BIOGRAPHICAL SKETCH (NIH)

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NAME: **Woo-Ping Ge**

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

POSITION TITLE: Assistant Professor, Children's Research Institute, Department of Neuroscience, Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center

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
East China Normal University, China	B.S.	07/2000	Biochemistry
Institute of Neuroscience, Chinese Academy of Sciences, China (Mentors: Shumin Duan & Mu-ming Poo)	Ph.D.	07/2005	Neurobiology
University of California, San Francisco (Mentor: Lily Jan)	Postdoc	12/2011	Developmental Neurobiology

Please refer to the Biographical Sketch sample in order to complete sections A, B, C, and D of the Biographical Sketch.

A Personal Statement

During graduate school, I worked on the crosstalk between neurons and glial cells in the brain. As a postdoctoral fellow and then associate specialist in Lily Jan's lab at UCSF, my research has broad interests in glial cell generation and the development of brain vasculature. After establishing my laboratory at UT Southwestern in Sep. 2013, our focus is to understand (1) gliovascular interaction in the brain, (2) the mechanisms underlying neuronal injury and repair in the brain under ischemia, (3) glioma-glia cell interactions. We also devote a lot of our effort in the establishment of new approaches/tools to study glioma-stromal cell interaction, brain injury and repair *in vivo*. Our long-term goal is to develop novel therapeutic targets for treating patients with ischemic stroke or brain tumors.

B. Positions and Honors

Positions, Employment

2006.04–2006.05 Visiting Scholar, Lab of Chi-Keung Chan, Institute of Physics Academia Sinica, Taiwan
2006.07–2006.11 Research Associate, Lab of Zuoren Wang, Institute of Neuroscience, Chinese Academy of Sciences
2011.12–2013.08 Associate Specialist, Lab of Lily Jan, University of California, San Francisco
2013.09–present Assistant Professor, Pediatrics & Neuroscience, Children's Research Institute, Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center

Honors-Awards

2003 Chinese Academy of Sciences Di-AO Award
2006 50 Excellent Ph.D. Theses of Chinese Academy of Sciences in 2006
2007 China's Top 10 Advances in Basic Research in 2006

2007	Human Frontier Science Program Long-term Fellowship Award
2008	100 Excellent Ph.D. Theses of China
2010	The National Natural Science Award (China, the 2nd contributor)
2011	NINDS Pathway to Independence Award (K99/R00)
2017	Bugher-AHA Dan Adams Thinking Outside the Box Award (The Henrietta B. and Frederick H. Bugher Foundation)

C. Contribution to Science

1. Development of a method to precisely control focal ischemia with magnetic forces

The precise manipulation of microcirculation in mice can facilitate mechanistic studies of brain injury and repair after ischemia, but this manipulation remains a technical challenge, particularly in conscious mice. We developed a technology that uses micromagnets to induce aggregation of magnetic nanoparticles to reversibly occlude blood flow in microvessels. This allowed induction of ischemia in a specific cortical region of conscious mice of different postnatal age, including neonatal stages, with precise spatiotemporal control but without surgical intervention of the skull or artery. When combined with longitudinal live-imaging approaches, this technology facilitated the discovery of a feature of the ischemic cascade: selective loss of smooth muscle cells in juveniles but not adults shortly after onset of ischemia and during blood reperfusion.

a. Jia JM, Chowdary PD, Gao X, Ci B, Li W, Mulgaonkar A, Plautz EJ, Hassan G, Kumar A, Stowe AM, Yang SH, Zhou W, Sun X, Cui B*, **Ge WP*** Control of cerebral ischemia with magnetic nanoparticles. ***Nat Methods***. 14(2):160-166 (2017).

