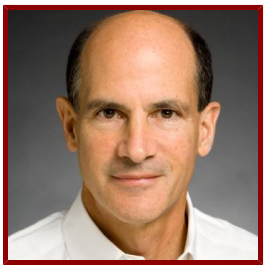
Stanford



Thomas Rando, MD, PhD

Professor of Neurology

NIH Biosketch available Online

Bio

ACADEMIC APPOINTMENTS

- Professor, Neurology
- Member, Bio-X
- Member, Cardiovascular Institute
- Member, Wu Tsai Neurosciences Institute

ADMINISTRATIVE APPOINTMENTS

- Founding Director, Muscular Dystrophy Association Clinic, Stanford Medical Center, (1999-2003)
- Director, Geriatric Research, Education, and Clinical Center (GRECC), Palo Alto VA Medical Center, (2000-2007)
- Chief, Neurology Service, Palo Alto VA Medical Center, (1996- present)
- Deputy Director, Stanford Center on Longevity, Stanford University, (2006- present)
- Director, Rehabilitation Research & Development Center of Excellence, Palo Alto VA Medical Center, (2009- present)
- Director, The Glenn Laboratories for the Biology of Aging, Stanford University School of Medicine, (2011- present)

HONORS AND AWARDS

- Frederick E. Terman Fellowship, Stanford University (1996)
- Paul Beeson Physician Faculty Scholar in Aging, American Federation for Aging Research (1999)
- Ellison Medical Foundation Senior Scholar Award in Aging, The Ellison Medical Foundation (2004)
- NIH Director's Pioneer Award, NIH (2005)
- NIH Transformative R01 (coPI with Dr. Tony Wyss-Coray), NIH (2013)
- Member, American Association for the Advancement of Science (2015)
- Member, National Academy of Medicine (2016)
- Member, American Academy of Arts and Sciences (2020)

PROFESSIONAL EDUCATION

- MD, Harvard Medical School , Medicine (1987)
- PhD, Harvard University , Cell and Develomental Biology (1987)
- AB, Harvard College , Biochemistry (1979)

LINKS

- Lab website: http://randolab.stanford.edu/
- Personal Web site: http://randolab.stanford.edu/

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

A major interest of the lab is the mechanism by which stem cells maintain a quiescent state, are activated to undergo proliferative expansion and differentiation, and undergo self-renewal. We focus specifically on stem cells from skeletal muscle, but study comparable processes in stem cells other mesenchymal tissue (e.g. fat) and epithelia (e.g. skin, gut, and neuro-epithelia). Our studies have focused primarily on the Notch and Wnt signaling pathways in these processes.

We have found that activation of the Notch signaling pathway is critical to the transition of muscle stem cells ("satellite cells") from a quiescent state to one of active proliferation. The regulation of Notch signaling by its inhibitor Numb appears to determine lineage progression and cell fate determination. Numb is found to be localized asymmetrically in dividing progenitor cells and may be involved in the process of satellite cell self-renewal. We subsequently found that activation of the Wnt signaling pathway occurs during muscle injury when satellite cells are proliferating. There appears to be an antagonistic interaction between Notch and Wnt signaling in activated satellite cells during this process. Furthermore, we have found that the age-related impairment of muscle regeneration is due to a decline in effective Notch signaling, manifested initially as a failure of injured muscle to up-regulate the Notch ligand, Delta. We are currently exploring further the regulation of the Notch and Wnt signaling pathways during satellite cell activation, the mechanisms underlying the transcriptional control of Delta expression, and epigenetic processes that may account for age-related changes in these pathways. Our near-term goals are to identify the key signaling processes that control satellite cell activation and lineage progression in order to enhance muscle regeneration.

Current studies are focused on the role of post-transcriptional regulation of stem cell quiescence and activation. We have discovered unique sets of microRNAs that regulate these processes and show targets are important for maintaining quiescence of promotion cell cycle entry. Ongoing studies are also addressing the role of long, intergenic non-coding RNAs in regulating stem cell function.

Our studies of stem cell aging have focused on two major areas. First, we are using microarray and next-generation high throughput sequencing to derive molecular signatures of young and old stem cells and the transcriptional and epigenetic levels. Second, we have pioneered the use of heterochronic parabiosis to study potential mechanisms of rejuvenation whereby an aged stem cell is ‘reprogrammed’ to become a young stem cell. We have been intrigued by possibility of aging being viewed as an epigenetic state, at least in part, and we are testing this hypothesis in various models in vivo and in vitro.

