BIOGRAPHICAL SKETCH

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NAME: **Thomas A. Rando, MD, PhD**

eRA COMMONS USER NAME (credential, e.g., agency login): **TRANDO**

POSITION TITLE: **Professor**

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
Harvard College, Cambridge, MA	AB	1979	Biochemistry
Harvard Medical School, Boston, MA	MD	1987	Medicine
Harvard University, Cambridge, MA	PhD	1987	Cell Biology
Stanford University, Stanford, CA	Postdoc	1994	Molecular Pharmacology

A. Personal Statement

The main focus of my laboratory is the biology of stem cells and the intersection between the biology of aging and stem cell biology. We have been at the forefront of studying how environmental influences affect the aging of stem cells and how alterations of those environmental factors can in fact delay or reverse age related changes. A main focus of our laboratory is to study the basic mechanisms of stem cell aging and its relationship to organismal longevity. Most of our work has focused on skeletal muscle stem cells as a model system, and this focus also relates to our longstanding interest in the muscular dystrophies and other disorders of muscle. In addition to these major research interests and Contributions to Science listed in section C, I have taken leadership roles in the areas of programmatic development, service to organizations, and mentoring of students, fellows, and junior faculty. Programmatically, I have directed centers of aging research and regenerative medicine, and I have directed clinical programs in neurology and geriatrics. I have served on boards and study sections for foundations and granting agencies nationally and internationally, and I have organized or co-organized numerous international meetings. As a mentor, I have trained/mentored more than 50 graduate students, postdoctoral fellows, and visiting scientists. Most of my former trainees have gone on to successful independent careers in academics and industry.

B. Positions and Honors

Professional Experience

1987-1988	Intern in Medicine, Massachusetts General Hospital, Boston, MA
1988-1990	Resident in Neurology, UCSF, San Francisco, CA
1990-1991	Chief Resident in Neurology, UCSF, San Francisco, CA
1991-1994	Postdoctoral Fellow, Department of Molecular Pharmacology, Stanford University
1995-2002	Assistant Professor, Department of Neurology and Neurological Sciences, Stanford University
2000-2003	Founding Director, MDA Clinic, Stanford University Medical Center
2000-2007	Director, GRECC, Veterans Affairs Medical Center, Palo Alto, CA
2002-2009	Associate Professor, Department of Neurology and Neurological Sciences, Stanford University
2009-2018	Director, Rehab R&D CoE/REAP, "The Center for Tissue Regeneration, Repair, and Restoration" (CTR^3), Veterans Affairs Medical Center, Palo Alto, CA
1996-present	Chief of Service, Neurology Service, Veterans Affairs Medical Center, Palo Alto, CA
2006-present	Deputy Director, Stanford Center on Longevity, Stanford University
2009-present	Professor, Department of Neurology and Neurological Sciences, Stanford University
2011-present	Director, Glenn Center for the Biology of Aging, Stanford University

Honors and Awards

1979 David McCord Scholarship for Contribution to the Arts, Harvard College
1979 Summa cum laude, thesis, Department of Biochemistry, Harvard College
1979 Magna cum laude, AB, Department of Biochemistry, Harvard College
1981 Medical Scientist Training Program Award
1985 Grass Fellowship in Neurophysiology
1987 Visiting Scholar in Neurology, National Hospital at Queens Square, London
1991 Sandoz Award for Outstanding Resident in Neurology
1991 Dana Fellowship in Neuroscience
1992 Howard Hughes Medical Institute Postdoctoral Research Fellowship for Physicians
1994 Faculty Award, Program in Molecular and Genetic Medicine, Stanford University
1995 Junior Faculty Research Award, American Academy of Neurology
1996 Frederick E. Terman Fellowship, Stanford University
1997 Young Investigator Award, Department of Veterans Affairs
1999 Paul Beeson Physician Faculty Scholar, American Federation for Aging Research
2002 Elected Member, American Neurological Association
2004 Ellison Medical Foundation Senior Scholar Award in Aging
2005 NIH Director's Pioneer Award
2007 Schober Award, German Society for Geriatrics and Gerontology
2007 F.L. McNaughton Lecturer, Montreal Neurological Institute
2008 Breakthroughs in Gerontology (BIG) Award, American Federation for Aging Research
2009 Bennett J. Cohen Award, University of Michigan Center for Biogerontology
2010 Roy Huffington Distinguished Lecturer, Baylor College of Medicine
2010 MERIT Award, National Institute on Aging
2012 Miles Alpern Levin Memorial Lecturer, Oregon Health & Science University
2013 Cheves Smythe Distinguished Lecturer, University of Texas Health Science Center
2013 Transformative Research Award, National Institutes of Health
2014 Member, National Advisory Council, NIA
2014 Earl P. Benditt Memorial Lecturer, University of Washington
2014 George Drummond Memorial Lecturer, University of Calgary
2014 Inaugural Lecturer, Manus C. Kraff Lecture, Northwestern Feinberg School of Medicine
2014 Faulkner Lectureship in Physiology, University of Michigan School of Medicine
2015 Fellow, American Association for the Advancement of Science
2016 Senior Visiting Fellow, Institute for Advanced Study, HKUST, Hong Kong
2016 Elected Member, National Academy of Medicine (NAM) (formerly, Institute of Medicine (IOM))
2018 Honorary Professorship, Chinese Academy of Medical Science, Peking Union Medical College
2019 Honorary Skou Professorship, Aarhus University, Aarhus, Denmark
2020 Elected Member, American Academy of Arts and Sciences

