## A. SCIENTIFIC ABSTRACT

X-linked severe combined immune deficiency (X-SCID) is the most common form of SCID, and is caused by mutations in the γc receptor gene. γc is a component of the high-affinity receptors for interleukin-2, -4, -7, -9, and -15. In heterozygous females and bone marrow transplant (BMT) recipients, lymphocytes expressing the normal γc have a profound selective advantage over lymphocytes expressing the mutant gene. BMT is the conventional therapy for X-SCID, but the outcome of BMT is sub-optimal in patients who lack a histocompatible sibling donor. Gene therapy may provide a new therapeutic approach to X-SCID that would overcome some of the problems associated with BMT, most notably the need for pre-BMT chemotherapy, graft-versus-host disease and poor humoral immunity post-BMT. Our hypothesis is that transduction of CD34+ cells from X-SCID patients with a normal γc gene will result in generation of functional T and B lymphocytes. The selective advantage of transduced cells may allow clinical benefit, even if the number of transduced CD34+ cells is limited. We have demonstrated transduction and expression of γc cDNA into CD34+ cells, and normalization of γc-mediated signalling through the IL-2 receptors by retroviral-mediated transduction of the normal γc cDNA into X-SCID cells. The present study may be of benefit to patients with X-SCID and provide important information on gene therapy for other primary immune deficiencies.