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: Zao C. Xu

eRA COMMONS USER NAME (credential, e.g., agency login): ZXU123

POSITION TITLE: 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
Guangzhou Medical College, China	M.D.	1982	Medicine
Sun Yat-sen Univ. of Medical Sciences, China	M.S.	1986	Neuroanatomy
University of Tennessee, Memphis.	Ph.D.	1990	Neuroscience

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

A. Personal Statement

The long-term goal of my research is to reveal the mechanisms of brain injury following acute neurological disorders and develop clinical interventions. I have more than 30 years of experience in neuroscience research using electrophysiological, morphological and molecular biological approaches. My research has been funded continuously by NIH and AHA, as well as other agents, since 1994. As a PI or Co-PI of these studies, I have established a solid ground, both scientifically and technically, for the success of the current proposed studies. I have the fortune to work with a group of talented, hard working collaborators at Indiana University School of Medicine and around the world. I have published more than 70 papers in peer review journals and 11 book chapters in neuroscience. In summary, I have a demonstrated tract record of successful and productive research related to the current proposal. I will be responsible to execute all aspects of the proposed project if it is funded.

B. Positions and Honors:

1990 - 1992 **Postdoctoral Research Associate**, University of Tennessee, Memphis. Department of Anatomy and Neurobiology.
1992 - 1997 **Assistant Professor**, University of Tennessee, Memphis. Department of Neurology.
1998 - 2004 **Associate Professor**, Indiana University School of Medicine, Department of Anatomy & Cell Biology.
2004 - Present **Professor**, Indiana University School of Medicine, Department of Anatomy & Cell Biology.

Other Experience and Professional Memberships

Bachelor of Medicine with Honor, Guangzhou Medical College,
Neuroscience Center of Excellence Predoctoral Fellowship,
The First Place, poster competition, Neuroscience Memphis Chapter,

Visiting Professor, The First Military Medical University, P. R. China.
Visiting Professor, Sun Yat-Sen University of Medical Sciences, P. R. China.
Visiting Professor, Jinan University School of Medicine, P.R. China.
Special Adjunct Professor, Guangzhou Medical College, P. R. China.
John D. Ryan Award for Distinguished contribution to international programs and studies. Indiana University

Professional Service

International

External Assessor of Earmarked Research Grant (ERG), Hong Kong	2000 - Present
Lecturer of IBRO School of Neuroscience, Hong Kong	2004
National Natural Science Foundation of China	2010 - Present

National

American Heart Association National Peer Review Committee	(2000 – 2001)
American Heart Association Peer Review Committee (Bain 3/4)	(2001 – 2005, 2012 - 2015)
NIH/NINDS ZNS1 SRB-H Committee	(2004)
NIH/NIGMS ZGM1 TWD-6 Committee	(2014-Present)

Society Memberships:

Society for Neuroscience	1987 -
American Heart Association (Stroke Council)	1994 -
Int. Soc. of Cerebral Blood Flow & Metabolism	1995 –

C. Contribution to Science

1. Neural transplantation

   My early research focused on the fate of rat embryonic neurons implanted into the adult brain. Using light and electron microscopy and in vivo intracellular recording and staining techniques, I demonstrated that the implanted embryonic neurons survive in the graft and make synaptic connections with the host neurons. However, most of the axons of the implanted neurons grow within the graft tissue and the morphology of some of the terminals is abnormal. The evoked synaptic potentials between the graft and host neurons also differ from those of control ones. These studies are among the first ones to show the nature of transplanted neurons at the cellular and synaptic levels. The results of these studies also provide a base for the current research on the survival, migration and differentiation of stem cells after implantation.

   - Xu, Z. C., Wilson, C.J. and Emson, P.C. (1989) Restoration of the corticostriatal projection in rat neostriatal grafts: electron microscopic analysis. Neuroscience 29(3): 539-550.
   - Xu, Z. C., Wilson, C. J. and Emson, P. C. (1991) Restoration of thalamostriatal projections in rat neostriatal grafts: electron microscopic analysis. J. Comp. Neurol. 303:22-34
   - Xu, Z. C., Wilson, C. J. and Emson, P. C. (1991) Synaptic potentials evoked in spiny neurons in rat neostriatal grafts by cortical and thalamic stimulation. J. Neurophysiol. 65(3):477-493
   - Xu, Z. C., Wilson, C. J. and Emson, P. C. (1992) Morphology of intracellularly stained spiny neurons in rat striatal graft. Neuroscience 48(1): 95-110.

2. Pathophysiology after cerebral ischemia

   My major contribution to science is to characterize the electrophysiological changes of ischemia-vulnerable and ischemia-resistant neurons after transient cerebral ischemia using in vivo and in vitro preparations. We discover a late-depolarizing postsynaptic potential in CA1 pyramidal neurons after ischemia, which might be associated with the excitotoxic cell death. We also demonstrate that enhancement of A-type potassium currents protect neurons against ischemia. These results shade lights on the mechanisms of selective cell death after ischemia and provide a foundation to develop agents to reduce brain damage after ischemia. In addition, we also investigate the mechanisms of seizures/epilepsy after ischemia in diabetic animals.

