BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Song, Juan	Assistant Professor
eRA COMMONS USER NAME (credential, e.g., agency login): JUAN_SONG	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of California, Berkeley	Ph.D	2007	Neuroscience
Johns Hopkins University	Postdoctoral	2007-2013	Adult Neurogenesis

A. Personal Statement

I have the expertise, leadership, training, expertise and motivation necessary to successfully carry out the proposed research project. Adult neurogenesis occurs in a unique microenvironment (niche) and recapitulates the complete neural developmental process in a mature central nervous system. Our primary research interests are: 1) To identify the circuit mechanisms that regulate neural circuit organization and function at distinct stages of adult neurogenesis, including activation and fate choice of quiescent neural stem cells, survival of proliferating neural progenitors, and synaptic integration of newborn neurons; 2) To understand how circuit-level information-processing properties are remodeled by the integration of new neurons into existing circuits and how dysregulation of this process may contribute to various neurological and mental disorders. Our long-range goals are to translate general principles aoverning neural network function into directions relevant for understanding neuropsychiatric diseases, such as schizophrenia and autism, and neuronal replacement therapy for brain injuries, such as stroke and Alzheimer's disease. We are addressing these questions using a combination of innovative and multifaceted approaches, including *in vivo* multi-channel recording, patch-clamp electrophysiology, calcium imaging, optogenetics and chemogenetics, clonal analysis for lineage tracing/fate mapping of adult neural stem/progenitor cells, high-resolution confocal microscopy, and sophisticated mouse genetic models. A list of related publications from my postdoc work to support the ongoing projects is as below:

a. Kim JY, Liu CY, Zhang F, Duan X, Wen Z, <u>Song J</u>, Feighery E, Lu B, Rujescu D, St Clair D, Christian K, Callicott JH, Weinberger DR, Song H, Ming GL (2012). Interplay between DISC1 and GABA signaling regulates neurogenesis in mice and risk for schizophrenia. *Cell* 148(5):1051-64

b. <u>Song J,</u> Zhong C, Bonaguidi MA, Sun G, Hsu D, Gu Y, Meletis K, Huang J, Ge S, Enikolopov G, Deisseroth K, Luscher B, Christian K, Ming GL, Song H (2012). Neuronal circuitry mechanism regulating adult quiescent neural stem-cell fate decision. *Nature* 489: 150-154

c. <u>Song J</u>, Sun J, Moss J, Wen Z, Sun G, Hsu D, Zhong C, Davoudi H, Christian K, Toni N, Ming GL, Song H (2013). Parvalbumin interneurons mediate neuronal circuitry-neurogenesis coupling in the adult hippocampus. *Nature Neuroscience* 16(12):1728-30

d. Zhou M, Li W, Huang S, <u>Song J</u>, Kim JY, Tian X, Kang E, Liu C, Balaji J, Zhou Y, Parivash SN, Zhou Y, Ehninger D, He L, Song H, Ming GL, Silva AJ (2013) mTOR inhibition ameliorates cognitive and affective deficits caused by Disc1 knockdown specifically in adult-born dentate granule neurons. *Neuron* 77(4):647-54

e. Duan Y, Wang SH, <u>Song J</u>, Mironova Y, Ming GL, Kolodkin A, and Giger RJ (2014). Semaphorin 5A inhibits synaptogenesis in early postnatal- and adult-born hippocampal dentate granule cells. *eLife* Oct 14;3 (*doi: 10.7554/eLife.04390*)

B. Positions, Honors and Professional Experiences

Positions and Employment

2013-	Assistant professor, University of North Carolina, Chapel Hill
2007-2013	Postdoctoral fellow, Johns Hopkins University School of Medicine
2001-2007	Graduate Student Researcher, University of California, Berkeley
Honors	
2015	Junior Faculty Career Development Award (UNC)
2014	Janett Rosenberg Trubatch Career Development Award (Society for Neuroscience)
2014-2018	American Heart Association Scientist Development Award
2014-2017	Whitehall Foundation Award
2014-2016	NARSAD Young Investigator Award (Brain and Behavioral Research Foundation)
2013	Alfred Blalock Young Investigator Award (Johns Hopkins University)
2012	Julius Axelrod Postdoctoral Travel Award (Society for Neuroscience)
2011-2013	Maryland Stem Cell Research Foundation Postdoctoral Fellowship
2011	Keystone Symposia Scholarship (Adult Neurogenesis)
2008-2011	Life Sciences Research Foundation Postdoctoral Fellowship
2004-2006	Graduate Student Travel Grant, University of California, Berkeley
2004-2006	Merit-based Predoctoral Training Fellowship, University of California, Berkeley

Professional Experience

Guest Editor

Neural plasticity (Special Issue)

Ad hoc reviewer

Neuron, Nature Neuroscience, Cell Stem Cell, Journal of Neuroscience, Developmental Neurobiology, European Journal of Neuroscience; Journal of Neurochemistry, Neuroscience

Membership:

Society for Neuroscience

C. Contribution to Science (*: corresponding author; #: equal contribution)

1. The early publications during my graduate school addressed how seizure is suppressed using Drosophila as a model system. Studies of human seizure disorders have revealed that susceptibility to seizures is largely influenced by genetic factors. In addition to causing epilepsy, genetic factors can also suppress seizures and epileptogenesis. Discovery of seizure-suppressor genes is challenging in mammals, however, such genes are readily identified and analyzed in a Drosophila model of epilepsy. Seizure-suppressor mutations in Drosophila are a novel class of second-site mutations that reverse the epilepsy phenotype of seizure-sensitive mutants. These mutations are a potentially powerful approach for identifying targets for anti-epileptic drugs. My accomplishments explored the potential of this approach, particularly: 1) Established an electrophysiology-based protocol for examining seizuresuppressor mutations utilizing a *Drosophila* mutation affecting the gap junction channel and reverse genetics. 2) Conducted a forward-genetics screen for new seizure-suppressor mutations, utilizing transposon mutagenesis, and discovered a novel mutation affecting DNA topoisomerase I. Mutations of topoisomerase I are especially effective at reverting the seizure phenotype of Drosophila epilepsy mutants. A creative model for seizure-suppression based on neuronal apoptosis is proposed and validated experimentally. 3) Based on the seizure suppression property of DNA topoisomerase I, I examined DNA topoisomerase I inhibitors as a promising new class of anti-epileptic drugs in Drosophila seizure models. DNA topoisomerase I inhibitors are a class of drug FDA-approved for cancer treatment, but not previously thought to be useful as anti-epileptic drugs.

a. <u>Song J*</u> and Tanouye M (2006). Seizure suppression by *shakB*², a gap junction mutation in *Drosophila*. *J. Neurophysiology* 95 (2): 627-635.

b. <u>Song J*</u>, Hu J and Tanouye M (2007). Seizure suppression by *top1* mutations in *Drosophila*. *J. Neuroscience* 27 (11): 2927-2937.

c. <u>Song J*</u>, and Tanouye M (2007). Role for *para* sodium channel gene 3' UTR in the modification of *Drosophila* seizure susceptibility. *Dev Neurobiol* 67(14):1944-56.

d. <u>Song J*</u>, Parker L, Hormozi L and Tanouye M (2008). DNA topoisomerase I inhibitors ameliorate seizure-like behaviors and paralysis in a Drosophila model of epilepsy. *Neuroscience* 156(3):722-728.

2. Adult neurogenesis arises from neural stem cells within specialized niches. Neuronal activity and experience, presumably acting upon this local niche, regulate multiple stages of adult neurogenesis, from neural progenitor proliferation to new neuron maturation, synaptic integration and survival. Whether local neuronal circuitry has a direct impact on adult neural stem cells is unknown. To address this fundamental question, I have developed a novel system to study the interaction between niche components and adult neurogenesis. This system combines an optogenetic approach to selectively manipulate the activity of specific local interneuron subtypes and a genetic approach to sparsely label adult neural stem cells and their progeny for lineage-tracing and fate mapping. Using this system I identified, for the first time, dentate gyrus parvalbumin-expressing interneurons as a critical and unique niche component that conveys hippocampal circuit activity to the regulation of neural stem cell activation, proliferating neural progenitor survival, and immature neuron integration and excitatory synapse formation. Together, these studies uncovered fundamental circuit mechanisms by which local network activity regulates endogenous adult neurogenesis at distinct developmental stages.

a. <u>Song J</u>, Zhong C, Bonaguidi MA, Sun G, Hsu D, Gu Y, Meletis K, Huang J, Ge S, Enikolopov G, Deisseroth K, Luscher B, Christian K, Ming GL, Song H (2012). Neuronal circuitry mechanism regulating adult quiescent neural stem-cell fate decision. *Nature* 489: 150-154 (*Featured in Cell Stem Cell, Nat Rev Neurosci, BioEssays, F1000 must read*)

b. <u>Song J</u>, Sun J, Moss J, Wen Z, Sun G, Hsu D, Zhong C, Davoudi H, Christian K, Toni N, Ming GL, Song H (2013). Parvalbumin interneurons mediate neuronal circuitry-neurogenesis coupling in the adult hippocampus. *Nature Neuroscience* 16(12):1728-30

c. <u>Song J*</u>, Crowther AJ, Olsen RHJ, Song H, and Ming GL (2014) A diametric mode of neuronal circuitry-neurogenesis coupling in the adult hippocampus via parvalbumin interneurons. *Neurogenesis* 1:e29949; <u>http://dx.doi.org/10.4161/neur.29949</u>

