CURRICULUM VITAE

Tim Mendler Townes
Department of Biochemistry and Molecular Genetics
Schools of Medicine and Dentistry
University of Alabama at Birmingham
Birmingham, Alabama 35294
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PERSONAL INFORMATION:

Married: Peggy B. Townes
Children: 4

DEGREES:

B.S. (Zoology) June 1973, University of Tennessee
M.S. (Zoology) December 1975, University of Tennessee
Ph.D. (Microbiology) August 1980, University of Tennessee

POSITIONS HELD:

Professor Emeritus
Department of Biochemistry and Molecular Genetics,
Schools of Medicine and Dentistry, University of Alabama at Birmingham
October 1, 2016 to present.

Professor, Department of Biochemistry and Molecular Genetics,
Professor, Department of Medicine, Division of Hematology/Oncology
Schools of Medicine and Dentistry, University of Alabama at Birmingham
October 1, 1992 to September 30, 2016.

Chairman and James C. and Elizabeth T. Lee Professor
Department of Biochemistry and Molecular Genetics
Schools of Medicine and Dentistry
University of Alabama at Birmingham
April 2001- December 31, 2015

Founder and Director
UAB Stem Cell Institute
April 1, 2010- to December 31, 2015

Associate Professor, Department of Biochemistry
Schools of Medicine and Dentistry
University of Alabama at Birmingham
October 1, 1989 to September 30,1992.

Assistant Professor, Department of Biochemistry
Schools of Medicine and Dentistry
University of Alabama at Birmingham
August 1, 1984 to September 30, 1989.

Postdoctoral Fellow, Department of Microbiology and Molecular Genetics
University of Cincinnati College of Medicine
January 1980 to July 1984.

Personal Statement

Dr. Townes' major research interest is the regulation of gene expression during development. He studies the human hemoglobin genes as a model system and translates the understanding of basic mechanisms of globin gene regulation into strategies to correct hemoglobinopathies such as sickle cell disease. His paper in Nature Genetics (Nature Genetics. 2010; 42:742-4) provided new insights into the mechanism of hemoglobin switching and provides a foundation for new drug and cell therapies. A report from his laboratory in collaboration with Rudolf Jaenisch [Science. 2007; 318:1920-3) demonstrated the conversion of skin cells into induced pluripotent stem cells (iPSCs), the efficient correction of the sickle gene, and a safe and effective cure for sickle cell disease in a humanized mouse model. In recent studies, Dr. Townes' group has used CRISPR/Cas enhanced gene replacement to correct mutations in iPSCs derived from skin fibroblasts of UAB patients with Sickle Cell Disease [Scientific Reports (Nature) 6:30422] and Severe Combined Immunodeficiency (Cell Reports 12:1668-77). Most recently, the Townes laboratory has developed modifications of the Cas9 protein that permit formation of stable Cas9 RNP + ssODN complexes that efficiently correct the sickle mutation in patient bone marrow and umbilical cord blood stem cells (unpublished). The Cas9 modifications reduce on-target indels, reduce off-target effects, and increase cell viability. These results suggest that modified Cas9 complexes can be developed for treatment of a number of hereditary and acquired blood disorders including, sickle cell disease, severe combined immunodeficiency, and beta-thalassemia.

AD HOC REVIEWER:

Science
Nature
Nature Genetics
Nature Medicine
Blood
Genes and Development
Proceedings of the National Academy of Sciences
Journal of Biological Chemistry
Molecular and Cellular Biology

GRANT REVIEW

Numerous Ad Hoc NIH grant review committees 1986-present
Member, NIH College of CSR Reviewers, 2010-2012
NIH, ELB (formerly Hematology-1) study section, 2002-2006

ADVISORY COUNCILS

NIH, Advisory Committee of the DDIR, 2018-2023
NIH, Board of Scientific Counselors (BSC) of NHGRI, 2016-2021
NIH, Board of Scientific Counselors (BSC) of NIDDK, 2011-2016
Chair, NIDDK BSC, 2015-2016
NIH, Sickle Cell Disease Advisory Group, NHLBI, 1998-2002
NHLBI, Gene Therapy Resource Program, Scientific Review Board, 2008-2017

SELECTED INVITED LECTURES:

