20 years of ASGCT and gene therapy.

1995

Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy.

Stuart H. Orkin, MD and Arno Motulsky, MD
Co-Chairs
December 7, 1995

- No evidence of clinical benefit to date despite 100 protocols
- Significant deficiencies in the basic science underpinning
- Only a few clinical trials designed to yield useful basic information
- Overselling of studies is rampant, which hinders confidence and progress
20 years of ASGCT and gene therapy.

1996

American Society of Gene Therapy established

American Society of Gene Therapy

Gene Therapy
20 years of ASGCT and gene therapy.

1996

Development of Lentivirus vectors

In Vivo Gene Delivery and Stable Transduction of Nondiving Cells by a Lentiviral Vector

Luigi Naldini, Ulrike Blömer, Philippe Gallay, Daniel Ory, Richard Mulligan, Fred H. Gage, Inder M. Verma,* Didier Trono

A retroviral vector system based on the human immunodeficiency virus (HIV) was developed that, in contrast to a murine leukemia virus-based counterpart, transduced heterologous sequences into HeLa cells and rat fibroblasts blocked in the cell cycle, as well as into human primary macrophages. Additionally, the HIV vector could mediate stable in vivo gene transfer into terminally differentiated neurons. The ability of HIV-based viral vectors to deliver genes in vivo into nondividing cells could increase the applicability of retroviral vectors in human gene therapy.

Science 272: 263. 1996.
Multiple crucial steps in preclinical development of AAV2 as a gene therapy vector, including these landmark papers in mice and in a canine disease model.

Efficient Long-Term Gene Transfer into Muscle Tissue of Immunocompetent Mice by Adeno-Associated Virus Vector

XIAO XIAO,1,2 JUAN LI,1,2 AND RICHARD JUDE SAMULSKI1,3*

Gene Therapy Center1 and Department of Pharmacology3 University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599, and Somatic Therapy Corporation, Alameda, California 945012


Long-term correction of canine hemophilia B by gene transfer of blood coagulation factor IX mediated by adeno-associated viral vector

ROLAND W. HERZOG1, EDMUND Y. YANG2, LINDA B. COUTO2, J. NATHAN HAGSTROM1, DAN ELWELL1, PAUL A. FIELDS1, MELINDA BURTON1, DWIGHT A. BELLINGER1, MAROONIE S. RIAO1, KENNETH M. BRINKHOUR1, GREGORY M. POULAKHOS3, TIMOTHY C. NICHOLS1, GARY I. KURTZMAN1 & KATHRYNE A. HIGH1,3

Nat Med 5: 56, 1999
Effective suicide gene therapy transfer to T cells allowing mitigation of graft-versus-host disease following donor lymphocyte infusion in allogeneic transplantation recipients.
20 years of ASGCT and gene therapy.

1998

First ASGT annual meeting, Seattle

George Stamatoyannopoulos, MD, Dr.Sci
Founding President, ASGCT
Patient Dies During a Trial Of Therapy Using Genes

New York Times, Sept. 29, 1999

Death of 18 year-old patient Jesse Gelsinger following administration of an adenoviral vector carrying the ornithine decarboxylase gene in a gene therapy protocol.
20 years of ASGCT and gene therapy.

2000

Launch of *Molecular Therapy*, official journal of ASGT

*In der Verma, PhD*
*Founding Editor-in-Chief*
Development of novel serotypes of AAV with increased efficiency and extended tropism as gene therapy vectors

Novel adeno-associated viruses from rhesus monkeys as vectors for human gene therapy

Guang-Ping Gao, Mauricio R. Alvira, Lili Wang, Roberto Calcedo, Julie Johnston, and James M. Wilson*
20 years of ASGCT and gene therapy.

**2002**

5th Annual Meeting attendance peaks with 2,885 attendees
20 years of ASGCT and gene therapy.

2002

Clinical benefit of hematopoietic stem cell retrovirus-mediated gene therapy for X-SCID

Retroviral transfer of IL2R gene to hematopoietic stem and progenitor cells of boys with X-linked severe combined immunodeficiency (SCID)

Gene Therapy of Human Severe Combined Immunodeficiency (SCID)–X1 Disease

Marina Cavazzana-Calvo,1,2,3 Salima Heccel-Bey,1,2,3 Geneviève de Saint Basile,1 Fabian Gross,2 Eric Yvon,3 Patrick Nusbaum,2 Françoise Selz,1 Christophe Hue,1,2 Stéphanie Certain,1 Jean-Laurent Casanova,1,4 Philippe Bousso,2 Françoise Le Deist,1 Alain Fischer1,2,4,5

[Graphs showing data over time]
20 years of ASGCT and gene therapy.

2003

Insertional mutagenesis and proto-oncogenic activation-mechanism of geno toxicity

Science 302: 415, 2003
20 years of ASGCT and gene therapy.

2003
First regulatory approval of a gene therapy product

Gendecine, a cancer treatment consisting of a replication-incompetent adenovirus vector expressing wild-type p53 approved in China
20 years of ASGCT and gene therapy.

