The promise of stem cell-based gene therapy

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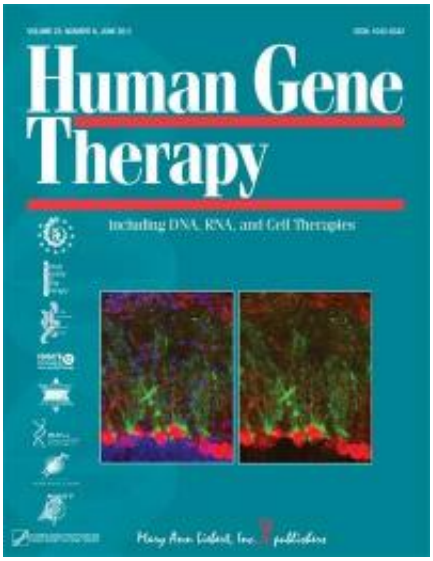

Human Gene Therapy, the official journal of the European Society of Gene and Cell Therapy, British Society for Gene Therapy, French Society of Cell and Gene Therapy, German Society of Gene Therapy, and five other gene therapy societies is an authoritative peer-reviewed journal published monthly in print and online that presents reports on the transfer and expression of genes in mammals, including humans. Related topics include improvements in vector development, delivery systems and animal models, particularly in the areas of cancer, heart disease, viral disease, genetic disease and neurological disease, as well as ethical, legal and regulatory issues related to the gene transfer in humans. Credit: © Mary Ann Liebert Inc., publishers

Sophisticated genetic tools and techniques for achieving targeted gene delivery and high gene expression levels in bone marrow will drive the successful application of gene therapy to treat a broad range of diseases.

Examples of these cutting-edge methods are presented in a series of five provocative articles in the latest issue of *Human Gene Therapy*.

Barese and Dunbar highlight the advances in gene marking techniques that are enabling selection and targeting of specific immune cell populations for cell and gene therapy. The success of marking studies will help optimize gene transfer for immunotherapeutics and improve patient survival, conclude the authors in the review article "Contributions of Gene Marking to Cell and Gene Therapies."

Giordano et al. explore the use of PCR and next-generation DNA sequencing methods to identify specific gene products that are associated with successful long-term transfer of therapeutic genes to bone marrow. They report their findings in the research article entitled "Clonal Inventory Screens Uncover Monoclonality Following Serial Transplantation of MGMTP140K-Transduced Stem Cells and Dose-Intense Chemotherapy."

As a model for therapeutic gene delivery to bone marrow and peripheral blood cells to treat lysosomal storage disorders, Walia et al. describe successful gene replacement in a primate model of Farber disease. The study, "Autologous Transplantation of Lentivector/Acid Ceramidase-Transduced Hematopoietic Cells in Nonhuman Primates," reports the ability to replace acid ceramidase (AC) gene activity and reduced ceramide levels in blood cells transduced with the AC gene.

Hunter et al. present a study that compares the use of a human gene promoter with a mouse promoter-enhancer for achieving high levels of gene expression in a dog model of leukocyte adhesion deficiency type 1. "Gene Therapy for Canine Leukocyte Adhesion Deficiency with Lentiviral Vectors Using the Murine Stem Cell Virus and Human Phosphoglycerate Kinase Promoters" describes the study results.

Evidence to support the effective use of chromatin insulators—a class of DNA regulatory elements—to improve the expression and safety of gene transfer vectors is the focus of the Methods Review by David Emery entitled "The Use of Chromatin Insulators to Improve the Expression and Safety of Integrating Gene Transfer Vectors."

"Bone marrow-directed gene therapy was the first model considered in the treatment of genetic diseases and remains one of the most successful models in terms of clinical efficacy," says James M. Wilson, MD, PhD, Editor-in-Chief, and Director of the Gene Therapy Program, Department of Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia.

More information: The articles are available free online at www.liebertpub.com/hum

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