University of Pittsburgh Medical Center (UPMC), Oct. 2018
Oxford University Pembroke College, Sept. 2018
Vertex Pharmaceuticals, Boston, May 2018
American Physiological Society Conference on Sickle Cell Disease, Washington DC, Nov. 2017
28th Annual Vascular Biology and Hypertension Symposium, Birmingham, AL, May 2017
8th Cuban Congress on Hematology, Havanna, May 2017
Washington University, Dept. of Biochemistry, Seattle WA, April, 2017
Hemoglobin Switching Meeting, Asilomar, Pacific Grove CA, Sept. 2016
Amer. Soc. Hematology, CRISPR/Cas Meeting, Washington D.C., July 2016
South African Hematology meeting, Johannesburg, May 2016
BioMarin Pharmaceutical Inc., Novato, CA, Jan. 2016
Editas Medicine, Inc., Boston, Jan. 2016
American Society of Hematology, Orlando, Dec. 2015
New York Academy of Sciences/Cooley's Anemia Foundation 10th Symposium, Chicago, Oct. 2015
American Society of Gene and Cell Therapy, New Orleans, May 2015
American Association of Blood Banking, Philadelphia, Dec. 2014
Oxford University, England, Sept 2014
American Society of Hematology, New Orleans, Dec. 2013
3nd CUHK International Symposium on Stem Cell Biology and Regenerative Medicine, Hong Kong, Nov 2013
Hacettepe University, Ankara, Turkey, Oct. 2013
University of Virginia, Charlottsville, Sept. 2013
Global Blood Therapeutics, San Francisco, Jan. 2013
Children's Hospital of Cincinnati, Nov. 2012
Beaumont Hospital Grand Rounds, Detroit, Sept. 2012
National Taiwan University, Taiwan, June 2012
Chung-Shan Medical University, Taiwan, June 2012
Yang-Ming Medical University, Taiwan, June 2012
Hemoglobin Switching Meeting, Asilomar, California June 2012
NHLBI-Biomedicine Lecture Series, March 2012
National Association of Professors of Medicine meeting, Tucson, AZ, Feb. 2012
Isis, Pharmaceuticles, Carlsbad, CA, Jan. 2012
NIH Workshop; Genomic Opportunities for Studying Sickle Cell Disease, San Deigo, 2012
Sickle Cell in Focus, London, 2011
Albert Einstein, College of Medicine, New York, 2011
NIH, Herrick Symposium, 100 Years After Discovery of Sickle Cell Disease, Bethesda, 2010
Conference on Sickle Cell Disease and Thalassemia, Capetown, South Africa, 2010
University of Utah, School of Medicine, 2010
Hemoglobin Switching Meeting, Oxford, England 2010
Vanderbilt University, Nashville, 2010
UC Davis School of Medicine/Sacramento State, Sacramento, 2010
Southern Society for Clinical Investigation, New Orleans, 2010
University of Minnesota, Minneapolis, 2009
Washington University, St. Louis, 2009
American Society of Gene Therapy, San Diego, 2009
University of Colorado Health Science Center, 2009
Cincinnati Children's Hospital, 2009
10th FISV Congress, Keynote Speaker, Riva del Garda, Italy, 2008
Hemoglobin Switching Meeting, Asilomar, CA, 2008
NIH, Bethesda, Maryland, 2008

