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Research Interests

Our research primarily focuses on elucidating the biological function of proteins, protein-protein, and protein-nucleotide complexes and utilizes this information in the context of human disease. we primarily use solution-state NMR spectroscopy to unravel the structure, interaction, and dynamics of these biological molecules in a quantitative manner. We have been particularly interested in the function of ion channels, receptors, phosphatases, kinases, metabolic enzymes, and multidrug resistance proteins, which play critical roles in biology and pathology, hence are attractive drug targets.

Significant Contributions in understanding biological mechanisms

- Inhibition and gating mechanism of the potassium channel KcsA (*JMB*, 2002; *Structure*, 2003; *Biochem J*, 2004; *JBC*, 2007; *PNAS*, 2010; *JBC*, 2010; *JBC*, 2012)
- Mechanosensitive activation and regulation of $\alpha\beta$ T-cell receptor (*JMB*, 2008; *JBC*, 2009; *J Immunol*, 2010)
- Structure of calcineurin-NAFT complex and its NFAT dephosphorylation mechanism (*Structure*, 2007; *Structure*, 2014)
- Allosteric activation mechanism of p38α MAPK by it substrates (*Nat Struct Mol Biol*, 2014)
- Dynamic multidrug recognition and transcriptional regulation of multidrug transcriptional repressors (*Sci Rep*, 2014; S*ci Rep*, 2017; *PNAS*, 2019).

In addition, I have developed an array of novel of solution-state NMR techniques and methods to tackle large/challenging biological systems and to develop compounds based on the structural information of complexes.

- The distance measurement techniques for accurate identification of protein-protein as well as protein-ligand interfaces (*JACS*, 2005; *JACS*, 2008; *Prog Nucl Magn Reson Spect*, 2009; *J Mol Graph Model*, 2011)
- Multidimensional correlation techniques, especially those utilizing low-γ nuclei direct detection in combination with stable isotope labeling technique, for assignment and

detection of large and supra (>100 ns) molecular weight proteins (*J Biomol NMR*, 2007; *JACS*, 2008; *JACS*, 2010; *J Biomol NMR*, 2010a; *J Biomol NMR*, 2010b; *J Biomol NMR*, 2011a; *J Biomol NMR*, 2011b; *Rec. Dev. Biomol. NMR*, 2012; *J Biomol NMR*, 2015b; *J Biomol NMR*, 2015c; *J Biomol NMR*, 2016a; *J Biomol NMR*, 2016b; *Nat Methods*, 2019)

- Sparse sampling and reconstitution techniques for rapid, quantitative, and high resolution reconstitution of multidimensional NMR spectra (*JACS*, 2010; *J Biomol NMR*, 2015a)
- Strategy for quantitative analysis of dynamics in protein-protein and protein-ligand complexes for the simultaneous acquisition of structure and dynamics information at atomic resolution (*Sci Rep*, 2014, *Angew Chem Int Ed*, 2016; *Molecules*, 2017).
- Strategies for structure-based drug development, in order to utilize the structure information to improve the human life (*J Med Chem*, 2013; *Angew Chem Int Ed*, 2014; *ChemMedChem*, 2015, *J Med Chem*, 2015).

A set of these technologies are patented and transferred to the major pharmaceutical companies in Japan through direct collaborations. Our research expertise is not limited to the structural biology using NMR, we have used X-ray crystallography, biochemistry, and cell biology, to carry out interdisciplinary work that addresses the big picture and validates the structural findings.

Details of some research achievements are follows.

Dynamic ligand recognition by multidrug-binding proteins

Multidrug resistance (MDR) systems are conserved in all three kingdoms of life, representing the most basic defense shared among organisms, and those of pathogenic bacteria and cancers are a major challenge for medication. However, the molecular mechanism by which multidrug-binding transcription factors (MDTF) recognize a variety of compounds with high affinity and regulate the transcription of MDR genes remains elusive.