C. Contributions to Science

Complete List of Published Work in PubMed: http://www.ncbi.nlm.nih.gov/pubmed/?term=rando+ta

1. Stem cell biology. Our laboratory has been at the forefront of studies of stem cell biology, using the muscle stem cell as a model system. We have focused on molecular mechanisms that are central to stem cell function and how those mechanisms are impaired during aging. These advances have addressed many questions that apply to tissue-specific stem cells throughout the body and related to such fundamental processes as the regulation of cell fate, asymmetric cell division, and post-transcriptional processing.

   Boutet SC, Disatnik M-H, Chan LS, Iori K, Rando TA (2007) Regulation of Pax3 by proteasomal degradation of mono-ubiquitinated protein in skeletal muscle progenitors. **Cell**, *130*: 349-362.

   Brack AS, Conboy IM, Conboy MJ, Shen J, Rando TA (2008) A temporal switch from Notch to Wnt signaling in muscle stem cells is necessary for normal adult myogenesis. **Cell Stem Cell**, *2*: 50-59.

   Boutet SC, Cheung TH, Quach NL, Liu L, Prescott SL, Edalati A, Iori K, Rando TA (2012) Alternative polyadenylation mediates microRNA regulation of muscle stem cell function. **Cell Stem Cell**, *10*: 327-336. (PMCID: PMC3306803)

   de Morree A, Klein JDD, Gan Q, Farup J, Urtasun A, Kanugovi A, Bilen B, van Velthoven CTJ, Quarta M, Rando TA (2019) Alternative polyadenylation of Pax3 controls muscle stem cell fate and muscle function. **Science**, *366*: 734-738. (PMCID: pending)

2. Biology of Aging. We have explored the mechanisms of stem cell aging and have pioneered the use of parabiosis (in the form of heterochronic parabiosis) to study aging processes. These studies have formed the basis of an expanding area of aging research, with numerous follow up studies demonstrating the enhancement of aged cell and tissue function by heterochronic parabiosis, and then beyond parabiosis to identify factors in the blood that play an important role in age-related phenotypes.

   Conboy IM, Conboy MJ, Wagers AJ, Girma E, Weissman IL, Rando TA (2005) Rejuvenation of aged progenitor cells by exposure to a young systemic environment. **Nature**, *433*: 760-764.

   Brack AS, Conboy MJ, Lee M, Roy S, Kuo CJ, Keller C, Rando TA (2007) Increased Wnt signaling during aging alters myogenic stem cell fate and increases fibrosis. **Science**, *317*: 807-810.

   Villeda SA, Luo J, Mosher KI, Zou B, Britschgi M, Bieri G, Stan TM, Fainberg N, Ding Z, Eggel A, Lucin KM, Czirr E, Park JS, Couillard-Després S, Aigner L, Li G, Peskind ER, Kaye JA, Quinn JF, Galasko DR, Xie XS, Rando TA, Wyss-Coray T (2011) Age-related changes in the systemic milieu regulate adult neurogenesis. **Nature**, *477*: 90-95. (PMCID: PMC3170097)

   Brett JO, Arjona M, Ikeda M, Quarta M, de Morrée A, Egner IM, Perandini LA, Ishak HD, Goshayeshi A, Benjamin DI, Both P, Rodriguez-Mateo C, Betley MJ, Wyss-Coray T, Rando TA (2020) Exercise rejuvenates quiescent skeletal muscle stem cells in old mice through restoration of Cyclin D1. **Nature Metabol**, *2*: 307-317. (PMCID: PMC7323974)

3. Muscle regeneration and muscular dystrophy research. We have studied the factors that contribute to muscle regeneration and that are responsible for aberrant regeneration, including fibrosis and adipogenesis, such as occurs during aging and in the setting of diseases such as the muscular dystrophies. Recently, we have developed novel tools for the non-invasive assessment of disease activity in the dystrophies to monitor natural history and therapeutic responses.

