BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Blau, Helen M	Donald E. and Delia B. Baxter Foundation Professor Director, Baxter Laboratory for Stem Cell Biology
eRA COMMONS USER NAME BLAU.HELEN	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of York, York, England	B.A.	1969	Biology
Harvard University, Cambridge, MA	M.A.	1970	Biology
Harvard University, Cambridge, MA	Ph.D.	1975	Biology
University of California, San Francisco, CA	Postdoctoral	1975-1978	Medical Genetics/ Biochem. & Biophysics

A. Personal Statement.

I am a full professor, PI, and Director of the Baxter Laboratory for Stem Cell Biology, with 34 years of experience running my own laboratory and research program including three PIs and approximately 80 others including research scientists, staff members and trainees. The Blau Laboratory is focused on cell and molecular approaches to regenerative medicine for acquired and inherited diseases. I have a long-term interest in Duchenne Muscular Dystrophy (DMD), spanning the early discovery of defective myoblast proliferation, the role of fast fiber deterioration, myoblast clinical trials, and most recently the demonstration of a role for telomere shortening in the development and etiology of the disease. Importantly, for this grant, the combined dystrophin null (mdx) telomerase null (mdx/mTR^{KO}) mouse model closely approximates all the features of DMD, enabling novel analyses of the etiology of the disease and tests of therapeutic strategies. Here we propose an integrated multidisciplinary preclinical test of an innovative combination therapy for the cardiorespiratory failure that leads to death of DMD patients.

B. Positions and Honors.

1969-1975	Predoctoral Fellow, Department of Biology, Harvard University, Cambridge, MA
1975-1978	Postdoctoral Fellow, Dept. of Biochem. & Biophysics, Div. of Medical Genetics, U.C.S.F., CA
1978-1986	Assistant Professor, Molecular Pharmacology, Stanford University School of Medicine, CA
1986-1991	Associate Professor, Molecular Pharmacology, Stanford University School of Medicine, CA
1991-2002	Professor, Molecular Pharmacology/Chemical and Systems Biology, Stanford University School of Medicine, CA
1997-2002	Chair, Molecular Pharmacology, Stanford University School of Medicine, CA
1997-present	Director, Gene Therapy Technology, Stanford University School of Medicine, CA
1999-present	Donald E and Delia B. Baxter Professor, Stanford University School of Medicine, CA
2002-present	Professor, Microbiology and Immunology, Stanford University School of Medicine, Stanford, CA
2002-present	Director, Baxter Laboratory for Stem Cell Biology, Stanford University School of Med., CA

Honors:

Basil O'Connor Starter Research Award (1978-81); Mellon Foundation Faculty Fellow (1979-80); William M. Hume Faculty Scholar (1981-84); Research Career Development Award, National Institutes of Health (1984-89); SmithKline and Beecham Junior Faculty Scholar Award (1989-1991); election as Fellow of the American Association for the Advancement of Science (1991); Senior WICB Career Recognition Award of the American Society for Cell Biology (1992); President, Society for Developmental Biology (1994-1995); Yvette Mayent-Rothschild Visiting Professorship, Instituts Curie and Pasteur, Paris (1995); NIH MERIT Award (1995-2005); election to Institute of Medicine of the National Academy of Sciences (1995); Nobel Forum Lecturer, Karolinska Inst., Sweden (1995); election to American Academy of Arts and Sciences (1996); National Advisory Council, NIH Institute on Aging (1996-2000); FASEB Excellence in Science Award (1999); Donald E. and Delia B. Baxter Endowed Professor (1999-present); NIH Director's Lecture (2000); McKnight Technological Innovations for Neuroscience Award (2001); Council Member, American Society for Cell Biology (2002-2004); President, International Society of Differentiation (2002-2004); Honorary Doctorate, University of Nijmegen, Holland

(2003); Council Member, Institute of Medicine (IOM) (2004-2009); Harvard Board of Overseers (2004-2010); Member, NIH Committee to Review Biology of Aging Program for the National Institute of Aging (summer and fall, 2005); Scientific Advisory Board, Ellison Medical Foundation (2007-present); NIH Peer Review Advisory Committee (PRAC) (2009-2010); Fulbright Senior Scholar Award (2007 & 2011); NIH Challenge Grant (2009-2011); Keynote speaker, French Academy of Sciences (2010 & 2012); AACR-Irving Weinstein Found. Distinguished Lecture (2011); Mayent-Rothschild Visiting Professor, Inst. Curie, Paris (2011); NIH Director's Transformative Research Award (2012-2017).

C. Selected publications (from total of 180+ peer reviewed)

Blau, H.M., Brazelton, T.R. and Weimann, J.M. (2001) The evolving concept of a stem cell: Entity or function? Cell 105:829-841.

Weimann, J.M., Johansson, C.B., Trejo, A. and Blau, H.M. (2003) Stable reprogrammed heterokaryons form spontaneously in Purkinje neurons in adult brain after BMT. Nature Cell Biol. 5(11):959-966.