Translational Genetics (TGen), Phoenix, Arizona, 2008
Jackson Labs, Bar Harbor Maine, 2008
University of Utah, School of Medicine, 2008
University of Cincinnati School of Medicine, Jerry Lingrel 35 yrs Celebration, 2007
Hemoglobin Switching Meeting, Oxford England, St. John's College, 2006
Frontiers in Human Embryonic Stem Cell Research, Stanford University, 2005
International Cooley's Anemia Symposium, Orlando, 2005
Hemoglobin Switching meeting, Orcus Island, 2004
Univ of North Carolina at Chapel Hill, Dept. of Cell Biology, 2004
Sangamo, Inc, Richmond, California, 2004
Tulane School of Medicine, Biochemistry, New Orleans, 2003
SUNY Buffalo, Biochemistry, 2003
Children Hospital of Los Angeles, University of Southern California, March 2003
AMGDB Annual Meeting, Costa Rica, January 2003
Hemoglobin Switching Meeting, Oxford, England, Oct. 2002
Hospital For Sick Children, Dept of Genetics, Toronto, April, 2002
8th International Hemoglobinopathy Meeting, Athens, Greece, Oct. 2001
Mouse Models of Human Genetic Disease meeting, Jackson Laboratory, Bar Harbor, 2001
National Sickle Cell Disease meeting, Philadelphia, 2000
International Hemoglobin Switching meeting, Orcus Island, 2000
Baxter/Somatogen, Boulder Co., 2000
American Society of Hematology, Gene Therapy for Hemoglobinopathies, New Orleans, 1999
12th Czech and Slovak Hematological Conference, Prague, 1999
Meharry Medical College, Nashville, 1999
Geron Corporation, Menlo Park, 1999
Vanderbilt University, Dept of Hematology, Nashville, 1998
Roslin Institute, Edinburgh, Scotland, 1998
XVIIIth International Congress of Genetics, Beijing, China, 1998
Genetics Institute, Boston, 1998
Brown University, Dept. of Biochemistry, Providence, 1997
Genentech, Inc., San Fransiciso, 1997
Seventh Cooley's Anemia Symposium, Boston, 1997
Washington University, Biology and Biomedical Sciences, St. Louis, 1997
International Congress on Human Genetics, Rio de Janeiro, 1996
International Conference on Hemoglobin Switching, Orcus Island, 1996
Mt. Sinai School of Medicine, Brookdale Center for Molecular Biology, New York, 1996
Red Cell Gordon Conference, New Hampshire, 1996
University of Minnesota, School of Medicine, Dept. of Human Genetics, 1995
NIH Sickle Cell Advisory Committee, Wash. D.C., 1995
International Conference on Hemoglobinopathies, Paris, France 1994
International Conference on Hemoglobin Switching, Orcus Island, 1994
University of Pennsylvania, Dept. of Human Genetics, 1994
American Society of Hematology, St. Louis, 1994, 1993
NIH Sickle Cell Disease Conference, Wash. D.C., 1993
2nd Queenstown Molecular Biology Meeting, New Zealand, 1992
LSU School of Medicine, Dept. of Biochem. and Molecular Biol.,1992
Univ. of Texas, Southwestern Medical School, Dept. of Biochem., 1991
Amgen Inc., Alameda CA, 1991
University of North Carolina at Chapel Hill, Dept. of Biochemistry and Biophysics, 1991
St. Jude's Children's Hospital, Department of Biochemistry, Memphis,1991
University of Calgary, Department of Genetics, Canada,1991
Molecular Genetics of Development Meeting, Wash. D.C., 1990

Eli Lilly, US-USSR Transgenic Animal Workshop, Indianapolis, IN, 1990
International Meeting on Hemoglobin Switching, Wash. D.C., 1990
Washington University School of Medicine, Dept. of Hematology/Oncology, 1990
European Molecular Biology Labs, Heidelberg, Germany, 1989
Case Western Reserve, Department of Genetics, Cleveland, 1989
Stanford University, Medical Scientist Training Program, Palo Alto, CA. 1988
Duke Medical School, Department of Medicine and Hematology, Durham, 1988
International Congress on Thalassemia, Heraklion, Crete, 1987
University of Pennsylvania, Department of Biology, Philadelphia,1987

FACULTY RECRUITMENT

Ching-Yi Chen, Ph.D., Assistant Professor, 2002
Igor Chesnokov, Ph.D., Assistant Professor, 2002
Kirill Popov, Ph.D., Associate Professor, 2003
Natalia Kedishvili, Ph.D., Associate Professor, 2003
Tom Ryan, Ph.D., Assistant Professor, 2004
Hengbin Wang, Ph.D., Assistant Professor, 2004
Dmitry Vassylyev, Ph.D., Professor, 2005
Matthew Renfrow, Ph.D., Assistant Professor, 2006
David Schneider, Ph.D., Assistant Professor, 2007
Jin-Biao Ma, Ph.D., Assistant Professor, 2007
Clint Lothrop, Ph.D., DVM, Professor, 2007
Kejin Wu, Ph.D., Assistant Professor, 2011
Xinyang Zhao, Ph.D., Assistant Professor, 2011
Keith Giles, Ph.D., Assistant Professor, 2011
Rui Zhou, Ph.D., Assistant Professor, 2011
Hao Jiang, Ph.D., Assistant Professor, 2011
Chad Petit, Ph.D., Assistant Professor, 2012
Will Placzek, Ph.D., Assistant Professor, 2012
Marek Napierala, Ph.D. Assistant Professor, 2013

