

**BIOGRAPHICAL SKETCH**

NAME		POSITION TITLE	
Taisuke Tomita		Professor	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
The University of Tokyo, Tokyo, Japan	B.S.	1995	Pharmaceutical Science
The University of Tokyo, Tokyo, Japan	M.S.	1997	Pharmaceutical Science
The University of Tokyo, Tokyo, Japan	Ph.D.	2000	Pharmaceutical Science
Washington University in St. Louis	Visiting Scientist	2004-2005	Notch Biology

**Positions**

1997-2003	Instructor in Laboratory of Neuropathology and Neuroscience, Graduate School of Pharmaceutical Sciences, The University of Tokyo, Japan
2003-2006	Assistant Professor in Laboratory of Neuropathology and Neuroscience, Graduate School of Pharmaceutical Sciences, The University of Tokyo, Japan
2006-2014	Associate Professor in Laboratory of Neuropathology and Neuroscience, Graduate School of Pharmaceutical Sciences, The University of Tokyo, Japan
2014-present	Professor in Laboratory of Neuropathology and Neuroscience, Graduate School of Pharmaceutical Sciences, The University of Tokyo, Japan
2017-present	Adjunct Professor in Laboratory of Brain and Neurological Disorders, Graduate School of Pharmaceutical Sciences, The University of Tokyo, Japan

**Editor and Editorial Advisory Board**

2006-2015	A member of Editorial Board of Molecular Neurodegeneration
2012-present	A member of Editorial Board of PLoS ONE
2013-present	A member of Editorial Board of the Journal of Biological Chemistry
2016-present	A member of Editorial Board of Scientific Reports
2018-present	A member of Editorial Board of JoVE
2018-present	Associate Editor of Neuroscience Research

**Honors and Awards**

2000-2001	Recipient of the research fellowship from the Tokyo Biochemical Research Foundation
2004-2005	Recipient of JSPS postdoctoral fellowships for research abroad
2010	Presentation Award from Japan Society for Dementia Research
2011	48 <sup>th</sup> Erwin von Balz prize
2013	Basic Research Award from Japan Society for Dementia Research
2015	NAGASE Foundation Award 2015

**Professional Membership**

The Japanese Biochemical Society  
The Pharmaceutical Society of Japan  
Japan Society for Dementia Research (Council from 2007, Auditor from 2017)  
The Molecular Biology Society of Japan  
The Japan Neuroscience Society  
Society for Neuroscience  
The American Society for Biochemistry and Molecular Biology  
ISTAART

International Proteolysis Society (Asian Council from 2016)

