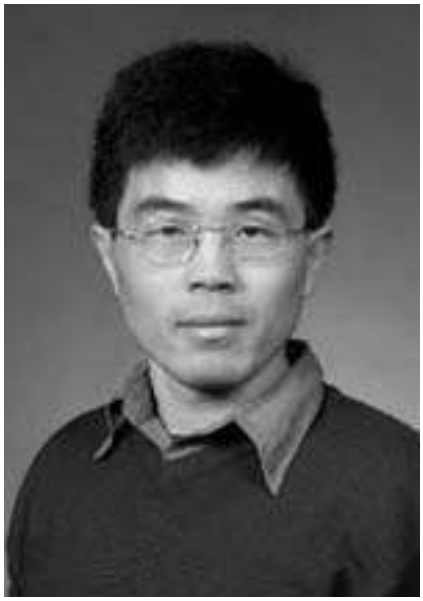
Houhui Xia, MSc, PhD
Assistant Professor of Cell Biology & Anatomy, and Neuroscience



Education

1998-2003 Postdoc, Stanford University
1993-1997 PhD, University of California, San Francisco, CA
1989-1992 MSc , University of Minnesota, Twin Cities
1984-1988 BSc, Peking University, Beijing, China

Positions

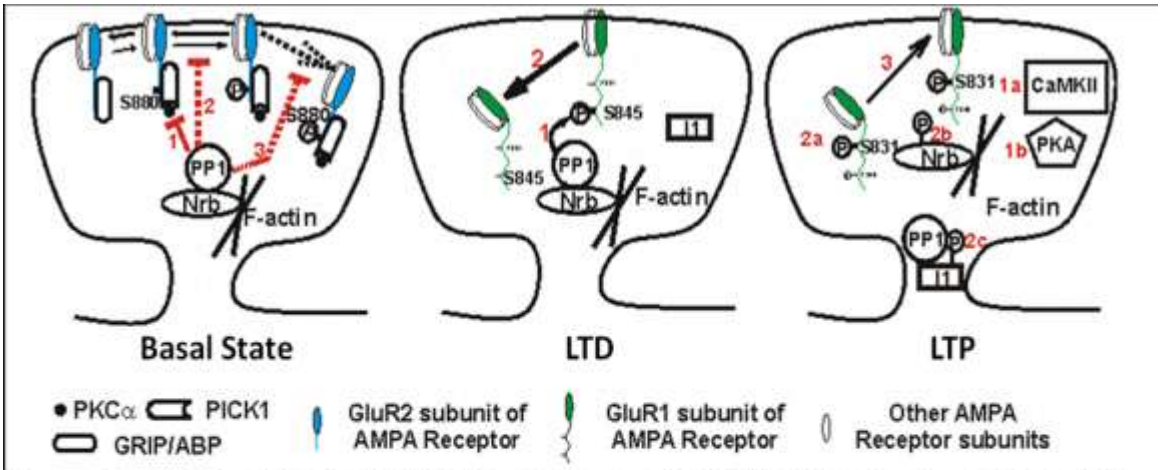
2003 – present Assistant Professor of Cell Biology and Anatomy, and Neuroscience; Neuroscience Center,
LSU Health Sciences Center, New Orleans, LA

2002-2003 Postdoctoral fellow; Department of Molecular and Cellular Physiology, Stanford University, CA
1998-2002 Postdoctoral fellow; Department of Psychiatry, Stanford University, CA;

Current Research

<u>NMDA receptor signaling, protein phosphatase-1 (PP1) and CREB mediated gene transcription</u>

Synapse has been shown to undergo persistent modifications in response to different patterns of activity and this change has been hypothesized to underlie the experience-dependent modifications in our brain, including learning and memory. We are currently focusing on the reversible phosphorylation mechanisms of synaptic plasticity, playing critical roles in both short term modifications in the synaptic protein composition (see schematics below) and in CREB mediated gene transcription process which provides new proteins for long term modification of the synapses. We use primary hippocampal cultures and organotypic hippocampal slice culture as our model systems to address these questions. Techniques used include electrophysiological recordings of synaptic transmission, molecular biology for manipulating genes involved in the signaling pathway from NMDA receptor activation to synaptic strength medication and confocal/two-photon microscopy for localization studies of key proteins in these pathways. The results from our study will provide insights in therapeutic interventions in many diseases in which synaptic functions are compromised, for example, mental retardation and epilepsy.



