

Principal Investigator/Program Director
(Last, First, Middle)

Akiko Hayashi-Takagi

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.

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NAME Akiko Hayashi-Takagi	POSITION TITLE Full professor		
eRA COMMONS USER NAME ahavash4			
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing,</i>			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Gunma University Graduate School of Medicine	M.D	1999	Medicine
Gunma University Graduate School of Medicine	Ph.D.	2005	Medicine

Positions and Employment

1999-2001	Medical Residency, Psychiatry, Gunma University Graduate School of Medicine, Japan
2001-2007	Seimou Hospital, Japan, attending (2 days/week)
2005-2007	Postdoctoral fellow, Lab for Molecular Dynamics of Mental Disorders, RIKEN, Japan
2007-2010	Postdoctoral fellow/Research associate, Department of Psychiatry, Johns Hopkins University School of Medicine, USA
2010-2016	Assistant professor, Center for Disease Biology and Integrative Medicine, Faculty of Medicine, The University of Tokyo, Japan
2016-present	Full professor, Lab of Medical Neuroscience, Institute for Molecular and Cellular Regulation, Gunma University

Honors

2008	Young investigator award, NARSAD, USA
2010	Academic Award, Japanese Society of Biological Psychiatry
2015	Young Investigator Award, Japan Neuroscience Society

A. Publications (CA, corresponding author)**Original paper**

- Hayashi-Takagi A (CA), Yagishita S, Nakamura M, Shirai F, Wu Y, Loshbaugh AL, Kuhlman B, Hahn KM, Kasai H. **Labelling and optical erasure of synaptic memory traces in the motor cortex.** *Nature* (Article): in press (2015)
- Yagishita S, Hayashi-Takagi A, Ellis-Davies GCR, Urakubo H, Ishii S, Kasai H. **A critical time window for dopamine actions on the structural plasticity of dendritic spines.** *Science* 345(6204):1616-20 (2014)

