

## *Biography*

Name: Hisashi Doi, DSc.  
Place of Birth: Osaka-shi, Osaka Pref., Japan  
Year of Birth: 1971  
Nationality: Japanese  
Present Position: Team Leader, Laboratory for Labeling Chemistry, RIKEN Center for Biosystems Dynamics Research (BDR)

### Education:

1989–1993 Department of Chemistry and Materials Technology, Kyoto Institute of Technology (Supervisor: Prof. Akira Oku)  
1993–2000 Ph. D. Course, Department of Chemistry, Nagoya University (Supervisor: Prof. Ryoji Noyori)  
2000 Nov. Ph. D. degree (DSc)

### Career:

2000–2003 JSPS Research Fellow (2001–2002, research activities at Uppsala University (Supervisor: Prof. Bengt Långström)  
2003–2005 Technical Assistant, Gifu University  
2005–2005 Member of Preparatory Office, RIKEN Molecular Imaging Research Program (MIRP)  
2005–2007 Research Scientist, MIRP  
2007–2008 Deputy Team Leader of Molecular Probe & Drug Design Laboratory, MIRP  
2008–2009 Unit Leader of Drug Synthesis & Molecular Probing Unit, RIKEN Center for Molecular Imaging Science (CMIS)  
2009–2013 Team Leader of Molecular Imaging Labeling Chemistry Team, CMIS  
2013–2018 Team Leader of Labeling Chemistry Team, RIKEN Center for Life Science Technology (CLST)  
2018–present Laboratory for Labeling Chemistry, RIKEN Center for Biosystems Dynamics Research (BRD)

### Membership:

- The Chemical Society of Japan
- The Society of Synthetic Organic Chemistry, Japan
- The Kinki Chemical Society Japan
- Japanese Society for Chemical Biology
- The Japanese Society for Molecular Imaging

### Awards:

Erwin von Bälz 1<sup>st</sup> Preis 2007 for Molecular Imaging Research, Joint prize by Yasuyoshi Watanabe, Masaaki Suzuki, Hirotaka Onoe, Hisashi Doi, Yasuhiro Wada, Yosky Kataoka, and Shuichi Enomoto

### Field of research:

PET Radiochemistry, Organometallic Chemistry, Organic Chemistry, Medicinal Chemistry

### Others:

- Senior radiation protection supervisor
- Guest associate professor (2007–2009) and Guest professor (2010–2014); Hamamatsu University School of Medicine
- Guest professor (2010–present); Osaka City University Graduate School of Medicine and Faculty of Medicine
- Guest professor (2011–2014); Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Science
- Guest associate professor (2011–2017) and Guest Professor (2018–present); Gifu University United Graduate School of Drug Discovery and Medical Information Science
- Guest professor (2016–present); Tokushima University Graduate School of Biomedical Sciences
- Executive board member, Japanese Society for Molecular Imaging (May 2021–present)

