BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Blau, Helen M.

eRA COMMONS USER NAME (credential, e.g., agency login): BLAU.HELEN

POSITION TITLE: Donald E. and Delia B. Baxter Foundation Professor
Director, Baxter Laboratory for Stem Cell Biology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	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 extensive experience running my own laboratory and research program including three PIs and approximately 75 trainees and staff. I am a committed mentor of postdocs with a strong history of training postdocs for academic careers and strongly support the goals of IRACDA. I am a co-inventor on 21 patents, 9 currently licensed, and my work is consistently high profile, with one quarter of my publications in *Science, Cell,* and *Nature* journals. My laboratory's research encompasses cell and molecular approaches to regenerative medicine for acquired and inherited diseases with an emphasis on understanding and elucidating the nature of cell plasticity. Our work has focused on Duchenne Muscular Dystrophy, telomeres, muscle stem calls, and the role of transient inactivation of tumor suppressors. A central interest is the elucidation of the mechanisms underlying and directing changes in muscle stem cell fate in aging, dystrophy, and diabetes. This knowledge is key to our understanding of stem cell reprogramming, self-renewal and expansion and tissue regeneration with a view toward medical applications for increasing muscle function and extending healthspan.

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 (now 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
2002-present Professor, Microbiology and Immunology, and member, Institute for Stem Cell Biology and Regenerative Medicine, Stanford University School of Medicine, Stanford, CA
2002-present Director, Baxter Laboratory for Stem Cell Biology, Stanford University School of Med., CA

Honors and Awards:

1978-1981 Basil O'Connor Starter Research Award
1979-1980 Mellon Foundation Faculty Fellow
1981-1984 William M. Hume Faculty Scholar

1984-1989	Research Career Development Award, National Institutes of Health
1989-1991	SmithKline and Beecham Junior Faculty Scholar Award
1991	Election as Fellow of the American Association for the Advancement of Science
1992	Senior WICB Career Recognition Award of the American Society for Cell Biology
1994-1995	President, Society for Developmental Biology
1995	Yvette Mayent-Rothschild Visiting Professorship, Instituts Curie and Pasteur, Paris
1995	Election to Institute of Medicine of the National Academy of Sciences
1995	Nobel Forum Lecturer, Karolinska Institute, Stockholm, Sweden
1995-2005	NIH MERIT Award
1996	Election to American Academy of Arts and Sciences
1996-2000	National Advisory Council, NIH Institute on Aging
1999	FASEB Excellence in Science Award
1999-present	Donald E. and Delia B. Baxter Endowed Professor
2000	NIH Director's Lecture
2001	McKnight Technological Innovations for Neuroscience Award
2002-2004	Council Member, American Society for Cell Biology
2002-2004	President, International Society of Differentiation
2003	Honorary Doctorate, University of Nijmegen, Holland
2004-2010	Harvard Board of Overseers
2005	Member, NIH Committee to Review Biology of Aging Program for the National Institute of Aging
2007-2014	Scientific Advisory Board, Ellison Medical Foundation
2009-2010	NIH Peer Review Advisory Committee (PRAC)
2007, 2011	Fulbright Senior Scholar Award
2009-2011	NIH Challenge Grant
2010, 2012	Keynote/Plenary Speaker, French Academy of Science, Paris, France
2011	AACR-Irving Weinstein Foundation Distinguished Lecture
2011, 2013	Mayent-Rothschild Visiting Professor, Institut Curie, Paris, France
2011-2017	NIH Director's Transformative Research Award
2011-2017	Pew Scholars Program National Advisory Committee
2014	Thomas Hunt Morgan Lecturer Award, University of Kentucky
2015	Stanford OTL Outstanding Inventor Award (2015)
2015-2019	Council Member, American Academy of Arts and Sciences
2015	Glenn Award for Research in Biological Mechanisms of Aging

C. CONTRIBUTION TO SCIENCE

1. Cell Plasticity and Differentiation

My early work on cell plasticity challenged the long-standing dogma that the state of differentiated cells is fixed and terminal. I showed that differentiated mammalian cells are plastic and reversible, constituting a paradigm shift in the understanding of mammalian cell differentiation. This work also demonstrated that a change in the stoichiometry of trans-acting regulators induces nuclear reprogramming, providing the scientific underpinnings for induction of pluripotent stem cells (iPSCs) by transcription factor overexpression. My current work capitalizes on the unique ability of the heterokaryon system-- the foundation for much of this work-- to generate "snapshots" of the sequential molecular, transcriptional, and epigenetic events in the remodeling of cell fate in the first minutes to hours of reprogramming. Using this approach, my laboratory has identified several novel early regulators crucial to the initiation of reprogramming to iPSCs. This body of work has established the basis for diverse approaches (transcription factor overexpression) now being used to control cell fate decisions, which is considered the bedrock for modern stem cell research and regenerative medicine. I served as the PI for all of these publications.

a. Blau, H.M., Chiu, C.-P. and Webster, C. (1983) Cytoplasmic activation of human nuclear genes in stable heterokaryons. Cell 32:1171-1180.
b. Chiu, C.P. and Blau, H.M. (1984) Reprogramming cell differentiation in the absence of DNA synthesis. Cell 37:879-887.
c. 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. PMCID: PMC2906123.
d. Brady, J.J., Li, M., Suthram, S., Jiang, H., Wong, W.H. and Blau, H.M. (2013) Early role for IL-6 signaling

during generation of induced pluripotent stem cells revealed by heterokaryon RNA-Seq. Nature Cell Biology 15(10):1244-1252. PMCID: PMC4100556.

