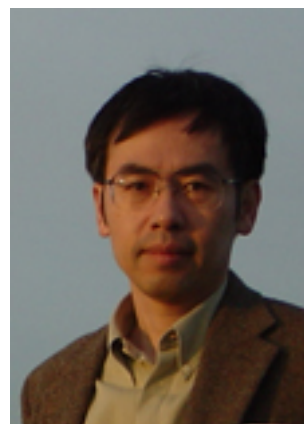


Curriculum Vitae

Name: **Takaomi C. Saido**
Date of Birth: August 7, 1959
Place of Birth: Kobayashi-shi, Miyazaki, JAPAN



Present occupation

Position: Laboratory Head
Institution: Laboratory for Proteolytic Neuroscience
RIKEN Brain Science Institute
2-1 Hirosawa, Wako-shi, Saitama 351-0198
Email: saido@brain.riken.jp
Phone: +81-48-467-9715
Fax: +81-48-467-9716

Education

1978-1982 B.A. University of Tsukuba
1982-1985 & 1986-1988
Ph. D University of Tokyo Graduate School
1985-1986 Visiting Scholar Cornell University

Academic appointments

1988-1997 Research Scientist, Tokyo Metropolitan Institute of Medical Science
1992 Visiting Scientist, Scripps Institute
1997-present Laboratory Head, RIKEN Brain Science Institute
1997-2012 Visiting Professor, Yokohama City Medical School
1997-2006 Visiting Professor, Tohoku University School of Medicine
1999-2009 Visiting Professor, University of Tsukuba School of Medicine
2004 Visiting Professor, University of Nagoya School of Medicine
2005 Visiting Professor, Institute for Frontier Medical Sciences, University of Kyoto
2006 Visiting Professor, Graduate School of Agricultural and Life Sciences, University of Tokyo
2008-present Visiting Professor, Waseda University
2009-2010 Visiting Professor, Japan Women's College

Awards and honors

1985	Rotary International Fellowship
1995	Young Investigator Award, Japanese Biochemical Society
2002	Journal of Biochemistry Excellent Paper Prize
2003	BSI Flagship Prize
2003	Neuroscience Research Excellent Paper Prize
2004	Outstanding contributor award, Alzheimer Research Forum
2007	Toshihiko Tokizane Memorial Award

Memberships and committee assignments in professional societies

1982-present	Japanese Biochemical Society
1984-1986	Japanese Biophysical Society
1993-present	Japanese Pharmaceutical Society
1994-present	Society for Neuroscience, USA
1996-present	Councilor, Japanese Society for Dementia (councilor)
1996- present	Japanese Society for Proteases and Inhibitors
1997- present	Japanese Society for Neuroscience
1998- present	Japanese Society for Neurochemistry

Major research interests

Metabolism of amyloid β peptide in brain
 Pathophysiological roles of calpain in the brain
 Animal models of Alzheimer's disease
 Presymptomatic markers for brain aging and Alzheimer's disease

Publications in international journals (in English only)

1. Toyoshima, S. Saido, T.C., Makishima, F., Osawa, T. (1983). Induction of increased calcium uptake in liposomes having membrane proteins of chicken erythrocytes by S-adenosylmethionine. *Biochem. Biophys. Res. Commun.* 114, 1126-1131.
2. Seki, H., Saido, T.C., Iseki, K., Whitney, F., Wong, S. (1984). Uptake kinetics of micro-organisms in the sulfuretum of Saanich Inlet, British Columbia, Canada. *Arch. Hydrobiol.*, 100, 73-82.
3. Saido, T.C., Toyoshima, S., Osawa, T. (1987). Protein-O-carboxymethyltransferase from cytosol and membranes of chicken erythrocytes. *J. Biochem.* 102, 319-326.
4. Magae, J., Osada, H., Fujiki, H., Saido, T.C., Suzuki, K., Nagai, K., Yamasaki, M., Isono, K. (1990). Morphological changes of human myeloid leukemia K562 cells by a protein phosphatase inhibitor, tautomycin. *Proc. Japan Acad.* 66, 209-212.

5. Osada, S., Mizuno, K., Saido, T.C., Akita, Y., Suzuki, K., Kuroki, T., Ohno, S. (1990). A phorbol ester receptor/protein kinase, nPKC η , a new member of the protein kinase C family predominantly expressed in lung and skin. *J. Biol. Chem.* 265, 22434-22440.
6. Sorimachi, H., Ohmi, S., Emori, Y., Kawasaki, H., Saido, T.C., Ohno, S., Minami, Y., Suzuki, K. (1990). A novel member of the calcium-dependent cysteine protease family. *Biol. Chem. Hoppe-Seyler* 371, 171-176.
7. Kobayashi, Y., Yamamoto, K., Saido, T.C., Kawasaki, H., Oppenheim, J.T., Matsushima, K. (1990). Identification of calcium-activated neutral protease as a processing enzyme of human interleukin 1 α . *Proc. Natl. Acad. Sci. USA* 87, 5548-5552.
8. Ohno, S., Akita, Y., Hata, A., Osada, S., Kubo, K., Konno, Y., Akimoto, K., Mizuno, K., Saido, T.C., Kuroki, T., Suzuki, K. (1991). Structural and functional diversities of a family of signal transducing protein kinases, protein kinase C; two distinct classes of PKC, conventional cPKC and novel nPKC. *Advances in Enzyme Regulation* 31, 287-303.
9. Mori, A., Aizawa, H., Saido, T.C., Kawasaki, H., Mizuno, K., Murofushi, H., Suzuki, K., Sakai, H. (1991). Site-specific phosphorylation by protein kinase C inhibits assembly-promoting activity of microtubule-associated protein. *Biochemistry* 30, 9341-9346.
10. Mizuno, K., Kubo, K., Saido, T.C., Akita, Y., Osada, S., Kuroki, T., Ohno, S., Suzuki, K. (1991). Structure and properties of a ubiquitously expressed protein kinase C, nPKC δ . *Eur. J. Biochem.* 202, 931-940.
11. Saido, T.C., Mizuno, K., Suzuki, K. (1991). Proteolysis of protein kinase C by calpain: effect of acidic phospholipids. *Biomed. Biochim. Acta* 50, 485-489.
12. Osada, S., Mizuno, K., Saido, T.C., Suzuki, K., Kuroki, T., Ohno, S. (1992). A new member of protein kinase C family, nPKC θ , predominantly expressed in skeletal muscle. *Mol. Cell. Biol.* 12, 3930-3938.
13. Suzuki, K., Saido, T.C., Hirai, S. (1992). Modulation of cellular signals by calpain. *Ann. N. Y. Acad. Sci.* 674, 218-227.
14. Saido, T.C., Mizuno, K., Konno, Y., Osada, S., Ohno, S., Suzuki, K. (1992). Purification and characterization of protein kinase C ϵ from rabbit brain. *Biochemistry* 31, 482-490.
15. Saido, T.C., Nagao, S., Shiramine, M., Tsukaguchi, M., Sorimachi, H., Murofushi, H., Tsuchiya, T., Ito, H., Suzuki, K. (1992). Autolytic transition of μ -calpain as resolved by antibodies distinguishing between the pre- and post-autolysis forms. *J. Biochem.* 111, 81-86.
16. Saido, T.C., Shibata, M., Takenawa, T., Murofushi, H., Suzuki, K. (1992). Positive regulation of μ -calpain action by polyphosphoinositides. *J. Biol. Chem.* 267, 24585-24590.
17. Mizuno, K., Saido, T.C., Ohno, S., Tamaoki, T., Suzuki, K. (1993). Staurosporine-related compounds, K252a and UCN-01, inhibit both cPKC and nPKC. *FEBS Lett.* 330, 114-116.
18. Sorimachi, H., Toyama-Sorimachi, N., Saido, T.C., Kawasaki, H., Sugita, H., Miyasaka, M., Arahata, K., Suzuki, K. (1993). Muscle-specific calpain, p94, is degraded by autolysis immediately after translation, resulting in disappearance from muscle. *J. Biol. Chem.* 268, 10593-10605.
19. Yamaura, I., Tani, E., Saido, T.C., Suzuki, K., Minami, N., Maeda, Y. (1993). Calpain-calpastatin system of canine basilar artery in vasospasm. *J. Neurosurg.* 79, 537-543.

20. Saido, T.C., Suzuki, H., Yamazaki, H., Tanoue, K., Suzuki, K. (1993). In situ capture of μ -calpain activation in platelets. *J. Biol. Chem.* 268, 7422-7426.
21. Saido, T.C., Yokota, M., Nagao, S., Yamaura, I., Tani, E., Tsuchiya, T., Suzuki, K., Kawashima, S. (1993). Spatial resolution of fodrin proteolysis in postischemic brain. *J. Biol. Chem.* 268, 25239-25243.
22. Satake, A., Itoh, K., Shimmoto, M., Saido, T.C., Sakuraba, H., Suzuki, Y. (1994). Distribution of lysosomal protective protein in human tissues. *Biochem. Biophys. Res. Commun.*, 205, 38-43
23. Akita, Y., Ohno, S., Yajima, Y., Konno, Y., Saido, T.C., Mizuno, K., Chida, K., Osada, S., Kuroki, T., Kawashima, S., Suzuki, K. (1994). Overexpression of Ca²⁺-independent protein kinase C isozyme, nPKC ϵ increases the secretion of prolactin from thyrotropin-releasing hormone-stimulated rat pituitary GH4C1 cells. *J. Biol. Chem.* 269, 4653-4660.
24. Yokota, M., Saido, T.C., Miyaji, K., Tani, E., Kawashima, S., Suzuki, K. (1994). Stimulation of protein-tyrosine phosphorylation in gerbil hippocampus after global forebrain ischemia. *Neurosci. Lett.* 168, 69-72.
25. Nagao, S., Saido, T.C. (corresponding author), Akita, Y., Tsuchiya, T., Suzuki, K., Kawashima, S. (1994). Calpain-calpastatin interactions in epidermoid carcinoma KB cells. *J. Biochem.* 115, 1178-1184.
26. Sorimachi, H., Saido, T.C., Suzuki, K. (1994). New era of calpain research, discovery of tissue-specific calpains. *FEBS Lett.*, 343, 1-5.
27. Saito, Y., Saido, T.C., Sano, K., Kawashima, S. (1994). The calpain-calpastatin system is regulated differentially during human neuroblastoma cell differentiation to Schwannian and neuronal cells. *FEBS Lett.*, 353, 327-331.
28. Saido, T.C., Nagao, S., Shiramine, M., Tsukaguchi, M., Yoshizawa, T., Sorimachi, H., Ito, H., Tsuchiya, T., Kawashima, S., Suzuki, K. (1994). Distinct kinetics of subunit autolysis in mammalian m-calpain activation. *FEBS Lett.* 346, 263-267.
29. Saido, T.C., Sorimachi, H., Suzuki, K. (1994). Calpain: new perspectives in molecular diversity and physiological-pathological involvement. *FASEB J.*, 8, 814-822.
30. Saido, T.C., Yokota, M., Maruyama, K., Yamao-Harigaya, W., Tani, E., Ihara, Y., Kawashima, S. (1994). Spatial resolution of the primary β -amyloidogenic process induced in postischemic brain. *J. Biol. Chem.* 269, 15253-15257.
31. Hong, D.-h., Huan, J., Ou, B.-r., Yeh, J.-y., Saido, T.C., Cheeke, P.R., Forsberg, N.E. (1995). Protein kinase C isoforms in muscle cells and their regulation by phorbol ester and calpain. *Biochim. Biophys. Acta*, 1267, 45-54.
32. Yoshida, K., Inui, M., Harada, K., Saido, T.C., Sorimachi, Y., Ishihara, T., Kawashima, S., Sobue, K. (1995). Reperfusion of rat heart after brief ischemia induces proteolysis of caldesmon (non-erythroid spectrin or fodrin) by calpain. *Circ. Res.*, 77, 603-610.
33. Mizuno, K., Noda, K., Ueda, Y., Hanaki, H., Saido, T.C., Ikuta, T., Kuroki, T., Tamaoki, T., Hirai, S., Osada, S., Ohno, S. (1995). UCN-01, an anti-tumor drug, is a selective inhibitor of the conventional PKC subfamily. *FEBS Lett.* 359, 259-261.
34. Blomgren, K., Kawashima, S., Saido, T.C., Karlsson, J.-O., Hagberg, H. (1995). Subcellular distribution of calpains and fodrin degradation after neonatal hypoxic ischemia. *Brain Res.*, 684, 143-149.
35. Blomgren, K., McRae, A., Bona, E., Gilland, E., Saido, T.C., Karlsson, J.-O., Hagberg, H. (1995). Degradation of fodrin and MAP2 after neonatal cerebral hypoxic-ischemia. *Brain Res.*, 684, 136-142.