TEACHING

Cell and Molecular Biology III Co-Coursemaster 1985-present
Dental and/or Medical Biochemistry, Prokaryotic and Eukaryotic Gene Regulation, 1985-present
Advanced Eukaryotic Molecular Genetics Journal Club, 1986-present
Advanced Eukaryotic Molecular Genetics Course 1992, 1994, 1998, 2000
Medical Biochemistry Course Master 2001-2006

GRADUATE STUDENT TRAINING

Past students; year Ph.D. granted
Thomas Ryan, Ph.D., 1990
John Caterina, Ph.D., 1993
Joe Sun, MS, 1994
Kevin Pawlik, Ph.D., 1995
Steve McCune, MD-PhD, 1995
David Donze, PhD, 1996
Joe Sun, PhD, 1998
Wenyong Chen, PhD, 1999
Dominic Ciavatta, PhD, 1999

Susan Farmer, Ph.D., 2002
Kumar Pandya, Ph.D., 2002
Howard Masuoka, MD-PhD, 2002
Dana Levasseur 2003
Andrea Svendsen 2006
Li-Chen (Jane) Wu, 2008
Chia-Wei Chang, 2009
Yi-Shin Lai, 2011
Chao LI, 2015

Graduate student thesis committees: more than 75 since 1984

Present laboratory personnel:
Total of 7 scientists, postdocs and students

PUBLICATIONS:

Townes, T. and Fuhr, J.E. (1977) Protection by Cycloheximide from Hyperthermic Inhibition of Protein Synthesis in Human Reticulocytes. **Life Sciences** 20:585-592.

Fuhr, J.E., Yang, T.J., Townes, T. and Overton, M. (1977) Effect of Dibutyl Cyclic Adenosine 5' Monophosphate on Protein Synthesis in L5A8Y Cells After Hyperthermia. **J. National Cancer Institute** 59:1469-1473.

Riggsby, W.S., Torres-Bauza, L.J., Wills, J.W. and Townes, T. (1982) DNA Content, Kinetic Complexity, and the Ploidy Question in Candida albicans. **Mol. Cell. Biology** 2:853-862.

Lingrel, J.B., Shapiro, S.G., Townes, T., Wernke, S. and Schon, E.A.(1983) Globin Gene Structure, Linkage, and Evolution. In **DNA Recombinant Technology**, Vol. II: Applications, S.Woo, ed. (CRC Press, Inc., FL).

Shapiro, S.G., Schon, E.A., Townes, T. and Lingrel, J.B. (1983) Sequence and linkage of the goat epsilon I and epsilon II beta-globin genes.. **J. Mol. Biol**. 169:31-35.

Townes, T., Shapiro, S.G., Wernke, S.M. and Lingrel, J.B. (1983) Duplication of a four-gene set during the evolution of the goat beta-globin locus produced genes now expressed differentially in development. **J. Biol. Chem**. 259:1896-1900.

Lingrel, J.B., Townes, T., Shapiro, S.G., Spence, S.E., Liberator, P.A.and Wernke, S.M. (1983) Organization, Structure and Expression of the Goat Globin Genes. In **Globin Gene Expression and Hematopoietic Differentiation**, pp. 131-139, G. Stamatoyannopoulos and A.W. Nienhuis, eds. (Alan R. Liss, Inc., New York).

Townes, T.M., Fitzgerald, M. and Lingrel, J.B. (1984) Triplication of a Four Gene Set During Evolution of the Goat beta-Globin Locus Produced Three Genes Now Expressed Differentially During Development. **Proc. Natl. Acad Sci**. 81:6589-6593.

Lingrel, J.B., Townes, T.M., Shapiro, S.G., Wernke, S.M., Liberator, P.A. and Menon, A.G. (1985) Structural organization of the alpha and beta globin loci of the goat. In **Globin Gene Expression and Hematopoietic Differentiation**, G. Stamatoyannopoulous and A.W. Nienhuis, eds. (Alan RLiss, Inc).