With regard to studies of muscular dystrophies, a major interest is the development of fibrosis and adiposis. We have intriguing data that the impairment of regeneration and the development of these pathological changes may arise, at least in part, from the conversion of muscle stem cells from the myogenic lineage to other mesenchymal lineages. These finding parallel what we have found in aged muscle as well. We are currently developing mouse models that will serve as “degeneration reporter mice” and “regeneration reporter mice” that will allow the assessment of disease progression and response to treatment non-invasively.

Teaching

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Paras Minhas

Doctoral Dissertation Co-Advisor (AC)

Ronghao Zhou

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)
- Neurosciences (Phd Program)

Publications

PUBLICATIONS

- **Exercise reprograms the inflammatory landscape of multiple stem cell compartments during mammalian aging** *Cell Stem Cell*
  Liu, L., Kim, S., Buckley, M., Reyes, J., Kang, J., Tian, L., Wang, M., Lieu, A., Mao, M., Mateo, C., Ishak, H., Jeong, M., Wu, et al
  2023; 30 (1-17)
- **Tubastatin A maintains adult skeletal muscle stem cells in a quiescent state ex vivo and improves their engraftment ability in vivo.** *Stem cell reports*
  Arjona, M., Goshayeshi, A., Rodriguez-Mateo, C., Brett, J. O., Both, P., Ishak, H., Rando, T. A.
  2022; 17 (1): 82-95
- **Exercise plasma boosts memory and dampens brain inflammation via clusterin.** *Nature*
  De Miguel, Z., Khoury, N., Betley, M. J., Lehallier, B., Willoughby, D., Olsson, N., Yang, A. C., Hahn, O., Lu, N., Vest, R. T., Bonanno, L. N., Yerra, L., Zhang, et al
  2021
- **Cells, scaffolds, and bioactive factors: Engineering strategies for improving regeneration following volumetric muscle loss.** *Biomaterials*
  Eugenis, I., Wu, D., Rando, T. A.
  2021; 278: 121173
- **Hairless regulates heterochromatin maintenance and muscle stem cell function as a histone demethylase antagonist.** *Proceedings of the National Academy of Sciences of the United States of America*
  Liu, L., Rodriguez-Mateo, C., Huang, P., Huang, A., Lieu, A., Mao, M., Chung, M., Yang, S., Yu, K., Charville, G. W., Gan, Q., Rando, T. A.
  2021; 118 (37)
- **RNA splicing programs define tissue compartments and cell types at single-cell resolution** *ELIFE*
  Olivieri, J., Dehghannasiri, R., Wang, P. L., Jang, S., de Morree, A., Tan, S. Y., Ming, J., Wu, A., Consortium, T., Quake, S. R., Krasnow, M. A., Salzman, J.
  2021; 10
- **Regeneration, Rejuvenation, and Replacement: Turning Back the Clock on Tissue Aging.** *Cold Spring Harbor perspectives in biology*
  Rando, T. A., Jones, D. L.
  2021
- **Context-dependent modulation of aggressiveness of pediatric tumors by individual oncogenic RAS isoforms.** *Oncogene*
  Bauer, J., Cuvelier, N., Ragab, N., Simon-Keller, K., Nitzki, F., Geyer, N., Botermann, D. S., Elmer, D. P., Rosenberger, A., Rando, T. A., Biressi, S., Fagin, J. A., Saur, et al
  2021
- **Electrical stimulation of human neural stem cells via conductive polymer nerve guides enhances peripheral nerve recovery.** *Biomaterials*
  Song, S., McConnell, K. W., Amores, D., Levinson, A., Vogel, H., Quarta, M., Rando, T. A., George, P. M.
  2021; 275: 120982
- **Computational modeling of malignant ascites reveals CCL5-SDC4 interaction in the immune microenvironment of ovarian cancer.** *Molecular carcinogenesis*
  Kim, S. n., Han, Y. n., Kim, S. I., Lee, J. n., Jo, H. n., Wang, W. n., Cho, U. n., Park, W. Y., Rando, T. A., Dhanasekaran, D. N., Song, Y. S.
  2021
- **Asynchronous, contagious and digital aging.** *Nature aging*
  Rando, T. A., Wyss-Coray, T.
  2021; 1 (1): 29-35
- **Targeting microRNA-mediated gene repression limits adipogenic conversion of skeletal muscle mesenchymal stromal cells.** *Cell stem cell*

Wosczyna, M. N., Perez Carbajal, E. E., Wagner, M. W., Paredes, S. n., Konishi, C. T., Liu, L. n., Wang, T. T., Walsh, R. A., Gan, Q. n., Morrissey, C. S., Rando, T. A.

