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## BIOGRAPHICAL SKETCH

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NAME: Brunet, Anne

eRA COMMONS USER NAME: BRUNET, ANNE

POSITION TITLE: Michele and Timothy Barakett Professor of Genetics

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
Ecole Normale Supérieure, Paris, France	B.S.	06/1992	Genetics and Cell Biology
University of Nice, Nice, France	Ph.D.	06/1997	Cell Biology
Harvard Medical School, Boston, MA	Postdoctoral	12/2003	Neuroscience

### A. Personal Statement

I hold the Michele and Timothy Barakett Chair at Stanford, serving as a Professor of Genetics. My laboratory has developed an innovative line of investigation to understand aging based on the integration of model organisms with diverse lifespans. We are interested in identifying pathways involved in delaying aging in response to external stimuli such as availability of nutrients, and we made the exciting discovery that lifespan extension can be inherited in a transgenerational epigenetic manner in *C. elegans*. We are excited to address complex questions about aging in vertebrates, focusing on brain aging and rejuvenation. We have embarked on a systematic and functional characterization of aging mechanisms in the regenerative stem cell niches of the adult brain<sup>1-4</sup>. We have also pioneered the naturally short-lived African killifish as a powerful model to identify new principles of vertebrate aging and ‘suspended animation’.

An essential aspect of my lab is its track-record of mentoring and training. My mentoring philosophy is to foster creativity and provide the most supportive environment for trainees to test their creative and independent ideas. Since I started my lab at Stanford, I have been training 24 graduate students and 30 post-doctoral fellows. This is a vibrant team, which benefits from interdisciplinary approaches and diverse backgrounds. I am proud that all graduate students and post-doctoral fellows who graduated from our lab had first author papers. Importantly, 18 trainees from our lab have secured faculty positions at top academic institutions, including MIT, Princeton University, Duke University, USC, University College London, Washington University, Yale University, University of Washington, and UCSF. I am also proud that other students and post-doctoral fellows in the lab have gotten attractive leadership positions in industry and started innovative aging start-ups. I take mentoring very seriously and have been awarded the Stanford University Postdoctoral Association Mentoring Award.

### Citations

1. Dulken BW, Buckley MT, Navarro Negredo P, Saligrama N, Cayrol R, Leeman DS, George BM, Boutet SC, Hebestreit K, Pluvinage JV, Wyss-Coray T, Weissman IL, Vogel H, Davis MM, **Brunet A** (2019). Single-cell analysis reveals T cell infiltration in old neurogenic niches. *Nature*, 571:205-210.
2. Hu CK, Wang W, Brind’Amour J, Singh PP, Reeves GA, Lorincz MC, Sanchez Alvarado A, **Brunet A** (2020) Vertebrate diapause preserves organisms long-term via Polycomb complex members. *Science*, 367: 870-874.
3. Ruetz T, Pogson AN, Kashiwagi CM, Gagnon SD, Morton B, Sun ED, Na J, Yeo RW, Leeman DS, Morgens DW, Tsui CK, Li A, Bassik MC, and **Brunet A** (2024). CRISPR-Cas9 screens reveal regulators of ageing in neural stem cells. *Nature*, 634:1150-1159.
4. Sun ED, Zhou OY, Hauptschein M, Rappoport N, Xu L, Navarro Negredo P, Liu L, Rando TA, Zou J, **Brunet A** (2025). Spatial transcriptomic clocks reveal cell proximity effects in brain aging. *Nature*, 638:160-171.

## **B. Positions, Scientific Appointments and Honors**

### **Positions and Employment**

2023- Director, Glenn Center for the Biology of Aging, Stanford University, Stanford CA  
2015- Michele and Timothy Barakett Professor of Genetics, Stanford University, Stanford, CA  
2014- Professor, Department of Genetics, Stanford University, Stanford, CA  
2011-2023 Co-director, Glenn Center for the Biology of Aging, Stanford University, Stanford, CA  
2011-2014 Associate Professor, Department of Genetics, Stanford University, Stanford, CA  
2004-2011 Assistant Professor, Department of Genetics, Stanford University, Stanford, CA

