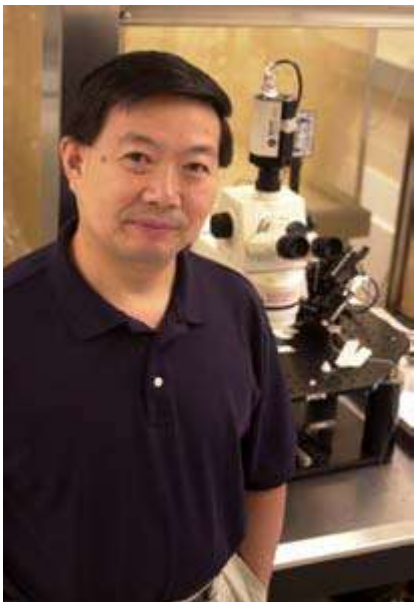
**Youming Lu, PhD, MD**
Professor of Neurology and Neuroscience
Bollinger Professor of Alzheimer's Diseases



**EDUCATION**

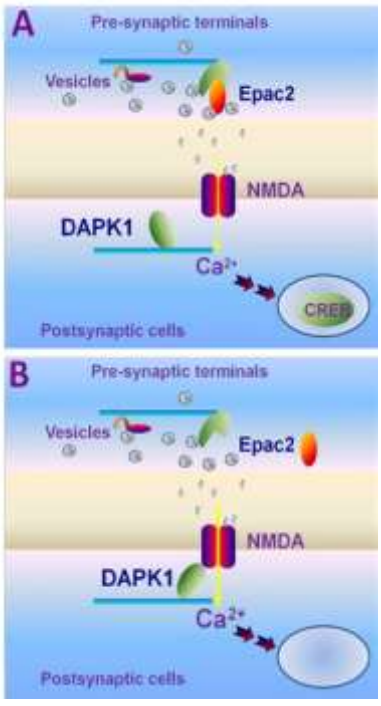
1996-1999 PhD, University of Toronto, Canada
1993-1995 Postdoctoral Fellow, University of California, Irvine
1990-1993 Postdoctoral Fellow, Novartis, Basal, Switzerland
1987-1990 MS, China Pharmaceutical University, China
1980-1985 MD, SMMU Naval Medical College, China

**POSITIONS**

2008- Professor, LSU School of Medicine, New Orleans
2004-2008 Associate Professor, University of Central Florida, Orlando 2000-2004 Assistant Professor, University of Calgary, Calgary

**CURRENT RESEARCH**

Glutamate is a major excitatory transmitter in the mammalian central nervous system (CNS) and plays an essential role in neural development, excitatory synaptic transmission, and plasticity. In cases of brain injury such as stroke, however, glutamate accumulates at synapses, resulting in extensive stimulation of its receptors that can eventually be toxic to neurons. Although excess stimulation of glutamate transmission contributes to neuronal death, blocking it totally could be deleterious to animals and humans because targeting glutamate synapses would block the synaptic physiological function as well. My long-term objective is to explore an ideal approach for treatment of some neurological disorders and brain injury by targeting the specific glutamate "cell death signals" whereby the pathological effects of glutamate transmission is selectively blocked, leaving the physiological action unaffected. To achieve this goal, I am currently investigating the specific cellular and molecular signaling processes that cause the aberrant changes of glutamate transmission with two independent research projects, as summarized in the following working model:




**Cell death signals induce the aberrant changes of synaptic transmission**

(**A**) Under physiological conditions, excitatory neurotransmitter glutamate releases from the pre-synaptic terminals through synaptic vesicle fusion events, in which Epac, an exchange factor directly activated by cAMP, is involved. Released glutamate binds to its receptors on the post-synaptic sites. One of the principle glutamate receptors is NMDA receptor. Activation of NMDA receptor allows physiological $Ca^{2+}$ influx and in turn induces gene expression, neuronal growth, synaptic transmission and plasticity. (**B**) I have two independent research projects on the aberrant changes of synaptic transmission. Project one is targeting to the pre-synaptic terminals, in which Epac mutation deteriorates glutamate release event. We have recently generated the mutant mice with deficiency in expression of Epac genes, and found that declined synaptic transmission links to the learning and social behavioral deficits in the Epac mutants. Project two is focusing on the post-synaptic glutamate receptors. We have discovered that ischemia recruits DAPK1, death-associated protein kinase 1, into the NMDA receptor complex, and induces toxic $Ca^{2+}$ influx through the receptor channels. We have thus generated the null mutant mice lacking the DAPK1 gene and found that genetic deletion of DAPK1 protects against brain cell death from diseases.