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- **Functional redundancy of type I and type II receptors in the regulation of skeletal muscle growth by myostatin and activin A.** *Proceedings of the National Academy of Sciences of the United States of America*

  Lee, S., Lehar, A., Liu, Y., Ly, C. H., Pham, Q., Michaud, M., Rydzik, R., Youngstrom, D. W., Shen, M. M., Kaartinen, V., Germain-Lee, E. L., Rando, T. A.

  2020

- **Transplantation of insulin-like growth factor-1 laden scaffolds combined with exercise promotes neuroregeneration and angiogenesis in a preclinical muscle injury model** *BIOMATERIALS SCIENCE*

  Alcazar, C. A., Hu, C., Rando, T. A., Huang, N. F., Nakayama, K. H.

  2020; 8 (19): 5376–89

- **Exercise rejuvenates quiescent skeletal muscle stem cells in old mice through restoration of Cyclin D1.** *Nature metabolism*

  Brett, J. O., Arjona, M., Ikeda, M., Quarta, M., de Morrée, A., Egner, I. M., Perandini, L. A., Ishak, H. D., Goshayeshi, A., Benjamin, D. I., Both, P., Rodríguez-Mateo, C., Betley, et al

  2020; 2 (4): 307-317

- **Taking the Next Steps in Regenerative Rehabilitation: Establishment of a New Interdisciplinary Field.** *Archives of physical medicine and rehabilitation*

  Willett, N. J., Boninger, M. L., Miller, L. J., Alvarez, L. n., Aoyama, T. n., Bedoni, M. n., Brix, K. A., Chisari, C. n., Christ, G. n., Dearth, C. L., Dyson-Hudson, T. A., Evans, C. H., Goldman, et al

  2020

- **Ageing hallmarks exhibit organ-specific temporal signatures.** *Nature*

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  2020

- **Stem cell therapy for muscular dystrophies.** *The Journal of clinical investigation*

  Biressi, S. n., Filareto, A. n., Rando, T. A.

  2020

- **Aging of the skeletal muscle extracellular matrix drives a stem cell fibrogenic conversion**

  Stearns-Reider, K. M., D'Amore, A., Beezhold, K., Rothrauff, B., Cavalli, L., Wagner, W. R., Vorp, D. A., Tsamis, A., Shinde, S., Zhang, C., Barchowsky, A., Rando, T. A., Tuan, et al

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- **ARDD 2020: from aging mechanisms to interventions.** *Aging*

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  2020; 12

- **Transient non-integrative expression of nuclear reprogramming factors promotes multifaceted amelioration of aging in human cells.** *Nature communications*

  Sarkar, T. J., Quarta, M. n., Mukherjee, S. n., Colville, A. n., Paine, P. n., Doan, L. n., Tran, C. M., Chu, C. R., Horvath, S. n., Qi, L. S., Bhutani, N. n., Rando, T. A., Sebastiano, et al

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- **A single-cell transcriptomic atlas characterizes ageing tissues in the mouse.** *Nature*

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  Cable, J., Fuchs, E., Weissman, I., Jasper, H., Glass, D., Rando, T. A., Blau, H., Debnath, S., Oliva, A., Park, S., Passegue, E., Kim, C., Krasnow, et al

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- **mTORC1 underlies age-related muscle fiber damage and loss by inducing oxidative stress and catabolism** *AGING CELL*

  Tang, H., Inoki, K., Brooks, S. V., Okazawa, H., Lee, M., Wang, J., Kim, M., Kennedy, C. L., Macpherson, P. D., Ji, X., Van Roekel, S., Fraga, D. A., Wang, et al

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Wosczyna, M. N., Konishi, C. T., Carbajal, E., Wang, T. T., Walsh, R. A., Gan, Q., Wagner, M. W., Rando, T. A.
2019; 27 (7): 2029-+