2. Identification of local generation of glia as a major astrocyte source in the postnatal brain

The majority of glial cells are produced after birth; their numbers increase 6- to 8-fold within the first three postnatal weeks in rodents. The mechanism by which most glial cells are produced remains unknown. In my most recent studies, I developed two novel methods: *in vivo* imaging of single-cell behavior in postnatal day (P)0–8 mouse brains and whole-cell recording of cells at different mitotic stages in brain slices. Using these tools, I found that local proliferation of astrocytes constitutes a major glial source in the early postnatal brain. This study provides direct evidence of local generation of astrocytes within the cerebral cortex as a major astrocyte source outside of the known neurogenic regions, which include the ventricular zone(VZ) and the subventricular zone (SVZ).

a. **Ge WP**, Miyawaki A, Gage FH, Jan YN, Jan LY. Local generation of glia is a major astrocyte source in postnatal cortex. ***Nature.*** 484, 376-380 (2012) [PMCID: PMC3777276]

3. Characterization of properties of dividing NG2 glia in the brain

As the major proliferating cell type in the mammalian central nervous system, NG2 glial cells account for 5-8% of the glial cell population and form synaptic contacts with neurons. I reported that NG2 glial cells divide while maintaining their differentiation, including morphological features, such as the elaboration of multiple complex cellular processes and physiological features including active glutamatergic and GABAergic synaptic responses. It is generally believed that dividing cells gain complex features of differentiation only after exiting the cell cycle because cell division and differentiation are both under such tight regulation that their coexistence is deemed unlikely. These findings provide a clear counterexample of the widely perceived incompatibility between cell division and differentiation.

a. **Ge WP**, Zhou W, Luo Q, Jan LY, Jan YN. (2009). Dividing glial cells maintain differentiated properties including complex morphology and functional synapses. ***Proc Natl Acad Sci U S A***. 106(1):328-333. [PMCID: PMC2610014].

4. Identification of long-term plasticity in neuron-to-glia signaling

Glial cells in the mammalian central nervous system are usually classified as astrocyte, oligodendrocyte, microglia, and NG2 glial cell. My work shows that neuronal signaling to both astrocytes and NG2 glial cells exhibits **LTP-like plasticity** following tetanus stimulation of Schaffer collaterals (SC). The elevated SC-evoked astrocyte depolarization is due to an increased extracellular K^+ accumulation accompanying LTP of neuronal synapses. In NG2 glial cells receiving direct glutamatergic synaptic inputs from neurons,

the persistent enhancement of postsynaptic currents requires intracellular Ca^{2+} elevation that is induced by activation of Ca^{2+} permeable AMPA receptors. The finding in astrocyte indicates astrocyte will play a critical role in the clearance of extracellular potassium during the expression LTP, whereas the finding of neuron-NG2 glia LTP involve Ca^{2+}-permeable AMPARs reveals a novel form of the plasticity of neuron-glia signaling and suggests additional sites for information storage in the brain.

a. **Ge WP***, Yang XJ*, Zhang Z, Wang HK, Shen W, Deng QD, Duan S. Long-term potentiation of neuron-glia synapses mediated by $Ca2^{+}$-permeable AMPA receptors. ***Science***. 312(5779):1533-1537 (2006). (*- co-first author)
b. **Ge WP**, Duan S. Persistent enhancement of neuron-glia signaling mediated by increased extracellular K^{+} accompanying long-term synaptic potentiation. ***J Neurophysiol.*** 97(3):2564-2569 (2007).

Complete List of Published Works in My Bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/woo-ping.ge.1/bibliography/41748484/public/?sort=date&direction=ascending