Townes, T.M., Chen H.Y., Lingrel, S.B., Palmiter, R.D. and Brinster,R.L. (1985) Expression of human beta-globin genes in transgenic mice: effects of a flanking metallothionein-human growth hormone fusion gene. **Mol. Cell. Biol**., 5:1977-1983.

Townes, T.M., Lingrel, J.B., Brinster, R.L. and Palmiter, R.D. (1985) Erythroid-specific expression of human beta-globin genes in transgenic mice.. **EMBO J**., 4:1715-1723.

Dunham, R.A., Eash, J., Askins, J. and Townes, T.M. (1987) Transfer of the Metallothionein-Human Growth Hormone Fusion Gene into Channel Catfish. **Trans. Amer. Fisheries Soc**., 116:87-91.

Townes, T.M., Behringer, R., Hammer, R.E., Brinster, R.L., and Palmiter, R.D. (1987) Multiple sequences regulate human beta-globin gene expression in transgenic mice. In **Globin Gene Expression and Hematopoietic Differentiation,** G. Stamatoyannopoulous and A.W. Nienhuis, eds. (Alan R. Liss, Inc.).

Behringer, R., Hammer, R.E., Brinster, R.L., Palmiter, R.D. and Townes, T.M. (1987) Two 3' sequences direct adult erythroid-specific expression of human beta-globin genes in transgenic mice. **Proc. Natl. Acad. Sci**., 84:7056-7060.

Ryan, T.M., Behringer, R.R., Townes, T.M., Palmiter, R.D. and Brinster, R. L. (1989) High-level erythroid expression of human alpha-globin genes in transgenic mice. **Proc. Natl. Acad. Sci.** 86, 37-41.

Ryan, T.M., Behringer, R.R., Martin, N.C., Townes, T.M., Palmiter, R.D. and Brinster (1989) A single erythroid-specific DNase I super-hypersensitive site activates high levels of human beta-globin gene expression in transgenic mice. **Genes and Development** 3:314-323.

Townes, T.M., Ryan, T.M., Behringer, R.R., Palmiter, R.D. and Brinster, R.L. (1989) DNase I super-hypersensitive sites direct high level erythroid expression of human alpha-, beta- and betaS- globin genes in transgenic mice. Genes In Transgenic Mice. In **Hemoglobin Switching**, G. Stamatoyannopoulos and A.W. Nienhuis, eds. (Alan R.Liss, Inc.).

Behringer, R.R., T.M. Ryan, M. P. Reilly, T. Asakura, T.M., Palmiter, R.D., Brinster, R.L. and Townes, T.M. (1989) Synthesis of Functional Human Hemoglobin in Transgenic Mice, **Science**, 245: 971-973.

Ryan, T.M., Townes, T.M., Reilly, M. P., Asakura, T., Palmiter, R.D., Brinster, R.L. and Behringer, R.R. (1990) Human Sickle Hemoglobin In Transgenic Mice, **Science**, 247: 566-568.

Behringer, R.R., Ryan, T.M., Palmiter, R.D., Brinster, R.L. and Townes, T.M. (1990) Human gamma- to beta-globin gene switching in transgenic mice. **Genes and Development** 4: 380-389.

Townes, T.M. and Behringer, R.R. (1990) Human Globin Locus Activation Region (LAR): Role in Temporal Control, **Trends In Genetics** 6: 219-223.

Caterina, J. J., Ryan, T. M., Pawlik, K. M., Palmiter, R. D., Brinster, R. L., Behringer, R. R. and Townes, T. M. (1991) Human □-globin Locus Control Region (LCR): Analysis of the 5' HS 2 Site in Transgenic Mice. **Proc. Natl. Acad. Sci.,** 88:1626-1630.

Reilly, M.P., McCune, S.L., Ryan, T.M., Townes, T.M., Katsumata, M. and Asakura, T. (1994) Preparation of Recombinant Hemoglobin in Transgenic Mice, **Methods in Enzymology** 231, Hemoglobins, Part B, Biochemical and Analytical Methods; Everse, J., Vandergriff, K.D. and Winslow, R.M., eds. (Academic Press, New York)

Townes, T.M., Ryan, T.M., Caterina, J.J., Pawlik, K.M., Palmiter, R.D., Brinster, R.L., Behringer, R.R. (1991) Human Globin Gene Regulation in Transgenic Mice. In **The Regulation of Hemoglobin Switching**, G. Stamatoyannopoulos and A.W. Nienhuis, eds. (Johns Hopkins Press).