By using NMR, we showed that an MDTF, LmrR, samples various conformations with different apertures in the ligand-binding site in the free state, while the conformations preferable to each ligand were selected upon the binding (Panel A, Sci. Rep., 2014). We also found that the regions allosteric to the ligand-binding site enhance the random fluctuation upon the binding to ligands, which entropically achieve a high-affinity interaction (Panel B). In addition, in the Staphylococcus aureus MDTF, QacR, the compound's size defines the induced activation levels through the fraction of the active conformation in the conformational equilibrium (Proc. Natl. Acad. Sci. USA, 2019). These results highlight the unique strength of NMR to unveil the dynamic molecular mechanism of proteins.

Identification and utilization of cryptic sites.
Protein-protein interactions (PPIs) contain many attractive drug targets. However, PPI-targeted drug discovery has been challenging since PPI sites are flat and wide and unsuitable for small molecules to bind. It is known that several successful PPI inhibitors bind to "cryptic sites" a dynamically formed ligand-interacting pocket that is not apparent in the absence of a ligand. Cryptic sites have been found only after discovering ligand and following structural analysis of the complexes (Panel A). However, if there is any strategy to discover and utilize cryptic sites in advance, we can accelerate the development of the PPI inhibitors and inhibitors of other difficult-to-target proteins.
By using NMR, we have found that a small fraction of cryptic sites already in the open conformation in Bcl-xL, an anti-cancer PPI inhibitor target, even in the absence of ligand (Panel B). We also obtained an allosteric mutant that stabilizes cryptic site open conformation and proved that the mutant could screen the hit compound more efficiently than the wild-type protein (Panel C). These results indicate that the druggability of proteins, including PPIs, can be improved by controlling the conformational equilibrium by using NMR.

Dynamic ligand optimization by the FCT method
The thermodynamic properties of ligand-receptor interactions attract attention due to their relation to the binding specificity. However, designing ligands with preferable thermodynamic properties is challenging. We developed a strategy to experimentally evaluate the local dynamics and the surface complementarity of ligands in the receptor-bound state by forbidden-coherence-transfer (FCT) analysis and utilized the information to ligand optimization (Panel A). The FCT method was originally developed in L. Kay's group (http://pound.med.utoronto.ca/), for protein dynamics analysis; however, we extended the method to dynamic ligand optimization (Angew. Chemie. Int. Ed., 2016; Molecules, 2017).
By applying the FCT method to the interaction between the MEF2A peptide and the p38α MAP kinase, the dynamics and surface complementarity of the MEF2A methyl groups in the p38α-bound state were quantitatively analyzed. Based on the information, we introduced a rational modification to the MEF2A peptide and obtained a ligand with higher affinity and better thermodynamic properties (higher enthalpic contribution for binding) than those of the original ligand (Panel B). The ligand is expected to show an improved specificity to its receptor, which is beneficial for the structure-guided lead-optimization.

Heteronuclear-direct detections
The application of solution NMR to high molecular weight (HMW) systems is still challenging, especially for those exceeding 100 kDa. The limitation mainly comes from signal losses due to fast transverse relaxation in HMW systems. While proton (1H) is the most commonly used as the detecting nucleus, the acceleration of relaxation in HMW systems is the most substantial among other nuclei.
To overcome this limitation, we have developed heteronuclear-direct detection experiments that are applicable to the >100 kDa systems. Those experiments use low γ-nuclei, such as 13C,

and 15N for detection. Although the intrinsic sensitivities of these nuclei are lower than that of 1H, the slower relaxation yields a superior sensitivity in the non-deuterated or hard-to-deuterate conditions. Our latest examples are N-CRINPT (J. Med. Chem., 2020) and FC-TROSY (Nat. Methods., 2019). N-CRINEPT presents a structural fingerprint of an analog of a therapeutic monoclonal antibody at low storage temperature, under various prescription solution conditions (Panel A). FC-TROSY successfully provides the structural information from the aromatic sidechains of the 180-kDa α7 single-ring of the 20S proteasome core particle (Panel B). FC-TROSY is expected to provide a powerful background-free spectrum in in-cell NMR methods.