36. Bednarski, E., Vanderklish, P., Gall, C., Saido, T.C., Bahr, B.A., Lynch, G. (1995). Translational suppression of calpain I reduces NMDA-induced spectrin proteolysis and pathophysiology in cultured hippocampal slices. *Brain Res.*, 694, 147-157.
37. Vanderklish P., Saido, T.C., Gall, C., Arai, A., Lynch, G. (1995). Proteolysis of spectrin by calpain accompanies theta-burst stimulation in cultured hippocampal slices. *Mol. Brain Res.*, 32, 25-35.
38. Harigaya, Y., Shoji, M., Kawarabayashi, T., Kanai, M., Nakamura, T., Iizuka, T., Igeta, Y., Saido, T.C., Sahara, N., Mori, H., Hirai, S. (1995). Modified amyloid β -protein ending at 42 or 40 with different solubility accumulates in the brain of Alzheimer's disease. *Biochem. Biophys. Res. Commun.*, 211, 1015-1022.
39. Yokota, M., Saido, T.C., Tani, E., Kawashima, S., Suzuki, K. (1995). Three distinct phases of fodrin proteolysis induced in postischemic hippocampus: involvement of calpain and unidentified protease. *Stroke*, 26, 1901-1907.
40. Igarashi, K., Kaneda, M., Yamaji, A., Saido, T.C., Kikkawa, U., Ono, Y., Inoue, K., Umeda, M. (1995). A novel phosphatidylserine-binding peptide motif defined by an anti-idiotypic monoclonal antibody: localization of phosphatidylserine-specific binding sites on protein kinase C and phosphatidylserine decarboxylase. *J. Biol. Chem.*, 270, 29075-29078.
41. Martin, S.J., O'Brien, G.A., Nishioka, W.K., Mahboubi, A., Saido, T.C., Green, D.R. (1995). Proteolysis of fodrin (nonerythroid spectrin) during apoptosis. *J. Biol. Chem.*, 270, 6425-6428.
42. Saito, Y., Maruyama, K., Saido, T.C., Kawashima, S. (1995). N23K, a gene transiently up-regulated during neuronal differentiation, encodes a precursor protein for a newly identified neuropeptide Nociceptin. *Biochem. Biophys. Res. Commun.*, 217, 539-545.
43. Eto, A., Akita, Y., Saido, T.C. (corresponding author), Suzuki, K., Kawashima, S. (1995). The role of calpain-calpastatin system in thyrotropin releasing hormone-induced selective down-regulation of a protein kinase C isozyme, nPKC ϵ , in rat pituitary GH4C1 cells. *J. Biol. Chem.*, 270, 25115-25120.
44. Du, X., Saido, T.C. (two first authors), Tsubuki, S., Indig, F.E., Williams, M.J., Ginsberg, M.H. (1995). Calpain cleavage of the cytoplasmic domain of the integrin β 3 subunit. *J. Biol. Chem.*, 270, 24146-26152.
45. Saido, T.C., Iwatsubo, T., Mann, D.M.A., Shimada, H., Ihara, Y., Kawashima, S. (1995). Dominant and differential deposition of distinct β -amyloid peptide species, A β N3(pE), in senile plaques. *Neuron*, 14, 457-466.
46. Yamashima, T., Saido, T.C., Takita, M., Miyazawa, A., Yamano, J., Miyakawa, A., Nishijo, H., Ono, T., Yamashita, J., Yoshioka, T. (1996). Transient brain ischemia provokes Ca²⁺ mobilization, PIP2 overexpression and calpain activation prior to delayed CA-1 neuronal death in monkeys. *Eur. J. Neurosci.*, 8, 1932-1944.
47. Kume, H., Maruyama, K., Tomita, T., Iwatsubo, T., Saido, T.C., Obata, K. (1996). Molecular cloning of a novel basic helix-loop-helix protein from the rat brain. *Biochem. Biophys. Res. Commun.*, 219, 526-530.
48. Inomata, M., Hayashi, M., Ohno-Iwashita, Y., Tsubuki, S., Saido, T.C., Kawashima, S. (1996). Involvement of calpain in integrin-mediated signal transduction. *Arch. Biochem. Biophys.*, 328, 129-134.
49. Kanai, Y., Kanai-Azuma, M., Noce, T., Saido, T.C., Shiroishi, T., Hayashi, Y., Yazaki, K. (1996). Identification of two Sox17 mRNA isoforms, with and without the HMG-box region, and their differential expression in mouse spermatogenesis. *J. Cell Biol.*, 133, 667-681.

50. Lemere, C.A., Blusztajn, J.K., Yamaguchi, H., Wisniewski, T., Saido, T.C., Selkoe, D.J. (1996). Sequence of deposition of heterogeneous amyloid β -peptides and apo E in Down syndrome: implications for initial events in amyloid plaque formation. *Neurobiol. Disease*, 3, 16-32.
51. Yokota, M., Saido, T.C., Tani, E., Yamaura, I., Minami, N. (1996). Cytotoxic fragment of amyloid precursor protein accumulates in hippocampus after global forebrain ischemia. *J. Cereb. Blood Flow Metabol.*, 16, 1219-1223.
52. Saito, Y., Maruyama, K., Kawano, J., Yamagishi, K., Saido, T.C., Kawashima, S. (1996). Molecular cloning and characterization of a novel form of neuropeptide precursor gene as a developmentally regulated molecule. *J. Biol. Chem.*, 271, 15615-15622.
53. Saido, T.C., Yamao-Harigaya, W., Iwatsubo, T., Kawashima, S. (1996). Amino- and carboxyl-terminal heterogeneity of β -amyloid peptides deposited in human brain. *Neurosci. Lett.*, 215, 173-176.
54. Iwatsubo, T., Saido, T.C., Mann, D.M.A., Lee, V.M.-Y., Trojanowski, J.Q. (1996). Full-length $A\beta(1-42(43))$ as well as amino-terminally modified and truncated $A\beta(42(43))$ deposit in diffuse plaques. *Am. J. Pathol.*, 149, 1823-1830.
55. Lemere, C.A., Lopera, F., Kosik, K.S., Lendon, C.L., Ossa, J., Saido, T.C., Yamaguchi, H., Ruiz, A., Martinez, A., Madrigal, L., Hincapie, L., Arango L., J.C., Anthony, D.C., Koo, E.H., Goate, A.M., Selkoe, D.J., Arango V., J.C. (1996). The E280A Presenilin 1 mutation leads to a distinct Alzheimer's disease phenotype: Increased $A\beta(42)$ deposition and severe cerebellar pathology. *Nature Medicine*, 2, 1146-1150.
56. Maruyama, K., Tomita, T., Shinozaki, K., Kume, H., Asada, H., Saido, T.C., Ishiura, S., Iwatsubo, T., Obata, K. (1996). Familial Alzheimer's disease-linked mutations at Val717 of amyloid precursor protein are specific for the increased secretion of $A\beta(42(43))$. *Biochem. Biophys. Res. Commun.*, 227, 730-735.
57. Blomgren, K., McRae, A., Elmered, A., Kawashima, S., Saido, T.C., Ono, T., Hagberg, H. (1997). The calpain proteolytic system in neonatal hypoxic-ischemia. *Ann. New York Acad. Sci.*, 825, 104-119.
58. Kuda, T., Shoji, M., Arai, H., Kawashima, S., Saido, T.C. (1997). Reduction of plasma glutamyl aminopeptidase activity in sporadic Alzheimer's disease. *Biochem. Biophys. Res. Commun.*, 231, 526-530.
59. Tomita, T., Maruyama, K., Saido, T.C., Kume, H., Shinozaki, K., Tokuhiko, S., Capell, A., Walter, J., Gruenberg, J., Haass, C., Iwatsubo, T., Obata, K. (1997). The presenilin 2 mutation (N141I) linked to familial Alzheimer's disease (Volga German families) increases the secretion of amyloid β protein ending at $A\beta(42(43))$. *Proc. Nat. Acad. Sci. USA*, 94, 2025-2030.
60. Mann, D.M.A., Iwatsubo, T., Pickering-Brown, S.M., Owen, F., Saido, T.C., Perry, R.H. (1997). Preferential Deposition of amyloid β protein ($A\beta$) in the form of $A\beta(40)$ in Alzheimer's disease is associated with a gene dosage effect of the apolipoprotein E E4 allele. *Neurosci. Lett.*, 221, 81-84.
61. Mann, D.M.A., Pickering-Brown, Byatt, N.N., Wright, A.E., Owen, F., Iwatsubo, T., Saido, T.C. (1997). An intronic polymorphism in the presenilin-1 gene does not influence the amount or molecular form of the amyloid β protein deposited in Alzheimer's disease. *Neurosci. Lett.*, 222, 57-60.
62. Saito, Y., Maruyama, K., Saido, T.C., Kawashima, S. (1997). Overexpression of a neuropeptide nociceptin/orphanin FQ precursor gene, N23K/N27K, induces neurite outgrowth in mouse NS20Y cells. *J. Neurosci. Res*, 48, 397-406.