Our working model on teh role of PP1 binding protein neurabin (Nrb) in bidirectional synaptic plasticity. *Basal State*: Nrb-targeted PP1 inhibits PKCα (Step 1), thus indirectly blocks GluR2 phosphorylation at serine 880 (Step 2) and the decrease of GluR2 surface expression (Step 3). During *LTD*, Nrb-targeted PP1 dephosphorylate GluR1 at serine 845 (Step 1), leading to AMPA Receptor endocytosis (Step 2). *LTP* stimulus activates CaMKII (Step 1a) and PKA (Step 1b). CaMKII phosphorylates GluR1 at serine 831 (Step 2a) while PKA phosphorylates Nrb at serine 461 (Step 2b) and I1 at threonine 35 (Step 2c), resulting in transfer of PP1 from Nrb to I1 and subsequent PP1 inhibition by I1. Inhibition of PP1 thus will relieve CaMKII inactivation and GluR1 dephosphorylation, leads to AMPA receptor surface insertion (Step 3).

Research Interests and Goals

Molecular mechanisms of synaptic plasticity: NMDA receptor signaling and CREB mediated gene transcription

Awards/Recognitions/Lectures

2006-2008	NARSAD Young investigator award
2004-2006	NARSAD Young investigator award
1999-2002	NRSA Individual Postdoctoral F32 Fellowship, Stanford University (RC Malenka, Preceptor)
1995	NIH predoctoral training fellow, UCSF (DS Bredt, Preceptor)
1984	Freshman math competition prize, 1984 Peking University, China

Key Recent Papers

Gao J., Siddoway B., Huang Q. and **Xia, H**. Inactivation of CREB mediated gene transcription by HDAC targeted protein phosphatase. Biochem Biophys Res Commun. (2009) 379:1-5.

Hu XD, Huang Q, Yang X and **Xia, H.** Differential regulation of AMPA receptor trafficking by neurabin-targeted synaptic protein phosphatase-1 in synaptic transmission and long-term depression in hippocampus Journal of Neuroscience (2007) 27:4674-86

Hu XD, Huang Q, Roadcap DW, Shenolikar SS and **Xia, H**. Actin-associated neurabin-protein phosphatase-1 complex regulates hippocampal plasticity. Journal of Neurochemistry (2006) 98:1841-51.

Deisseroth K, Mermelstein PG, **Xia H** and Tsien RW. Signaling from synapse to nucleus: the logic behind the mechanisms. Curr Opin Neurobiol (2003) 13:76-80.

Xia H, von Zastrow M, Malenka RC. A novel anterograde trafficking signal present in the N-terminal extracellular domain of ionotropic glutamate receptors. J Biol Chem (2002) 277:47765-47769.

Braithwaite S, **Xia H**, Malenka RC. Differential Roles of NSF and GRIP in AMPA receptor cycling. Proc Natl Acad Sci USA (2002) 99:7096-7101.

Morishita W, Connor JH, **Xia H**, Quinlan E, Shenolikar S, Malenka RC. Regulation of synaptic strength by protein phosphatase 1 Neuron (2001) 32:1133-1148.

Xia H, Hornby ZD, Malenka RC. An ER retention signal explains differences in surface expression of NMDA and AMPA receptor subunits. Neuropharmacology (2001) 41:714-723.

Lüscher C, **Xia H**, Beattie EC, Carroll RC, von Zastrow M, Malenka RC, Nicoll RA. Role of AMPA receptor cycling in synaptic transmission and plasticity. Neuron (1999) 24:649–658.

Funding

"Distinct roles of Neurabin and Spinophilin in Synaptic Transmission and Plasticity"
Principal Investigator: Houhui Xia, Ph.D.
Agency: NINDS/NIH (R01 NS 060879-01A2). Period: 03/01/2009-02/28/2014

"Neurabin and Inhibtor-1 compete for PP1 binding in LTD and LTP expression"
Principal Investigator: Houhui Xia, Ph.D.
Agency: National Science Foundation (IOS-0824393). Period: 09/01/2008-08/31/2011