### Publications

#### **【Original Articles】**

- (1) Takatani, S., Tahara, T., Tsuji, M., Ozaki, D., Shibata, N., Hashizume, Y., Suzuki, M., Onoe, H., Watanabe, Y., Doi, H., “Synthesis of L-[5-<sup>11</sup>C]Leucine and L- $\alpha$ -[5-<sup>11</sup>C]Methylleucine via Pd<sup>0</sup>-mediated <sup>11</sup>C-Methylation and Microfluidic Hydrogenation: Potentiality of Leucine PET Probes for Tumor Imaging”, *ChemMedChem*, 2021, in press. (doi: 10.1002/cmdc.202100255) **This paper won Very Important Paper (VIP) designation and was selected as the front cover of the journal. Additionally, this paper was introduced as a news article in a chemistry magazine *ChemistryViews*.**
- (2) Doi, H., Goto, M., Sato, Y., “Pd<sup>0</sup>-Mediated Cross-Coupling of [<sup>11</sup>C]Methyl Iodide with Carboxysilane for Synthesis of [<sup>11</sup>C]Acetic Acid and Its Active Esters: <sup>11</sup>C-Acetylation of Small, Medium, and Large Molecules”, *Eur. J. Org. Chem.*, 3970–3979, (2021). (doi: 10.1002/ejoc.202100638) **This paper was selected as the front cover of the journal.**
- (3) Watanabe, Y., Mawatari, A., Aita, K., Sato, Y., Wada, Y., Nakaoka, T., Onoe, K., Yamano, E., Akamatsu, G., Ohnishi, A., Shimizu, K., Sasaki, M., Doi, H., Senda, M., “PET imaging of <sup>11</sup>C-labeled thiamine tetrahydrofurfuryl disulfide, vitamin B<sub>1</sub> derivative: First-in-human study”, *Biochem. Biophys. Res. Commun.*, **555**, 7–12 (2021). (doi: 10.1016/j.bbrc.2021.03.119)
- (4) Nozaki, S., Nakatani, Y., Mawatari, A., Shibata, N., Hume, W. E., Hayashinaka, E., Wada, Y., Doi, H., Watanabe, Y., “<sup>18</sup>F-FIMP: a LAT1-specific PET probe for discrimination between tumor tissue and inflammation”, *Sci. Rep.* **9**, 15718 (2019). (doi: 10.1038/s41598-019-52270-x)
- (5) Takeuchi, J., Kikukawa, T., Saito, H., Hasegawa, I., Takeda, A., Hatsuta, H., Kawabe, J., Wada, Y., Mawatari, A., Igesaka, A., Doi, H., Watanabe, Y., Shimada, H., Kitamura, S., Higuchi, M.,