- Gao, T. M., Pulsinelli, W. A. and Xu, Z. C. (1998) Prolonged potentiation and depression of synaptic transmission in CA1 pyramidal neurons induced by lethal ischemia in vivo. Neuroscience 87:371-383.
- Ren, Yubo, Li Xiaoda and Xu, Z. C. (1997) Asymmetrical protection of neostriatal neurons from transient forebrain ischemia by unilateral dopamine depletion. Exp. Neurol. 146:250-257.
- Chi, X. X. and Xu, Z. C. (2000) Differential changes of potassium currents in CA1 neurons after transient forebrain ischemia. J. Neurophysiol. 84:2834-2843.
- Pang Z., Deng, P., Ruan, Y. and Xu, Z. C. (2002) Depression of fast excitatory synaptic transmission in large aspiny neurons of neostriatum after transient forebrain ischemia. J. Neurosci. 22: 10948-10957.
- Deng, P., Pang, ZP., Lei, Z., Shikano, S., Xiong, Q., Harvey, B., London, B., Wang, Y., Li, M. and Xu, Z. C. (2011) Up-regulation of A-type potassium currents protects neurons against cerebral ischemia. JCBFM 31: 1823-1835. **Feature Article**
- Lei, Z., Zhang, H., Liang, Y., Cui, Q., Xu, Z. and Xu, Z. C. (2014) Reduced expression of IA channels is associated with post-ischemic seizures in hyperglycemic rats. J. Neurosci Res. 92:1775–1784.
- Xia, Zhigang Lei, Zhongshan Shi, Dave Guo, Henry Su, Yiwen Ruan, Zao C. Xu (2016) Enhanced autophagy signaling in post-ischemia seizures under diabetic conditions. Brain Res. 1643:18-26.
- Zhigang Lei, Hui Zhang, Yanling Liang, Zao C. Xu (2016) Reduced expression of I_A channels is associated with post-ischemic seizures. Epilepsy Res. 124:40-48.

3. Pathogenesis of brain and spinal cord injury

   Another direction of my research is the mechanisms of neuronal injury after traumatic brain injury or spinal cord injury. We have shown that alteration of ion channels such as Ih and IA might contribute to neuron injury after TBI and up-regulation of inflammation related signals also play a role in this pathological process.

   - Deng, P. and Xu, Z. C. (2011) Contribution of Ih to neuronal damage in the hippocampus after traumatic brain injury. J. Neurotrauma. 28(7): 1173-1183.
   - Lei, Z., Deng, P., Li, J. and Xu, Z. C. (2012) Alterations of A-type potassium channels in hippocampal neurons after traumatic brain injury. J Neurotrauma. 29: 235-245
   - Deng, L., Deng, P., Ruan, Y., Xu, Z. C., Liu, N., Smith, G. and Xu, X. M. (2013) A Novel Growth-Promoting Pathway Formed by GDNF-Overexpressing Schwann Cells Promotes Propriospinal Axonal Regeneration, Synapse formation, and Partial Recovery of Function after Spinal Cord Injury. J. Neurosci. 33:5655–5667

4. Pain research

   In collaboration with other investigators, we have shown that enhanced presynaptic transmitter release in the anterior frontal cortex might contribute to the chronic pain and up-regulation of Thrombospondin-4 in spinal cord dorsal horn neurons is involved in spinal sensitization and neuropathic pain.

   - Zhao, MG., Ko, SW., Toyoda, H., Wu, LJ., Xu, H., Li, JG., Jia, Y., Xu, ZC. and Zhuo, M. (2006) Enhanced presynaptic neurotransmitter release in the anterior cingulate cortex of the mice with chronic pain. J. Neurosci. 26:8923-8930.
   - Kim, D., Li, KW., Boroujerdi, A., Yu,Y., Zhou, CY., Deng, P., Park, J., Zhang, X., Lee, J., Corpe, M., Sharp, K., Steward, O., Eroglu, C., Barres, B., Zaucke, F., Xu, Z. C., and Luo, ZD (2012) Thrombospondin-4 contributes to spinal sensitization and neuropathic pain states. J. Neurosci. 32: 8977-8987.
   - Li, J., Wu, M., Zhuo. M. and Xu, Z. C. (2013) Alteration of neuronal activity after digit amputation in rat anterior cingulate cortext. Int. J. PPP 5 (1): 43-51.

List of Published work in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/zao.xu.1/bibliography/40796451/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

AHA 14GRNT20410061, Xu (PI) 07/01/2014 - 06/30/2017 (no cost extension)
"PKC modulation of K+ after ischemia"

The project is to reveal a novel mechanism that protein kinase C mediated enhancement of IA contribute to neuronal survival after ischemia.
Role: PI

CURE Jin (PI) 12/01/2014 – 11/30/2017
"Targeting HMGB1 signaling for preventing posttraumatic epileptogensis"

The project will test the hypothesis that activation of HMGB1-TLR4 signaling contributes to PTE and that blocking this pathway following TBI will prevent PTE.
Role: Co-P.I.

ISPBIF 020915 Rodgers (PI) 7/1/2015 – 6/30/2017
"Investigation of a Novel Hemoadsorption System in Rats with Traumatic Brain Injury application"

The project will use a newly developed technique to absort the inflammatory factors in the blood circulation and reduced the neuronal damage after traumatic brain injury with hemorrhage shock.
Role: Co-P.I.

Completed Research Support

R21 NS071238 Xu (PI) 07/01/2010 – 06/30/2013
"K+ current and selective cell death after ischemia"

The project is to investigate the contribution of potassium currents in neuronal survival or death after transient cerebral ischemia.
Role: P. I.

R01 NS046341 Luo (PI) 02/01/2010 – 01/31/2014
"Mechanism of calcium channel Cava2d1 protein mediated neuropathic pain"

The project is to reveal the role of alteration of calcium channel Cava2d1 protein expression in spinal cord neurons in neuropathic pain.
Role: Co-PI