Caterina, J. J., Ciavatta, D. J., Donze, D., Behringer, R. R. and Townes, T. M. (1994) Multiple elements in human beta-globin locus control region 5' HS 2 are involved in enhancer activity and position-independent, transgene expression. **Nucleic Acid. Res**., 22:1006-1011.

Caterina, J. J., Donze, D., Sun, C.-W., Ciavatta, D. J. and Townes, T.M. (1994) Cloning and Functional Characterization of LCR-F1: A bZIP Transcription Factor That Activates Erythroid-Specific, Human Globin Gene Expression, **Nucleic Acids Res**., 22, 2383-2391.

McCune, S.L., Reilly, M.P., Chomo, M.J., Asakura, T. and Townes, T.M. (1994) Recombinant Human Hemoglobins Designed For Gene Therapy Of Sickle Cell Disease, **Proc. Natl. Acad. Sci**., 91, 9852-9856.

McCune, S. L. and Townes, T. M. (1994) Retroviral vector sequences inhibit human beta-globin gene expression in transgenic mice. **Nucleic Acids Res**. 22:4477-4481.

Donze, D., Townes, T.M. and Bieker, J.J. (1995) Role of erythroid Kruppel-like factor in human gamma- to beta-globin gene switching., **J. Biol. Chem**. 270: 1955-1959.

Pawlik, K.M. and Townes, T.M. (1995) Autonomous, erythroid-specific DNase I hypersensitive site formed by human beta-globin locus control region (LCR) 5' HS 2 in transgenic mice. **Dev. Biol**. 169:728-732.

Pawlik, K.M., Sun, C.-W. J., Higgins, N. P. and Townes, T.M. (1995) End Joining of Genomic DNA and Transgene DNA in Fertilized Mouse Eggs, **Gene**, 165: 173-181.

Ciavatta, D., Ryan, T.M. Farmer, S. and Townes, T.M. (1995) Mouse model of human beta zero thalassemia: targeted deletion of the mouse beta maj- and beta min-globin genes in embryonic stem cells. **Proc. Natl. Acad. Sci**. 92: 9259-9263.

Luhovy, M., Mccune, S., Dong, J.Y., Prchal, J.F., Townes, T.M. and Prchal. J.T. (1996) Stable Transduction of Recombinant Adeno-Associated Virus into Hematopoietic Stem Cells from Normal and Sickle Cell Patients, **Biology of Blood and Marrow Transplantation** 2:24-30.

Donze, D., Jeancake, P.H. and Townes, T.M. (1996) Activation of delta-globin gene expression by erythroid Krupple-like factor: a potential approach for gene therapy of sickle cell disease. **Blood** 88:4051-4057.

Farmer, S., Sun, C.-W., Winnier, G.E., Hogan, B.L.M. and Townes, T.M. (1997) The bZIP Transcription Factor LCR-F1 Is Essential For Mesoderm Formation in Mouse Development, **Genes & Development**, 11: 786-798.

Chen, W., Bailey, E., Dong, Jian-Yun and Townes, T. M. (1997) Reactivation of Silenced, Virally Transduced Genes by Inhibitors of Histone Deacetylase, **Proc. Natl. Acad. Sci**., 94: 5798-5803.

Ryan, T.M., Ciavatta, D. and Townes, T.M. (1997) Knockout/Transgenic Mouse Model of Sickle Cell Disease, **Science**, 278: 873-876.

Graubert, T.A., Hug, B.A., Wesselschmidt, R., Hsieh, C.L., Ryan, T.M., Townes, T.M., Ley, T.J. (1998) Stochastic, Stage-specific Mechanisms Account for the Variegation of a Human Globin Transgene. **Nucleic Acids Res** 26 :2849-2858.

Chen, W. and Townes, T.M. (2000) Molecular Mechanism for Silencing Virally Transduced Genes Involves Histone Deacetylation and Chromatin Condensation. **Proc. Natl. Acad. Sci**., 97:377-382.