2003–04

Elucidation of vector integration patterns

Science 300: 1749, 2003

Transcription Start Regions in the Human Genome Are Favored Targets for MLV Integration

Xiaolin Wu, Yuan Li, Bruce Crise, Shawn M. Burgess

Distinct Genomic Integration of MLV and SIV Vectors in Primate Hematopoietic Stem and Progenitor Cells

Fred Bushman, PhD
University of Pennsylvania, Philadelphia, Pennsylvania

Retroviral DNA Integration: ASLV, HIV, and MLV Show Distinct Target Site Preferences


PLoS Biology: E423 2004

PLoS Biology: E234, 2004
20 years of ASGCT and gene therapy.

2008

Derivation of human induced pluripotent stem cells

Shinya Yamanaka, MD, PhD
Kyoto University, Kyoto, Japan

James Thomson, PhD
University of Wisconsin, Madison, Wisconsin
20 years of ASGCT and gene therapy.

2008

Pioneering AAV gene therapy clinical trials for inherited form of blindness

**ORIGINAL ARTICLE**

**BRIEF REPORT**

*Safety and Efficacy of Gene Transfer for Leber’s Congenital Amaurosis*

Albert M. Maguire, M.D., Francesca Simoneelli, M.D., Eric A. Pierce, M.D., Ph.D., Edward N. Pugh, Jr., Ph.D., Federico Mingozzi, Ph.D., Jeannette Bensisiali, Ph.D., Sandro Bentil, M.D., Kathleen A. Marshall, C.G.T, Francesco Testa, M.D., Enrico M. Bucolo, D.V.M., Bettina Rossi, M.D., Arndt Luchsinger, Ph.D., Velder R. Aruda, M.D., Barbara Ronke, M.D., Edwin Stone, M.D., Ph.D., Janice Sun, M.S., Jonathan Jacobs, Ph.D., Lou DelCollo, Ph.D., Richard Hertle, M.D., Jianxiong Ma, M.D., Ph.D., T. Michael Redmond, Ph.D., Xiaoxiao Zhu, M.D., Bernd Hanss, Ph.D., Olga Zilemas, Ph.D., Kenneth S. Ziderman, M.D., Ph.D., Maureen G. Maguire, Ph.D., J. Fraser Wright, Ph.D., Nicholas J. Vage, M.D., Jennifer Weilman McDonnell, M.S., Alberto Auricchio, M.D., Katherine A. High, M.D., and Jean Bennett, M.D., Ph.D.


**ORIGINAL ARTICLE**

**BRIEF REPORT**

*Effect of Gene Therapy on Visual Function in Leber’s Congenital Amaurosis*


Clinical benefit of hematopoietic stem cell retrovirus gene therapy for adenosine deaminase-deficient SCID
20 years of ASGCT and gene therapy.

2009
ASGT changes name to reflect integration of gene and cell therapies
Positive clinical trial results using hematopoietic stem cell lentiviral gene therapy for central nervous system metabolic/storage disorders

Science 326: 818, 2009

Lentiviral Hematopoietic Stem Cell Gene Therapy Benefits Metachromatic Leukodystrophy

Science 341: 2003
20 years of ASGCT and gene therapy.

2011

Successful AAV8 gene therapy for hemophilia B

Adenovirus-Associated Virus Vector–Mediated Gene Transfer in Hemophilia B

Amit Nathwani, MB, ChB, PhD
University College, London, United Kingdom

Arthur W. Nienhuis, MD
St. Jude Children’s Research Hospital, Memphis, Tennessee

Katherine A. High, MD
Spark Therapeutics

Andrew M. Davidoff, MD
St. Jude Children’s Research Hospital, Memphis, Tennessee
Dramatic clinical responses to chimeric antigen receptor engineered T Cells for CD19+ lymphoid malignancies

Blood 116: 4099, 2010

20 years of ASGCT and gene therapy.

2012
Launch of Molecular Therapy Nucleic Acids, an open-access ASGCT journal

John Rossi, PhD
Founding Editor-in-Chief
2012

European Commission approves Glybera, the first approved gene therapy in Europe

AAV Vector delivering the lipoprotein lipase gene to patients with genetic hypercholesterolemia
Discovery of CRISPR/Cas9 and utilization of this system to perform targeted gene editing in mammalian cells

2012–13

Jennifer Doudna, PhD
University of California, Berkeley, California

Emmanuelle Charpentier, PhD
Umea Center for Microbial Research, Umeå Sweden

George Church, PhD
Harvard Medical School, Boston, Massachusetts

Feng Zhang, PhD
MIT, Cambridge, Massachusetts
20 years of ASGCT and gene therapy.

2013

FDA approval of Kynamro ( mipomersen), an antisense oligonucleotide inhibitor of ApoB-100, for use in patients with hypercholesterolemia

Articles

Mipomersen, an apolipoprotein B synthesis inhibitor, for lowering of LDL cholesterol concentrations in patients with homozygous familial hypercholesterolaemia: a randomised, double-blind, placebo-controlled trial

Prof Frederick J Raal, MD, Raul D Santos, MD, Dirk J Blom, MD, Prof A David Marais, MD, Min-Ji Charng, MD, William C Cromwell, MD, Robin H Lachmann, MRCP, Daniel Gaudet, MD, Ju L Tan, MB BS, Scott Chasan-Taber, PhD, Diane L Tribble, PhD, Johann D Flaim, PhD, Stanley T Crooke, MD

Lancet 375: 998, 2010
20 years of ASGCT and gene therapy.