- Suhara, T., Itoh, Y., “Amyloid-Negative Dementia in the Elderly is Associated with High Accumulation of Tau in the Temporal Lobes”, *Open Biomed. Eng. J.* **13**, 55–66 (2019). (doi: 10.2174/1874120701913010055)
- (6) Watanabe, K., Nozaki, S., Goto, M., Kaneko, K., Hayashinaka, E., Irie, S., Nishiyama, A., Kasai, K., Fujii, K., Wada, Y., Mizuno, K., Mizuseki, K., Doi, H., Watanabe, Y., “PET imaging of <sup>11</sup>C-labeled coenzyme Q<sub>10</sub>: Comparison of biodistribution between [<sup>11</sup>C]ubiquinol-10 and [<sup>11</sup>C]ubiquinone-10”, *Biochem. Biophys. Res. Commun.*, **512**, 611–615 (2019). (doi: 10.1016/j.bbrc.2019.03.073)
- (7) Ose, T., Autio, J. A., Ohno, M., Nishigori, K., Tanki, N., Igesaka, A., Mori, T., Doi, H., Wada, Y., Nakajima, I., Watabe, H., Hayashi, T., “A novel tungsten-based fiducial marker for multi-model brain imaging”, *J. Neurosci. Methods* **323**, 22–31 (2019). (doi: 10.1016/j.jneumeth.2019.04.014)
- (8) Goto, M., Nishiyama, A., Yamaguchi, T., Watanabe, K., Fujii, K., Watanabe, Y., Doi, H., “Synthesis of <sup>11</sup>C-labeled ubiquinone and ubiquinol via Pd<sup>0</sup>-mediated rapid C-[<sup>11</sup>C]methylation using [<sup>11</sup>C]methyl iodide and 39-demethyl-39-(pinacolboranyl)ubiquinone”, *J. Labelled Compd. Radiopharm.* **62**, 86–94 (2019). (doi: 10.1002/jlcr.3700) **This research was adopted as the cover image and recognized as the top 10% most downloaded papers 2018–2019 in the journal.**
- (9) Takahashi, K., Hosoya, T., Onoe, K., Takashima, T., Tanaka, M., Ishii, A., Nakatomi, Y., Tazawa, S., Takahashi, K., Doi, H., Wada, Y., Watanabe, Y., “Association between aromatase in human brains and personality traits”, *Sci. Rep.* **8**, 16841 (2018). (doi: 10.1038/s41598-018-35065-4)
- (10) Nozaki, S., Mawatari, A., Nakatani, Y., Hayashinaka, E., Wada, Y., Nomura, Y., Kitayoshi, T., Akimoto, K., Ninomiya, S., Doi, H., Watanabe, Y., “PET Imaging Analysis of Vitamin B<sub>1</sub> Kinetics with [<sup>11</sup>C]Thiamine and its Derivative [<sup>11</sup>C]Thiamine Tetrahydrofurfuryl Disulfide in Rats”, *Mol. Imaging Biol.* **20**, 1001–1007 (2018). (doi: 10.1007/s11307-018-1186-y)
- (11) Doi, H., Kida, T., Nishino, K., Nakatsuji, M., Sakamoto, S., Shimizu, S., Teraoka, Y., Tamura, Y., Kataoka, Y., Inui, T., “Solubility-Improved 10-*O*-Substituted SN-38 Derivatives with Antitumor Activity”, *ChemMedChem* **12**, 1715–1722 (2017). (doi: 10.1002/cmdc.201700454)
- (12) Morizane, A., Kikuchi, T., Hayashi, T., Mizuma, H., Takara, S., Doi, H., Mawatari, A., Glasser, M. F., Shiina, T., Ishigaki, H., Itoh, Y., Okita, K., Yamasaki, E., Doi, D., Onoe, H., Ogasawara, K., Yamanaka, S., Takahashi, J., “MHC matching improves engraftment of iPSC-derived neurons in non-human primates”, *Nat. Commun.* **8**:385 (2017). (doi: 10.1038/s41467-017-00926-5)
- (13) Nozaki, S., Ozaki, N., Suzuki, S., Goto, M., Mawatari, A., Nakatani, Y., Hayashinaka, E., Doi, H., Wada, Y., Watanabe, Y., “Development of diagnostic techniques for early rheumatoid arthritis using positron emission tomography with [<sup>11</sup>C]PK11195 and [<sup>11</sup>C]ketoprofen tracers”, *Mol. Imaging Biol.* **19**, 746–753 (2017). (doi: 10.1007/s11307-016-1039-5)
- (14) Yokoyama, C., Mawatari, A., Kawasaki, A., Takeda, C., Onoe, K., Doi, H., Newman-Tancredi, A., Zimmer, L., Onoe, H., “Marmoset serotonin 5-HT<sub>1A</sub> receptor mapping with a biased agonist PET probe <sup>18</sup>F-F13714: comparison with an antagonist tracer <sup>18</sup>F-MPPF in awake and anaesthetized state”, *Int. J. Neuropsychopharmacol.* **19**(12), 1–12 (2016). (doi: 10.1093/ijnp/pyw079)
- (15) Doi, H., Sato, K., Shindou, H., Sumi, K., Koyama, H., Hosoya, T., Watanabe, Y., Ishii, S., Tsukada, H., Nakanishi, K., Suzuki, M., “Blood-Brain Barrier Permeability of Ginkgolide: Comparison of the Behavior of PET Probes 7 $\alpha$ -[<sup>18</sup>F]Fluoro- and 10-*O*-*p*-[<sup>11</sup>C]Methylbenzyl Ginkgolide B in Monkey and Rat Brains”, *Bioorg. Med. Chem.* **24**, 5148–5157 (2016). (doi: 10.1016/j.bmc.2016.08.032)
- (16) Ohnishi, A., Senda, M., Yamane, T., Mikami, T., Nishida, H., Nishio, T., Akamatsu, G., Ikari, Y., Kimoto, S., Aita, K., Sasaki, M., Shinkawa, H., Yamato, Y., Shukuri, M., Mawatari, A., Doi, H., Watanabe, Y., Onoe, H., “Exploratory human PET study of the effectiveness of <sup>11</sup>C-ketoprofen methyl ester, a potential biomarker of neuroinflammatory processes in Alzheimer’s disease”, *Nucl.*