63. Saido, T.C. (1998). Alzheimer's disease as proteolytic disorders: Anabolism and catabolism of β -amyloid. *Neurobiol. Aging*, 19, S69-S75.
64. Saido, T.C., Kawashima, S., Tani, E., Yokota, M. (1997). Up- and down-regulation of calpain inhibitor polypeptide, calpastatin, in postischemic hippocampus. *Neurosci. Lett.*, 227, 75-78.
65. Russo, C., Saido, T.C., DeBusk, L.M., Tabaton, M., Gambetti, P., Teller, J.K. (1997). Heterogeneity of water-soluble amyloid β -peptide in Alzheimer's disease and Down's syndrome brains. *FEBS Lett.* 409, 411-416.
66. Yamazaki, T., Haass, C., Saido, T.C., Omura, S., Ihara, Y. (1997). Specific increase in amyloid β -protein42 secretion ratio by calpain inhibition. *Biochemistry* 36, 8377-8383.
67. Kouchi, Z., Saido, T.C., Ohyama, H., Maruta, H., Suzuki, K., Tanuma, S. (1997). The restrictive proteolysis of α -fodrin to a 120 kDa fragment is not catalyzed by calpains during thymic apoptosis. *Apoptosis* 2, 84-89.
68. Yamazaki, M., Suga, Y., Ishidoh, K., Saido, T.C., Kawashima, S., Suzuki, K., Kominami, E., Ogawa, H. (1997). Cytoplasmic processing of human profilaggrin by active μ -calpain. *Biochem. Biophys. Res. Commun.*, 235, 652-656.
69. Didier, M., Xu, M., Berman, S.A., Saido, T.C., Bursztajn, S. (1997). Involvement of three glutamate receptor ϵ subunits in the formation of N-methyl-D-aspartate receptors mediating excitotoxicity in primary cultures of mouse cerebellar granule cells. *Neuroscience*, 78, 1129-1146.
70. Yan, S.D., Fu, J., Soto, C., Chen, X., Zhu, H., Al-Mohanna, F., Collison, K., Zhu, A., Stern, E., Saido, T., Tohyama, M., Ogawa, S., Roher, A., Stern, D. (1997). ERAB: A novel intracellular amyloid- β peptide binding protein which mediates neurotoxicity in Alzheimer's disease. *Nature* 389, 689-695.
71. Schoenwaelder, S.M., Kulkarni, S., Salem, H.H., Imajoh-Ohmi, S., Yamao-Harigaya, W., Saido, T.C., Jackson, S.P. (1997). Distinct substrate specificities and functional roles for the 78 and 76 kDa forms of μ -calpain in human platelets. *J. Biol. Chem.*, 272, 24876-24884.
72. Shin, R.-W., Ogino, K., Kondo, A., Saido, T.C., Trojanowski, J.Q., Kitamoto, T., Tateishi, J. (1997). Amyloid β -protein (A β) 1-40 but not A β 1-42 contributes experimental formation of Alzheimer disease amyloid fibrils in rat brain. *J. Neurosci.* , 17, 8187-8193.
73. Tekirian, T.L., Saido, T.C., Markesbery, W.R., Russell, M.J., Wekstein, D.R., Patel, E., Geddes, J.W. (1998). Amino terminus heterogeneity of Parenchymal and Cerebrovascular β -amyloid deposits in aged human, canine, and polar bear brains. *J. Neuropathol. Exp. Neurol.*, 57, 76-94.
74. Sorimachi, Y., Harada, K., Saido, T.C., Ono, T., Kawashima, S., Yoshida, K. (1997). Downregulation of calpastatin in rat heart after brief ischemia and reperfusion. *J. Biochem.* 122, 743-748.
75. Inomata, M., Nomura, K., Takehana, M., Saido, T.C., Kawashima, S., Shumiya, S. (1997). Evidence for involvement of calpain in the cataractogenesis in Shumiya Cataract Rat. *Biochim. Biophys. Acta*, 1362, 11-23.
76. Schmidt, M.L., Lee, V.M.-Y., Saido, T.C., Perl, D., Schuck, T., Iwatsubo, T., Trojanowski, J.Q. (1998). Amyloid plaques in Guam ALS and Parkinsonism-dementia complex contain species of A β similar to those found in the amyloid plaques of Alzheimer's disease. *Acta Neuropathol.*, 1362, 11-23.
77. Oyama, F., Sawamura, N., Kobayashi, K., Morishima-Kawashima, M., Kuramochi, T., Ito, M., Tomita, T., Maruyama, K., Saido, T.C., Iwatsubo, T.,

- Capell, A., Walter, J., Grunberg, J., Ueyama, Y., Haass, C., Ihara, Y. (1998). Mutant presenilin 2 transgenic mouse: Effect on an age-dependent increase of amyloid β -protein (A β)₄₂ in brain. *J. Neurochem.*, 71, 313-322.
78. Frautschy, S.A., Yang, F., Irrizarry, M., Hyman, B., Saido, T.C., Hsiao, K., Cole, G.M. (1998). Microglial response to amyloid plaques in APP^{sw} transgenic mice. *Am. J. Pathol.*, 152, 307-317.
79. Tokuhiro, S., Tomita, T., Iwata, H., Kosaka, T., Saido, T.C., Maruyama, K., Iwatsubo, T. (1998). The presenilin 1 mutation (M146V) linked to familial Alzheimer's disease attenuates the neuronal differentiation of NTera 2 cells. *Biochem. Biophys. Res. Commun.*, 244, 751-755.
80. Shinozaki, K., Maruyama, K., Kume, H., Tomita, T., Saido, T.C., Iwatsubo, T., Obata, K. (1998). The presenilin 2 loop domain interacts with the μ -calpain C-terminal region. *Int. J. Mol. Med.*, 1, 797-799.
81. Sudoh, S., Kawamura, Y., Sato, S., Wang, R., Saido, T.C., Oyama, F., Sakaki, Y., Komano, H., Yanagisawa, K. The presenilin 1 mutations linked to familial Alzheimer's disease elevate a production of N-terminally truncated A β ₄₂ variant, A β ₁₁₋₄₂, which is generated through distinct processing pathway from A β ₁₋₄₂. (1998). *J. Neurochem.*, 1535-1543.
82. Funato, H., Yoshimura, M., Yamazaki, T., Saido, T.C., Ito, Y., Yokofujita, J., Odaka, R., Ihara, Y. (1998). Astrocytes containing amyloid β -protein (A β -positive granules) are associated with A β ₄₀-positive diffuse plaques in the aged human brain. *Am. J. Pathol.*, 152, 983-992.
83. Kimura, Y., Koga, H., Araki, N., Mugita, N., Fujita, N., Takeshima, H., Nishi, T., Yamashima, T., Saido, T.C., Yamasaki, T., Moritake, K., Saya, H., Nakao, M. (1998). The involvement of calpain-dependent proteolysis of the tumor suppressor NF2 (merlin) in schwannomas and meningiomas. *Nature Med.*, 8, 915-922.
84. Ono, Y., Shimada, H., Sorimachi, H., Richard, I., Saido, T.C., Beckmann, J.S., Ishiura, S., Suzuki, K. (1998). Functional defects of a muscle-specific calpain, p94, caused by mutations associated with Limb-Girdle muscular dystrophy type 2A. *J. Biol. Chem.*, 273, 17073-17078.
85. Yamaguchi, H., Sugihara, S., Ogawa, A., Saido, T.C., Ihara, Y. (1998). Diffuse plaques associated with astroglial amyloid β protein, possibly showing a disappearing stage of senile plaques. *Acta Neuropathol.*, 95, 217-222.
86. Meredith, J.Jr., Mu, Z., Saido, T.C., Du, X. (1998). Cleavage of the cytoplasmic domain of the integrin β 3 subunit during endothelial cell apoptosis. *J. Biol. Chem.*, 273, 19525-19531.
87. Akiyama, H., Mori, H., Saido, T.C., Kondo, H., Ikeda, K., McGeer, P.L. (1998). Occurrence of the diffuse deposits with numerous amyloid β -protein(A β)-containing glial cells in the cerebral cortex of patients with Alzheimer's disease. *Glia*, 4, 324-331.
88. Tomita, T., Tokuhiro, S., Hashimoto, T., Aiba, K., Saido, T.C., Maruyama, K., Iwatsubo, T. (1998). Molecular dissection of domains in mutant presenilin 2 that mediate overproduction of amyloidogenic forms of amyloid β peptides. *J. Biol. Chem.*, 273, 21153-21160.
89. Frautschy, S.A., Horn, D.L., Sigel, J.J., Harris-White, M.E., Mendoza, J.J., Yang, F., Saido, T.C., Cole, G.M. (1998). Protease inhibitor coinfusion with amyloid β -protein results in enhanced deposition and toxicity in rat brain. *J. Neurosci.*, 18, 8311-8321.

90. Hiwasa, T., Nakamura, Y., Ozaki, T., Kondo, K., Saido, T., Nakagawara, A. and Sakiyama, S. (1998). Down-regulation of protein kinase α and γ and enhanced TPA-induced neurite formation in DAN-transfected neuroblastoma cells. *FEBS Lett.*, 440, 25-28.
91. Ishidoh, K., Saido, T.C., Kawashima, S., Hirose, M., Watanabe, S., Sato, N., Kominami, E. (1998). Multiple processing of procathepsin L to cathepsin L *in vivo*. *Biochem. Biophys. Res. Commun.*, 252, 202-207.
92. Kitagawa, K., Matsumoto, M., Saido, T.C., Ohtuki, T., Kuwabara, K., Yagita, Y., Mabuchi, T., Yanagihara, T., Hori, M. (1999). Species differences in fodrin proteolysis in the ischemic brain. *J. Neurosci. Res.*, 643-649.
93. Honda, T., Yasutake, K., Nihonmatsu, N., Merchen, M., Takahashi, H., Murayama, O., Murayama, M., Sato, K., Omori, A., Tsubuki, S., Saido, T.C., Takashima, A. (1999). Dual roles of proteasome in the metabolism of presenilin 1. *J. Neurochem.*, 72, 255-261.
94. Hosoda, R., Saido, T.C., Otvos, L.Jr., Arai, T., Mann, D.M.A., Lee, V.M.-Y., Trojanowski, J.Q., Iwatsubo, T. (1998). Quantitation of modified amyloid β peptides in Alzheimer disease and down syndrome brains *J. Neuropathol. Exp. Neurol.*, 57, 1089-1095.
95. Yokota, M., Tani, E., Tsubuki, S., Yamaura, I., Nakagaki, I., Hori, S., Saido, T.C. (1999). Calpain inhibitor entrapped in liposome rescues ischemic neuronal damage. *Brain research*, 819, 8-14.
96. Kubo, H., Matsushita, M., Kotani, M., Kawasaki, H., Saido, T.C., Kawashima, S., Katagiri, C., Suzuki, A. (1999). Molecular basis for oviductin-mediated processing from gp43 to gp41, the predominant glycoproteins of *Xenopus* egg envelopes. *Dev. Genet.*, 25, 123-129.
97. Eto, A., Saido, T.C., Fukushima, K., Tomioka, S., Imai, S., Nishizawa, T., Hanada, N. (1999). Inhibitory effect of a self-derived peptide on glycosyltransferase of *Streptococcus mutans*. Possible novel anticaries measures. *J. Biol. Chem.*, 274, 15797-15802.
98. Saido, T.C. (2000). Involvement of polyglutamine endolysis followed by pyroglutamate formation in the pathogenesis of triplet repeat/polyglutamine-expansion diseases. *Med. Hypotheses*, 54, 427-429.
99. Ray, S.K., Shields, D.C., Saido, T.C., Matzelle, D.C., Wilford, G.G., Hogan, E.L., Banik, N.L. (1999). Calpain activity and translational expression increased in spinal cord injury. *Brain Res.*, 816, 375-380.
100. Nakagawa, Y., Nakamura, M., McIntosh, T.K., Rodriguez, A., Berlin J.A., Smith, D.H., Saatman, K.E., Raghupathi, R., Clemens, J., Saido, T.C., Schmidt, M.L., Lee, V.M.-Y., and Trojanowski, J.Q. (1999). Traumatic brain injury in young PDAPP transgenic mice induces marked ipsilateral hippocampal atrophy and diminished A β deposition during aging. *J. Comp. Neurol.*, 411, 390-398.
101. Kulkarni, S., Saido, T.C., Suzuki, K., Fox, J.E.B. (1999). Calpain mediates integrin-induced signals at a point upstream of rho family members. *J. Biol. Chem.*, 274, 21265-21275.
102. Blomgren, K., Hallin, U., Anderson, A.-L., Puka-Sundvall, M., Bahr, B.A., McRae, A., Saido, T.C., Kawashima, S., Hagberg, H. (1999). Calpastatin is up-regulated in response to hypoxia and is a suicide substrate to calpain after neonatal cerebral hypoxia-ischemia. *J. Biol. Chem.*, 274, 14046-14052.
103. Koike, H., Seki, H., Kouchi, Z., Ito, M., Kinouchi, T., Sorimachi, H., Saido, T.C., Maruyama, K., Suzuki, K., Ishiura, S. (1999). Thimet oligopeptidase cleaves the