   Urciuolo A, Quarta M, Morbidoni V, Gattazzo F, Molon S, Grumati P, Montemurro F, Tedesco F, Cossu G, Vozzi G, *Rando TA, *Bonaldo P (2013) Collagen VI regulates satellite cell self-renewal and muscle regeneration. **Nature Commun**, *4*: 1964. (PMCID: PMC3682802) (*co-senior authors)

   Heredia JE, Mukundan L, Chen F, Mueller AA, Deo R, Locksley RM, Rando TA, Chawla A (2013) Type 2 innate immunity stimulates proliferation of fibro/adipogenic progenitors to facilitate muscle regeneration. **Cell**, *153*: 376-388. (PMCID: PMC3663598)

   Biressi S, Miyabara EH, Gopinath SD, Carlig PMM, Rando TA (2014) A Wnt-TGFβ2 axis induces a fibrogenic program in muscle stem cells of dystrophic mice. **Science Transl Med**, *6*: 267-279. (PMCID: PMC4350665)

   Mueller AA, van Velthoven CT, Fukumoto K, Cheung TH, Rando TA (2016) Intronic polyadenylation of PDGFRα in resident stem cells attenuates muscle fibrosis. **Nature**, *540*: 276-279.(PMCID: PMC5384334)

4. Epigenetics and stem cell function. Our laboratory has been at the forefront of studies of adult stem cell epigenetics and the epigenetics of stem cell aging. We have explored both the epigenetic status of cells of different ages and the regulators of those epigenetic states. Our long term goal is to understand the relationship between epigenetic status and cellular state, including cellular age, and how epigenetic regulators are central to establishing and maintaining those states.

   Rando TA, Chang HY (2012) Aging, rejuvenation, and epigenetic reprogramming: Resetting the aging clock. **Cell**, *148*: 46-57. (PMCID: PMC3336960)

   Liu L, Cheung TH, Charville GW, Hurgo BMC, Leavitt T, Shih J, Brunet A, Rando TA (2013) Chromatin modifications as determinants of muscle stem cell quiescence and chronological aging. **Cell Reports**, *4*: 189-204. (PMCID: PMC4103025)

   Benayoun BA, Pollina EA, Uçar D, Mahmoudi S, Karra K, Wong ED, Devarajan K, Daugherty A, Kundaje A, Mancini E, Hitz BC, Gupta R, Rando TA, Baker JC, Snyder MP, Cherry JM, Brunet A (2014) H3K4me3 breadth is linked to cell identity and transcriptional consistency. **Cell**, *158*: 673-688. (PMCID: PMC4137894)

   Liu L, Charville GW, Cheung TH, Yoo B, Santos PJ, Schroeder M, Rando TA (2018) Impaired Notch signaling leads to a decrease in p53 activity and mitotic catastrophe in aged muscle stem cells. **Cell Stem Cell**, *23*: 544–556. (PMCID: PMC6173623)

5. The biology of quiescence. Our lab has made a major contribution to the understanding of the regulation of cellular quiescence. Using both in vivo and in vitro models, we have demonstrated key signaling pathways that maintain and regulate the quiescent state.

Cheung TH, Quach NL, Liu L, Charville GW, Liu L, Park L, Edalati A, Yoo B, Hoang P, Rando TA (2012) Maintenance of muscle stem cell quiescence by microRNA-489. **Nature**, *482*: 524-528. (PMCID: PMC3292200)