We also have initiated and been a part of several collaborative projects and recently we found that lipid kinase PI5P4Kβ is an intracellular GTP sensor for metabolism and tumorigenesis through a collaborative research with cell biologist and X-ray crystallographer (*Mol Cell*, 2016). Due to the importance of PI5P4Kβ in tumorigenesis, we are currently seek for the specific inhibitor for PI5P4Kβ. Initial hits were obtained by *in silico* + NMR screening. Compounds with improved activity were currently under development, utilizing the structural information of PI5P4Kβ-compound complex structure.

Education

2004:	Ph.D. in Biophysics – The University of Tokyo, Tokyo, Japan
2001:	M.S. in Biophysics – The University of Tokyo, Tokyo, Japan
1999:	B.S. in Pharmacy – The University of Tokyo, Tokyo, Japan

Professional Experience

2003/4-2005/3	JSPS Special Research Fellow – Japan Society for Promotion of Science
2004/4-2005/3	Post-doctoral Fellow – Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, Japan (Supervisor: Prof. Ichio Shimada)
2005/4-2010/3	Post-doctoral Fellow – Biochemistry and Molecular Pharmcology Harvard Medical School, Boston, USA (Supervisor: Prof. Gerhard Wagner)
2006/4-2008/3	JSPS Overseas Fellow – Japan Society for Promotion of Science
2010/4-2013/3	Researcher – Biomedicinal Information Research Center, National Institute of Advanced Industrial Science and technology, Tokyo, Japan

2014/4-2017/3	Senior Researcher – Molecular Profiling Research Center for Drug Discovery, National Institute of Advanced Industrial Science and technology, Tokyo, Japan
2014/10-2018/3	(Additional post) Faculty – Presto, Japan Science and Technology Agency, Tokyo, Japan
2017/4-2021/10	Team Leader – Structural Modality Research team, Molecular Profiling Research Center for Drug Discovery, National Institute of Advanced Industrial Science and technology, Tokyo, Japan
2021/10-Present	Professor – Laboratory of Physical Chemistry, Graduate Schools of Pharmaceutical Sciences, The University of Tokyo Tokyo, Japan
2017/11-Present	(Additional post) Councilor- Nuclear Magnetic Resonance Society of Japan

Honors, Scholarships, and Prizes

Year	***Name of Honor/Prize***	***Awarding Institution***
2001-2003	Scholarship for Graduate Students	The Japan Scholarship Foundation
2003-2005	Research Fellowships for Young Scientists	Japan Society for Promotion of Science
2005	Postdoctoral Fellowship	The Mochida Memorial Foundation
2005	Postdoctoral Fellowship	The Uehara Memorial Foundation
2006-2008	Research Fellowships for Research Abroad	Japan Society for Promotion of Science
2010	Best Presentation Award for Young Scientists	The Spectroscopical Society of Japan
2017	Research Award (¥3,000,000)	Mochida Memorial Foundation for Medical and Pharmaceutical Research
2017	Natural Science Award (¥3,000,000)	The Naito Foundation
2020	Yong Scientist Award	The NMR society of Japan
2017	Pharmaceutical Science Award (¥2,000,000)	The Takeda Science Foundation