- full-length Alzheimer amyloid precursor protein at beta-secretase cleavage site in COS cells. *J. Biochem.*, 126, 235-242.
104. Koriyama, H., Kouchi, Z., Umeda, T., Saido, T.C., Ishiura, S., Suzuki, K. (1999). Proteolytic activation of protein kinase δ and ϵ by caspase-3 in U937 cells during chemotherapeutic agent-induced apoptosis. *Cell. Signal.*, 11, 831-838.
105. Koike, H., Tomioka, S., Sorimachi, H., Saido, T.C., Maruyama, K., Okuyama, A., Fujisawa-Sehara, A., Ohno, S., Suzuki, K., Ishiura, S. (1999). MDC9 has an α -secretase activity responsible for processing the amyloid precursor protein. *Biochem. J.*, 343, 371-375.
106. Fukumoto, H., Tomita, T., Matsunaga, H., Ishibashi, Y., Saido, T.C., Iwatsubo, T. (1999). Primary cultures of neuronal and non-neuronal rat brain cells secrete similar proportions of amyloid β peptides ending at A β 40 and A β 42. *NeuroReport*, 10, 2965-2969.
107. Shields, D.C., Schaecher, K.E., Saido, T.C., Banik, N. (1999). A putative mechanism of demyelination in multiple sclerosis by a proteolytic enzyme, calpain. *Proc. Natl. Acad. Sci. U.S.A.*, 96, 11486-11491.
108. Iwata, N., Tsubuki, S., Takaki, Y., Watanabe, K., Sekiguchi, M., Hosoki, E., Kawashima-Morishima, M., Lee, H.-J., Hama, E., Sekine-Aizawa, Y., Saido, T.C. (2000). Identification of the major A β 1-42-degrading catabolic pathway in brain parenchyma: Suppression leads to biochemical and pathological deposition. *Nat. Med.*, 6, 143-151.
109. Shimokata, H., Yamada, Y., Nakagawa, M., Okubo, R., Saido, T.C., Funakoshi, A., Miyasaka, K., Ohota, S., Tsujimoto, G., Tanaka, M., Ando, F., Niino, N. (2000). Distribution of geriatric disease-related genotypes in the National Institute for Longevity Sciences, Longitudinal Study of Aging (NILS-LSA). *J. Epiderm.*, S46-55.
110. Russo, C., Schettini, G., Saido, T.C., Hulette, C., Lippa, C., Lannfelt, L., Ghetti, B., Gambetti, P., Tabaton, M., Teller, J.K. (2000). Preferential deposition of truncated amyloid- β peptides in brain of presenilin 1 gene mutation carriers. *Nature*, 405, 531-532.
111. Nakagawa, Y., Reed, L., Nakamura, M., McIntosh, T.K., Smith, D.H., Saatman, K.E., Raghupathi, R., Clemens, J., Saido, T.C., Lee, V.M.-Y., Trojanowski, J.Q. (2000). Brain trauma in aged transgenic mice induces regression of established A β deposit. *Exper. Neurol.*, 163, 244-252.
112. Lankiewicz, S., Luetjens, C.M., Bui, N.T., Krohn, A.J., Poppe, M., Cole, G.C., Nicholson, D.W., Saido, T.C., Prehn, H.M. (2000). Activation of calpain I converts excitotoxic neuron death into a caspase-independent cell death. *J. Biol. Chem.*, 275, 17064-17071.
113. Takeuchi, A., Irizarry, M.C., Duff, K., Saido, T.C., Hsiao, Ashe K., Hasegawa, M., Mann D.M.A., Hyman, B.T., Iwatsubo, T. (2000). Age-related A β deposition in transgenic mice overexpressing both Alzheimer mutant presenilin 1 and β amyloid precursor protein is not associated with global neuronal loss. *Am. J. Pathol.*, 157, 331-339.
114. Hiwasa, T., Arase, Y., Kikuno, K., Hasegawa, R., Sugaya, S., Kita, K., Saido, T., Yamamori, H., Maki, M., Suzuki, N. (2000). Increase in ultraviolet sensitivity by overexpression of calpastatin in ultraviolet-resistant UVr-1 cells derived from ultraviolet-sensitive human R5a cells. *Cell Death Differ.*, 7, 531-537.

115. Iwata, N., Tsubuki, S., Hama, E., Takaki, Y., Shirotani, K., Saido, T.C. (2000). Clearance of amyloid β -peptide from brain: transport or metabolism? *Nat. Med.*, 6, 718-719.
116. Harigaya, Y., Saido, T.C., Eckman, C.B., Prada, C.-M., Shoji, M., Younkin, S. (2000). Amyloid beta protein starting pyroglutamate at position 3 is a major component of the amyloid deposits in the Alzheimer's disease brain. *Biochem. Biophys. Res. Commun.*, 276, 422-427.
117. Saido, T. C. (2000). Degradation of amyloid- β peptide: a key to Alzheimer pathogenesis, prevention, and therapy. *NeuroSci. News*, 5(3) 52-62.
118. Lee, H.-J., Tomioka, M., Takaki, Y., Masumoto, H., Saido, T.C. (2000). Molecular cloning and expression of aminopeptidase A isoforms from rat hippocampus. *Biochim. Biophys. Acta*, 1493, 273-278.
119. Takaki, Y., Iwata, N., Tsubuki, S., Taniguchi, S., Toyoshima, S., Lu, B., Gerard, N.P., Gerard, C., Lee, H.-J., Shirotani, K., Saido, T.C. (2000). Biochemical Identification of the neutral endopeptidase family member responsible for the catabolism of amyloid β peptide in brain. *J. Biochem.*, 128, 897-902.
120. Kawarabayashi, T., Younkin, L.H., Saido, T.C., Shoji, M., K. Hsiao, A., Younkin, S.G. (2001). Age-dependent changes in brain, cerebrospinal fluid, and plasma amyloid β protein in the Tg2576 transgenic mouse model of Alzheimer's disease. *J. Neurosci.*, 21, 372-381.
121. Koike, H., Kouchi, Z., Kinouchi, T., Maeda, T., Sorimachi, H., Saido, T.C., Maruyama, K., Okuyama, A., Suzuki, K., Ishiura, S. (2000). Metabolism of amyloid precursor protein in COS cells transfected with a beta-secretase candidate. *Cytotechnol.*, 33, 213-219.
122. Kitagaki, H., Tomioka, S., Yoshizawa, T., Sorimachi, H., Saido, T.C., Ishiura, S., Suzuki, K. (2000). Autolysis of calpain large subunit inducing irreversible dissociation of stoichiometric heterodimer of calpain. *Biosci. Biotechnol. Biochem.*, 64, 689-695.
123. Shoji, M., Kawarabayashi, T., Sato, M., Sasaki, A., Saido, T.C., Matsubara, E., Yomidokoro, Y., Kanai, M., Shizuka, M., Ishiguro, K., Ikeda, M., Harigaya, Y., Okamoto, K., Hirai, S. (2000). Age-related amyloid beta protein accumulation induces cellular death and macrophage activation in transgenic mice. *J. Pathol.*, 191, 93-101.
124. Yamaguchi, A., Yamamoto, N., Akamatsu, N., Saido, T.C., Kaneda, M., Umeda, M., Tanoue, K. (2000). PS-liposome and ox-LDL bind to different sites of the immunodominant domain (#155-183) of CD 36: a new study with GS95, a new anti-CD36 monoclonal antibody. *Thromb. Res.*, 97, 317-326.
125. Maruyama, K., Usami, M., Kametani, F., Tomita, T., Iwatsubo, T., Saido, T.C., Mori, H., Ishiura, S. (2000). Molecular interactions between presenilin and calpain: inhibition of m-calpain protease activity by presenilin-1, 2 and cleavage of presenilin-1 by m-, mu-calpain, *Int. J. Mol. Med.*, 5, 269-273.
126. Taniguchi, S., Fujita, Y., Takahashi, H., Hayashi, S., Kakita, A., Murayama, S., Saido, T.C., Hisanaga, S., Iwatsubo, T., Hasegawa, M. (2001). Degradation of p35 to p25 in postmortem human and rat brains. *FEBS Lett*, 46-50.
127. Sekine-Aizawa, Y., Hama, E., Watanabe, K., Tsubuki, S., Kanai-Azuma, M., Kanai, Y., Arai, H., Aizawa, H., Iwata, N., Saido, T.C. (2001). Matrix metalloproteinase (MMP) system in brain: Identification and characterization of brain-specific MMP highly expressed in cerebellum. *Eur. J. Neurosci.*, 13, 935-948.

128. Bialkowska, K., Kulkarni, S., Du, X., Goll, D.E., Saido, T.C., Fox, J.E.B. (2000). Evidence that beta3 integrin-induced Rac activation involves the calpain-dependent formation of integrin clusters that are distinct from the focal complexes and focal adhesions that form as Rac and RhoA become active. *J. Cell Biol.*, 151, 685-695.
129. Shirotani, K., Tsubuki, S., Iwata, N., Takaki, Y., Harigaya, W., Maruyama, K., Kiryu-Seo, S., Kiyama, H., Iwata, H., Tomita, T., Iwatsubo, T., Saido, T.C. (2001). Neprilysin degrades both amyloid β peptides 1-40 and 1-42 most rapidly and efficiently among thiorphan- and phosphoramidon-sensitive endopeptidases. *J. Biol. Chem.*, 276, 21895-21901.
130. Choi, W.-S., Lee, E.-H., Chung, C.-W., Jung, Y.-K., Jin, B.K., Kim, S.U., Oh, T.H., Saido, T.C., Oh, Y.J. (2001). Cleavage of Bax is mediated by caspase-dependent or -independent calpain activation in dopaminergic neuronal cells: Protective role of Bcl-2. *J. Neurochem.*, 77, 1531-1541.
131. Iwata, N., Tsubuki, S., Takaki, Y., Shirotani, K., Lu, B., Gerard, N.P., Gerard, C., Hama, E., Lee, H.-J., Saido, T.C. (2001). Metabolic regulation of brain A β by neprilysin. *Science*, 292, 1550-1552.
132. Kaneko, T., Yamashima, T., Tohma, Y., Nomura, M., Imajoh-Ohmi, S., Saido, T.C., Nakao, M., Saya, H., Yamamoto, H., Yamashita, J. (2001). Calpain-dependent proteolysis of merlin occurs by oxidative stress in meningiomas: a novel hypothesis for tumorigenesis. *Cancer*, 92, 2662-2672.
133. Hama, E., Shirotani, K., Masumoto, H., Sekine-Aizawa, Y., Aizawa, H., Saido, T.C. (2001). Clearance of extracellular and cell-associated amyloid β peptide by viral expression of neprilysin in primary culture. *J. Biochem.*, 130, 721-726.
134. Russo, C., Schettini, G., Saido, T.C., Gambetti, P., Tabaton, M., Teller, J.T. (2001). N-Terminally truncated amyloid β peptides and Alzheimer's disease. *Neurobiol. Aging*, 22, 345.
135. Kitazume, S., Tachida, Y., Oka, R., Shirotani, K., Saido, T.C., Hashimoto, Y. (2001). Alzheimer's β -secretase, β -site amyloid precursor protein-cleaving enzyme, is responsible for cleavage secretion of a golgi-resident sialyltransferase. *Proc. Natl. Acad. Science, USA*, 98, 13554-13559.
136. Kim, J.E., Han, B.S., Choi, W.S., Eom, D.S., Lee, E.H., Oh, T.H., Markelonis, G.J., Saido, T.C., Lee, G.E., Chung, I.K., Oh, Y.J. (2001) Temporospatial sequence of cellular events associated with etoposide-induced neuronal cell death : role of antiapoptotic protein Bcl-X_L. *J. Neurosci. Res.*, 66, 1074-1082.
137. Fukami, S., Watanabe, K., Iwata, N., Haraoka, J., Lu, B., Gerard, N.P., Gerard, C., St. George-Hyslop, P., Saido, T.C. (2002). A β -degrading endopeptidase, neprilysin, in mouse brain: Synaptic and axonal localization inversely correlating with Ab pathology. *Neurosci. Res.*, 43, 39-56.
138. Shirotani, K., Tsubuki, S., Lee, H.-J., Maruyama, K., Saido, T.C. (2002). Generation of amyloid b peptide with pyroglutamate at position 3 in primary cortical neurons. *Neurosci. Lett.*, 327, 25-28.
139. Fukami, S., Iwata, N., Saido, T.C. (2002). Therapeutic strategies of Alzheimer's disease through manipulation of Ab metabolism: a focus on A β -degrading enzyme, neprilysin. *Drug Development Research*, 56, 171-183.
140. Takahashi, M., Fukami, S., Iwata, N., Inoue, K., Itohara, S., Itoh, H., Haraoka, J., Saido, T.C. (2002). *In vivo* glioma growth requires host-derived matrix metalloproteinase 2 for maintenance of angioarchitecture. *Pharmacol. Res.*, 46, 155-163.