- Med. Biol.* **43**, 438–444 (2016). (doi: 10.1016/j.nucmedbio.2016.04.005)
- (17) Shukuri, M., Mawatari, A., Ohno, M., Suzuki, M., Doi, H., Watanabe, Y., Onoe, H., “Detection of cyclooxygenase-1 in activated microglia during amyloid plaque progression: PET studies in Alzheimer’s disease model mice”, *J. Nucl. Med.* **57**, 291–296 (2016). (doi: 10.2967/jnumed.115.166116)
- (18) Tahara, T., Zhang, Z., Ohno, M., Hosaka, N., Hirao, Y., Suzuki, M., Doi, H., Onoe, H., “A novel <sup>11</sup>C-labeled thymidine analog, [<sup>11</sup>C]AZT, for tumor imaging by positron emission tomography”, *EJNMMI Research* **5**:45 (2015). (doi: 10.1186/s13550-015-0124-0)
- (19) Doi, H., Mawatari, A., Kanazawa, M., Nozaki, S., Nomura, Y., Kitayoshi, T., Akimoto, K., Suzuki, M., Ninomiya, S., Watanabe, Y., “Synthesis of <sup>11</sup>C-Labeled Thiamine and Fursultiamine for In Vivo Molecular Imaging of Vitamin B<sub>1</sub> and Its Prodrug Using Positron Emission Tomography”, *J. Org. Chem.* **80**, 6250–6258 (2015). (doi: 10.1021/acs.joc.5b00685)
- (20) Goto, M., Mizuma, H., Wada, Y., Suzuki, M., Watanabe, Y., Onoe, H., Doi, H., “<sup>11</sup>C-Labeled Capsaicin and Its In Vivo Molecular Imaging in Rats by Positron Emission Tomography”, *Food and Nutrition Sciences* **6**, 216–220 (2015). (doi: 10.4236/fns.2015.62022)
- (21) Han, C., Doi, H., Kimura, J., Nakao, Y., Suzuki, M., “<sup>11</sup>C-Labeling of the C(1)-C(10) Dihydroxy Acid Moiety for the Study on the Synthesis of Kulokekahilide-2 PET Tracer”, *Int. J. Org. Chem.* **4**, 269–277 (2014). (doi: 10.4236/ijoc.2014.44029)
- (22) Zhang, Z., Doi, H., Koyama, H., Watanabe, Y., Suzuki, M., “Efficient synthesis of [<sup>11</sup>C]zidovudine and its analogs by convenient one-pot palladium(0)-copper(I) co-mediated rapid C-[<sup>11</sup>C]methylation”, *J. Label. Compd. Radiopharm.* **57**, 540–549 (2014). (doi: 10.1002/jlcr.3213)
- (23) Suzuki, M., Takashima-Hirano, M., Ishii, H., Watanabe, C., Sumi, K., Koyama, H., Doi, H., “Synthesis of <sup>11</sup>C-labeled retinoic acid, [<sup>11</sup>C]ATRA, via an alkenylboron precursor by Pd(0)-mediated rapid C-[<sup>11</sup>C]methylation”, *Bioorg. Med. Chem. Lett.*, **24**, 3622–3625 (2014). (doi: 10.1016/j.bmcl.2014.05.041)
- (24) Ohnishi, A., Senda, M., Yamane, T., Sasaki, M., Nishio, T., Mikami, T., Ikari, Y., Nishida, H., Shukuri, M., Takashima, T., Mawatari, A., Doi, H., Watanabe, Y., Onoe, H., “Human whole-body biodistribution and dosimetry of a new PET tracer, [<sup>11</sup>C]ketoprofen methyl ester, for imagings of neuroinflammation”, *Nucl. Med. Biol.* **41**, 594–599 (2014). (doi: 10.1016/j.nucmedbio.2014.04.008)
- (25) Mukai, H., Ozaki, D., Cui, Y., Kuboyama, T., Yamato-Nagata, H., Onoe, K., Takahashi, M., Wada, Y., Imanishi, T., Kodama, T., Obika, S., Suzuki, M., Doi, H., Watanabe, Y., “Quantitative evaluation of the improvement in the pharmacokinetics of a nucleic acid drug delivery system by dynamic PET imaging with <sup>18</sup>F-incorporated oligodeoxynucleotides”, *J. Control. Release.* **180**, 92–99 (2014). (doi: 10.1016/j.jconrel.2014.02.014)
- (26) Yamanaka, H., Yokoyama, C., Mizuma, H., Kurai, S., Finnema, S.J., Halldin, C., Doi, H., Onoe, H., “A possible mechanism of the nucleus accumbens and ventral pallidum 5 HT1B receptors underlying the antidepressant action of ketamine: a PET study with macaques”, *Transl. Psychiatry* **4**, e342 (2014). (doi: 10.1038/tp.2013.112)
- (27) Takahashi, K., Hosoya, T., Onoe, K., Doi, H., Nagata, H., Hiramatsu, T., Li, X., Watanabe, Y., Wada, Y., Takashima, T., Suzuki, M., Onoe, H., Watanabe, Y., “[<sup>11</sup>C]Cetrozole: an improved C-[<sup>11</sup>C]methylated PET probe for aromatase imaging in the brain”, *J. Nucl. Med.*, **55**, 852–857 (2014).
- (28) Koyama, H., Doi, H., Suzuki, M., “Evaluation of TIOH Effect for Pd<sup>0</sup>-Mediated Cross-Coupling of Methyl Iodide and Excess Boronic Acid Ester Toward Fabrication of [<sup>11</sup>C]CH<sub>3</sub>-Incorporated PET Tracer”, *Int. J. Org. Chem.*, **3**, 220–223 (2013).
- (29) Kimura, T., Sako, T., Siqin, Hosokawa-Muto, J., Cui, Y., Wada, Y., Kataoka, Y., Doi, H., Sakaguchi, S., Suzuki, M., Watanabe, Y., Kuwata, K., “Synthesis of <sup>11</sup>C-Labeled Antiprion GN8