Grantsmanship

Year(s)	*Title/Type/Direct Cost/Role*
2010-2012:	Development of novel stable isotope labeling methods for the structural analysis of high molecular weight drug discovery target proteins Grants-in-Aid for Research Activity Start-up, ￥2,420,000 Role: Principal Investigator (2010/04/01-2012/03/31)
2011-2012:	NMR analysis of structural fluctuation and function of prokaryotic multidrug resistance transporter Grant-in-Aid for Scientific Research on Innovative Areas, ¥5,400,000 Role: Principal Investigator (04/2011-03/2012)
2011-2013:	Structural analysis of mitochondrial inner membrane transporters Grant-in-Aid for Young Scientists (B), ¥3,300,000 Role: Principal Investigator (04/2011-03/2013)
2012-2013:	Basic study toward NMR structural analysis of human membrane proteins Grant-in-Aid for Scientific Research (B), ¥1,500,000 Role: Co-Investigator (04/2012-03/2013)
2013-2015	Structural dynamics analysis of kinase complexes by integrated use of X-ray and NMR Grant-in-Aid for Scientific Research on Innovative Areas, ¥7,000,000 Role: Principal Investigator (04/2013-03/2015)
2014-2017	NMR analysis of dynamic drug recognition and regulation of multidrug transcriptional factors Grant-in-Aid for Young Scientists (A), ¥4,200,000 Role: Principal Investigator (04/2014-03/2015, terminated by PRESTO promotion)
2014-2018	Functional dynamics of multidrug transcriptional factors Japan Science and Technology Agency, PRESTO, ¥40,000,000 Role: Principal Investigator (10/2014-03/2018)
2015-2018	Development of NMR approach for NMR structural analysis of human membrane proteins Grant-in-Aid for Scientific Research (B), ¥1,500,000 Role: Co-Investigator (04/2015-03/2018)
2017-2021	In situ functional analyses of membrane proteins by NMR Grant-in-Aid for Specially Promoted Research, ¥40,000,000 Role: Co-Investigator (04/2017-03/2021)
2018-2020	Collaborative research for development of small molecule inhibitors for difficult-to-target protein-protein interactions

JSPS - ISF Joint Program, ¥4,000,000
Role: Principal Investigator (04/2018-03/2020)

2019-2020 NMR method to obtain structural fingerprints of an intact monoclonal antibody acquired under formulated storage conditions.
Grant-in-Aid for challenging Exploratory Research, ¥4,800,000
Role: Principal Investigator (06/2019-03/2021)

2020-2021 Dynamic molecular interaction between protein and ligand in molecular crowding condition
Grant-in-Aid for Scientific Research on Innovative Areas, ¥3,800,000
Role: Principal Investigator (04/2020-03/2021)

2020-2022 Development of dynamic Structure based drug development for lead optimization and improvement of druggability of human proteome.
Grant-in-Aid for Scientific Research (B), ¥13,600,000
Role: Principal Investigator (04/2020-03/2021)

Technological and Scientific Innovation

Title	*Description*
Reconstitution method of membrane protein for ligand interaction analysis by NMR	**Inventors:** Koh Takeuchi (AIST, JBiC) , Ichio Shimada (AIST) **Submitted:** 10/8/2003 (JP2003-350094) **Published:** 04/28/2005 (JP2005-112800).
Machine, method and program for identification of binding site	**Inventors:** Yuya Kodama (Ajinomoto Co.), Koh Takeuchi (AIST), Hideo Takahashi (AIST), Ichio Shimada (AIST) **Submitted:** 12/25/2012 (PCT/JP2013/085330).
Screening of drug candidates by NMR	**Inventors:** Koh Takeuchi (AIST), Yuji Tokunaga (JBiC), Ichio Shimada (AIST) **Submitted:** 08/21/2015 (JP2015-163548).
GTP SENSOR PROTEIN PI5P4Kβ INHIBITOR	**Inventors:** Koh Takeuchi, Toshiya Senda, Atsuo Sasaki, Yoshifumi Fukunishi **Submitted:** 12/05/2017 (US201762594814P). **Published:** 06/13/2019 (WO2019111792A1)

Complete Publication List

Cumulative: citations: 3046 (h-index 32, i10-index 60)
Last 5-years: citations: 1544 (h-index 20, i10-index 42)

1) Tsuji Y, Aoyama T, **Takeuchi K**, Homma Ki, Takahashi H, Nakajima Y, Shimada I, Natori S. Identification and characterization of an antibacterial peptide of the 26-kDa protease of Sarcophaga peregrina with antibacterial activity. *J Biochem*, **130**, 313-318, (2001).