3. Hayashi-Takagi A, Araki Y, Nakamura M, Vollrath B, Duron SG, Yan Z, Kasai H, Haganir RL, Campbell DA, Sawa A. **PAKs inhibitors ameliorate schizophrenia-associated dendritic spine deterioration in vitro and in vivo during late adolescence.**
Proc Natl Acad Sci USA 111 (17): 6461-6466 (2014)
4. Miyazaki J, Tsurui H, Hayashi-Takagi A, Kasai H, Kobayashi T. **Sub-diffraction resolution pump-probe microscopy with shot-noise limited sensitivity using laser diodes.**
Optics EXPRESS 22 (8): 9024-9032 (2014)
5. 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 75 (5):414-424 (2014)
6. Hayama T, Noguchi J, Watanabe S, Ellis-Davies GCR, Hayashi-Takagi A, Takahashi N, Matsuzaki M. & Kasai H. **GABA promotes the competitive selection of dendritic spines by controlling local Ca²⁺ signaling.**
Nat Neuroscience 16 (10):1409-1416 (2013)
7. Kato T, Hayashi-Takagi A, Toyota T, Yoshikawa T, Iwamoto K. **Gene expression analysis in lymphoblastoid cells as a potential biomarker of bipolar disorder.**
J Hum Genet. 56 (11): 779-783 (2011)
8. Koga M, Serritella AV, Messmer MM, Hayashi-Takagi A, Hester LD, Snyder SH, Sawa A, Sedlak TW. **Glutathione is a physiologic reservoir of neuronal glutamate.**
Biochem Biophys Res Commun. 409 (4): 596-602 (2011)
9. Ishizuka K, Kamiya A, Oh EC, Kanki H, Seshadri S, Robinson JF, Murdoch H, Dunlop AJ, Kubo K, Furukori K, Huang B, Zeledon M, Hayashi-Takagi A, Okano H, Nakajima K, Houslay MD, Katsanis N, Sawa A. **DISC1-dependent switch from progenitor proliferation to migration in the developing cortex.**
Nature 473 (7345): 92-96 (2011)
10. Wang Q, Charych EI, Pulito VL, Lee JB, Graziane NM, Crozier RA, Revilla-Sanchez R, Kelly MP, Dunlop AJ, Murdoch H, Taylor N, Xie Y, Pausch M, Hayashi-Takagi A, Ishizuka K, Seshadri S, Bates B, Kariya K, Sawa A, Weinberg RJ, Moss SJ, Houslay MD, Yan Z, Brandon NJ. **The psychiatric disease risk factors DISC1 and TNK1 interact to regulate synapse composition and function.**
Mol Psychiatry 16 (10):1006-1023 (2011)
11. Hayashi-Takagi A, Takaki M, Graziane N, Seshadri S, Murdoch H, Dunlop AJ, Makino Y, Seshadri AJ, Ishizuka K, Srivastava DP, Xie Z, Baraban JM, Houslay MD, Tomoda T, Brandon NJ, Kamiya A, Yan Z, Penzes P, Sawa A. **Disrupted-in-Schizophrenia-1 (DISC1) regulates spines of the glutamate synapse via Rac1.**
Nat Neuroscience 13(3): 327-332(2010)
12. Seshadri S, Kamiya A, Groh B, Prikulus I, Kano S, Hayashi-Takagi A, Ishizuka K, Wong P, Korth C, Anton E, and Sawa A. **Disrupted-in-Schizophrenia-1 expression is regulated by Neuregulin signaling: involvement of Neuregulin, ErbB receptors, Akt, and BACE1.**
Proc Natl Acad Sci USA 107 (12): 5622-5627 (2010)
13. Yasumoto F, Hayashi A, Kamiya A, Negishi T, Yoshikawa Y, Sawa A. **Genetic manipulation of brain cultures from the primates: a novel tool for molecular studies of neuropsychiatric disorders.**
Mol Psychiatry 13(2): 116-118 (2008)
14. Sawamura N, Ando T, Maruyama Y, Fujimuro M, Mochizuki H, Honjo K, Shimoda M, Toda H, Sawamura-Yamamoto T, Makuch LA, Hayashi A, Ishizuka K, Cascella NG, Kamiya A, Ishida N, Tomoda T, Hai T, Furukubo-Tokunaga K, Sawa A. **Nuclear DISC1 regulates CRE-mediated gene transcription and sleep homeostasis in the fruit fly.**
Mol Psychiatry 13(12):1138-1148 (2008)

15. Hayashi A, Kasahara T, Kametani M, Toyota T, Yoshikawa T, Kato T. **Aberrant endoplasmic reticulum stress response in lymphoblastoid cells from patients with bipolar disorder.**
Int J Neuropsychopharmacol. 12 (1): 33-43 (2009)
16. Hayashi A, Kasahara T, Kametani M, Kato T. **Attenuated BDNF-induced upregulation of GABAergic markers in neurons lacking Xbp1.**
Biochem Biophys Res Commun. 376(4): 758-763 (2008)
17. Hayashi A, Kasahara T, Iwamoto K, Ishiwata M, Kametani M, Kakiuchi C, Furuichi T, Kato T. **The role of brain-derived neurotrophic factor (BDNF)-induced XBP1 splicing during brain development.**
J Biol Chem. 282(47): 34525-34534 (2007)
18. Kakiuchi C, Ishiwata M, Hayashi A, Kato T. **XBP1 induces WFS1 through an endoplasmic reticulum stress response element-like motif in SH-SY5Y cells.**
J Neurochem. 97(2): 545-555 (2006)
19. Ohnishi H, Kaneko Y, Okazawa H, Miyashita M, Sato R, Hayashi A, Tada K, Nagata S, Takahashi M, Matozaki T. **Differential localization of Src homology 2 domain-containing protein tyrosine phosphatase substrate-1 and CD47 and its molecular mechanisms in cultured hippocampal neurons.**
J Neurosci. 25(10): 2702-2711 (2005)
20. Miyashita M, Ohnishi H, Okazawa H, Tomonaga H, Hayashi A, Fujimoto TT, Furuya N, Matozaki T. **Promotion of neurite and filopodium formation by CD47: roles of integrins, Rac, and Cdc42.**
Mol Biol Cell 15(8): 3950-3963 (2004)
21. Hayashi A, Ohnishi H, Okazawa H, Nakazawa S, Ikeda H, Motegi S, Aoki N, Kimura S, Mikuni M, Matozaki T. **Positive regulation of phagocytosis by SIRPbeta and its signaling mechanism in macrophages.**
J Biol Chem. 279(28): 29450-29460 (2004)
22. Sato R, Ohnishi H, Kobayashi H, Kiuchi D, Hayashi A, Kaneko Y, Honma N, Okazawa H, Hirata Y, Matozaki T. **Regulation of multiple functions of SHPS-1, a transmembrane glycoprotein, by its cytoplasmic region.**
Biochem Biophys Res Commun. 309(3): 584-590 (2003)