141. Iwata, N., Takaki, Y., Fukami, S., Tsubuki, S., Saido, T.C. (2002). Region-specific reduction of A β -degrading endopeptidase, neprilysin, in mouse hippocampus upon aging. *J. Neurosci. Res.*, 70, 493-500.
142. Hattori, C., Asai, M., Oma, Y., Kino, Y., Sasagawa, N., Saido, T.C., Maruyama, K., Ishiura, S. (2002). BACE1 interacts with nicastrin. *Biochem. Biophys. Res. Commun.*, 293, 1228-1232.
143. Tomioka, M., Shirotani, K., Iwata, N., Lee, H.J., Yang, F., Cole, G.M., Seyama, Y. Saido, T.C. (2002). In vivo role of caspases in excitotoxic neuronal death: generation and analysis of transgenic mice expressing baculovirus caspase inhibitor, p35, in postnatal. *Brain Res. Mol. Brain Res.*, 108, 18-32.
144. Mori, C., Spooner, E.T., Wisniewski, K.E., Wisniewski, T.M., Yamaguchi, H., Saido, T.C., Tolan, D.R., Selkoe, D.J., Lemere, C.A. (2002). Intracellular A β 42 accumulation in Down syndrome brain. *Amyloid*, 9, 88-102.
145. Kuwano, K., Nisimura, I., Uetsuki, T., Saido, T.C., Yoshikawa, K. (2002). Activation of calpain in cultured neurons overexpressing Alzheimer amyloid precursor protein. *Brain Res. Mol. Brains Res.*, 107, 166-175.
146. Dare, E., Tofighi, R., Vettori, M.V., Momoi, T., Poli, D., Saido, T.C., Mutti, A., Ceccatelli, S. (2002). Styrene 7,8-oxide induces caspase activation and regular DNA fragmentation in neuronal cells, *Brain Res.*, 933, 12-22
147. Kitazume, S., Tachida, Y., Oka, R., Kotani, N., Ogawa, K., Suzuki, M., Dohmae, N., Takio, K., Saido, T.C., Hashimoto, Y. (2003). Characterization of α 2,6-sialyltransferase cleavage by Alzheimer's β -secretase (BACE1). *J. Biol. Chem.*, 278, 14865-14871.
148. Saito, T., Takaki, Y., Iwata, N., Trojanowski, J., Saido T.C. (2003). Perspectives: Alzheimer's disease, neuropeptide, neuropeptidase, and A β metabolism. *Science (SAGE-KE)*, <http://sageke.sciencemag.org/cgi/content/full/sageke;2003/3/pe1>.
149. Kitazume, S., Saido T.C., Hashimoto, Y. (2003). Alzheimer's β -secretase cleaves a glycosyltransferase as a physiological substrate. *Glycoconjugate J.*, 278, 14865-14871.
150. Tsubuki, S., Takaki, Y., Saido, T.C. (2003) Dutch, Flemish, Italian, and Arctic mutations of APP and resistance of A β to physiologically relevant proteolytic degradation. *Lancet*, 361, 1957-1958.
151. Zhang, J., Miyamoto, K., Hashioka, S., Hao, H. P., Murao, K., Saido, T.C., Nakanishi, H. (2003). Activation of μ -calpain in developing cortical neurons following methylmercury treatment. *Develop. Brain Res.*, 142, 105-110.
152. Porn-Ares, I., Saido, T.C., Tommy, A., Ares, M. P.S. (2003) Oxidized low-density lipoprotein induces calpain-dependent cell death and ubiquitination of caspase-3 in HMEC-1 endothelial cells. *Biochem. J.*, 374, 403-411.
153. Yokota, M., Saido, T.C., Kamitani, H., Tabuchi, S., Satokata, I., Watanabe, T. (2003). Calpain induces proteolysis of neuronal cytoskeleton in ischemic gerbil forebrain. *Brain Res.*, 984, 122-132.
154. Rami, A., Volkmann, T., Agarwal, R., Schoninger, S., Nuernberger, F., Saido, T.C., Winckler, J. (2003). β 2-adrenergic receptor responsiveness of the calpain-calpastatin system and attenuation of neuronal death in rat hippocampus after transient global ischemia. *Neurosci. Res.*, 47, 373-382.
155. Wang, D.-S., Iwata, N., Hama, E., Saido, T.C., Dickson, D.W. (2003). Oxidized neprilysin in aging and Alzheimer's disease brains. *Biochem. Biophys. Res. Commun.*, 310, 236-241.

156. Yamashima, T., Tonchev, A.B., Tsukada, T., Saido, T.C., Imajoh-Ohmi, S., Momoi, T., Kominami, E. (2003). Sustained calpain activation associated with lysosomal rupture executes necrosis of the postischemic CA1 neurons in primates. *Hippocampus*, 13, 791-800.
157. Inoue, H., Tsukita, K., Iwasato, T., Suzuki, Y., Tomioka, M., Tateno, M., Nagao, M., Kawata, A., Saido, T.C., Miura, M., Misawa, H., Itohara, S., Takahashi, R. (2003). The crucial role of caspase-9 in the disease progression of transgenic ALS mouse model. *EMBO J.*, 22, 6665-6674.
158. Wakutani, Y., Watanabe, K., Adachi, Y., Wada-Isoe, K., Urakami, K., Ninomiya, H., Saido, T.C., Hashimoto, T., Iwatsubo, T., Nakashima, K. (2004). Novel amyloid precursor protein missense mutation in probable Alzheimer's disease. *J. Neurol. Neurosurg. Psych.*, 75, 1039-1042.
159. Iwata, N., Mizukami, H., Shirotani, K., Takaki, Y., Muramatsu, S., Gerard, N., Gerard, C., Ozawa, K., Saido, T.C. (2004). Presynaptic localization of neprilysin contributes to efficient clearance of amyloid β peptide in mouse brain. *J. Neurosci.*, 24, 991-998.
160. Kimura, T., Shuto, D., Kasai, S., Liu, P., Hidaka, K., Hamada, T., Hayashi, Y., Hattori, C., Asai, M., Kitazume, S., Saido, T.C., Ishiura, S., Kiso, Y. (2004). KMI-358 and KMI-370, highly potent and small-sized BACE1 inhibitors containing phenylmorstatine. *Bioorg. & Med. Chem. Lett.*, 14, 1527-1531.
161. Kitazume, S., Saido, T.C., Hashimoto, Y. (2004). Alzheimer's β -secretase cleaves a glycosyltransferase as a physiological substrate. *Glycoconjugate J.*, 20, 59-62.
162. Hama, E., Shirotani, K., Iwata, N., Saido, T.C. (2004). Effects of neprilysin chimeric proteins targeted to subcellular compartments on amyloid β peptide clearance in primary neurons. *J. Biol. Chem.*, 279, 30259-30264.
163. Sato, K., Higuchi, M., Iwata, N., Saido, T.C., Sasamoto, K. (2004). Fluoro-substituted and ^{13}C -labeled styrylbenzene derivatives for detecting brain amyloid plaques. *Eur. J. Med. Chem.*, 39, 573-578.
164. Ladrech, S., Guillon, M., Saido, T.C., Lenoir, M. (2004). Calpain activity in the Amikacin-damaged rat cochlea. *J. Comp. Neurol.*, 477, 149-160.
165. Funamoto, S., Morishima-Kawashima, M., Tanimura, Y., Hirotani, N., Saido, T.C., Ihara, Y. (2004). Truncated carboxyl-terminal fragments of β -amyloid precursor protein are processed to amyloid β -proteins 40 and 42. *Biochemistry*, 43, 13532-13540.
166. Bialkowska, K., Saido, T.C., Fox, J.E.B. (2004). SH3 domain of spectrin participates in the activation of Rac in specialized calpain-induced integrin signaling complexes. *J. Cell Science*, 118, 381-395.
167. Shin, R.W., Saido, T.C., Maeda, M., Kitamoto, T. (2005). Novel α -secretase cleavage of Alzheimer's amyloid β precursor protein in the endoplasmic reticulum of COS7 cells. *Neurosci. Lett.*, 376, 14-19.
168. Saito, T., Iwata, N., Tsubuki, S., Takaki, Y., Takano, J., Huang, S.-H., Suemoto, T., Higuchi, M., Saido, T.C. (2005). Somatostatin regulates brain amyloid β peptide, $\text{A}\beta_{42}$, through modulation of proteolytic degradation. *Nat. Med.*, 11, 434-439.
169. Qi-Takahara, Yue, Morishima-Kawashima, M., Tanimura, Y., Dolios, G., Hirotani, N., Horikoshi, Y., Kametani, F., Maeda, M., Saido, T.C., Wang, R., Ihara, Y. (2005). Longer forms of amyloid β protein: Implications for the mechanism of intramembrane cleavage by γ -secretase. *J. Neurosci.*, 25, 436-445.