Rodgers JT, King KY, Brett JO, Cromie MJ, Charville GW, Maguire KK, Brunson C, Mastey N, Liu L, Tsai C-R, Goodell MA, Rando TA (2014) mTORC1 controls the adaptive transition of quiescent stem cells from G_0 to G_{Alert}. **Nature**, *510*: 393-396. (PMCID: PMC4065227)

van Velthoven CTJ, de Morree A, Egner IM, Brett JO, Rando TA (2017) Transcriptional profiling of quiescent muscle stem cells in vivo. **Cell Reports**, *21*: 1994-2004. (PMCID: PMC5711481)

de Morree A, Klein JDD, Gan Q, Farup J, Urtasun A, Kanugovi A, Bilen B, van Velthoven CTJ, Quarta M, Rando TA (2019) Alternative polyadenylation of Pax3 controls muscle stem cell fate and muscle function. **Science**, *366*: 734-738. (PMCID: PMC7046176)

D. Additional Information: Research Support and/or Scholastic Performance

ACTIVE

P01 AG036695 (PI/PD: Rando) 6/1/17 – 5/31/22
NIH/NIA
"Molecular regulation of stem cell aging"

The primary goal of this project is study transcriptional and epigenetic changes that define stem cell aging.

R37 MERIT Award AG023806 (PI: Rando) 8/1/15 – 4/30/21
NIH/NIA
"Notch signaling and satellite cell activation"

The primary goal is to study the role of the Notch signaling pathway in muscle-specific stem cells.

R01 AG055755 (PI: Rando) 9/1/17 – 5/31/22
NIH/NIA
"Complement components as mediators of cell and tissue aging"

The primary goal of this grant is to explore the role of components of the complement cascade in regulating stem cell function and stem cell aging.

R01 AR073248 (PI: Rando) 4/1/18 – 3/31/23
NIH/NIAMS
"Molecular regulation of stem cell quiescence"

The primary goal of this grant is to study the regulation and dynamics of stem cell quiescence

R01 AG057433 (PIs: Suh (Einstein), Rando) 9/15/17 – 5/31/21
NIH/NIA
"From in vivo to in vitro heterochronic parabiosis to identify geronic factors"

The primary goal of this grant is to study the mechanism of anti-geronic factors

R01 AG052962 (PIs: Lee (UConn), Rando) 9/15/17 – 5/31/21
NIH/NIA
"TGF-beta family members and their binding proteins in aging skeletal muscle"

The primary goal of this grant is to explore the role of TGF-beta family members in the process of tissue aging.

I01 BX002324 BLR&D Merit Review (PI: Rando) 10/1/13 – 9/30/21
Department of Veterans Affairs
"Regulation of muscle fibrosis in response to injury and aging"

The primary goal of this project is to study the role of fibroadipogenic progenitors in the generation of muscle fibrosis in diseases and aging

I01 RX001222 RR&D Merit Review (PI: Rando) 1/1/14 – 9/30/22
Department of Veterans Affairs:
“Muscle stem cell therapy for volumetric muscle loss”

The primary goal of this project is to study how muscle stem cell therapy can be enhanced to treat volumetric muscle loss.

P2C HD086843 (PIs: Ambrosio; Univ. Pittsburg; Rando) 12/1/15 – 6/30/25
NIH/NCMRR
“Alliance for Regenerative Rehabilitation Research & Training (AR3T)"

The primary goal of this grant is to establish a national network that will expand scientific knowledge, expertise and methodologies in “Regenerative Rehabilitation”.

COMPLETED IN PAST THREE YEARS

T-R01 (Transformative R01) AG047820 (PIs: Rando, Wyss-Coray) 10/1/13 – 5/31/19
NIH/NIA
“A new muscle-brain axis underlying the cognitive benefits of physical activity”

The primary goal was to explore the molecular pathways by which physical activity can lead to improved cognitive function, focusing specifically on factors released from muscle.

SPiRE Award RX002234 (PI: Rando) 7/1/16 – 6/30/18
Department of Veterans Affairs
“The effect of exercise on neural innervation in the treatment of volumetric muscle loss”

The primary goal was to test different forms of exercise to promote functional recovery in mouse models of volumetric muscle loss treated with stem cell therapies.

Neuromuscular Disease Research Grant (PI: Rando) 8/1/15 – 7/31/18
Muscular Dystrophy Association
“Non-invasive imaging of disease progression and treatment response in mdx mice”

The overall objective of this project was the development of mouse models, so-called "reporter mice", that will be of greatest value for testing cell and gene therapy in terms of altering the progression of muscular dystrophies.

R01 AR062185 (PI: Rando) 12/1/11 – 8/31/17
NIH/NIAMS
“The regulation and function of Pax3 in muscle stem cells”

The primary goal was to study the expression of Pax3 in different populations of adult muscle stem cells.