Chen, W., Wu, X., Liu, H., Zhang, M, Lai, L, Ciavatta, D., Kappes, J. and Townes, T. (2000) Lentiviral transduction of murine hematopoietic stem cells that mediate long term reconstitution of lethally irradiated mice, **Stem Cells** 18:352-359.

Ryan, T. M., Sun, C-W., and Townes, T. M. (2000) Human gamma-globin gene promoter element regulates human beta-globin gene developmental specificity. **Nucleic Acids Res**. 28:2736-2740.

Divoky, V., Zhi Yong Liu, Z.Y., Ryan, T.M., Townes, T.M. and Prchal, J.T. (2001) Homozygous Knockin of Mutant Human Erythropoietin Receptor Produces Severe Mouse Model of Polycythemia, **Proc. Natl. Acad. Sci**. 98:986-991.

Aslan M, Ryan TM, Adler B, Townes TM, Parks DA, Thompson JA, Tousson A, Gladwin MT, Patel RP, Tarpey MM, Batinic-Haberle I, White CR, Freeman BA. (2001) Oxygen radical inhibition of nitric oxide-dependent vascular function in sickle cell disease, **Proc. Natl. Acad. Sci**. 98:15215-15220.

Pandya K, Donze D, Townes T (2001) Novel transactivation domain in Erythroid Kruppel-like factor (EKLF), **J. Biol. Chem.** 276:8239-8243.

Masuoka, H. and Townes, T.M. (2002) Targeted disruption of the ATF4 gene results in severe fetal anemia, **Blood** 99:736-735.

Pandya, K and Townes, T.M. (2002) Basic Residues within the Kruppel Zinc Finger DNA Binding Domains Are the Critical Nuclear Localization Determinants of EKLF/KLF-1. **J. Biol. Chem**. 277:16304-16312.

Bradley MB, Sattler RM, Raftopoulos H, Ward M, Grossman IR, Townes TM, Ryan TA, Bank A. (2002) Correction of phenotype in a thalassemia mouse model using a nonmyeloablative marrow transplantation regimen. **Biol Blood Marrow Transplant**. 8:453-461.

Aslan M, Ryan TM, Townes TM, Coward L, Kirk MC, Barnes S, Alexander CB, Rosenfeld SS, Freeman BA. (2003) Nitric oxide-dependent generation of reactive species in sickle cell disease. Actin tyrosine induces defective cytoskeletal polymerization. **J Biol Chem**. 278:4194-4204.

Bennett EM, Anand R, Allan PW, Hassan AE, Hong JS, Levasseur DN, McPherson DT, Parker WB, Secrist JA 3rd, Sorscher EJ, Townes TM, Waud WR, Ealick SE. (2003) Designer gene therapy using an Escherichia coli purine nucleoside phosphorylase/prodrug system. **Chem Biol**. 10:1173-1181.

Levasseur, DN, Ryan, TM, Pawlik, KM and Townes, TM (2003) Correction of a mouse model of sickle cell disease: lentiviral/antisickling beta-globin gene transduction of unmobilized, purified hematopoietic stem cells. **Blood**. 102:4312-4319.

Roybal CN, Yang S, Sun CW, Hurtado D, Vander Jagt DL, Townes TM, Abcouwer SF. (2004) Homocysteine increases the expression of vascular endothelial growth factor by a mechanism involving endoplasmic reticulum stress and transcription factor ATF4. **J Biol Chem.** 279:14844-14852.

Hong JS, Waud WR, Levasseur DN, Townes TM, Wen H, McPherson SA, Moore BA, Bebok Z, Allan PW, Secrist JA 3rd, Parker WB, Sorscher EJ. (2004) Excellent in vivo bystander activity of fludarabine phosphate against human glioma xenografts that express the escherichia coli purine nucleoside phosphorylase gene. **Cancer Res**. 64:6610-5.

Yang X, Matsuda K, Bialek P, Jacquot S, Masuoka HC, Schinke T, Li L, Brancorsini S, Sassone-Corsi P, Townes TM, Hanauer A, Karsenty G. (2004) ATF4 is a substrate of RSK2 and an essential regulator of osteoblast biology; implication for Coffin-Lowry Syndrome. **Cell** 117:387-98.

