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: **Brunet, Anne**

eRA COMMONS USER NAME (credential, e.g., agency login): **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 a productive line of investigation to understand aging and rejuvenation. To tackle the complexity of aging and longevity, we use model organisms with diverse lifespans – worms, killifish, and mice. We are interested in identifying the genetic and epigenetic mechanisms underlying aging and the pathways involved in suspending or reversing aging in response to external stimuli[1]. We are excited to understand the mechanisms of brain aging and rejuvenation[2]. Importantly, we have pioneered the naturally short-lived African killifish as a new model to identify principles underlying aging and 'suspended animation'[3,4].

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 innovative and independent ideas. Since I started my lab at Stanford, I have been training 20 graduate students and 24 post-doctoral fellows. This is an inclusive team, which benefits from diversity of approaches and backgrounds. I am proud that all graduate students and post-doctoral fellows who graduated from our lab had first author papers and that trainees from our lab secured positions at academic institutions, including Max Planck Institute, USC, University College London, Brown University, and Harvard Medical School. 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.

[1] Navarro Negredo P, Yeo RW, and Brunet A (2020). Aging and rejuvenation of neural stem cell niches. **Cell Stem Cell**, 27: 202-223.

[2] Leeman DS, Hebestreit K, Ruetz T, Webb AE, McKay A, Pollina EA, Dulken BW, Zhao X, Yeo RW, Ho TT, Mahmoudi S, Devarajan K, Passegué E, Rando TA, Frydman J, and Brunet A (2018). Lysosome activation clears aggregates and enhances quiescent neural stem cell activation during aging. **Science**, 359: 1277-1283.

[3] 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. PMCID: PMC7111535

[4] Ruetz T, Kashiwagi CM, Morton B, Yeo RW, Leeman DS, Morgens DW, Tsui CK, Li A, Bassik MC, and Brunet A (2021). *In vitro* and *in vivo* CRISPR-Cas9 screens reveal drivers of aging in neural stem cells of the brain. **BioRxiv (under review at Nature).** Doi: 10.1101/2021.11.23.46972

B. Positions, Scientific Appointments and Honors

Positions and Employment

2015-	Michele and Timothy Barakett Professor of Genetics, Stanford University, Stanford, CA
2014-	Professor, Department of Genetics, Stanford University, Stanford, CA
2011-	Co-director, Glenn Laboratories 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

2020-	External Advisory Board, American Heart Association - Allen Institute
2020-	Editorial Board, *Cell Stem Cell*
2019-	External Advisory Board, Nathan Shock Center, University of Washington
2017-	Editorial Board, *Genes & Development*
2015-	Editorial Board, *Cell Reports*
2015-2016	Chair of NIH Study Section (CMAD)
2012-2015	Permanent Member of NIH Study Section (CMAD)
2012-	Editorial Board, *Aging Cell*
2011-2016	Member of *Faculty of 1000*
2011-2013	Reviewer for the Ellison Medical Foundation
2011-	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

2021	Keynote Lecture – EMBO|EMBL Symposium – Metabolism Meets Epigenetics
2021	NIH Florence Mahoney Lecture on Aging, Bethesda, MD
2018	NIH Director Transformative Research Award
2017	Sager Lecture - Marine Biological Laboratory Friday Evening Lecture, Woods Hole
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 *summa cum laude* from Ecole Normale Supérieure, Paris

C. Contribution to Science

Complete List of Published Work in MyBibliography:

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

1. **Mode of action of FOXO transcription factors**
   My early work as a postdoctoral fellow in Michael Greenberg's lab addressed the regulation and molecular mechanism of action of the pro-longevity FOXO Forkhead 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 by the protein deacetylase SIRT1. 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.

   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. Brunet A, Datta SR and Greenberg ME (2001) Transcription-dependent and -independent control of neuronal survival by the PI3K-Akt signaling pathway. **Curr Opin Neurobiol,** 11: 297-305.
   c. 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.
   d. 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.

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. I 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.

   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. PMCID: PMC2680339
   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. PMCID: PMC3246132
   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. PMCID: PMC4635044
   d. Brunet A and Rando T (2017). Interaction between epigenetic and metabolism in stem cell aging. **Current Opinion in Cell Biology**, 45:1-7.

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. More recently have also explored the intriguing relationship between chromatin modifications and lipid metabolism.

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. PMCID: PMC3075006
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. PMCID: PMC3368121
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. PMCID: PMC5391274
d. Papsdorf K and Brunet A (2019). Linking Lipid Metabolism to Chromatin Regulation in Aging. **Trends Cell Biol**, 29:97-116. PMCID: PMC6340780

4. **Stem cell aging and rejuvenation**
My lab has also developed mammalian models to address complex questions about brain aging and rejuvenation. We have embarked on an effort to unbiasedly characterize aging in the regenerative neural stem cell region in the adult mammalian brain.

a. Leeman DS, Hebestreit K, Ruetz T, Webb AE, McKay A, Pollina EA, Dulken BW, Zhao X, Yeo RW, Ho TT, Mahmoudi S, Devarajan K, Passegué E, Rando TA, Frydman J, and Brunet A (2018). Lysosome activation clears aggregates and enhances quiescent neural stem cell activation during aging. **Science**, 359: 1277-1283. PMCID: PMC5915358
b. 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. PMCID: PMC7111535
c. Yeo RW**,** Zhou OY**,** Zhong B, Sharmin M, Ruetz TZ**,** Hollenhorst CN, Kundaje A, Dunn AR, and Brunet A (2021) Chromatin accessibility dynamics of neurogenic niche cells reveal a reversible decline in neural stem cell migration during aging. **BioRxiv (in revision at Nature)**. Doi: 10.1101/2021.03.29.437585
d. Ruetz T, Kashiwagi CM, Morton B, Yeo RW, Leeman DS, Morgens DW, Tsui CK, Li A, Bassik MC, and Brunet A (2021). *In vitro* and *in vivo* CRISPR-Cas9 screens reveal drivers of aging in neural stem cells of the brain. **BioRxiv (under review at Nature)** Doi: 10.1101/2021.11.23.46972

5. **Pioneering the African turquoise killifish as a new model for studying vertebrate longevity**
Finally, my lab is pioneering 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 has developed genome editing of several aging and longevity genes. We are excited to ask unique questions about vertebrate aging in this unique new system to understand the regulation of aging and 'suspended animation'.

a. Valenzano DR, Sharp S, Brunet A (2011) Transposon-mediated transgenesis in the short-lived African killifish *Nothobranchius furzeri*, a vertebrate model for aging. **G3, Genes Genome Genetics** 1: 531-538. *Cover article.* PMCID: PMC3276177
b. 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. PMCID: PMC4684691
c. 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. PMCID: PMC4344913
d. 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. PMCID: PMC7532943