Corbel, S.Y., Lee, A., Yi, L., Duenas, J., Brazelton, T.R., Blau, H.M. and Rossi, F.M.V. (2003) Contribution of hematopoietic stem cells to skeletal muscle. Nature Medicine 9(12):1528-1532.

Pomerantz, J. and Blau, H.M. (2004) Nuclear reprogramming: A key to regenerative medicine. Nature Cell Biol. 6:810-816.

Sacco, A., Doyonnas, R., Kraft, P., Vitorovic, S. and Blau H.M. (2008) Self-renewal and expansion of single transplanted muscle stem cells. Nature 456:502-506. PMCID: PMC2919355.

Lutolf, M.P., Gilbert, P.M. and Blau, H.M. (2009) Designing materials to direct stem-cell fate. Nature 462(7272):433-441. PMCID: PMC2908011.

Bhutani, N., Brady, J.J., Damian, M., Sacco, A., Corbel, S.Y. and Blau, H.M. (2009) Reprogramming towards pluripotency requires AID-dependent DNA demethylation. Nature 463(7284):1042-1047.

Yamanaka, S. and Blau, H.M. (2010) Nuclear reprogramming to a pluripotent state by three approaches. Nature 465:704-712. PMCID: PMC2901154.

Pajcini, K.V., Corbel, S.C., Sage, J., Pomerantz, J.H. and Blau, H.M. (2010) Transient inactivation of Rb and ARF yields regenerative cells from postmitotic mammalian muscle. Cell Stem Cell 7(2):198-213. PMCID: PMC2919350.

Gilbert, P.M., Havenstrite, K.L., Magnusson, K.E.G., Sacco, A., Leonardi, N.A., Kraft P., Nguyen, N.K., Thrun, S., Lutolf, M.P. and Blau, H.M. (2010) Substrate elasticity regulates skeletal muscle stem cell self-renewal in culture. Science 329(5995):1078-1081. PMCID: PMC2929271.

Sacco, A., Mourkioti, F., Tran, R., Choi, J., Llewellyn, M., Kraft, P., Shkreli, M., Delp, S., Pomerantz, J. H., Artandi, S.E. and Blau, H.M. (2010) Short telomeres and stem cell exhaustion model Duchenne muscular dystrophy in mdx/mTR mice. Cell 143:1-13. PMCID: PMC3025608.

Bhutani, N, Burns, D.M. and Blau, H.M. (2011) DNA demethylation dynamics. Cell 146(6):866-872. PMCID: PMC3236603.

Gilbert, P.M., Corbel, S., Doyonnas, R., Havenstrite, K., Magnusson, K. and Blau, H.M. (2012) A single cell bioengineering approach to elucidate mechanisms of adult stem cell self-renewal. Integr. Biol. 4:360-367. PMCID: PMC3325106.

Bhutani, N., Decker, M.N., Brady, J.J., Bussat, R.T., Burns, D.M., Corbel, S.Y. and Blau, H.M. (2012) Critical role for AID in initiation of reprogramming to induced pluripotency, FASEB J. 27(3):1107-13. PMCID: Blau, H.M. (2012) Redefining differentiation: reshaping our ends. Nature Cell Biology 14(6):558. – *Invited Turning Point Commentary.*

D. Research Support

Ongoing Research Support (Blau, H. M.)

NIH R01 AG009521 MERIT award Blau (PI) 04/01/86-04/30/15

Activators of Human Muscle Genes - The goal of this grant is to investigate maintenance and generation of muscle stem cells using myoblasts and pre-adipocytes using techniques to assess global transcriptional and epigenetic changes essential to distinguish nuclear reprogramming contributions of each cell type in bi-species heterokayrons.

NIH R01 HL096113 Blau (PI) 04/28/09-02/28/14

Regulation of Hematopoietic Stem Cell Fate in Bioengineered Niches - The specific aims of this proposal are 1) to study the influence of single extrinsic factors on HSC maintenance; 2) to investigate the mechanisms of action of candidate extrinsic factors on HSC self-renewal; and 3) to identify *in vitro* predictive parameters that correlate with HSC expansion and to use these parameters to screen a small protein library.

NIH R01 AG020961 Blau (PI) 05/15/02-07/31/14

Regulation of Muscle Stem Cell Fate - This grant focuses on (1) elucidating biophysical niche signals in muscle stem cell function in artificial niches and (2) using young mouse muscle stem cells to examine the differences that arise from elasticity that is typical of the tissue from which the cells derive relative to standard tissue culture plastic which is 5 orders of magnitude more rigid. We are developing a new hydrogel technology: non-swelling gels of different rigidity.