3. Adult neurogenesis recapitulates the whole process of neuronal development in a mature central nervous system, from proliferation and fate specification of adult neural progenitors, morphogenesis, migration, axon/dendritic development, and finally synapse formation, culminating in the full integration of new neurons into the existing circuitry. Cumulative evidence suggests that new neurons participate in specific brain functions and aberrant adult neurogenesis may contribute to brain disorders. During my postdoctoral studies, I use adult mouse hippocampal neurogenesis as an experimental model system to elucidate molecular mechanisms regulating the neuronal development. Furthermore, I use this system to explore novel functions of risk genes for mental disorders in neuronal development during the adult stage. Knowledge gained from these studies provide the basis for understanding the etiology of neurological diseases and mental disorders and have important implications for neuronal replacement therapy.

a. Kim JY, Liu CY, Zhang F, Duan X, Wen Z, <u>Song J</u>, Feighery E, Lu B, Rujescu D, St Clair D, Christian K, Callicott JH, Weinberger DR, Song H, Ming GL (2012). Interplay between DISC1 and GABA signaling regulates neurogenesis in mice and risk for schizophrenia. *Cell* 148(5):1051-64

b. Zhou M, Li W, Huang S, Song J, Kim JY, Tian X, Kang E, Liu C, Balaji J, Zhou Y, Parivash SN, Zhou Y. Ehninger D. He L. Song H. Ming GL. Silva AJ (2013) mTOR inhibition ameliorates cognitive and affective deficits caused by Disc1 knockdown specifically in adult-born dentate granule neurons. Neuron 77(4):647-54

c. Jang M, Kitabatake Y, Bonaguidi, MA, Sun J, Song J, Kang E, Jun H, Zhong C, Su Y, Guo J, Wang M, Sailor K, Kim JY, Gao Y, Christian KM, Ming GL, Song H (2013). Secreted frizzled-related protein 3 regulates activity-dependent adult hippocampal neurogenesis. Cell Stem Cell 12(2):215-23

d. Duan Y, Wang SH, Song J, Mironova Y, Song H, Kolodkin A, and Giger RJ (2014). Semaphorin 5A inhibits synaptogenesis in early postnatal- and adult-born hippocampal dentate granule cells. eLife Oct 14;3 (doi: 10.7554/eLife.04390)

4. In my new lab at UNC, we have ongoing efforts to apply novel tools in addressing fundamental questions on adult neurogenesis regulation and function at the circuitry and molecular levels. We have established collaborations with serval labs both within and outside UNC with considerable expertise in these areas.

a. Vardy E, Robinson JE, Li C, Olsen, R.H.J., DiBerto, J.F., Sassano F.M., Huang X.P., Zhu, H., Urban DJ, Rittiner JE, Crowley(Capik) NA, Song J, Kash T.L., Malanga C.J., Krashes M., Roth B.L. (2015). A DREADD for multiplexing chemogenetic interrogation of neural circuits. **Neuron** 20:86(4):936-46.

b. Shin J, Berg DA, Zhu Y, Shin JY, **Song J**, Bonaguidi MA, Enikolopov G, Nauen DW, Christian KM, Ming GL, and Song H (2015). Single-cell RNA-seg with Waterfall reveals molecular cascades underlying adult neurogenesis. Cell Stem Cell (in press).

Complete List of Published Work in MyBibliography:

http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/47791935/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

1. Whitehall Foundation

Neural circuits regulating synapse dynamics of adult-born neurons The goal of this project is to investigate how inhibitory neural circuits mediated by local interneurons regulate spine dynamics of adult-born neurons in the hippocampus. Role: PI

2. Junior Faculty Career Development Award (UNC) Song (PI) 1/1/2015-12/31/2015

Neural Circuits Regulating Adult Neurogenesis

The goal of this project is to investigate the neural circuitry mechanisms regulating adult hippocampal neurogenesis in the mouse. Role: PI

3. R21 MH106939

Mapping Global Brain Connectivity Mediated by DISC1 Gene in Adult-born Neurons The goal of this project is to investigate brain circuitry connectivity mediated by newborn neurons with mental disorder risk gene DISC1 deficiency in the adult mouse hippocampus. Role: PI

4. American Heart Association

Local circuitry mechanism underlying stroke induced neurogenesis in the adult hippocampus The goal of this project is to investigate how local neural circuits mediated by parvalbumin interneurons impact adult neurogenesis upon brain injuries. Role: PI

Song (PI) 06/01/2015 - 05/31/2020

07/01/2014 -6/30/2018

07/01/2014 - 6/30/2017

Song (PI)

Song (PI)

5. Brain and Behavior Foundation (NARSAD)

Role of NKCC1 in parvalbumin-expressing interneurons for psychiatric disorders The goal of this project is to examine the role of NKCC1 in parvalbumin interneurons in regulation of prefrontal cortical circuitry properties and how that impact cognitive and affective affect behaviors. Role: PI

Song (PI)

6. P60-AA011605

Crews (PI) 12/01/2014-11/30/2016

01/15/2014 - 01/14/2016

Molecular and Cellular Pathogenesis in Alcoholism

The goal of this pilot project is to investigate the impact of adolescent binge drinking on basal forebrain cholinergic neurons and adult hippocampal neurogenesis in the mouse model. Role: Co-Investigator