2. Telomeres and Duchenne Muscular Dystrophy

Duchenne Muscular Dystrophy (DMD) is a major cause of death in childhood with an estimated worldwide incidence of 1 in 3,500 boys. There is no effective therapy, and the widely used mouse model that lacks dystrophin (mdx) exhibits only a very mild form of the disease. My laboratory has discovered that in DMD, reduced telomere length leads to exhaustion of stem cells in skeletal muscle and mitochondrial failure in cardiac muscle. We developed a mouse model with the dystrophin mutation and shorted telomeres, which faithfully recapitulates the skeletal muscle and cardiac defects of DMD patients. Moreover, the findings in mice held true for patients; in the cardiac cells of hearts of DMD patients, but not normal age-matched human hearts, telomere lengths are significantly shorter. Thus we have developed the only rodent model that recapitulates the devastating skeletal muscle weakness and dilated cardiomyopathy that causes premature death in children with DMD, providing novel mechanistic insights into DMD and enabling tests of novel therapeutic interventions. I served as the PI for all of these studies.

a. 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.
b. Mourkioti, F., Kustan, J., Kraft, P., Day, J.W., Zhao, M.-M., Kost-Alimova, M., Protopopov, A., DePinho, R.A., Bernstein, D., Meeker, A. K. and Blau, H.M. (2013) Role of telomere dysfunction in cardiac failure in Duchenne muscular dystrophy. Nature Cell Biology 15(8):895-904. PMCID: PMC3774175.
c. Ramunas, J., Yakubov, E., Brady, J. J., Corbel, S. Y., Holbrook, C., Brandt, M, Stein, J., Santiago, J.G., Cooke, J.P. and Blau, H.M. (2015). Transient delivery of modified mRNA encoding TERT rapidly extends telomeres in human cells. The FASEB Journal, fj.14-259531. PMCID: PMC4415018.

3. Muscle Repair and Regeneration by Muscle Stem Cells

A major barrier in regenerative medicine and drug discovery aimed at muscle repair has been the difficulty in purifying and maintaining in an active state sufficient quantities of active populations of muscle stem cells. My laboratory has developed a combination of novel technologies, including creating bioengineered microenvironments, developing single cell tracking algorithms, and a non-invasive bioluminescence assay for monitoring muscle stem cell engraftment, muscle repair and self renewal in living mice. We found that in aging, two-thirds of muscle stem cells develop a cell autonomous defect, overturning the prevailing view that tissue-extrinsic factors such as systemic factors, are largely responsible for the decreased regeneration observed with aging. Our platform has enabled screening for and identifying a drug capable of enhancing the numbers and function of the aged muscle stem cell population. Remarkably, we found that transplantation of treated aged stem cell populations into injured muscles of aged mice restores muscle strength to a level comparable to that of young mice. This work has broad therapeutic implications for using autologous cells to treat muscle wasting and immobilization due to bone fractures, which plague the increasingly aged population. I have served as the PI for all of these studies.

a. 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.
b. 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.
c. Chenouard, N., Smal, I., de Chaumont, F., Maška, M., Sbalzarini, I.F., Gong, Y., Cardinale, J., Carthel, C., Coraluppi, S. Winter, M., Cohen, A.R., Godinez, W.J., Rohr, K., Kalaidzidis, Y. Liang, L., Duncan, J., Shen, H., Xu, Y., Magnusson, K.E.G., Jaldén, J., Blau, H.M., Paul-Gilloteaux, P., Roudot, P., Kervrann, C., Waharte, F., Tinevez, J-Y., Shorte, S.L., Willemse, J., Celler, K., van Wezel, G.P., Dan, H-W., Tsai, Y-S., Ortiz de Solórzano, E., Olivo-Marin, J-C., and Meijering, E. (2014). Objective comparison of particle tracking methods. Nature Methods 11(3):281-289. PMCID: PMC4131736.
d. Cosgrove, B.D., Gilbert, P.M., Porpiglia, E., Mourkioti, F., Lee, S.P., Corbel, S.Y., Llewellyn, M.E., Delp, S.L. and Blau, H.M. (2014). Rejuvenation of the muscle stem cell population restores strength to injured aged muscles. Nature Medicine 20(3):255-264. PMCID: PMC3949152.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/helen.blau.1/bibliography/40647444/public/?sort=date&direction=ascending