170. Takano, J., Tomioka, M., Tsubuki, T., Higuchi, M., Iwata, N., Itohara, S., Maki, M., Saido, T.C. (2005). Calpain mediates excitotoxic DNA fragmentation via mitochondrial pathways: evidence from calpastatin-mutant mice. *J. Biol. Chem.*, 280, 16175-16184.
171. Higuchi, M., Tomioka, M., Takano, J., Shirotani, K., Iwata, N., Masumoto, H., Maki, M., Itohara, S., Saido, T.C. (2005). Distinct mechanistic roles of calpain and caspase activation in neurodegeneration as revealed in mice over-expressing their specific inhibitors. *J. Biol. Chem.*, 280, 15229-15237.
172. Higuchi, M., Iwata, N., Matsuba, Y., Sato, K., Sasamoto, K., Saido T.C. (2005). ¹⁹F- and ¹H-MRI detection of amyloid- β peptide *in vivo*. *Nat. Neurosci.*, 8, 527-533.
173. Kokubo, H., Saido, T.C., Iwata, N., Helms, J.B., Shinohara, R., Yamaguchi, H. (2005). Part of membrane-bound A β exists in rafts within senile plaques in Tg2576 mouse brain. *Neurobiol. Aging*, 26, 409-418.
174. Kambe, A., Yokota, M., Saido, T.C., Sakokata, I., Fujikawa, H., Tabushi, S., Kamitani, H., Watanabe, T. (2005). Spatial resolution of calpain-catalyzed proteolysis in focal cerebral ischemia. *Brain Res.*, 1040, 36-43.
175. Hayashi, M., Koshihara, Y., Ishibashi, H., Yamamoto, S., Tsubuki, S., Saido, T.C., Kawashima, S., Inomata, M. (2005). Involvement of calpain in osteoclastic bone resorption. *J. Biochem.*, 137, 331-338.
176. Sato, T., Tanimura, Y., Hirotsu, N., Saido, T.C., Morishima-Kawashima, M., Ihara, Y. (2005). Blocking the cleavage at midportion between γ - and ϵ - sites remarkably suppresses the generation of amyloid b-protein. *FEBS Lett.*, 579, 2907-2912.
177. Kokubo, H., Kaye, R., Glabe, C.G., Saido, T.C., Iwata, N., Helms, J.B., Yamaguchi, H. (2005). Oligomeric proteins ultrastructurally localize to cell processes, especially to axon terminals with higher density, but not to lipid rafts in Tg2576 mouse brain. *Brain Res.*, 1045, 224-228.
178. Hama, E., Saido, T.C. (2005). Etiology of sporadic Alzheimer's disease: somatostatin, neprilysin, and amyloid β peptide. *Med. Hypotheses*, 65, 498-500.
179. Maruyama, M., Higuchi, M., Takaki, Y., Matsuba, Y., Tanji, H., Nemoto, M., Tomita, N., Matsui, T., Iwata, N., Mizukami, H., Muramatsu, S., Ozawa, K., Saido, T.C., Arai, H., Sasaki, H. (2005). Cerebrospinal fluid neprilysin is reduced in prodromal Alzheimer's disease. *Ann. Neurol.*, 57, 832-842.
180. Higuchi, M., Iwata, N., Saido, T.C. (2005). Understanding molecular mechanisms of proteolysis in Alzheimer's disease: progress toward therapeutic interventions. *Biochim. Biophys. Acta*, 1751, 60-67.
181. Piccini, A., Russo, C., Gliozzi, A., Relini, A., Vitali, A., Borghi, R., Giliberto, L., Armirotti, A., D'Arrigo, C., Bachi, A., Cattaneo, A., Canale, C., Torrassa, S., Saido, T.C., Markesbery, W., Gambetti, P., Tabaton, M. (2005). β Amyloid is different in normal aging and in Alzheimer disease. *J. Biol. Chem.*, 280, 34186-34192.
182. Iwata, N., Higuchi, M., Saido, T.C. (2005). Metabolism of amyloid- β peptide and Alzheimer's disease. *Pharmacol. Ther.*, 108, 129-148.
183. Yoshida, T., Ohno-Matsui, K., Ichinose, S., Sato, T., Iwata, N., Saido, T.C., Hisatomi, T., Mochizuki, M., Morita, I. (2005). The potential role of amyloid β in the pathogenesis of age-related macular degeneration. *J. Clin. Invest.*, 115, 2793-2800.
184. Ogawa, T., Kiryu-Seo, S., Tanaka, M., Iwata, N., Saido, T.C., Watanabe, Y., Kiyama, H. (2005). Altered expression of neprilysin family members in the

- pituitary gland of sleep-disturbed rats, an animal model of severe fatigue. *J. Neurochem.*, 95, 1156-1166.
185. Thal, D.R., Capetillo-Zarate, E., Schultz, C., Rub, U., Saido, T.C., Yamaguchi, H., Haass, C., Griffin, W.S., Del Tredici, K., Braak, H., Ghebremedhin, E. (2005). Apolipoprotein E co-localizes with newly formed amyloid β -protein (A β) deposits lacking immunoreactivity against N-terminal epitopes of A β in a genotype-dependent manner. *Acta Neuropathol. (Berl)*, 110, 459-471.
186. Mouri, A., Zou, L.B., Iwata, N., Saido, T.C., Wang, D., Wang, M.W., Noda, Y., Nabeshima, T. (2005). Inhibition of neprilysin by thiorphan(i.c.v.) cause an accumulation of amyloid β and impairment of learning and memory. *Behav. Brain Res.*, 168, 83-91.
187. Zou, L.B., Mouri, A., Iwata, N., Saido, T.C., Wang, D., Wang, M.W., Mizoguchi, H., Noda, Y., Nabeshima, T. (2005). Inhibition of neprilysin by infusion of thiorphan into the hippocampus cause an accumulation of amyloid β and impairment of learning and memory. *J. Pharmacol. Exp. Ther.*, 314, 334-340.
188. Asai, M., Hattori, C., Iwata, N., Saido, T.C., Sasagawa, N., Szabo, B., Hashimoto, Y., Maruyama, K., Tanuma, S., Kiso, Y., Isihura, S. (2006). The novel β -secretase inhibitor KMI-429 reduces amyloid β peptide production in amyloid precursor protein transgenic and wild-type mice. *J. Neurochem.*, 96, 533-540.
189. Nakagawa, K., Kitazume, S., Oka, R., Maruyama, K., Saido, T.C., Sato, Y., Endo, T., Hashimoto, Y. (2006). Sialylation enhances the secretion of neurotoxic amyloid- β peptides. *J. Neurochem.*, 99, 924-923.
190. Harigaya, Y., Tomidokoro, Y., Ikeda, M., Sasaki, A., Kawarabayashi, T., Matsubara, E., Kanai, M., Saido, T.C., Younkin, S.G., Shoji, M. (2005). Type-specific evolution of amyloid plaque and angiopathy in APPsw mice. *Neurosci. Lett.*, 395, 37-41.
191. Saido, T.C., Iwata, N. (2006). Metabolism of amyloid β peptide and pathogenesis of Alzheimer's disease towards presymptomatic diagnosis, prevention and therapy. *Neurosci. Res.* 54, 235-253.
192. Fujiwara, H., Iwasaki, K., Seki, T., He, M., Maruyama, M., Tomita, N., Kudo, Y., Higuchi, M., Saido, T.C., Maeda, S., Takashima, A., Hara, M., Ohizumi, Y., Arai, H. (2006). Uncaria rhynchophylla, a Chinese medical herb, has potent antiaggregation effects on Alzheimer's β -amyloid proteins. *J. Neurosci. Res.*, 84, 427-433.
193. Huang, S.M., Mouri, A., Kokubo, H., Nakajima, R., Suemoto, T., Higuchi, M., Staufenbiel, M., Noda, Y., Yamaguchi, H., Nabeshima, T., Saido, T.C., Iwata, N. (2006). Neprilysin-sensitive synapse-associated amyloid β peptide oligomers impair neuronal plasticity and cognitive function. *J. Biol. Chem.*, 281, 17941-17951.
194. Sumura, E., Kawarabayashi, T., Sasaki, A., Matsubara, E., Murakami, T., Wuhua, X., Tamura, S., Ikeda, M., Ishiguro, K., Saido, T.C., Westaway, D., St. Hyslop, G., Harigaya, Y., Abe, K. (2006). Enhanced accumulation of tau in doubly transgenic mice expressing mutant β APP and presenilin-1. *Brain Res.* 192-199.
195. Sato, T., Nyborg, A.C., Iwata, N., Dieh T.S., Saido, T.C., Dolde T. E., Wolfe, M.S. (2006). Signal peptide peptidase: biochemical properties and modulation by nonsteroidal anti-inflammatory drugs. *Biochemistry*, 45, 8649-8656
196. Araya, R., Noguchi, T., Yuhki, M., Kitamura, N., Higuchi, M., Saido, T.C., Seki, K., Itohara, S., Kawano, M., Tanemura, K., Takashima, A., Yamada, K., Kondoh, Y., Kanno, I., Wess, J., Yamada, M. (2006). Loss of M(5) muscarinic acetylcholine

- receptors leads to cerebrovascular and neuronal abnormalities and cognitive deficits in mice. *Neurobiol. Dis.*, 24, 334-344.
197. Cynis, H., Schilling, S., Bodnar, M., Hoffmann, T., Heiser, U., Saido, T.C., Demuth, H.U. (2006). Inhibition of glutaminyl cyclase alters pyroglutamate formation in mammalian cells. *Biochim. Biophys. Acta*, 1764, 1618-1625.
198. Higuchi, M., Saido, T.C., Sahara, T.(2006). Animal models of tauopathies. *Neuropathology*, 26, 491-497.
199. Wirths, O., Weis, J., Kaye, R., Saido, T.C., Bayer, T.A. (2007). Age-dependent axonal degeneration in an Alzheimer mouse model. *Neurobiol. Aging.*, 28, 1689-1699.
200. Kamei, H., Saito, T., Ozawa, M., Fujita, Y., Asada, A., Bibb, J.A., Saido, T.C., Sorimachi, H., Hisanaga, S.I. (2007). Suppression of calpain-dependent cleavage of the Cdk5 activator p35 to p25 by site-specific phosphorylation. *J. Biol. Chem.*, 282, 1687-1694.
201. Hori, Y., Hashimoto, T., Wakutani, Y., Urakami, K., Nakashima, K., Condron, M.M., Tsubuki, S., Saido, T.C., Teplow, D.B., Iwatsubo, T. (2006). The Tottori (D7N) and English (H6R) familial Alzheimer's disease mutations accelerate A β fibril formation without increasing protofibril formation. *J. Biol. Chem.*, 282, 4916-4923.
202. Asai, M., Iwata, N., Yoshikawa, A., Aizaki, Y., Ishiura, S., Saido, T.C., Maruyama, K.(2007) Berberine alters the processing of Alzheimer's amyloid precursor protein to decrease A β secretion. *Biochem. Biophys. Res. Commun.*, 352, 498-502.
203. Yoshiyama, Y., Higuchi, M., Zhang, B., Huang, S.M., Iwata, N., Saido, T.C., Maeda, J., Sahara, T., Trojanowski, J.Q., Lee, V.M. (2007) Synapse loss and microglial activation precede tangles in a P301S tauopathy mouse model. *Neuron*, 53, 337-351
204. Wang, J., Pignol, B., Chabrier, P.E., Saido, T.C., Lloyd, R., Tang, Y., Lenoir, M., Puel, J.L. (2007) A novel dual inhibitor of calpains and lipid peroxidation (BN8220) rescues the cochlea from sound trauma. *Neuropharmacology*, 52, 1426-1437.
205. Maeda, J., Ji, B., Irie, T., Tomiyama, T., Maruyama, M., Okauchi, T., Staufenbiel, M., Iwata, N., Ono, M., Saido, T.C., Suzuki, K., Mori, H., Higuchi, M., Sahara, T. (2007). Longitudinal, quantitative assessment of amyloid, neuroinflammation, and anti-amyloid treatment in a living mouse model of Alzheimer's disease enabled by positron emission tomography. *J. Neurosci.*, 27, 10957-10968.
206. Tachida, Y., Nakagawa, K., Saito, T., Saido, T.C., Honda, T., Saito, Y., Murayama, S., Endo, T., Sakaguchi, G., Kato, A., Kitazume, S., Hashimoto, Y. (2008). Interleukin-1 β upregulates TACE to enhance α -cleavage of APP in neurons: Resulting decrease in A β production. *J. Neurochem.*, 47, 1387-1393.
207. Hirata-Fukae, C., Li, H-F., Hoe, H.S., Gray, A.J., Minami, S.S., Hamada, K., Niikura, T., Hua, F., Tsukagoshi-Nagai, H., Horikoshi-Sakuraba, Y., Mughal, M., Rebeck, G.W., LaFerla, F.M., Mattson, M.P., Iwata, N., Saido, T.C., Klein, W.K., Duff, K.E., Aisen, P.S. & Matsuoka, Y. (2008). Females exhibit more extensive amyloid, but not tau, pathology in an Alzheimer transgenic model. *Brain Res.*, 1216, 92-103.
208. Vetrivel, K.S., Zhang, X., Meckler, X., Cheng, H., Lee, S., Gong, P., Lopes, K.O., Chen, Y., Iwata, N., Yin, K-J., Lee, J-M., Parent, A.T., Saido, T.C., Li, Y-M., Sisodia, S.S. & Thinakaran, G. (2008). Evidence that CD147 modulation of A β

