the treatment of this disorder. Transkaryotic Therapy is a gene therapy system in which a small number of skin cells are removed from a patient and stably modified with the gene for factor VIII so that the cells produce the factor VIII protein. The introduction of the factor VIII gene is done by non-viral means. The administration of cells with the correctly functioning factor VIII gene to hemophilia A patients may allow them to make sufficient factor VIII in their own bodies to prevent bleeding episodes. Thus a single administration of Transkaryotic Therapy could free the hemophilic patient from future bleeding episodes.

In the clinical study described in this application, a small skin biopsy will be performed on patients with severe hemophilia A, and fibroblasts will be isolated from the skin biopsy at TKT's manufacturing facility. A modified human factor VIII gene will then be inserted into the patient's fibroblasts. The fibroblasts will be grown and prepared for patient administration using manufacturing practices recommended by the U.S. Food and Drug Administration. Each patient will receive his own genetically-modified fibroblasts by implantation in the abdomen using a laparoscopic technique. The laparoscopic procedure will be performed by making a small incision the patient's abdominal wall, inserting a tube into the abdomen through the incision, and pushing the patient's cells through the tube into the implantation site. The laparoscopic procedure will be performed using standard procedures after giving the patients sufficient factor VIII to provide normal blood clotting levels.

While participating in the study patients will continue to receive their regular factor VIII replacement therapy as needed. The patients will be monitored intensively for twelve weeks following the cell implantation. After the three month intensive evaluation period, the patients will be evaluated periodically during the next 21 months. The total observational period will be of two years duration.