- Derivative and Evaluation of Its Brain Uptake by Positron Emission Tomography”, *ChemMedChem*, **8**, 1035–1039 (2013). (doi: 10.1002/cmdc.201300167)
- (30) Takashima, T., Shingaki, T., Katayama, Y., Hayashinaka, E., Wada, Y., Kataoka, M., Ozaki, D., Doi, H., Suzuki, M., Ishida, S., Hatanaka, K., Sugiyama, Y., Akai, S., Oku, N., Yamashita, S., Watanabe, Y., “Dynamic Analysis of Fluid Distribution in the Gastrointestinal Tract in Rats: PET Imaging after Oral Administration of Non-absorbable Marker, [<sup>18</sup>F]Deoxyfluoropoly(ethylene glycol)”, *Mol. Pharmaceutics*, **10**(6), 2261–2269 (2013).
- (31) Koyama, H., Zhang, Z., Ijuin, R., Siqin, Son, J., Hatta, Y., Ohta, M., Wakao, M., Hosoya, T., Doi, H., Suzuki, M., “Pd<sup>0</sup>-mediated rapid coupling of methyl iodide with excess amounts of benzyl- and cinnamylboronic acid esters: efficient method for incorporation of positron-emitting <sup>11</sup>C radionuclide into organic frameworks by coupling between two sp<sup>3</sup>-hybridized carbons”, *RSC Advances*, **3**, 9391–9401 (2013).
- (32) Miyazaki, S., Minami, T., Mizuma, H., Kanazawa, M., Doi, H., Matsumura, S., Lu, J., Onoe, H., Furuta, K., Suzuki, M., Ito, S., “The action site of the synthetic kainoid (2*S*,3*R*,4*R*)-3-carboxymethyl-4- (4-methylphenylthio)pyrrolidine-2-carboxylic acid (PSPA-4), an analogue of Japanese mushroom poison acromelic acid, for allodynia (tactile pain)”, *Eur. J. Pharmacol.*, **710**, 120–127 (2013). (doi: 10.1016/j.ejphar.2012.10.023)
- (33) Nakazawa, S., Yokoyama, C., Nishimura, N., Horisawa, T., Kawasaki, A., Mizuma, H., Doi, H., Onoe, H., “Evaluation of dopamine D<sub>2</sub>/D<sub>3</sub> and serotonin 5-HT<sub>2A</sub> receptor occupancy for a novel antipsychotic, lurasidone, in conscious common marmosets using small-animal positron emission tomography”, *Psychopharmacology* **225**, 329–339 (2013). (doi: 10.1007/s00213-012-2815-9)
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- (37) Suzuki, M., Takashima-Hirano, M., Koyama, H., Yamaoka, T., Sumi, K., Nagata, H., Hidaka, H., Doi, H., “Efficient synthesis of [<sup>11</sup>C]H-1152, a PET probe specific for Rho-kinases, highly potential targets in diagnostic medicine and drug development”, *Tetrahedron* **68**, 2336–2341 (2012). (doi: 10.1016/j.tet.2012.01.033)
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- (39) Shukuri, M., Takashima-Hirano, M., Tokuda, K., Takashima, T., Matsumura, K., Inoue, O., Doi, H., Suzuki, M., Watanabe, Y., Onoe, H., “In Vivo Expression of Cyclooxygenase-1 in Activated Microglia and Macrophages During Neuroinflammation Visualized by PET with <sup>11</sup>C-Ketoprofen Methyl Ester”, *J. Nucl. Med.*, **52**(7), 1094–1101 (2011).
- (40) Takashima-Hirano, M., Tazawa, S., Takahashi, K., Doi, H., Suzuki, M., “Efficient Synthesis of [<sup>11</sup>C]Ramelteon as a Positron Emission Tomography Probe for Imaging Melatonin Receptors