- levels is mediated by extracellular degradation of secreted A β . *J. Biol. Chem.*, 283, 19489-19498.
209. Wang, J., Ohno-Matsui, K., Yoshida, T., Kojima, A., Shimada, N., Nakahama, K., Safranov, O., Iwata, N., Saido, T.C., Mochizuki, M., Morita, I. (2008). Altered function of factor I caused by amyloid β : Implication for pathogenesis of age-related macular degeneration from drusen. *J. Immunol.*, 181, 712-720.
210. Cynis, H., Scheel, E., Saido, T.C., Schilling, S., Demuth, H.U. (2008). Amyloidogenic processing of amyloid precursor protein: evidence of a pivotal role of glutamyl cyclase in generation of pyroglutamate-modified amyloid- β . *Biochemistry*, 47, 7405-7413.
211. Nakajima, R., Takao, K., Huang, S.-M., Takano, J., Iwata, N., Miyakawa, T., Saido, T.C. (2008). Comprehensive behavioral phenotyping of calpastatin-knockout mice. *Mol. Brain*, 1(7), 1-15.
212. Nakazawa, T., Shimura, M., Mourin, R., Kondo, M., Yokokura, S., Saido, T.C., Nishida, L., Endo, S. (2009). Calpain-mediated degradation of G-substrate plays a critical role in retinal excitotoxicity for amacrine cells, *J. Neurosci. Res.*, 87, 141-1423.
213. Suzuki, T., Miyamoto, H., Nakahari, T., Inoue, I., Suemoto, T., Jiang, B., Hirota, Y., Itohara, S., Saido, T.C., Tsumoto, T., Sawamoto, K., Hensch, T.K., Delgado-Escueta, A.V., Yamakawa, K. (2009). Efhc1 deficiency causes spontaneous myoclonus and increase seizure susceptibility. *Hum. Mol. Genet.*, 18, 1099-1109.
214. Adachi, A., Kano, F., Saido, T.C., Murata, M. (2009). Visual screening and analysis for kinase-regulated membrane trafficking pathways that are involved in extensive β -amyloid secretion. *Genes Cells*, 14, 355-369.
215. Gonçalves, I., Nitulescu, M., Saido, T.C., Dias, N., Pedro, L.M., E. Fernandes. J.F., Ares, M.P., Pörn-Ares, I. (2009). Activation of calpain-1 in human carotid artery atherosclerotic lesions. *BMC Cardiovasc. Disord.*, 18, 9:26.
216. Fujiwara, H., Tabuchi, M., Yamaguchi, T., Iwasaki, K., Furukawa, K., Sekiguchi, K., Ikarashi, Y., Kudo, Y., Higuchi, M., Saido, T.C., Maeda, S., Takashima, A., Hara, M., Yaegashi, N., Kase, Y., Arai, H. (2009). A traditional medicinal herb *Paeonia suffruticosa* and its active constituent 1,2,3,4,6-penta-O-galloyl- β -D-glucopyranose have potent anti-aggregation effects on Alzheimer's amyloid β proteins in vitro and in vivo. *J. Neurochem.*, 109, 1648-1657.
217. Nishida, Y., Ito, S., Ohtsuki, S., Yamamoto, N., Takahashi, T., Iwata, N., Jishage, K.I., Yamada, H., Sasaguri, H., Yokota, S., Piao, W., Tomimitsu, H., Saido, T.C., Yanagisawa, K., Terasaki, T., Mizusawa, H., Yokota, T. (2009). Depletion of vitamin E increases A β accumulation by decreasing its clearances from brain and blood in a mouse model of Alzheimer disease. *J. Biol. Chem.*, 284, 33400-33408.
218. Choi, Y.S., Lee, B., Cho, H.Y., Reyes, I.B., Pu, X.A., Saido, T.C., Hoyt, K.R., Obrietan, K. (2009). CREB is a key regulator of striatal vulnerability in chemical and genetic models of Huntington's disease. *Neurobiol. Dis.*, 36, 259-268.
219. Nilsson, P., Iwata, N., Muramatsu, S-I., Tjernberg, L.O., Winblad, B., Saido T.C. (2010). Gene therapy in Alzheimer's disease -potential for disease modification. *J. Cell Mol. Med.* 14, 714-757.
220. Thal, D.R., Papassotiropoulos, A., Saido T.C., Griffin, W.S., Mrak, R.E., Kölsch, H., Tredici, K.D., Attems, J., Ghebremedhin, E. (2010). Capillary cerebral amyloid angiopathy identifies a distinct APOE epsilon4-associated subtype of sporadic Alzheimer's disease. *Acta Neuropathol.* 120, 169-183.

221. Asai, M., Iwata, N., Tomita, T., Iwatsubo, T., Ishiura, S., Saido, T.C., Maruyama, K. (2010). Efficient four-drug cocktail therapy targeting amyloid- β peptide for Alzheimer's disease. *J. Neurosci. Res.*, 88, 3588-3597.
222. Attems, J., Yamaguchi, H., Saido T.C., Thal, D.R. (2010). Capillary CAA and perivascular A β -deposition: two distinct features of Alzheimer's disease pathology. *J. Neurol. Sci.* 299, 155-162.
223. Zhang, G., Thomas, A.L., Marshall, A.L., Kernan, K.A., Su, Y., Zheng, Y., Takano, J., Saido, T.C., Eddy, A.A. (2011) Nicotinic acetylcholine receptor $\alpha 1$ promotes calpain-1 activation and macrophage inflammation in hypercholesterolemic nephropathy. *Lab. Invest.*, 91, 106-123.
224. Kitazume, S., Tachida, Y., Kato, M., Yamaguchi, Y., Honda, T., Hashimoto, Y., Wada, Y., Saito, T., Iwata, N., Saido, T., Taniguchi, N. (2010). Brain endothelial cells produce amyloid β from amyloid precursor protein 770 and preferentially secrete the O-glycosylated form. *J. Biol. Chem.*, 285, 40097-40103.
225. Gomes, J.R., Lobo, A.C., Melo, C.V., Inácio, A.R., Takano, J., Iwata, N., Saido, T.C., de Almeida, L.P., Wieloch, T., Duarte, C.B. (2011) Cleavage of the vesicular GABA transporter under excitotoxic conditions is followed by accumulation of the truncated transporter in tonsynaptic Sites. *J. Neurosci.* 31, 4622-4635.
226. Maeda, J., Zhang, M.R., Okauchi, T., Ji, B., Ono, M., Hattori, S., Kumata, K., Iwata, N., Saido, T.C., Trojanowski, J.Q., Lee, V.M., Staufenbiel, M., Tomiyama, T., Mori, H., Fukumura, T., Suhara, T., Higuchi, M. (2011) *In vivo* positron emission tomographic imaging of glial responses to amyloid- β and tau pathologies in mouse models of Alzheimer's disease and related disorders. *J. Neurosci.*, 31, 4720-4730.
227. Sato, K., Minegishi, S., Takano, J., Plattner, F., Saito, T., Asada, A., Kawahara, H., Iwata, N., Saido, T.C., Hisanaga, S-I. (2011) Calpastatin, an endogenous calpain-inhibitor protein, regulates the cleavage of the Cdk5 activator p35 to p25. *J. Neurochem.*, 117, 505-515.
228. Saito, T., Suemoto, T., Brouwers, N., Slegers, K., Funamoto, S., Mihira, M., Matsuba, Y., Yamada, K., Nilsson, P., Takano, J., Nishimura, M., Iwata, N., Van Broeckhoven, C., Ihara, Y., Saido, T.C. (2011) Potent amyloidogenicity and pathogenicity of A β 43. *Nat. Neurosci.*, 14, 1023-1032.
229. Takano, J., Mihira, N., Fujioka, R., Hosoki, E., Chishti, A.H., Saido, T.C. (2011) Vital role of the calpain-calpastatin system for placental integrity-dependent embryonic survival. *Mol. Cell Biol.*, 31, 4097-4106.
230. Asai, M., Yagishita, S., Iwata, N., Saido, T.C., Ishiura, S., Maruyama, K. (2011) An alternative metabolic pathway of amyloid precursor protein C-terminal fragments via cathepsin B in a human neuroglioma model. *FASEB J.*, 10, 3720-3730.
231. Yahata, N., Asai, M., Kitaoka, S., Takahashi, K., Asaka, I., Hioki, H., Kaneko, T., Maruyama, K., Saido, T.C., Nakahata T, Asada T, Yamanaka S, Iwata N, Inoue H. (2011) Anti-A β drug screening platform using human iPS cell-derived neurons for the treatment of Alzheimer's disease. *PLoS One.*, 6, e25788.
232. Ryu, M., Yasuda, M., Shi, D., Shanab, A.Y., Watanabe, R., Himori, N., Omodaka, K., Yokoyama, Y., Takano, J., Saido, T., Nakazawa T. (2012) Critical role of calpain in axonal damage-induced retinal ganglion cell death. *J. Neurosci. Res.*, 90, 802-815.
233. Higuchi, M., Iwata, N., Matsuba, Y., Takano, J., Suemoto, T., Maeda, J., Ji, B., Ono, M., Staufenbiel, M., Suhara, T., Saido, T.C. (2012) Mechanistic involvement