Zhou D, Ren JX, Ryan TM, Higgins NP, Townes TM. (2004) Rapid tagging of endogenous mouse genes by recombineering and ES cell complementation of tetraploid blastocysts. **Nucleic Acids Res**. 32:128 (online).

Foster KW, Liu Z, Nail CD, Li X, Fitzgerald TJ, Bailey SK, Frost AR, Louro ID, Townes TM, Paterson AJ, Kudlow JE, Lobo-Ruppert SM, Ruppert JM. (2005) Induction of KLF4 in basal keratinocytes blocks the proliferation-differentiation switch and initiates squamous epithelial dysplasia. **Oncogene** 24:1491-500.

Zhou D, Pawlik KM, Ren J, Sun C-W and Townes TM (2006) Differential Binding of EKLF To Embryonic/Fetal Globin Gene Promoters During Development. **J. Biol. Chem**. 281:16052-7

Wu L-C, Sun C-W, Ryan TM, Pawlik KM, Ren J and Townes TM (2006) Correction of Sickle Cell Disease by Homologous Recombination in Embryonic Stem Cells. **Blood** 108:1183-1188.

Pilon AM, Nilson DG, Zhou D, Sangerman J, Townes TM, Bodine DM, Gallagher PG. (2006) Alterations in expression and chromatin configuration of the alpha hemoglobin-stabilizing protein gene in erythroid Kruppel-like factor-deficient mice. **Mol Cell Biol** 26:4368-77.

Hanna J, Wernig M, Markoulaki S, Sun CW, Meissner A, Cassady JP, Beard C, Brambrink T, Wu LC, Townes TM*, Jaenisch R*. (2007) Treatment of Sickle Cell Anemia Mouse Model with iPS Cells Generated from Autologous Skin. **Science** 318:1920-1923. *communicating authors

Isbell TS, Sun CW, Wu LC, Teng W, Vitturi DA, Branch BG, Kevil CG, Peng N, Wyss JM, Ambalavanan N, Schwiebert L, Ren J, Pawlik, KM, Renfrow MB, Patel RP, Townes TM (2008) SNO–Hemoglobin Not Essential for Red Blood Cell Dependent Hypoxic Vasodilation. **Nature Medicine**. 14:773-777

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SOME ACCOMPLISHMENTS of my graduate students, postdoctoral fellows and collaborators are as follows:

(1) the first transgenic mice that express a correctly regulated human gene [EMBO J., 4:1715 (1985)]
(2) the competition model of human hemoglobin switching during development [Genes and Development 4: 380 (1990)]; [Trends In Genetics 6: 219 (1990)]
(3) the first mice that express functional human hemoglobin A and S [Science, 245: 971 (1989)]; [Science, 247: 566 (1990)]
(4) the first knockout mouse model of beta-thalassemia [Proc. Natl. Acad. Sci. 92: 9259 (1995)]
(5) the first mouse model of sickle cell disease [Science, 278: 873 (1997)]
(6) an early example of molecular memory in mammalian cells by reversible histone modification [Proc. Natl. Acad. Sci. 97:377 (2000)]
(7) the first correction of a disease utilizing induced pluripotent stem cells (iPS cells) and the first demonstration of homologous recombination in iPSC (collaboration with Jacob Hanna and Rudolf Jaenisch at MIT) [Science 318:1920 (2007)]
(8) the first demonstration of a protein directly involved in the competitive switch from human fetal to adult hemoglobin [J. Biol. Chem. 270: 1955 (1995); Nat. Genet. 42: 742 (2010)].
(9) one of three groups demonstrating the production of functional T lymphocytes from induced Pluripotent Stem Cells (iPSC) derived from SCID patient skin biopsy [Cell Reports 12, 1668-1677 (2015)]
(10) highly efficient and safe correction of the sickle mutation in iPSC with novel Adenoviral Vectors [Scientific Reports (Nature) 6:30422 (2016)]

Most recently, we have produced a modified CRISPR/Cas9 complex that can be electroporated into primary hematopoietic stem cells and correct the sickle mutation with high efficiency. Compared with wild-type Cas9, our modified recombinant Cas9 proteins have low toxicity, high specificity and high efficiency. Transplantation studies of corrected human CD34+ HSC/HSPC into NSG mice demonstrate high level correction in all cell lineages, and we have successfully cured our humanized mouse model of sickle cell disease.