2) **Takeuchi K,** Park E, Lee C, Kim J, Takahashi H, Swartz K, Shimada I. Solution structure of omega-grammotoxin SIA, a gating modifier of P/Q and N-type Ca^{2+} channel. *J Mol Biol*, **321**, 517-526 (2002).

3) **Takeuchi K**, Yokogawa M, Matsuda T, Sugai M, Kawano S, Kohno T, Shimada I. Structural basis of the KcsA K^+ channel and agitoxin2 pore-blocking toxin interaction by using the transferred cross-saturation method. *Structure*, **11**, 1381-1392, (2003).

4) Lee CW, Lee EH, **Takeuchi K**, Takahashi H, Shimada I, Sato K, Shin SY, Kim DH, Kim JI. Molecular basis of the high-affinity activation of type 1 ryanodine receptors by imperatoxin A. *Biochem J*, **377**, 385-394, (2004).

5) **Takeuchi K**, Takahashi H, Sugai M, Iwai H, Kohno T, Sekimizu K, Natori S, Shimada I. Channel-forming membrane permeabilization by an antibacterial protein, sapecin: determination of membrane-buried and oligomerization surfaces by NMR. *J Biol Chem*, **279**, 4981-4987, (2004).

6) Nakamura T, Takahashi H, **Takeuchi K**, Kohno T, Wakamatsu K, Shimada I. Direct determination of a membrane-peptide interface using the nuclear magnetic resonance cross-saturation method. *Biophys J*, **89**, 4051-4055, (2005).

7) Sakakura M, Takahashi H, Terasawa H, **Takeuchi K**, Fujii I, Shimada I. Backbone resonance assignments for the Fv fragment of catalytic antibody 6D9 complexed with a transition state analogue. *J Biomol NMR*, **33**, 282, (2005).

8) **Takeuchi K**, Shimada I. [Structural basis of the K+ channel inhibition by pore-blocking toxins, revealed by NMR]. *Tanpakushitsu Kakusan Koso*, **50**, 1297-1302, (2005).

9) Yokogawa M, **Takeuchi K**, Shimada I. Bead-linked proteoliposomes: a reconstitution method for NMR analyses of membrane protein-ligand interactions. *J Am Chem Soc*, **127**, 12021-12027, (2005).

10) Park S, **Takeuchi K**, Wagner G, Solution structure of the first SRC homology 3 domain of human Nck2. *J Biomol NMR*, **34**, 203-208, (2006).

11) **Takeuchi K**, Wagner G. NMR studies of protein interactions. *Curr Opin Struct Biol*, **16**, 109-117, (2006).

12) **Takeuchi K**, Ng E, Malia TJ, Wagner G. 1-^{13}C amino acid selective labeling in a $^{2}H^{15}N$ background for NMR studies of large proteins. *J Biomol NMR*, **38**, 89-98, (2007).

13) **Takeuchi K**, Roehrl MH, Sun ZY, Wagner G. Structure of the calcineurin-NFAT complex: defining a T cell activation switch using solution NMR and crystal coordinates. *Structure*, **15**, 587-597, (2007).

14) **Takeuchi K,** Takahashi H, Kawano S, Shimada I. Identification and characterization of the slowly exchanging pH-dependent conformational rearrangement in KcsA. *J Biol Chem*, **282**, 15179-15186, (2007).

15) **Takeuchi K,** Yang H, Ng E, Park S, Sun ZY, Reinherz EL, Wagner G. Structural and functional evidence that Nck interaction with CD3ε regulates T cell receptor activity. *J Mol Biol*, **180**, 704-716, (2008).

16) Igarashi S, Osawa M, **Takeuchi K**, Ozawa S, Shimada I. Amino acid-selective cross-saturation method for identification of proximal residue pairs in a protein−protein complex. *J Am Chem Soc*, **130**, 12168-12176, (2008).

17) **Takeuchi K**, Sun ZY, Wagner G. Alternate ^{13}C-^{12}C labeling for complete mainchain resonance assignments using Cα direct-detection with applicability toward fast relaxing protein systems. *J Am Chem Soc*, **130**, 17210-17211, (2008).