- of the calpain-calpastatin system in Alzheimer neuropathology. *FASEB J.*, 26, 1204-1217.
234. Abramowski, D., Rabe, S., Upadhaya, A.R., Reichwald, J., Danner, S., Staab, D., Capetillo-Zarate, E., Yamaguchi, H., Saido, T.C., Wiederhold, K.H., Thal, D.R., Staufenbiel, M. (2012) Transgenic expression of intraneuronal A β 42 but not A β 40 leads to cellular A β lesions, degeneration, and functional impairment without typical Alzheimer's disease pathology. *J. Neurosci.*, 32, 1273-1283.
235. Schlenzig, D., Rönicke, R., Cynis, H., Ludwig, H.H., Scheel, E., Reymann, K., Saido, T., Hause, G., Schilling, S., Demuth, H.U. (2012) N-terminal Pyroglutamate (pGlu) formation of Ab38 and Ab40 Enforces Oligomer Formation and Potency to Disrupt Hippocampal LTP. *J. Neurochem.*, 121, 774-784.
236. Schoch, K.M., Evans, H.N., Brelsfoard, J.M., Madathil, S.K., Takano, J., Saido, T.C., Saatman, K.E. (2012) Calpastatin overexpression limits calpain-mediated proteolysis and behavioral deficits following traumatic brain injury. *Exp. Neurol.*, 236, 371-382.
237. Kakiya, N., Saito, T., Nilsson, P., Matsuba, Y., Tsubuki, S., Takei, N., Nawa, H., Saido T.C. (2012) Cell-surface expression of the major A β degrading enzyme, neprilysin, depends on phosphorylation by MEK and dephosphorylation by protein phosphatase 1a. *J. Biol. Chem.*, 287, 29396-29372.
238. Yamashita, T., Hideyama, T., Hachiga, K., Teramoto, S., Takano, J., Iwata, N., Saido, T.C., Kwak, S. (2013) A role for calpain-dependent cleavage of TDP-43 in amyotrophic lateral sclerosis pathology. *Nat. Commun.*, 3:1307. doi:10.1038/ncomms2303.
239. Hübener, J., Weber, J.J., Richter, C., Honold, L., Weiss, A., Murad, F., Breuer, P., Wüllner, U., Bellstedt, P., Paquet-Durand, F., Takano, J., Saido, T.C., Riess, O., Nguyen, H.P. (2013) Calpain-mediated ataxin-3 cleavage in the molecular pathogenesis of spinocerebellar ataxia type 3 (SCA3). *Hum. Mol. Genet.*, 22, 508-18.
240. Iwata, N., Sekiguchi, M., Hattori, Y., Takahashi, A., Asai, M., Ji, B., Higuchi, M., Staufenbiel, M., Muramatsu, S., Saido T.C. (2013) Global brain delivery of neprilysin gene by intravascular administration of AAV vector in mice. *Sci. Rep.*, 3:1472. doi: 10.1038/srep01472.
241. Sörgjerd, K.M., Zako, T., Sakono, M., Stirling, P.C., Leroux, M.R., Saito, T., Nilsson, P., Sekimoto, M., Saido, T.C., Maeda, M. (2013) Human prefoldin inhibits amyloid- β (A β) fibrillation and contributes to formation of nontoxic A β aggregates. *Biochemistry*, 52, 3532-3542.
242. Frost, J.L., Le, K.X., Cynis, H., Ekpo, E., Kleinschmidt, M., Palmour, R.M., Ervin, F.R., Snigdha, S., Cotman, C.W., Saido, T.C., Vassar, R.J., St George-Hyslop, P., Ikezu, T., Schilling, S., Demuth, H.U., Lemere, C.A. (2013) Pyroglutamate-3 amyloid- β deposition in the brains of humans, non-human primates, canines, and Alzheimer disease-like transgenic mouse models. *Am. J. Pathol.*, 183, 369-381. doi: 10.1016/j.ajpath.2013.05.005.
243. Huang, Z., Rose, A.H., Hoffmann, F.W., Hashimoto, A.S., Bertino, P., Denk, T., Takano, J., Iwata, N., Saido, T.C., Hoffmann, P.R. (2013) Calpastatin Prevents NF- κ B-Mediated Hyperactivation of Macrophages and Attenuates Colitis. *J. Immunol.*, 191, 3778-3788. doi: 10.4049/jimmunol.1300972.
244. Maruyama, M., Shimada, H., Suhara, T., Shinotoh, H., Ji, B., Maeda, J., Zhang, M.R., Trojanowski, J.Q., Lee, V.M., Ono, M., Masamoto, K., Takano, H., Sahara, N., Iwata, N., Okamura, N., Furumoto, S., Kudo, Y., Chang, Q., Saido, T.C., Takashima, A., Lewis, J., Jang, M.K., Aoki, I., Ito, H., Higuchi, M. (2013) Imaging of tau pathology in a tauopathy mouse model and in Alzheimer patients compared to normal controls. *Neuron*, 79, 1094-1108. doi: 10.1016/j.neuron.2013.07.037.
245. Nilsson, P., Loganathan, K., Sekiguchi, M., Matsuba, Y., Hui, K., Tsubuki, S., Tanaka, M., Iwata, N., Saito, T., Saido, T.C. (2013) A β secretion and plaque

- formation depend on autophagy. *Cell Reports*, 5(19), 61-69, doi: 10.1016/j.celrep.2013.08.042.
246. Funamoto, S., Sasaki, T., Ishihara, S., Nobuhara, M., Nakano, M., Watanabe-Takahashi, M., Saito, T., Kakuda, N., Miyasaka, T., Nishikawa, K., Saido, T.C., Ihara, Y. (2013) Substrate ectodomain is critical for substrate preference and inhibition of γ -secretase. *Nat. Commun.*, 4:2529. doi:10.1038/ncomms3529.
247. Iwata, A., Nagata, K., Hatsuta, H., Takuma H., Bundo, M., Iwamoto, K., Tamaoka, A., Murayama, S., Saido, T., Tsuji, S. (2014) Altered CpG methylation in sporadic Alzheimer's disease is associated with APP and MAPT dysregulation. *Hum. Mol. Genet.*, 23, 648-656.
248. Saito, T., Matsuba, Y., Mihira, N., Takano, J., Nilsson, P., Itohara, S., Iwata, N., Saido, T.C. (2014) Single App knock-in mouse models of Alzheimer's disease. *Nat. Neurosci.*, 17, 661-663.
249. Nilsson, P., Saido, T.C. (2014) Dual roles for autophagy: Degradation and secretion of Alzheimer's disease A β peptide. *Bioessays*, 36, 570-578.
250. Nilsson, P., Saido, T.C. (2014) New mouse model of Alzheimer's. *ACS Chem. Neurosci.*, 5, 499-502.
251. Kudo-Sakamoto, Y., Akazawa, H., Ito, K., Takano, J., Yano, M., Yabumoto, C., Naito, A.T., Oka, T., Lee, J.K., Sakata, Y., Suzuki, J., Saido, T.C., Komuro, I. (2014) Calpain-dependent cleavage of N-cadherin is involved in the progression of post-myocardial infarction remodeling. *J. Biol. Chem.*, 289, 19408-19419.
252. Nilsson, P., Sekiguchi, M., Akagi, T., Izumi, S., Komori, T., Hu, K., Sörgjerd, K., Tanaka, M., Saito, T., Iwata, N., Saido, T.C. (2015) Autophagy-Related Protein 7 Deficiency in Amyloid β (A β) Precursor Protein Transgenic Mice Decreases A β in the Multivesicular Bodies and Induces A β Accumulation in the Golgi. *Am. J. Pathol.*, 185, 305-313.
253. Zhang, H., Wu, L., Pchitskaya, E., Zaharova, O., Saito, T., Saido, T., Bezprozvanny, I. (2015) Neuronal store-operated calcium entry and mushroom spine loss in amyloid precursor protein knock-in mouse model of Alzheimer's disease. *J. Neurosci.*, 35, 13275-13286.
254. Huang, Y., Skwarek-Maruszewska, A., Horré, K., Vandeweyer, E., Wolfs, L., Snellinx, A., Saito, T., Radaelli, E., Corthout, N., Colombelli, j., Lo, A. C., Aerschot, L. V., Callaerts-Vegh, Z., Trabzuni, D. Bossers, K., Verhaagen, J., Ryten, M., Munck, S., D'Hooge, R., Swaab, D. F., Hardy, J. Saido, T. C., De Strooper, B., Thathiah, A. (2015) GPR3 modulation of the amyloid plaque burden and memory in Alzheimer's disease. *Sci. Trans. Med.*, 309ra164. doi: 10.1126/scitranslmed.aab3492.
255. Kizuka, Y., Nakano, M., Kitazume, S., Saito, T., Saido, T.C., Taniguchi, N. (2015) Bisecting GlcNAc modification stabilizes BACE1 protein under oxidative stress conditions. *Biochem. J.* in press.

Editorial

1. *A β Metabolism and Alzheimer's Disease*. (Saido, T.C. ed.), Landes Bioscience (Georgetown, Tex), also available at www.eurekah.com (2003).

Books and book chapters

1. Suzuki, K., Sorimachi, H., Hata, A., Ohno, S., Emori, Y., Kawasaki, H., Saido, T.C., Imajoh-Ohmi, S., Akita, Y. (1990). Calcium-dependent protease, a novel molecular species, regulation of gene expression, and activation at the cell membrane. in *Neurotoxicity of Excitatory Amino Acids* (Guidotti, A. ed.), Raven Press (New York), pp. 79-93.
2. Saido, T.C., Shiramine, M., Tsukaguchi, M., Ito, H., Nagao, S., Tsuchiya, T., Suzuki, K. (1992). Autolytic activation of μ -calpain as probed by an active form-

- specific antibody. in Recent Advances in *Cellular and Molecular Biology*, Vol. 4 (Wegmann, R.J., and Wegmann, M.A. eds.), Peeters Press (Leuven), pp. 375-380.
3. Saido, T.C., Suzuki, K. (1993). Calpain: new aspects in activation processes and physiological roles. in *Innovations in Proteases and their inhibitors* (Aviles, F.X. ed.), Walter de Gruyter (Berlin), pp. 197-214.
 4. Saido, T.C., Yokota, M., Tani, E., Kawashima, S. (1997). Post-secretory catabolism of β -amyloid in brain. in *Alzheimer's Disease: Biology, Diagnosis and Therapeutics* (Iqbal, K., Winblad, B., Nishimura, T., Takeda, M., Wisniewski, H.M., eds.), John Wiley & Sons Ltd. (Chichester), pp. 337-346.
 5. Fox, J.E.B., Saido, T.C. (1999). Calpain in signal transduction. in *Calpain: Pharmacology and Toxicology of a calcium-dependent cellular protease* (Wang, K.K.W., Yuen, P.-w., eds.), Taylor & Francis. (Brisotol), pp. 103-126.
 6. Saido, T.C., Iwata, N. (2000). Catabolism of amyloid- β peptide in brain parenchyma. in *Neuroscientific Basis of Dementia* (Tanaka, C., Ihara, Y., and McGeer, P.L., eds.), Birkhauser Verlag, pp. 249-256.
 7. Lee, H.-J., Suzuki, K., Saido, T.C. (2000). Genes of Mammalian Proteinase. in *Role of Proteases in the Pathophysiology of Neurodegenerative Disease* (Banik, N.L. ed.) Plenum Press, New York.
 8. Iwata, N., Saido, T.C. (2001). Alzheimer's disease as a proteolytic disorder: catabolism and processing of amyloid β peptide. in *Mapping the progress of Alzheimer's and Parkinson's disease* (Mizuno, Y. ed.) Kluwer Academic/Plenum Publishers, New York.
 9. Saido, T.C. (2003). A β metabolism: from Alzheimer research to brain aging control. In *A β Metabolism and Alzheimer's Disease* (Saido, T.C. ed) Landes Bioscience (Georgetown, Tex) www.eurekah.com (2002).
 10. Saido, T.C., Nakahara, H. (2003). Proteolytic degradation of Ab by neprilysin and other peptidases. In *A β Metabolism and Alzheimer's Disease* (Saido, T.C. ed) Landes Bioscience (Georgetown, Tex) www.eurekah.com (2002).

***There are 89 other scientific publications including two books in Japanese.**