BIOGRAPHICAL SKETCH

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NAME: Santos J Franco

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

POSITION TITLE: Assistant 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
Colorado State University, Fort Collins CO	B.S.	05/00	Biological Sciences
University of Wisconsin, Madison WI	Ph.D.	08/05	Cellular & Molecular Biology
The Scripps Research Institute, La Jolla CA	Postdoctoral	07/13	Developmental Neurobiology

A. Personal Statement

My long-term career goal is to define the mechanisms that control development and function of neural circuits in the cerebral cortex and to understand how defects in this process lead to brain dysfunction and neurological disease. Toward this goal, I have been studying three related processes involved in the formation of neural circuits in the cerebral cortex: **1)** Coordination between cell-fate specification and neurogenesis in neural stem cells, **2)** Migration of newborn neurons to their proper laminar position in the cortex, and **3)** The cellular and molecular mechanisms that control dendrite arborization and synapse formation.

B. Positions and Honors

Positions and Employment

08/00-08/05	Graduate Student, Cellular and Molecular Biology Program, University of Wisconsin-Madison, Madison, WI
08/05-12/05	Postdoctoral Associate, Department of Pediatrics, University of Wisconsin- Madison, Madison, WI
01/06-04/09	Research Associate, Department of Cell Biology and Institute for Childhood and Neglected Diseases, The Scripps Research Institute, La Jolla, CA
05/09-07/13	Senior Research Associate, Department of Cellular and Molecular Neuroscience and Dorris Neuroscience Center, The Scripps Research Institute, La Jolla, CA
08/13-Present	Assistant Professor, Career Track, Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO
08/13-Present	Assistant Professor, Programs of Pediatric Stem Cell Biology and Developmental Origins of Health and Disease, Children's Hospital Colorado, Aurora, CO

Other Experience and Professional Memberships

2002-Present	Member, American Society for Cell Biology
2006-Present	Member, Society for Neuroscience
2006-2011	Member, NIH Neuroscience Blueprint Cre Driver Network

2010-2013	Associate Faculty Member, Faculty of 1000
2014-Present	Member, Society for Developmental Biology
2017-Present	Early Career Reviewer, Molecular Neurogenetics (MNG) Study Section

Honors and Awards

1997-1998	Colorado State University Natural Sciences Scholarship
1998	Western Alliance to Expand Student Opportunities
1999	McNair Scholars Program Summer Research Internship
1998	NIH Short-term Research Education Program to Increase Diversity (R25)
2000-2002	University of Wisconsin Advanced Opportunity Fellowship
2002-2005	NIH Kirschstein NRSA Molecular Biosciences Training Grant (T32)
2006-2009	NIH Research Supplement for Underrepresented Minorities (R01 supplement)
2009-2012	NIH Kirschstein NRSA Individual Postdoctoral Fellowship (F32)

C. Contribution to Science

1. I performed my Ph.D. thesis research with Dr. Anna Huttenlocher in the Department of Pediatrics at the University of Wisconsin. During my graduate studies, I investigated the molecular mechanisms of cell-matrix adhesion formation and turnover during cell migration. We found that cleavage of the focal adhesion protein talin 1 is by the calcium-dependent protease calpain 2 is required for focal adhesion disassembly during cell migration on extracellular matrix. We further identified the molecular mechanisms by which talin is targeted to focal adhesions in the first place. Together this body of work provided new insights into the cellular and molecular mechanisms by which cell-matrix adhesions are regulated during cell migration.

a. Franco S, Perrin B, Huttenlocher A. (2004). Isoform specific function of calpain 2 in regulating membrane protrusion. Exp Cell Res. Sep 10;299(1):179-87.
b. Franco SJ, Rodgers MA, Perrin BJ, Han J, Bennin DA, Critchley DR, Huttenlocher A. (2004). Calpain-mediated proteolysis of talin regulates adhesion dynamics. Nat Cell Biol. Oct;6(10):977-83.
c. Franco SJ, Huttenlocher A. (2005). Regulating cell migration: calpains make the cut. J Cell Sci. Sep 1;118(Pt 17):3829-38. Review.
d. Franco SJ, Senetar MA, Simonson WT, Huttenlocher A, McCann RO. (2006). The conserved C-terminal I/LWEQ module targets Talin1 to focal adhesions. Cell Motil Cytoskeleton. Sep;63(9):563-81.

2. My postdoctoral training was carried out with Dr. Ulrich Mueller in the Departments of Cell Biology and Cellular and Molecular Neuroscience at The Scripps Research Institute. During the first part of my postdoctoral studies, I investigated the cellular and molecular mechanisms by which newborn neurons migrate to their appropriate positions in the developing cerebral cortex. One of the best-known signaling pathways required for neuronal migration is the Reelin/Dab1 pathway. Using precisely timed conditional knockout of Dab1 in the developing mouse cerebral cortex, we found that Reelin/Dab1 signaling is essential only for a specific type of migration, called glia-independent somal translocation, but not other modes of migration. We further demonstrated that Reelin signaling accomplishes this task by activating Cadherin-based cell-cell adhesions via the GTPase Rap1 and the intermediate cell-cell adhesion molecules, Nectin 1 and Nectin 3. These studies elucidated the cellular and molecular mechanisms by which the Reelin/Dab1 signaling pathway controls neuronal migration to integrate newborn neurons into functional circuits in the cerebral cortex. Our work also provided a novel framework for future studies on the mechanisms by which Reelin and Dab1 control other aspects of brain function, including their emerging role in controlling synapse function in the mature brain. Our collaborators and we went on to show that Reelin and Dab1 are required beyond the developmental stages and function in the mature forebrain during synaptic plasticity and associative learning.

