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1973-1977	B.A., Chemistry, Albion College, Albion, MI
1977-1984	Ph.D., Biological Chemistry, University of Michigan Medical School, Ann Arbor, MI
1977-1984	M.D., University of Michigan Medical School, Ann Arbor, MI
1984-1986	Internship and Residency, Medical Services, Massachusetts General Hospital, Boston, MA
1986-1988	Postdoctoral Fellow, Whitehead Institute, Massachusetts Institute of Technology, Cambridge, MA
1988-1993	Assistant Professor to Associate Professor, Internal Medicine and Biological Chemistry, University of Michigan
1988-1993	Assistant Investigator, Howard Hughes Medical Institute, University of Michigan
1991-1993	Chief, Division of Molecular Medicine and Genetics, University of Michigan
1993-present	John Herr Musser Professor and Chair, Molecular and Cellular Engineering, University of Pennsylvania, Philadelphia, PA
1993-present	Director, Institute for Human Gene Therapy, University of Pennsylvania
1993-present	Professor of Medicine and Chief, Division of Medical Genetics, University of Pennsylvania
1993-present	Professor at the Wistar Institute, University of Pennsylvania

Honors

1976	Phi Beta Kappa, Albion College
1977-1980	National Science Foundation Predoctoral Fellowship, University of Michigan
1980-1984	Fellow in the Medical Scientist Training Program, University of Michigan
1982	Thomas Francis, Jr. Memorial Award, March of Dimes
1983	University of Michigan Student Achievement Award
1984	Medical Scientist Training Program Award for Excellence
1984	Dean's Award for Research Excellence
1984	William Dodd Robinson Award for Excellence in Internal Medicine
1989	Young Investigator's Award, Central Society for Clinical Research
1990	Hickman Lecturer, Central Society for Clinical Research
1991	Jerome W. Conn Award for Distinguished Research by a Junior Faculty Member
1992	Henry Russell Award for Outstanding Faculty Member, University of Michigan
1992	Distinguished Alumni Award, Albion College
1993	*Philadelphia Business Journal* Health Care Heroes Award
1998	Maurice Hilleman-Merck Research Laboratories Lecturer of the American Society for Virology
1998	Keynote Speaker, Albion College Opening Convocation

Constitutive and Regulated Expression in the Systemic Delivery of Erythropoietin Following Skeletal Muscle Transduction with DNA Viral Vectors

One of the objectives in our laboratory is to develop a system for regulated expression of recombinant genes encoding therapeutic secreted proteins from vectors injected into muscle. Adenoviral and adeno-associated viral vectors expressing erythropoietin or growth hormone from constitutive promoters were used to transduce skeletal muscle in mice with subsequent application to rhesus monkeys. Peak expression from adenoviral vectors is much higher than with AAV although it is less stable. In monkeys, serum erythropoietin from adenoviral vectors dropped 3-4 logs over the course of 1 year while that from AAV dropped only 4-fold over 11/2 years. For regulated expression of erythropoietin, mice and rhesus monkeys were administered two previously described rAAV vectors (*Science* **283**, 88-91; 1999). One vector constitutively expresses two chimeric proteins. These proteins are biologically inactive until they form a complex mediated by the presence of rapamycin. This ternary drug-protein complex functions as a transcriptional activator recognizing a unique DNA binding site present on the second vector upstream of the erythropoietin cDNA. Erythropoietin expression is controlled by dose and frequency of rapamycin administration. Six monkeys have received the described regulated expression system. In four monkeys, two cycles of rapamycin inducible expression have been observed with subsequent extinction of induction after 100 days following vector administration. One monkey has continued to show regulated expression of erythropoietin over 300 days with 9 cycles of intermittent drug administration while the other monkey has undergone 11 cycles of pharmacologic regulated erythropoietin expression for over 400 days. Our data support the feasibility of pharmacologically regulated transgene expression in primates. Mechanisms to explain heterogeneity in the stability of the regulated system in non-human primates is under evaluation. We are also developing modified vectors to improve the efficiency of the regulated system and screening analogs of rapamycin with superior safety profiles.