2014
First clinical trial of genome editing

Gene Editing of CCR5 in Autologous CD4 T Cells of Persons Infected with HIV

Pablo Tebas, M.D., David Stein, M.D., Winson W. Tang, M.D., Ian Frank, M.D., Shelley Q. Wang, M.D., Gary Lee, Ph.D., S. Kaye Spratt, Ph.D., Richard T. Surosky, Ph.D., Martin A. Giedlin, Ph.D., Geoff Nichol, M.D., Michael C. Holmes, Ph.D., Philip D. Gregory, Ph.D., Dale G. Ando, M.D., Michael Kalos, Ph.D., Ronald G. Collman, M.D., Gwendolyn Binder-Scholl, Ph.D., Gabriela Pless, M.D., Ph.D., Wei-Ting Hwang, Ph.D., Bruce L. Levine, Ph.D., and Carl H. June, M.D.


Pablo Tebas, MD
Carl June, MD
Bruce L. Levine, PhD
20 years of ASGCT and gene therapy.

2014

Launches of Molecular Therapy Methods and Clinical Development and Molecular Therapy Oncolytics, two additional open-access ASGCT journals

Matthew Porteus, PhD
Founding Editor-in-Chief, MTMCD

Yuman Fong, MD
Founding Editor-in-Chief, MTO
20 years of ASGCT and gene therapy.

2014

First clinical trial of iPSC-derived cells to regenerate tissue

Autologous Induced Stem-Cell–Derived Retinal Cells for Macular Degeneration

Michiko Mandai, M.D., Ph.D., Akira Watanabe, Ph.D., Yasuo Kurimoto, M.D., Ph.D., Yasuhiro Hiram, M.D., Ph.D., Chikako Morinaga, Ph.D., Takashi Daimon, Ph.D., Masashi Fujihara, M.D., Ph.D., Hiroshi Akimar, Ph.D., Noriko Sakai, B.S., Yumiko Shibata, M.S., Motoki Terada, Yul Nomiy, M.S., Shigeki Tanishima, B.S., Masahiro Nakamura, M.D., Ph.D., Hiroyuki Kamao, M.D., Ph.D., Sunao Sugita, M.D., Ph.D., Akishi Onishi, Ph.D., Tomoko Ito, Kanako Fujita, Shin Kawamura, M.D., Ph.D., Masahiro Go, Ph.D., Chikara Shihohara, Ph.D., Ken-Ichiro Hata, D.D.S., Ph.D., Masanori Sawada, M.D., Ph.D., Midori Yamamoto, Sachiko Ohta, Yasuo Ohara, B.S., Kenichi Yoshida, M.D., Ph.D., Junko Kuwahara, Yuko Kitano, M.S., Naoki Amano, M.S., Masafumi Umei, M.S., Fumio Kitaoka, Ph.D., Azusa Tanaka, Ph.D., Chihiro Okada, M.S., Naoko Takasu, M.S., Seishi Ogawa, M.D., Ph.D., Shinya Yamakita, M.D., Ph.D., and Masayo Takahashi, M.D., Ph.D.

20 years of ASGCT and gene therapy.

2015

Drs. Alain Fischer and Theodore Friedmann are awarded the prestigious Japan Prize for the proposal of the concept of gene therapy and its clinical applications

Alain Fischer, MD, PhD
Institut Imagine, Paris, France

Theodore Friedmann, MD
University of California, San Diego, California
European Commission approves Strimvelis, the first ex vivo gene therapy product worldwide

Retrovirus vector expressing the adenosine deaminase gene to treat patients with ADA-deficient SCID
20 years of ASGCT and gene therapy.

2016

FDA approval of the oligonucleotide drug Spinraza for spinal muscle atrophy

**Articles**

Treatment of infantile-onset spinal muscular atrophy with nusinersen: a phase 2, open-label, dose-escalation study

Dr Richard S Finkel, MD, Claudia A Chiriboga, MD, Jiri Vajsar, MD, John W Day, MD, Jacqueline Montes, EdD, Darryl C De Vivo, MD, Mason Yamashita, MD, Frank Rigo, PhD, Gene Hung, MD, Eugene Schneider, MD, Daniel A Norris, PhD, Shuting Xia, MS, C Frank Bennett, PhD, Kathie M Bishop, PhD

Use of “universal donor” TALEN-engineered CAR-T cells to achieve remission in a patient with refractory CD19+ acute leukemia

Remission in infant with refractory acute leukemia

Molecular remission of infant B-ALL after infusion of universal TALEN gene-edited CAR T cells

Waseem Qasim1,2,*, Hong Zhan1, Sujith Samarasinghe1, Stuart Adams1, Persis Amrolia1,2, Sian Stafford1, Katie Butler1, Christi... See all authors and affiliations

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