Review paper

1. Hayashi-Takagi A (CA), Vawter MP, Iwamoto K. **Peripheral biomarkers revisited: Integrative profiling of peripheral samples for psychiatric research.**
Biol Psychiatry 75 (12): 920-928 (2014)
2. Hayashi-Takagi A, Barker PB, Sawa A. **Readdressing synaptic pruning theory for schizophrenia: Combination of brain imaging and cell biology.**
Commun Integr Biol. 4 (2): 211-212 (2011)
3. Hayashi-Takagi A (CA), Sawa A. **Disturbed synaptic connectivity in schizophrenia: convergence of genetic risk factors during neurodevelopment.**
Brain Res Bull. 83 (3): 140-146 (2010)
4. Kasai H, Fukuda M, Watanabe S, Hayashi-Takagi A, Noguchi J. **Structural dynamics of dendritic spines in memory and cognition.**
Trends Neuroscience 33(3): 121-129 (2010)
5. Seshadri AJ, Hayashi-Takagi A (CA). **Gene manipulation with use of stereotaxic viral infection for psychiatric research: spatiotemporal components for schizophrenia.**
Prog Brain Res. 179: 17-27 (2009)

6. Jaaro-Peled H, Hayashi-Takagi A, Seshadri S, Kamiya A, Brandon NJ, Sawa A. **Neurodevelopmental mechanisms of schizophrenia: understanding disturbed postnatal brain maturation through Neuregulin-1 and DISC1.**

Trends Neuroscience 32 (9): 485-495 (2009)

B. Research Support

Ongoing Research Support

Scientific Research on Innovative Areas (Research in a proposed research area), Japan (2012-2017)

Examination of the dendritic spine of disease related mouse models and patient derived iPS cells

¥60,100,000

Role: PI

Grant-in-Aid for Scientific Research (B) (26293260), Japan (2014-2018)

Neurocomputation of schizophrenia pathophysiology based on the two-photon synaptic imaging in vivo.

¥14,000,000

Role: PI

Presto, JST, Japan (2015-2019)

Examination of synaptic stress response for the drug discovery of neuropsychiatric disorders.

¥40,000,000

Role: PI

Completed Research Support

Presto, JST, Japan (2010-2014)

Examination of relationship between dendritic spines in the prefrontal cortex and behavioral phenotypes by using optogenetics.

¥40,000,000

Role: PI

Grant-in-Aid for Young Scientist (A) (23689055), Japan (2010-2011)

Simulation of schizophrenia onset by using optogenetics

¥4,810,000

Role: PI

Grant-in-Aid for Young Scientist (B) (18790857), Japan. 4/1/2006-3/31/2007

To make a transgenic mouse, which displays fluorescence in the presence of the endoplasmic stress.

¥1,700,000

Role: PI

Postdoctoral Research Fellowship, Uehara Memorial Foundation, Japan. 4/1/2007-3/31/2008

Elucidation of SZ susceptibility molecular pathway, especially focusing on the protein-protein interaction.

¥3,400,000

Role: PI

Young investigator award, NARSAD, USA. 7/1/2008-6/30/2010

The goal of this project was to investigate the function of schizophrenia related factors on an activity-dependent dendritic spine formation. \$60,000.

Role: PI