NIH U01 HL100397 Blau & Cooke, J (Co-PIs) 09/30/09-04/30/16

Basic and Translational Research of iPSC-based Hematologic and Vascular Therapies

Project 1 PI: Discovery of Novel Regulators to Enhance iPSC Derivation and Differentiation of EC - The goal is to study nuclear reprogramming of somatic cells toward a human arterial endothelial cell (EC) fate; the regulators discovered in these experiments will be delivered as proteins to enhance iPSC generation and will be used in deriving arterial EC from iPSC more efficiently.

NIH R21 AR06235901 Heilshorn, S (PI) 09/01/11-08/31/13

3D Bioengineering Strategies to Mimic Human Skeletal Muscle Stem Cell Niches - We propose a 3D model of primary human skeletal muscle that utilizes an engineered extracellular matrix (eECM), gradients of chemotactic cues, and cellular patterning. Role: Co-PI

California Institute of Regenerative Medicine TR3-05501 Blau (PI) 11/01/12-10/31/15

Local Delivery of Rejuvenated Old Muscle Stem Cells to Increase Strength in Aged Patients - The goal of this Development Candidate Feasibility grant is to provide preclinical proof-of-concept for the translation of human muscle stem cells as a localized therapy for muscle atrophy in aged patients.

NIH 1R01 AR063963 Blau (PI) 09/13/12-08/31/17

(NIH DIRECTOR'S TRANSFORMATIVE RESEARCH AWARD) Telomere Extension using Nucleoside-modified mRNA as a Novel Therapeutic Tool - This project focuses on a collaboration between the Cooke and Blau labs for the development of a TERT therapeutic deliverable to muscle stem cells to treat Duchenne Muscular Dystrophy and potentially other major diseases in which short telomere length is implicated.

NIH 5U01HL099997– subcontract SR00002307 Blau (PI) 8/1/12-4/30/14

Ancillary Grant: Safe, Rapid Telomere Extension in Diverse Progenitor Cell Types - The goal of this grant it to optimize the telomere-extending nucleoside-modified mRNA cells developed in my lab. Our process allows safe and rapid extension of telomeres in progenitor cells and the optimized process will be made available to colleagues doing research in this are.

CIRM TR3-05501 Blau (PI) 10/01/12-09/30/15

Local Delivery of Rejuvenated Old Muscle Stem Cells to Increase Strength in Aged Patients - We propose to develop a human stem cell therapy to prevent and/or reverse localized skeletal muscle atrophy in muscles of the aged. Specifically, we aim to (1) refine a strategy we have developed that enables us to isolate muscle stem cells (MuSCs) from human muscle biopsies, (2) apply a strategy which we developed for murine MuSCs to human MuSCs that rejuvenates and expands the stem cells in culture to clinically useful numbers using a combined bioengineering and small molecule treatment, and (3) demonstrate that transplantation of human MuSCs results in increased *in vivo* force generation and strength in atrophied muscles of aged recipients.

NIH 1R21 AG04481501 Blau (PI) 6/01/13-5/31/15

Safe, Rapid Telomere Extension to Prevent and Treat Hypertension - Our goal in this project is to initiate translation of our uniquely enabling telomere extending drug toward human studies to help prevent or treat hypertension and the many other diseases exacerbated or caused by short telomeres.

Completed Research Support

NHLBI Progenitor Cell Biology Consortium Blau & Santiago (Co-PIs) 08/1/12-04/30/13

Safe, Rapid Telomere Extension in Diverse Progenitor Cell Types

California Institute of Regenerative Medicine RB1-01292 Blau (PI) 11/01/09-12/31/12

Molecular Mechanisms of Reprogramming towards Pluripotency

Bio-X IIP Blau & Santiago (Co-PIs) 01/01/11-12/31/12

Stanford Bio-X Pilot Project funding - Oxytocin Delivery During Pup Ultrasonic Vocalizations to Rescue Maternal Behavior

Stanford Cardiovascular Institute Blau (PI) 04/11/11-04/10/12

CVI Seed Grant - Direct readout of age-related perturbation of redox homeostasis using a novel method for metabolic imaging of the heart

Juvenile Diabetes Research Fdn. Kim, S (PI) 10/01/08-09/30/11
Directly Observed Development of Purified Human Pancreatic Progenitor Cells

Leukemia and Lymphoma Society TRP 6025 Blau (PI) 10/01/08-09/30/11
Bioengineered Niches to Control Human Follicular Lymphoma Cells

NIH RC1 AR059365 (NIH CHALLENGE GRANT) Santiago (PI) 09/30/09-08/31/11
Remote-control Mouse-implantable Micropumps for Establishment of Regenerative Capability

NIH P50 CA114747 Gambhir, S (PI) 09/15/10-08/31/11
Project 4: Development of a Novel Gadolinium-Based MRI Contrast Agent for Tracking Cancer Cells

California Institute of Regenerative Medicine RT1-01001-1 Blau (PI) 04/01/09-03/31/11
Regulation of Stem Cell Fate in Bioengineered Arrays of Hydrogel Microwells