BIOGRAPHICAL SKETCH

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NAME: WEI, JING

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

POSITION TITLE: Assistant Scientific Investigator

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Anhui University , Hefei	B.S.	07/2005	life science
Southeast University , Nanjing	Ph.D.	03/2011	neuroscience, genetics
SUNY- Buffalo, NY	Postdoctoral Fellow	12/2013	neuroscience

A. Personal Statement

My primary research interest is to understand the molecular and cellular basis underlying psychiatric disorders of neurodevelopmental origin, including autism spectrum disorders. I graduated from Southeast University in China with a PhD degree in *Genetic*s in 2011. My PhD thesis project, however, was conducted in Dr. Zhen Yan's laboratory at SUNY-Buffalo (2008-2011). During my graduate study, I received rigorous and systemic training in stress and stress-induced maladaptive changes of the brain circuits. My projects focused on how neuromodulators and disease susceptibility genes engage specific molecular and cellular substrates to shape synaptic circuit connectivity in the brain. I have used electrophysiological, biochemical, molecular and pharmacological approaches combined with murine behavioral assays to tackle a few very challenging questions related to both acute and chronic stress. I was also an integral part of a concerted lab research effort investigating the role of Shank3 protein in an autism mouse model. My productivity is reflected by 22 publications authored or coauthored in many solid scientific journals, with an H-Index of 14 and 569 total citations so far.

1. Wei J, Xiong Z, Lee JB, Cheng J, Duffney LJ, Matas E, Yan Z. Histone Modification of Nedd4 Ubiquitin Ligase Controls the Loss of AMPA Receptors and Cognitive Impairment Induced by Repeated Stress. J Neurosci. 2016 Feb 17;36(7):2119-30. PubMed PMID: 26888924; PubMed Central PMCID: PMC4756151.
2. Wei J, Yuen EY, Liu W, Li X, Zhong P, Karatsoreos IN, McEwen BS, Yan Z. Estrogen protects against the detrimental effects of repeated stress on glutamatergic transmission and cognition. Mol Psychiatry. 2014 May;19(5):588-98. PubMed PMID: 23835908.
3. Wei J, Graziane NM, Wang H, Zhong P, Wang Q, Liu W, Hayashi-Takagi A, Korth C, Sawa A, Brandon NJ, Yan Z. Regulation of N-methyl-D-aspartate receptors by disrupted-in-schizophrenia-1. Biol Psychiatry. 2014 Mar 1;75(5):414-24. PubMed PMID: 23906531; PubMed Central PMCID: PMC3864617.
4. Yuen EY, Wei J, Liu W, Zhong P, Li X, Yan Z. Repeated stress causes cognitive impairment by suppressing glutamate receptor expression and function in prefrontal cortex. Neuron. 2012 Mar 8;73(5):962-77. PubMed PMID: 22405206; PubMed Central PMCID: PMC3302010.

B. Positions and Honors

Positions and Employment

2008 - 2011 Research Scientist, University at Buffalo, Buffalo, NY
2011 - 2013 Postdoctoral Associate, University at Buffalo, Buffalo, NY
2013 - 2016 Research Associate, Buffalo VA Medical Center, Buffalo, NY
2014 - 2016 Research Assistant Professor, University at Buffalo, Buffalo, NY

April 2017 - Assistant Scientific Investigator, University of Arizona, Phoenix, AZ

Other Experience and Professional Memberships

2009 - Member, Society for Neuroscience
2013 - Affiliate Member, National Postdoctoral Association