### **Other Experience and Professional Memberships**

2022- Scientific Advisory Board, Calico Life Sciences  
2020- External Advisory Board, American Heart Association - Allen Institute, Salk Institute  
2020-2023 Editorial Board, *Cell Stem Cell*  
2019- External Advisory Board, Nathan Shock Center, University of Washington  
2017- Editorial Board, *Genes & Development*  
2015-2023 Editorial Board, *Cell Reports*  
2015-2016 Chair of NIH Study Section (CMAD)  
2012-2015 Permanent Member of NIH Study Section (CMAD)  
2012-2022 Editorial Board, *Aging Cell*  
2011-2016 Member of *Faculty of 1000*  
2011-2013 Reviewer for the Ellison Medical Foundation  
2011-2022 Editorial Board, *Longevity & Healthspan*  
2010-2012 Ad Hoc Reviewer for NIH Program Projects  
2009- Editorial Board, *Aging*  
2007- Reviewer for the American Federation for Aging Research (AFAR)

### **Honors**

2025 NIH Director's Pioneer Award  
2025 Elected member, American Academy of Arts and Sciences  
2023 NOMIS Award  
2022 Lurie Prize in Biomedical Sciences (FNIH)  
2022 Chan Zuckerberg Biohub Investigator  
2021 NIH Florence Mahoney Lecture on Aging, Bethesda, MD  
2018 NIH Director Transformative Research Award  
2015 Michele and Timothy Barakett Endowed Professorship  
2014 Bennett J. Cohen Award for Research in Aging  
2013 Koshland Lecture, UC Berkeley  
2012 Vincent Cristofalo 'Rising Star' Award in Aging Research  
2012 NIH Director's Pioneer Award  
2010 Mentoring Award from the Stanford University Post-doctoral Association  
2009 NARSAD New Investigator Award  
2009 Ellison Medical Foundation Senior Scholar Award  
2008 California Institute of Regenerative Medicine New Faculty Award  
2007 McCormick Award for Women in Science  
2007 Glenn Award for Research in Biological Mechanisms of Aging  
2006 Sloan Research Fellowship  
2005 Damon Runyon Scholar Award (*declined because of Pfizer/AFAR Award*)  
2005 Ellison Medical Foundation New Scholar Award (*declined because of Pfizer/AFAR Award*)  
2005 Pfizer/AFAR Innovation in Aging Research Award  
2003 La Caze-Policart Lacassagne Award from the French National Academy of Sciences  
2003 Harvard-Radcliffe Institute for Advanced Studies fellowship  
2000 Goldenson-Berenberg Postdoctoral Fellowship at Harvard Medical School  
2000 Medical Foundation (Charles King) Postdoctoral Fellowship

1998	Human Frontier Postdoctoral Fellowship
1997	EMBO Long-term Postdoctoral Fellowship
1993	EMBO Short-term Fellowship
1993	Ecole Normale Supérieure Pre-doctoral Fellowship
1992	BS <i>summa cum laude</i> from Ecole Normale Supérieure, Paris

## C. Contribution to Science

### 1. Mode of action of FOXO transcription factors

My early work as a postdoctoral fellow addressed the regulation and molecular mechanism of action of the pro-longevity FOXO transcription factor in mammalian cells. I found that FOXO was regulated by direct phosphorylation by the protein kinase AKT in response to insulin-PI3K signaling, and that this phosphorylation led to FOXO cytoplasmic retention and subsequent inhibition. I then showed that FOXO could also be regulated by stress stimuli, notably by deacetylation. My work established FOXO transcription factors as the nexus of growth factor and stress pathways in mammalian cells and served as a foundation for my laboratory to study the role of FOXO in neural stem cell homeostasis throughout lifespan.