- **Treatment of volumetric muscle loss in mice using nanofibrillar scaffolds enhances vascular organization and integration** *COMMUNICATIONS BIOLOGY*
  Nakayama, K. H., Quarta, M., Paine, P., Alcazar, C., Karakikes, I., Garcia, V., Abilez, O. J., Calvo, N. S., Simmons, C. S., Rando, T. A., Huang, N. F.
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- **Treatment of volumetric muscle loss in mice using nanofibrillar scaffolds enhances vascular organization and integration.** *Communications biology*
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- **mTORC1 underlies age-related muscle fiber damage and loss by inducing oxidative stress and catabolism.** *Aging cell*
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- **Models and Studies of Aging: Executive Summary of a Report from the U13 Conference Series** *JOURNAL OF THE AMERICAN GERIATRICS SOCIETY*
  Hurria, A., Carpenter, C. R., McFarland, F., Lundebjerg, N. E., de Cabo, R., Ferrucci, L., Studenski, S. A., Barzilai, N., Briggs, J. P., Ix, J. H., Kitzman, D. W., Kuchel, G. A., Musi, et al
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- **Stem Cell Quiescence: Dynamism, Restraint, and Cellular Idling** *CELL STEM CELL*
  van Velthoven, C. J., Rando, T. A.
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- **Stem Cell Quiescence: Dynamism, Restraint, and Cellular Idling.** *Cell stem cell*
  van Velthoven, C. T., Rando, T. A.
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- **Models and Studies of Aging: Executive Summary of a Report from the U13 Conference Series.** *Journal of the American Geriatrics Society*
  Hurria, A., Carpenter, C. R., McFarland, F., Lundebjerg, N. E., de Cabo, R., Ferrucci, L., Studenski, S. A., Barzilai, N., Briggs, J. P., Ix, J. H., Kitzman, D. W., Kuchel, G. A., Musi, et al
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- **Angiotensin receptor blockade mimics the effect of exercise on recovery after orthopaedic trauma by decreasing pain and improving muscle regeneration.** *The Journal of physiology*
  Tawfik, V. L., Quarta, M. n., Paine, P. n., Forman, T. E., Pajarinen, J. n., Takemura, Y. n., Goodman, S. B., Rando, T. A., Clark, J. D.
  2019
- **Chronic inflammation in the etiology of disease across the life span.** *Nature medicine*
  Furman, D. n., Campisi, J. n., Verdin, E. n., Carrera-Bastos, P. n., Targ, S. n., Franceschi, C. n., Ferrucci, L. n., Gilroy, D. W., Fasano, A. n., Miller, G. W., Miller, A. H., Mantovani, A. n., Weyand, et al
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- **Alternative polyadenylation of Pax3 controls muscle stem cell fate and muscle function.** *Science (New York, N.Y.)*
  de Morree, A. n., Klein, J. D., Gan, Q. n., Farup, J. n., Urtasun, A. n., Kanugovi, A. n., Bilen, B. n., van Velthoven, C. T., Quarta, M. n., Rando, T. A.
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- **Mesenchymal Stromal Cells Are Required for Regeneration and Homeostatic Maintenance of Skeletal Muscle.** *Cell reports*
  Wosczyna, M. N., Konishi, C. T., Perez Carbajal, E. E., Wang, T. T., Walsh, R. A., Gan, Q. n., Wagner, M. W., Rando, T. A.
  2019; 27 (7): 2029–35.e5
- **Honey bee Royalactin unlocks conserved pluripotency pathway in mammals** *NATURE COMMUNICATIONS*
  Wan, D. C., Morgan, S. L., Spencley, A. L., Mariano, N., Chang, E. Y., Shankar, G., Luo, Y., Li, T. H., Huh, D., Huynh, S. K., Garcia, J. M., Dovey, C. M., Lumb, et al
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- **Honey bee Royalactin unlocks conserved pluripotency pathway in mammals.** *Nature communications*
  Wan, D. C., Morgan, S. L., Spencley, A. L., Mariano, N., Chang, E. Y., Shankar, G., Luo, Y., Li, T. H., Huh, D., Huynh, S. K., Garcia, J. M., Dovey, C. M., Lumb, et al
  2018; 9 (1): 5078

- **Age-related declines in alpha-Klotho drive progenitor cell mitochondrial dysfunction and impaired muscle regeneration** *NATURE COMMUNICATIONS*
  Sahu, A., Mamiya, H., Shinde, S. N., Cheikhi, A., Winter, L. L., Vo, N. V., Stolz, D., Roginskaya, Tang, W. Y., Croix, C., Sanders, L. H., Franti, M., Van Houten, B., et al
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  2018; 9 (1): 4859