C. Contribution to Science

1. **Stress-induced maladaptive changes in the developing brain circuits:** Stress is a proven precursor to many chronic conditions, such as major depression and post-traumatic stress disorders (PTSD), often exacerbating existing illnesses. Considering that juveniles are more vulnerable to stress compared to adults, it is critical to study the underlying molecular mechanism for stressed adolescents. As a postdoctoral fellow, I was able to show that repeated stress dampened prefrontal cortex (PFC) glutamatergic transmission by facilitating glutamate receptor turnover in juvenile male rats, which caused the detrimental effect on PFC-dependent cognitive processes. The effects are dependent on activation of glucocorticoid receptors and the subsequent ubiquitin/proteasome-mediated degradation. In the follow-up study, I identified histone deacetylase 2 (HDAC2) as a key regulator for the glucocorticoid receptors-induced upregulation of Nedd4-1 expression in PFC in response to repeat stress. Moreover, I found that estrogen protects against the detrimental effects of stress on glutamatergic transmission and PFC-dependent cognition in juvenile females.

    a. Seo JS, **Wei J,** Qin L, Kim Y, Yan Z, Greengard P. Cellular and molecular basis for stress-induced depression. *Mol Psychiatry.* 2016 Jul 26;PubMed PMID: 27457815; PubMed Central PMCID: PMC5269558.
    b. **Wei J,** Xiong Z, Lee JB, Cheng J, Duffney LJ, Matas E, Yan Z. Histone Modification of Nedd4 Ubiquitin Ligase Controls the Loss of AMPA Receptors and Cognitive Impairment Induced by Repeated Stress. *J Neurosci.* 2016 Feb 17;36(7):2119-30. PubMed PMID: 26888924; PubMed Central PMCID: PMC4756151.
    c. **Wei J,** Yuen EY, Liu W, Li X, Zhong P, Karatsoreos IN, McEwen BS, Yan Z. Estrogen protects against the detrimental effects of repeated stress on glutamatergic transmission and cognition. *Mol Psychiatry.* 2014 May;19(5):588-98. PubMed PMID: 23835908.
    d. Yuen EY, **Wei J,** Liu W, Zhong P, Li X, Yan Z. Repeated stress causes cognitive impairment by suppressing glutamate receptor expression and function in prefrontal cortex. *Neuron.* 2012 Mar 8;73(5):962-77. PubMed PMID: 22405206; PubMed Central PMCID: PMC3302010.

2. **Regulation of glutamatergic synaptic transmission by DISC1, a major risk factor for schizophrenia:** Disrupted in schizophrenia 1 is a protein that in humans is encoded by the *DISC1* gene. Emerging studies have suggested that genetic variations of DISC1 and specific endophenotypes that are commonly associated with schizophrenia, depression and bipolar disorder. In Dr. Yan's lab, I examined the effect of DISC1 on NMDAR-mediated synaptic response and GABAergic transmission in cortical pyramidal neurons. I found that cellular knockdown DISC1 significantly increased NMDAR currents and the expression of NMDAR subunit, NR2A in cortical neurons. In addition, I discovered that DISC1 exerted an effect on GABAergic inhibitory transmission by regulating KIF5/microtubule-based GABAAR trafficking in the cortical neurons.

    a. **Wei J,** Graziane NM, Gu Z, Yan Z. DISC1 Protein Regulates γ-Aminobutyric Acid, Type A (GABAA) Receptor Trafficking and Inhibitory Synaptic Transmission in Cortical Neurons. *J Biol Chem.* 2015 Nov 13;290(46):27680-7. PubMed PMID: 26424793; PubMed Central PMCID: PMC4646017.
    b. **Wei J,** Graziane NM, Wang H, Zhong P, Wang Q, Liu W, Hayashi-Takagi A, Korth C, Sawa A, Brandon NJ, Yan Z. Regulation of N-methyl-D-aspartate receptors by disrupted-in-schizophrenia-1. *Biol Psychiatry.* 2014 Mar 1;75(5):414-24. PubMed PMID: 23906531; PubMed Central PMCID: PMC3864617.