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- (41) Takahashi, K., Onoe, K., Doi, H., Nagata, H., Yamagishi, G., Hosoya, T., Tamura, Y., Wada, Y., Yamanaka, H., Yokoyama, C., Mizuma, H., Takashima, T., Bergström, M., Onoe, H., Långström, B., Watanabe, Y., “Increase in hypothalamic aromatase in macaque monkeys treated with anabolic-androgenic steroids: PET study with [<sup>11</sup>C]vorozole”, *NeuroReport*, **22**, 326–330 (2011).
  - (42) Takashima-Hirano, M., Takashima, T., Katayama, Y., Wada, Y., Sugiyama, Y., Watanabe, Y., Doi, H., Suzuki, M., “Efficient sequential synthesis of PET Probes of the COX-2 inhibitor [<sup>11</sup>C]celecoxib and its major metabolite [<sup>11</sup>C]SC-62807 and in vivo PET evaluation”, *Bioorg. Med. Chem.*, **19**, 2997–3004 (2011).
  - (43) Koyama, H., Siqin, Zhang, Z., Sumi, K., Hatta, Y., Nagata, H., Doi, H., Suzuki, M., “Highly efficient syntheses of [methyl-<sup>11</sup>C]thymidine and its analogue 4’-[methyl-<sup>11</sup>C]thiothymidine as nucleoside PET probes for cancer cell proliferation by Pd<sup>0</sup>-mediated rapid C-[<sup>11</sup>C]methylation” *Org. Biomol. Chem.*, **9**, 4287–4294 (2011).
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