- a. **Brunet A**, Bonni A, Zigmond MJ, Lin MZ, Juo P, Hu LS, Anderson MJ, Arden KC, Blenis J, Greenberg ME (1999) Akt promotes cell survival by phosphorylating and inhibiting a Forkhead transcription factor. *Cell*, 96: 857-868.
- b. Tran H, **Brunet A**, Grenier JM, Datta SR, Fornace Jr AJ, DiStefano PS, Chiang LW and Greenberg ME (2002). DNA repair pathway stimulated by the Forkhead transcription factor FOXO3a (FKHRL1) through the GADD45 protein. *Science*, 296: 530-534. \*Equal contribution.
- c. **Brunet A**, Sweeney LB, Sturgill FJ, Chua KF, Greer PL, Lin Y, Tran H, Ross SE, Mostoslavsky R, Cohen H, Hu LS, Cheng H-L, Jedrychowsky M, Gygi SP, Sinclair DA, Alt FW, Greenberg ME (2004) Stress-Dependent Regulation of FOXO transcription factors by the SIRT1 Deacetylase. *Science*, 303: 2011-2015.
- d. Renault VM, Rafalski VA, Morgan AA, Salih DAM, Brett JO, Webb AE, Villeda SA, Thekkat PU, Guillerey C, Denko NC, Palmer TD, Butte AJ, and **Brunet A** (2009) FoxO3 regulates neural stem cell homeostasis. *Cell Stem Cell*, 5: 527-539.

### 2. Nutrient-sensing and metabolic pathways in longevity

In my own lab, I have been particularly interested in the role of nutrient-sensing and metabolic pathways in aging and longevity. We developed a new line of investigation combining *C. elegans* and mammalian cells to identify the role of the nutrient-sensing pathways such as the insulin-FOXO pathway and the AMP kinase (AMPK) pathway in longevity and associated cellular functions. More recently, we have investigated the role of glucose and lipid metabolism in aging cells.

- a. Greer EL and **Brunet A** (2009) Different dietary restriction regimens extend lifespan by both independent and overlapping genetic pathways in *C. elegans*. *Aging Cell*, 8: 113-127.
- b. Banko MR, Allen JJ, Schaffer BE, Wilker EW, Tsou P, White JL, Villen J, Wang B, Kim SR, Sakamoto K, Gygi SP, Cantley LC, Yaffe MB, Shokat KM, **Brunet A** (2011) Chemical genetic screen for AMPKα2 substrates uncovers a network of proteins involved in mitosis. *Mol Cell*, 44:878-892.
- c. Schaffer BE, Hertz NT, Levin RS, Maures TJ, Schoof ML, Hollstein PE, Benayoun BA, Banko MR, Shaw RJ, Shokat KM, **Brunet A** (2015) Identification of AMPK phosphorylation sites reveals a network of proteins involved in cell invasion and facilitates large-scale substrate prediction. *Cell Metab*, 22: 907-922.
- d. Papsdorf K, Miklas JW, Hosseini A, Cabruja M, Morrow CS, Savini M, Yu Y, Silva-Garcia CG, Haseley NR, Murphy LM, Yao P, de Launoit E, Dixon SJ, Snyder MP, Wang MC, Mair WB, and **Brunet A** (2023) Lipid droplets and peroxisomes are co-regulated to drive lifespan extension in response to mono-unsaturated fatty acids. *Nature Cell Biology*, 25: 1547.

### 3. Epigenomic regulation of aging and lifespan

My lab has set new ground in understanding how external signals that impact aging, including nutrients, are integrated in a stable, yet reversible manner. One of our most exciting discoveries is the importance of

epigenetic modifiers in longevity and the transgenerational inheritance of longevity by chromatin modifiers. We have discovered that epigenetic modifiers that catalyze the trimethylation of lysine 4 in histone H3 (H3K4me3) and H3K27me3 both influenced lifespan. We have also explored the intriguing relationship between chromatin modifications and lipid metabolism for the regulation of lifespan.

- a. Greer EL, Maures TJ, Hauswirth AG, Green EM, Leeman DS, Maro, GS, Han S, Banko MR, Gozani O, **Brunet A** (2010) Members of the H3K4 trimethylation complex regulate lifespan in a germline-dependent manner in *C. elegans*. ***Nature***, 466: 383-387.
- b. Greer EL, Maures TJ, Ucar D, Hauswirth AG, Mancini E, Lim JP, Benayoun BA, Shi Y, **Brunet A** (2011) Transgenerational epigenetic inheritance of longevity in *Caenorhabditis elegans*. ***Nature***, 479: 365-371.
- c. Han S, Schroeder EA, Silvia-Garcia CG, Hebestreit K, Mair WB, **Brunet A** (2017). Mono-unsaturated fatty acids link H3K4me3 modifiers to *C. elegans* lifespan. ***Nature***, 544: 185-190.
- d. Benayoun BA, Pollina EA, Singh PP, Mahmoudi S, Harel I, Casey KM, Dulken BW, Kundaje A, and **Brunet A** (2019). Remodeling of epigenome and transcriptome landscapes with aging in mice reveals widespread induction of inflammatory responses. ***Genome Research***, 29: 697-709.