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19) Yokogawa M, Muramatsu T, **Takeuchi K,** Osawa M, Shimada I. Backbone resonance assignments for the cytoplasmic regions of G protein-activated inwardly rectifying potassium channel 1 (GIRK1). *Biomol NMR Assign*, **3**, 125-128, (2009).

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21) Hyberts SG, **Takeuchi K**, Wagner G. Poisson-gap sampling and forward maximum entropy reconstruction for enhancing the resolution and sensitivity of protein NMR Data. *J Am Chem Soc*, **132**, 2145-2147, (2010).

22) **Takeuchi K**, Frueh D, Hyberts S, Sun ZY, Wagner G. High-resolution 3D CANCA NMR experiments for complete mainchain assignments using $C^{\circledcirc}$ direct-detection. *J Am Chem Soc*, **132**, 2945-2951, (2010).

23) Imai S, Osawa M, **Takeuchi K**, Shimada I. Structural basis underlying the dual gate properties of KcsA. *Proc Natl Acad Sci*, **107**, 6216-6221, (2010).

24) **Takeuchi K**, Frueh D, Sun ZY, Hiller S, Wagner G. CACA-TOCSY with alternate ^{13}C-^{12}C labeling: a $^{13}C^{\alpha}$ direct detection experiment for mainchain resonance assignment, dihedral angle information, and amino acid type identification. *J Biomol NMR*, **47**, 55-63, (2010).

25) **Takeuchi K**, Sun ZY, Park S, Wagner G. Autoinhibitory interaction in the multidomain adaptor protein Nck: possible roles in improving specificity and functional diversity. *Biochemistry*, **49**, 5634-5641, (2010)

26) **Takeuchi K**, Heffron G, Sun ZY, Frueh DP, Wagner G. Nitrogen-detected CAN and CON experiments as alternative experiments for main chain NMR resonance assignments. *J Biomol NMR*, **47**, 271-282, (2010).

27) Kim ST, Touma M, **Takeuchi K,** Sun ZY, Dave VP, Kappes DJ, Wagner G, Reinherz EL. Distinctive CD3 Heterodimeric Ectodomain Topologies Maximize Antigen-triggered Activation of $\alpha\beta$ T Cell Receptors. *J Immunol*, **185**, 2951-2959, (2010).

28) Yokogawa M, Osawa M, **Takeuchi K**, Mase Y, Shimada I. NMR analyses of the G$\beta\gamma$ binding and conformational rearrangements of the cytoplasmic pore of G protein-activated inwardly rectifying potassium channel 1 (GIRK1). *J Biol Chem*, **286**, 2215-2223, (2010).

29) **Takeuchi K**, Gal M, Takahashi H, Shimada I, Wagner G. HNCA-TOCSY-CANH experiments with alternate ^{13}C-^{12}C labeling: a set of 3D experiment with unique supra-sequential information for mainchain resonance assignment. *J Biomol NMR*, **49**, 17-26, (2011).

30) Milbradt AG, Kulkarni M, Yi T, **Takeuchi K**, Sun ZY, Luna RE, Selenko P, Näär AM, Wagner G. Structure of the VP16 transactivator target in the Mediator. *Nat Struct Mol Biol*, **18**, 410-418, (2011).

31) Sasaki AT, Carracedo A, Locasale JW, Anastasiou D, **Takeuchi K**, Kahoud ER, Haviv S, Asara JM, Pandolfi PP, Cantley LC. Ubiquitination of k-ras enhances activation and facilitates binding to select downstream effectors. *Sci Signal*, **4**, ra13, (2011).

32) Fukunishi Y, Mizukoshi Y, **Takeuchi K**, Shimada I, Takahashi H, Nakamura H. Protein-ligand docking guided by ligand pharmacophore-mapping experiment by NMR. *J Mol Graph Model*, **31**, 20-27, (2011).