**Publications (40 shown of 134)**

- **Tomita T**, Maruyama K, Saido TC, Kume H, Shinozaki K, Tokuhiko S, Capell A, Walter J, Gruenberg J, Haass C, Iwatsubo T, Obata K: The presenilin 2 mutation (N141I) linked to familial Alzheimer disease (Volga German families) increases the secretion of amyloid  $\beta$  protein ending at the 42nd (or 43rd) residue. **Proc Natl Acad Sci USA** 1997;**94**:2025-2030
- **Tomita T**, Tokuhiko S, Hashimoto T, Aiba K, Saido TC, Maruyama K, Iwatsubo T: Molecular dissection of domains in mutant presenilin 2 that mediate overproduction of amyloidogenic forms of amyloid  $\beta$  peptides: Inability of truncated forms of PS2 with familial Alzheimer's disease mutation to increase secretion of A $\beta$ 42. **J Biol Chem** 1998;**273**:21153-21160
- Naruse S, Thinakaran G, Luo J-J, Kusiak JW, **Tomita T**, Iwatsubo T, Qian X, Ginty, DD, Price, DL, Borchelt DR, Wong PC, Sisodia SS: Effects of PS1 deficiency on membrane protein trafficking in neurons. **Neuron** 1998;**17**:1213-1221
- **Tomita T**, Takikawa R, Koyama A, Morohashi Y, Takasugi N, Saido TC, Maruyama K, Iwatsubo T: C terminus of presenilin is required for overproduction of amyloidogenic A $\beta$ 42 through stabilization and endoproteolysis of presenilin. **J Neurosci** 1999;**19**:10627-10634
- Takahashi M, Dore S, Ferris CD, **Tomita T**, Sawa A, Wolosker H, Borchelt DR, Iwatsubo T, Kim S-H, Thinakaran G, Sisodia SS, Snyder SH: Amyloid precursor proteins inhibit heme oxygenase activity and augment neurotoxicity in Alzheimer's disease. **Neuron** 2000;**28**:461-473
- Okochi M, Steiner H, Fukumori A, Tani H, **Tomita T**, Tanaka T, Iwatsubo T, Kudo T, Takeda M, Haass C: Presenilins mediate a dual intramembranous  $\gamma$ -secretase cleavage of Notch-1. **EMBO J** 2002;**21**:5408-5416
- Kamenetz F, **Tomita T**, Seabrook G, Borchelt D, Iwatsubo T, Sisodia S, Malinow R: APP processing and synaptic function. **Neuron** 2003;**37**:925-937
- Takasugi N, **Tomita T**, Hayashi I, Tsuruoka M, Niimura M, Thinakaran G, Takahashi Y, Iwatsubo T: The role of presenilin cofactors in the  $\gamma$ -secretase complex. **Nature** 2003;**422**:438-441
- Takahashi Y, Hayashi I, Tominari Y, Rikimaru K, Morohashi Y, Kan T, Natsugari T, Fukuyama T, **Tomita T**, Iwatsubo T: Sulindac sulfide is a non-competitive  $\gamma$ -secretase inhibitor that preferentially reduces A $\beta$ 42 generation. **J Biol Chem** 2003;**278**:18664-18670
- Schroeter E-H, Ilagan MXG, Brunkan AL, Hecimovic S, Li Y-L, Xu M, Lewis HD, Saxena MT, Coonrod A, **Tomita T**, Iwatsubo T, Moore CL, Shearman M, Goate A, Wolfe MS, Kopan R: A presenilin dimer at the core of the  $\gamma$ -secretase enzyme: Insights from parallel analysis of Notch 1 and APP proteolysis. **Proc Natl Acad Sci** 2003;**100**:13075-13080
- Morohashi Y, Kan T, Tominari Y, Fuwa H, Okamura Y, Watanabe N, Sato C, Natsugari H, Fukuyama T, Iwatsubo T, **Tomita T**: C-terminal fragment of Presenilin is the molecular target of a dipeptidic  $\gamma$ -secretase-specific inhibitor DAPT (N-[N-(3,5-Difluorophenacetyl)-L-alanyl]-S-phenylglycine t-Butyl Ester). **J Biol Chem** 2006;**281**:14670-14676
- Sato C, Morohashi Y, **Tomita T**, Iwatsubo T: Structure of the catalytic pore of  $\gamma$ -secretase probed by the accessibility of substituted cysteines. **J Neurosci** 2006;**26**:12081-12088
- Hsieh H, Boehm J, Sato C, Iwatsubo T, **Tomita T**, Sisodia S, Malinow R: AMPAR removal underlies A $\beta$ -induced synaptic depression and dendritic spine loss. **Neuron** 2006;**52**:831-843
- Fuwa H, Konno Y, Takahashi Y, Sasaki M, Yokoshima S, Kan T, Fukuyama T, Natsugari H, **Tomita T**, Iwatsubo T: Divergent synthesis of multifunctional molecular probes to elucidate the enzyme specificity of dipeptidic  $\gamma$ -secretase inhibitors. **ACS Chem Biol** 2007;**2**:408-418
- Sato C, Takagi S, **Tomita T**, Iwatsubo T: The C-terminal PAL motif and transmembrane domain 9 of Presenilin 1 are involved in the formation of the catalytic pore of the  $\gamma$ -secretase. **J Neurosci** 2008;**28**:6264-6271
- Cheung KH, Shineman D, Müller M, Cárdenas C, Mei L, Yang J, **Tomita T**, Iwatsubo T, Lee VM, Foscett JK: Mechanism of Ca $^{2+}$  disruption in Alzheimer's disease by presenilin regulation of InsP(3) receptor channel gating. **Neuron** 2008;**58**:871-883
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- Watanabe N, Takagi S, Tominaga A, **Tomita T**, Iwatsubo T: Functional analysis of the transmembrane domains of presenilin 1: PARTICIPATION OF TRANSMEMBRANE DOMAINS 2 AND 6 IN THE FORMATION OF INITIAL SUBSTRATE-BINDING SITE OF  $\gamma$ -SECRETASE. **J Biol Chem** 2010;**285**:19738-19746
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- Ohki Y, Higo T, Uemura K, Shimada N, Osawa S, Funamoto S, Ihara Y, Berezovska O, Yokoshima S, Fukuyama T, **Tomita T**, Iwatsubo T: Phenylpiperidine-type  $\gamma$ -secretase modulators target the transmembrane domain 1 of presenilin 1. **EMBO J** 2011;**30**:4815-4824
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- **Tomita T**, Iwatsubo T: Structural biology of presenilins and signal peptide peptidases. **J Biol Chem** 2013;**288**:14673-14680
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