3. **Autism mouse model: *Shank3* knockout mouse model.** Autism is a developmental disorder characterized by impaired social interaction and repetitive behavior, may first identified in infants and

toddlers, and the prevalence in the United States is estimated at 1 in 68 births. Although autism costs U.S. citizens $236-262 billion annually, there is no specific treatment recommendations. Recent genetic studies have demonstrated that insufficiency of *Shank3* gene are associated with autism spectrum disorders. As a research assistant professor in Dr. Yan's lab, I participated in discovering the mechanisms and critical molecules involved in Shank3 regulation of NMDAR function. We found that *Shank3* mutation impaired NMDA receptor function in rat cortical cultures. Moreover, we also found that Shank3-deficient mice exhibit social deficits and diminished NMDA receptor synaptic function and synaptic distribution in prefrontal cortex, which was rescued by targeting actin regulators. The following publications demonstrate my contribution to the autism-related projects.

a. Duffney LJ, Zhong P, **Wei J,** Matas E, Cheng J, Qin L, Ma K, Dietz DM, Kajiwara Y, Buxbaum JD, Yan Z. Autism-like Deficits in Shank3-Deficient Mice Are Rescued by Targeting Actin Regulators. *Cell Rep.* 2015 Jun 9;11(9):1400-13. PubMed PMID: 26027926; PubMed Central PMCID: PMC4464902.
b. Duffney LJ, **Wei J,** Cheng J, Liu W, Smith KR, Kittler JT, Yan Z. Shank3 deficiency induces NMDA receptor hypofunction via an actin-dependent mechanism. *J Neurosci.* 2013 Oct 2;33(40):15767-78. PubMed PMID: 24089484; PubMed Central PMCID: PMC3787498.

4. **Other collaborative projects.** Huntington's disease (HD) is a devastating neurological disorder characterized by uncontrolled movements. Growing evidence suggests that HD is caused by the mutant huntingtin (htt) with an expanded polyglutamine (polyQ) repeat. In order to determine whether excitatory and inhibitory synaptic transmission synaptic inhibition is impaired in a mouse model of HD, we utilized electrophysiological and biochemical approaches, and identified that $GABA_AR$ or GluR2/huntingtin associated protein1 (HAP1)/kinesin family motor protein 5 (KIF5) complex was disrupted and dissociated from microtubules in the HD mouse model. Glycogen synthase kinase 3 (GSK-3) is a multifunctional kinase implicated in neuronal development, mood stabilization, and neurodegeneration. My PhD dissertation examined the impact of GSK-3 on AMPA receptor (AMPAR) channels, the major mediator of excitatory transmission, and found that GSK-3 regulates Rab5-mediated endocytosis of AMPAR via altering the GDI-Rab5 complex in cortical neurons.

a. Deng Y, Xiong Z, Chen P, **Wei J,** Chen S, Yan Z. β-amyloid impairs the regulation of N-methyl-D-aspartate receptors by glycogen synthase kinase 3. *Neurobiol Aging.* 2014 Mar;35(3):449-59. PubMed PMID: 24094580.
b. Yuen EY, **Wei J,** Zhong P, Yan Z. Disrupted GABAAR trafficking and synaptic inhibition in a mouse model of Huntington's disease. *Neurobiol Dis.* 2012 May;46(2):497-502. PubMed PMID: 22402331; PubMed Central PMCID: PMC3323696.
c. Mandal M, **Wei J,** Zhong P, Cheng J, Duffney LJ, Liu W, Yuen EY, Twelvetrees AE, Li S, Li XJ, Kittler JT, Yan Z. Impaired alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor trafficking and function by mutant huntingtin. *J Biol Chem.* 2011 Sep 30;286(39):33719-28. PubMed PMID: 21832090; PubMed Central PMCID: PMC3190808.
d. **Wei J,** Liu W, Yan Z. Regulation of AMPA receptor trafficking and function by glycogen synthase kinase 3. *J Biol Chem.* 2010 Aug 20;285(34):26369-76. PubMed PMID: 20584904; PubMed Central PMCID: PMC2924064.

Complete List of Published Work in My Bibliography:
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