Cellular Therapy and Transplantation (CTT), Vol. 2, No. 5, 2009
doi: 10.3205/ctt-2009-No5-abstract83

Abstract accepted for "Joint EBMT Pediatric Working Party – 3rd Raisa Gorbacheva Memorial Meeting on Hematopoietic Stem Cell Transplantation", Saint Petersburg, Russia, September 17–20, 2009

Gene therapy of hematopoietic stem cells

Gerard Wagemaker

Erasmus University Medical Center, Dept. Hematology, Rotterdam, The Netherlands

Correspondence: Gerard Wagemaker, Erasmus University Medical Center, Dept. Hematology, PO Box 2040, 3000 CA Rotterdam, The Netherlands, E-mail: editors@ctt-journal.com

Abstract

An estimated 24 million people in the European Union alone are affected by an inherited disorder based on a genetic defect. In humans, approximately 7,000 inherited diseases have been identified; in around 1/3 the genetic defect has been mapped and the function of the affected gene elucidated. Human suffering as well as health care costs are immense, and therefore the development of future curative therapy is a humanitarian, medical, societal, and economic necessity.

In patient numbers, the inherited diseases are most frequent in disorders of the blood cell producing system. This provides the rationale for a focus on hematopoietic stem cells as a prime target of gene therapy, solidly rooted in 40 years of experience with the clinical application of HSC transplantation for a variety of acquired and inherited disorders. In those disorders based on a monogenic defect, ex vivo gene correction of the patient's hematopoietic stem cells and transplantation of those cells is a realistic treatment concept. Due to the specific properties of the progeny of hematopoietic stem cells, curative approaches for disorders in other organ systems also turn out to be accessible to hematopoietic stem cell gene therapy, including disorders that affect the brain. In this overview the results of a European consortium's (www.gene-therapy.eu) translational research project—in which leading centers collaborated to prepare for the effective and safe gene therapy of selected example diseases that included severe combined immune deficiencies, red cell disorders, and lysosomal enzyme deficiencies—are presented. The research also required an in-depth analysis of the interaction of gammaretroviral and lentiviral vectors with stem cell genome expression levels, revealing new insights in hematopoietic stem cell genomics.

Keywords: inherited diseases, hematopoietic stem cell transplantation, HSCT, gene therapy