1. Zhang JM, Wang HK, Ye CQ, **Ge WP**, Chen Y, Jiang ZL, Wu CP, Poo MM, Duan S. (2003). ATP released by astrocytes mediates glutamatergic activity-dependent heterosynaptic suppression. ***Neuron***. 40(5):971-982.
2. Yang Y*, **Ge WP***, Chen Y, Zhang Z, Shen W, Wu C, Poo M, Duan S. (2003). Contribution of astrocytes to hippocampal long-term potentiation through release of D-serine. ***Proc Natl Acad Sci U S A***. 100(25):15194-15199. (*- co-first author). [PMCID: PMC299953]
3. Jin W, **Ge WP**, Xu J, Cao M, Peng L, Yung W, Liao D, Duan S, Zhang M, Xia J. (2006). Lipid binding regulates synaptic targeting of PICK1, AMPA receptor trafficking, and synaptic plasticity. ***J Neurosci***. 26(9):2380-2390.
4. **Ge WP***, Yang XJ*, Zhang Z, Wang HK, Shen W, Deng QD, Duan S. (2006). Long-term potentiation of neuron-glia synapses mediated by $Ca2^{+}$-permeable AMPA receptors. ***Science***. 312(5779):1533-1537. (*- co-first author).
5. Zhou W, **Ge WP**, Zeng S, Duan S, Luo Q. (2007) Identification and two-photon imaging of oligodendrocyte in CA1 region of hippocampal slices. ***Biochem Biophys Res Commun***. 352(3):598-602.
6. Zhang W, **Ge WP**, Wang ZA. (2007). A toolbox for light control of Drosophila behaviors through Channelrhodopsin mediated photoactivation of targeted neurons. ***Eur J Neurosci***. 26(9):2405-2416.
7. **Ge WP**, Duan S. (2007). Persistent enhancement of neuron-glia signaling mediated by increased extracellular K^{+} accompanying long-term synaptic potentiation. ***J Neurophysiol.*** 97(3):2564-2569.
8. Chung HJ*, **Ge WP***, Qian X, Wiser O, Jan YN, Jan LY. (2009). G protein-activated inwardly rectifying potassium channels mediate depotentiation of long-term potentiation. ***Proc Natl Acad Sci U S A***. 106(2):635-640. (*- co-first author). [PMCID: PMC2613041]
9. **Ge WP**, Zhou W, Luo Q, Jan LY, Jan YN Jan. (2009). Dividing glial cells maintain differentiated properties including complex morphology and functional synapses. ***Proc Natl Acad Sci U S A***.106(1):328-333. [PMCID: PMC2610014]
10. Lee HY, **Ge WP**, Huang W, He Y, Wang GX, Rowson-Baldwin A, Smith SJ, Jan YN, Jan LY. (2011) Bidirectional regulation of dendritic voltage-gated potassium channels by the fragile X mental retardation protein. ***Neuron.*** 72, 630-642. [PMCID: PMC3433402]
11. Ultanir SK, Hertz NT, Li G, **Ge WP**, Burlingame AL, Pleasure SJ, Shokat KM, Jan LY, Jan YN. (2012) Chemical genetic identification of NDR1/2 kinase substrates AAK1 and Rabin8 uncovers their roles in dendrite arborization and spine development. ***Neuron.*** 73, 1127-1142.
12. **Ge WP**, Miyawaki A, Gage FH, Jan YN, Jan LY. (2012) Local generation of glia is a major astrocyte source in postnatal cortex. ***Nature.*** 484, 376-380. [PMCID: PMC3777276]

Publication since Sep. 2013 (After I established my laboratory at UT Southwestern)

13. Yu D, Gustafson WC, Han C, Lafaye C, Noirclerc-Savoye M, **Ge WP**, Thayer DA, Huang H, Kornberg TB, Royant A, Jan LY, Jan YN, Weiss WA, Shu X. (2014) An improved monomeric infrared

fluorescent protein for neuronal and tumour brain imaging. ***Nat Commun.*** 5:3626. [PMCID: PMC4077998]
14. Shen Y, **Ge WP,** Li Y, Hirano A, Lee HY, Rohlmann A, Missler M, Tsien RW, Jan LY, Fu YH, Ptáček LJ (2015) Protein mutated in paroxysmal dyskinesia interacts with the active zone protein RIM and suppresses synaptic vesicle exocytosis. ***Proc Natl Acad Sci U S A.*** 112(10):2935-2941.
15. Ge WP*****, Jia JM. (2016) Local production of astrocytes in the cerebral cortex. ***Neuroscience***. 323:3-9. (Review)
16. Peng C, Gao X, Xu J, Du B, Ning X, Tang S, Bachoo RM, Yu M, **Ge WP*** (co-corresponding author) and Zheng J* Targeting orthotopic gliomas with renal-clearable luminescent gold nanoparticles. ***Nano Research*** (Accepted on Jan. 2, 2017).
17. Jia JM, Chowdary PD, Gao X, Ci B, Li W, Mulgaonkar A, Plautz EJ, Hassan G, Kumar A, Stowe AM, Yang SH, Zhou W, Sun X, Cui B*, **Ge WP*** (*co-corresponding author) (2016) Control of cerebral ischemia with magnetic nanoparticles. ***Nat Methods***. 14(2):160-166 (2017).