#### 4. Brain aging and rejuvenation

Importantly, my lab has also developed mammalian models to address complex questions about brain aging and rejuvenation. We have embarked on a systematic effort to unbiasedly characterize aging in the regenerative neural stem cell region in the adult mammalian brain, and we have identified key functional regulators that boost the function of old cells. We have also developed machine learning model to estimate the age of specific cells in the brain based on high-dimensional single cell and spatial transcriptomics datasets.

- a. Buckley MT, Sun E, Benson GM, Liu L, Schaum N, Xu L, Reyes JM, Goodell MA, Weissman IL, Wyss-Coray T, Rando TA and **Brunet A** (2023) Cell type-specific aging clocks to quantify aging and rejuvenation in neurogenic regions of the brain. ***Nature Aging***, 3:121-137.
- b. Yeo RW, Zhou OY, Zhong BL, Sun ED, Navarro Negredo P, Nair S, Sharmin M, Ruetz TJ, Wilson M, Kundaje A, Dunn AR, and **Brunet A** (2023) Chromatin accessibility dynamics of neurogenic niche cells reveal defects in neural stem cell adhesion and migration during aging. ***Nature Aging***, 3: 866-893.
- c. Ruetz T, Pogson AN, Kashiwagi CM, Gagnon SD, Morton B, Sun ED, Na J, Yeo RW, Leeman DS, Morgens DW, Tsui CK, Li A, Bassik MC, and **Brunet A** (2024). CRISPR-Cas9 screens reveal regulators of ageing in neural stem cells. ***Nature***, 634:1150-1159.
- d. Sun ED, Zhou OY, Hauptschein M, Rappoport N, Xu L, Navarro Negredo P, Liu L, Rando TA, Zou J, **Brunet A** (2025). Spatial transcriptomic clocks reveal cell proximity effects in brain aging. ***Nature***, 638:160-171.

#### 5. Pioneering the African turquoise killifish as a new model for studying vertebrate longevity

Finally, my lab has pioneered the naturally short-lived African turquoise killifish as a new model for aging and longevity in vertebrates. We have sequenced the genome of this fish and have developed genome editing technologies to mutate several aging and longevity genes. We are excited to ask unique questions about vertebrate aging in this new system and to understand the regulation and evolution of lifespan and 'suspended animation'.

- a. Valenzano DR, Benayoun BA, Singh PP, Zhang E, Etter PD, Hu CK, Clément-Ziza M, Willemsen D, Cui R, Harel I, Machado BE, Yee MC, Sharp SC, Bustamante CD, Beyer A, Johnson EA, **Brunet A** (2015) The African turquoise killifish genome provides insights into evolution and genetic architecture of lifespan. ***Cell***, 163: 1539-1554.
- b. Harel I, Benayoun BA, Machado M, Singh PP, Hu CK, Pech MF, Valenzano DR, Zhang E, Sharp SC, Artandi SE, **Brunet A** (2015) A Platform for rapid exploration of aging and diseases in a naturally short-lived vertebrate. ***Cell***, 160: 1013-1026.
- c. Hu CK, Wang W, Brind'Amour J, Singh PP, Reeves GA, Lorincz MC, Sanchez Alvarado A, **Brunet A** (2020) Vertebrate diapause preserves organisms long-term via Polycomb complex members. ***Science***, 367: 870-874.

- d. Singh PP, Reeves GA, Contrepolis K, Papsdorf K, Miklas JW, Ellenberger M, Hu CK, Snyder MP, and **Brunet A** (2024) Evolution of diapause in the African turquoise killifish by remodeling the ancient gene regulatory landscape. ***Cell***, 187:3338-3356.e30. doi: 10.1016/j.cell.2024.04.048.

**Complete List of Published Work in MyBibliography:**

<https://www.ncbi.nlm.nih.gov/myncbi/anne.brunet.1/bibliography/public/>