- **The regenerative rehabilitation collection: a forum for an emerging field** *NPJ REGENERATIVE MEDICINE*
  Ambrosio, F., Rando, T. A.
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- **Biomechanics show stem cell necessity for effective treatment of volumetric muscle loss using bioengineered constructs** *NPJ REGENERATIVE MEDICINE*
  Quarta, M., Lear, M., Blonigan, J., Paine, P., Chacon, R., Rando, T. A.
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- **Impaired Notch Signaling Leads to a Decrease in p53 Activity and Mitotic Catastrophe in Aged Muscle Stem Cells** *CELL STEM CELL*
  Liu, L., Charville, G. W., Cheung, T. H., Yoo, B., Santos, P. J., Schroeder, M., Rando, T. A.
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- **Rehabilitative exercise and spatially patterned nanofibrillar scaffolds enhance vascularization and innervation following volumetric muscle loss** *NPJ REGENERATIVE MEDICINE*
  Nakayama, K. H., Alcazar, C., Yang, G., Quarta, M., Paine, P., Doan, L., Davies, A., Rando, T. A., Huang, N. F.
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  Liu, L., Charville, G. W., Cheung, T. H., Yoo, B., Santos, P. J., Schroeder, M., Rando, T. A.
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- **Bioengineered Viral Platform for Intramuscular Passive Vaccine Delivery to Human Skeletal Muscle** *MOLECULAR THERAPY-METHODS & CLINICAL DEVELOPMENT*
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- **Monitoring disease activity noninvasively in the mdx model of Duchenne muscular dystrophy** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
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  Wosczyna, M. N., Rando, T. A.
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  Leeman, D. S., Hebestreit, K., Ruetz, T., Webb, A. E., McKay, A., Pollina, E. A., Dulken, B. W., Zhao, X., Yeo, R. W., Ho, T. T., Mahmoudi, S., Devarajan, K., Passegue, et al
  2018; 359 (6381): 1277–82

- **Regenerative Rehabilitation: Applied Biophysics Meets Stem Cell Therapeutics** *CELL STEM CELL*

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- **Inhibition of Methyltransferase Setd7 Allows the In Vitro Expansion of Myogenic Stem Cells with Improved Therapeutic Potential** *CELL STEM CELL*
  Judson, R. N., Quarta, M., Oudhoff, M. J., Soliman, H., Yi, L., Chang, C., Loi, G., Werff, R., Cait, A., Hamer, M., Blonigan, J., Paine, P., Doan, et al
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- **Bioengineered Viral Platform for Intramuscular Passive Vaccine Delivery to Human Skeletal Muscle.** *Molecular therapy. Methods & clinical development*
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- **The regenerative rehabilitation collection: a forum for an emerging field.** *NPJ Regenerative medicine*
  Ambrosio, F., Rando, T. A.
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- **Single-cell transcriptomics of 20 mouse organs creates a Tabula Muris.** *Nature*
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- **mTORC1 Activation during Repeated Regeneration Impairs Somatic Stem Cell Maintenance** *CELL STEM CELL*
  Haller, S., Kapuria, S., Riley, R. R., O'Leary, M. N., Schreiber, K. H., Andersen, J. K., Melov, S., Que, J., Rando, T. A., Rock, J., Kennedy, B. K., Rodgers, J. T., Jasper, et al
  2017; 21 (6): 806-+

- **Transcriptional Profiling of Quiescent Muscle Stem Cells In Vivo** *CELL REPORTS*
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  Tang, H., Kennedy, C. L., Lee, M., Gao, Y., Xia, H., Olguin, F., Fraga, D. A., Ayers, K., Choi, S., Kim, M., Tehrani, A., Sowb, Y. A., Rando, et al
  2017; 7: 14530

- **Staufen1 inhibits MyoD translation to actively maintain muscle stem cell quiescence** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  de Morree, A., van Velthoven, C. J., Gan, Q., Salvi, J. S., Klein, J., Akimenko, I., Quarta, M., Biressi, S., Rando, T. A.
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- **Bioengineered constructs combined with exercise enhance stem cell-mediated treatment of volumetric muscle loss** *NATURE COMMUNICATIONS*
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- **Aging of the skeletal muscle extracellular matrix drives a stem cell fibrogenic conversion** *AGING CELL*
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- **Evolved AAV Capsids for Intramuscular Passive Vaccine Administration to Human Skeletal Muscle**
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- **HGFA Is an Injury-Regulated Systemic Factor that Induces the Transition of Stem Cells into G(Alert)** *CELL REPORTS*
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  2017; 2: 4

- **Fleeting factors, turning back time** *NATURE BIOTECHNOLOGY*
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