## RESEARCH INTERESTS AND GOAL

I am interested in identifying and characterizing the specific cellular and molecular signaling processes that cause the aberrant changes of synaptic transmission and in applying this knowledge to develop practical strategies in the treatment of Alzheimer's disease and stroke.

## AWARDS AND RECOGNITION

• 2000-2006 New Investigator Award by Canada Institute for Health Research
• 2000-2005 Research Scholar Award by Alberta Heritage Foundation for Medical Research
• 1999-2001 Senior Research Fellowship by Canada Institute for Health Research
• 1997-1999 Tenable Merit Scholarship by University of Toronto
• 1997-1999 Laidlaw First Award by University of Toronto
• 1998-1999 Siminovitch Outstanding Research Award by University of Toronto.
• 1998 Joe A. Connolly Memorial Outstanding Research Award by University of Toronto
• 1996-1999 Doctoral Research Award by Medical Research Council of Canada
• 1991-1993 Postdoctoral Fellow by Ciba Foundation, Switzerland

## KEY PAPERS


- Kim, D., Frank, C.L., Dobbin, M.M., W. Tu., Peng, L.S., Lee, B-H., Giusti, P., Broodie, N., Mazitschek, R., Lu, Y and Tsai L-H (2008) Deregulation of HDAC1 by p25/cdk5 in neurotoxicity. Neuron 60, 801-817
- Peng, P.L., Zhong, X.F., Tu, W.H., Soundarapandian, M.M., Molner, P., Zhu, D.Y., Liu, S.H., and Lu, Y.M (2006) ADAR2-Dependent RNA Editing of AMPA Receptor Subunit GluR2 Determines Vulnerability of Neurons in Forebrain Ischemia. Neuron 49, 719-733.
- Liu, S.H., Lau, L., Wei, J.S., Zhu, D.Y., Zou, S., Sun, H.S., Fu, Y.P., Liu, F and Lu, Y.M (2004) Expression of Ca2+-permeable AMPA Receptor Channels Primes Cell Death in Transient Forebrain Ischemia. Neuron 43, 43-55
- Zhu, D.Y., Lau, L., Liu, S.H,. Wei, J.S and Lu, Y.M (2004) Activation of cAMP response element binding protein (CREB) after focal cerebral ischemia stimulates neurogenesis in the adult dentate gyrus. Proc. Natl. Acad. Sci. USA. 101, 9453-9457
- Wang, J., Liu, S.H., Fu, Y.P., Wang, J.H and Lu, Y.M (2003) Cdk5 activation induces CA1 pyramidal cell death by direct phosphorylating NMDA receptors. Nat. Neurosci. 6, 1039-1047
- Wang, J., Liu, S.H., Tu, W.H., Cochrane, K., Tran, L., Paw, J., Fu, Y.P and Lu, Y.M (2003) Interaction of calcineurin and GABAA receptor- γ2 subunit produces long-term depression at CA1 inhibitory synapses. J. Neurosci. 23, 826-836
- Liu, S.H., Wang, J and Lu, Y.M (2003) Generation of functional inhibitory neurons in the adult hippocampus. J. Neurosci. 23, 732-736.
- Zhu, D.Y., Liu, S.H., Sun, S.H and Lu, Y.M (2003) Expression of inducible nitric oxide synthase after focal cerebral ischemia stimulates neurogenesis in the adult animal dentate gyrus. J. Neurosci. 23, 223-229.
- Huang, Y.Q., Lu, W.Y., Ali, D.W., Pelkey, K.A., Pitcher, G.M., Lu, Y.M., Aoto, H., Roder, J.C., Sasaki, T., Salter, M.W and MacDonald, J.F (2001) CAK/Pyk2 Kinase Is a Signaling Link for Induction of Long-Term Potentiation in CA1 Hippocampus. Neuron 9, 485-496.
- Lu, Y.M., Mansuy, I.M., Kandel, E.R., and Roder, J. (2000). Calcineurin-mediated LTD of GABAergic inhibition underlies the increased excitability of CA1 neurons associated with LTP. Neuron 26, 197-205
- Lu, Y.M., Roder, J., Davidow, J., and Salter, M.W. (1998). Src activation in the induction of long-term potentiation in CA1 hippocampal neurons. Science 279, 1363-1967


## ACTIVE FUNDING


- R01 NS051383 (PI: Lu) 03/2006 – 02/2011 NIH/NINDS
  ADAR2-dependent RNA editing of AMPA receptor subunit GluR2 in ischemia

- R01 AG033282 (PI: Lu) 08/2008 - 07/2013 NIH/NIA
  DAPK1 regulation of NMDA receptor in ischemic neuronal death