

## ABSTRACT

Gaucher disease is an autosomal recessive storage disorder which causes an excess accumulation of glucocerebroside in bone marrow-derived cells called macrophages due to the functional absence of the enzyme glucocerebrosidase. Patients with Gaucher disease will be treated by gene therapy by inserting the cDNA for the normal glucocerebrosidase (GC) enzyme into hematopoietic stem cells (CD34+). Either G-CSF mobilized peripheral blood or bone marrow will be harvested from the patient and enriched for CD34+ cells. The CD34+ cells will be transduced with retroviral vector supernatant containing the cDNA for GC, over 72 hours in the presence of IL-3, IL-6 and stem cell factor. The transduced cells will be reinfused intravenously into the patient. Patients will be retreated four times 2 - 4 months apart if peripheral blood stem cells are treated. Bone marrow will be treated only one time. The patient will be monitored for any evidence of toxicity and for the number of cells containing the retroviral vector. If enough cells are found to contain the retroviral vector the cells of the subjects will also be evaluated for the expression of GC. It is hoped that the information obtained from this study will permit the development of gene therapy for Gaucher disease.