a. Franco SJ, Martinez-Garay I, Gil-Sanz C, Harkins-Perry SR, Müller U. (2011). Reelin regulates cadherin function via Dab1/Rap1 to control neuronal migration and lamination in the neocortex. Neuron. Feb 10;69(3):482-97.
b. Brunne B, Franco S, Bouché E, Herz J, Howell BW, Pahle J, Müller U, May P, Frotscher M, Bock HH. (2013). Role of the postnatal radial glial scaffold for the development of the dentate gyrus as revealed by reelin signaling mutant mice. Glia. Aug;61(8):1347-63.

c. Gil-Sanz C, Franco SJ, Martinez-Garay I, Espinosa A, Harkins-Perry S, Müller U. (2013). Cajal-Retzius Cells Instruct Neuronal Migration by Coincidence Signaling between Secreted and Contact-Dependent Guidance Cues. Neuron. Aug 7;79(3):461-77.
d. Trotter J, Lee GH, Kazdoba T, Crowell B, Domogauer J, Mahoney H, Franco SJ, Muller U, Weeber E, D'Arcangelo G. (2013). Dab1 is required for hippocampal synaptic plasticity and associative learning. J. Neurosci. Sep 25;33(39):15652-68.

3. At the end of my postdoctoral fellowship period, I was promoted to Senior Research Associate in Dr. Mueller's laboratory and began studying cell fate specification in the brain. In these studies, we uncovered an unexpected mechanism for projection neuron fate-specification from neural stem cells during development of the cerebral cortex. Using genetic fate-mapping experiments *in vivo*, we showed that there are distinct subtypes of neural progenitor cells in the cerebral cortex that are pre-specified to generate different functional classes of excitatory projection neurons. We also provided some first clues about the cellular mechanisms by which these different progenitor types generate neurons at distinct developmental time points. Our findings challenged the prevailing "common progenitor" hypothesis and provided a novel framework for answering a number of intriguing questions about how neurogenesis and cell-fate specification are coordinated to produce the appropriate types and numbers of neurons at the correct times.

a. Franco SJ, Gil-Sanz C, Martinez-Garay I, Espinosa A, Harkins-Perry SR, Ramos C, Müller U. (2012). Fate-restricted neural progenitors in the mammalian cerebral cortex. Science. Aug 10;337(6095):746-9.
b. Franco SJ, Müller U. (2013). Shaping our minds: stem and progenitor cell diversity in the mammalian neocortex. Neuron. Jan 9;77(1):19-34.
c. Gil-Sanz C, Espinosa A, Fregoso SP, Bluske KK, Cunningham CL, Martinez-Garay I, Zeng H, Franco SJ, Müller U. (2015). Lineage Tracing Using Cux2-Cre and Cux2-CreERT2 Mice. Neuron. May 20;86(4):1091-9.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/santos.franco.1/bibliograpahy/47342615/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

Linda Crnic Institute for Down Syndrome Grand Challenges Grant 04/01/2017-03/31/2018
Defects in Neurogenesis and Neuronal Migration in DS Mouse Models: Elucidating the Developmental and Molecular Mechanisms
The goal of this project is to investigate how key cellular processes of embryonic brain development are affected in a series of mouse models of Down syndrome.
Role: PI

Boettcher Foundation Webb-Waring Biomedical Research Award 07/01/2015-06/30-2018
Origins and Functions of Neuronal Diversity in the Cerebral Cortex
The goal of this project is to determine the molecular, developmental and functional properties of the neuron subtypes that are produced specifically by Cux2+ progenitors in the forebrain.
Role: PI

Pediatric Stem Cells Program Start-Up Funds, Children's Hospital Colorado 08/01/2013 – 07/31/2018
Cellular and Molecular Mechanisms of Brain Development and Neurological Disease
The goal of this project is to determine the molecular mechanisms by which fate-specification, neurogenesis and cell migration are temporally controlled and integrated to form layers of functionally related projection neurons in the cerebral cortex.
Role: PI

Completed Research Support

UL1 TR001082 (NCATS) Sokol, Ronald J (PI) 06/30/2015-05/31/2016
Novel Interactors of the Reelin Signaling Pathway and their Potential Roles in Healthy Brain Function and Alzheimer's Disease Pathology
The Colorado Clinical and Translational Sciences Institute (CCTSI) provides one-year pilot awards meant to encourage cross-disciplinary and collaborative research in clinical and translational science. The goal of this pilot study is to elucidate the molecular interactors of Dab1 at synapses in the normal brain to provide insights into the pathological consequences of perturbed Reelin signaling in the diseased human brain.
Role: PI