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35) Osawa M, **Takeuchi K**, Ueda T, Nishida N, Shimada I. Functional dynamics of proteins revealed by solution NMR. *Curr Opin Struct Biol*, **22**, 660-669, (2012).

36) Imai S, Osawa M, Mita K, Toyonaga S, Machiyama A, Ueda T, **Takeuchi K**, Oiki S, Shimada I. Functional Equilibrium of the KcsA Structure Revealed by NMR. *J Biol Chem*, **287**, 39634-39641, (2012).

37) **Takeuchi K**, Gal M, Shimada I, Wagner G. Low γ-nuclei detection experiments for bimolecular NMR. *Recent Developments in Biomolecular NMR*, 25-52, (2012).

38) Davis MI, Sasaki AT, Shen M, Emerling BM, Thorne N, Michael S, Pragani R, Boxer M, Sumita K, **Takeuchi K**, Auld DS, Li Z, Cantley LC, Simenov A. A homogeneous, high-throughput assay for phosphatidylinositol 5-phosphate 4-kinase with a novel, rapid substrate preparation. *PLoS One*, **8**, e54127, (2013).

39) Miyazawa-Ohnami M, **Takeuchi K**, Takano T, Sugiki T, Shimada I, Takahashi H, Perdeuteration and methyl-selective ^{1}H, ^{13}C-labeling by using a *Kluyveromyces lactis* expression system. *J Biomol NMR*, **57**, 297-304, (2013).

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43) Osawa M, Imai S, **Takeuchi K**, Shimada I. [Functional regulation mechanism of membrane protein revealed by Solution NMR analysis]. *Seibutu Buturi*, **53**, 236-241, (2013).

44) **Takeuchi K**, Tokunaga Y, Shimada I. [Experimental strategy of molecular recognition and application for drug development]. *Dozin Bioschience*, 291-203, (2013).

45) Ono K, **Takeuchi K**, Ueda H, Morita Y, Tanimura R, Shimada I, Takahashi H. Structure-based approach to improve a small-molecule inhibitor by the use of a competitive Peptide ligand. *Angew Chem Int Ed*, **53**, 2597-601, (2014).

46) Ueda T, **Takeuchi K**, Nishida N, Stampoulis P, Kofuku Y, Osawa M, Shimada I. Cross-saturation and transferred cross-saturation experiments. *Quart Rev Biophy*, **47**, 143–187, (2014).

47) Gal M, Li S, Luna RE, **Takeuchi K**, Wagner G. The LxVP and PxIxIT NFAT motifs bind jointly to overlapping epitopes on Calcineurin's catalytic domain distant to the regulatory domain. *Structure*, **22**, 1016-1027, (2014).

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49) **Takeuchi K**, Sun ZY, Li S, Gal M, Wagner G. NMR resonance assignments of the catalytic domain of human serine/threonine phosphatase calcineurin in unligated and PVIVIT-peptide-bound states. *Biomol NMR Assign*, **9**, 201-205, (2015).

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51) **Takeuchi K**, Tokunaga Y, Imai M, Takahashi H, Shimada I. Dynamic multidrug recognition by multidrug transcriptional repressor LmrR. *Sci Rep*, **4**, 6922, (2014).

52) Osawa M, Mase Y, Yokogawa M, **Takeuchi K**, Shimada I, Large protein complexes revealed by solution-state NMR: G proteins and G protein-activated inwardly rectifying potassium ion channel. Advances in Biological Solid-State NMR, 501-532

53) Mizukoshi Y, **Takeuchi K**, Arutaki M, Takizawa T, Hanzawa H, Takahashi H, Shimada I. Suppression of problematic compound oligomerization by cosolubilization of nondetergent sulfobetaines. *ChemMedChem*, **10**, 736-741, (2015).

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- *Genes to Cells* (The Molecular Biology Society of Japan/John Wiley & Sons Australia, Ltd)
- *International Journal of Oncology* (Spandidos Publications)
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