

## CURRICULUM VITAE

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### Education:

1992/4-1994/3 Stream Natural Science I, College of Arts and Sciences (Junior Division), The University of Tokyo  
1994/4-1996/3 Department of Biophysics and Biochemistry, Faculty of Science, The University of Tokyo  
Awarded the degree of BS in Biophysics and Biochemistry  
1996/4-1998/3 Department of Biophysics and Biochemistry, Graduate School of Science, The University of Tokyo  
Awarded the degree of MS in Biophysics and Biochemistry  
Work supervised by Lecturer Dr. Yutaka Muto  
1998/4-2001/3 Department of Biophysics and Biochemistry, Graduate School of Science, The University of Tokyo  
Awarded the degree of Ph.D. in Biophysics and Biochemistry for a thesis entitled “Structural Biological Studies of RNA-binding domains of human U2AF<sup>65</sup>”.  
Work supervised by Professor Dr. Shigeyuki Yokoyama

### Research experience:

1998/4-2001/3 Research Fellow of the Japan Society for the Promotion of Science (DC1)  
2001/4-2004/8 Postdoctoral research fellow at Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, supervised by Professor Dr. Gerhard Wagner  
2004/9-2005/3 Research associate at Genomic Science Center, RIKEN

2005/3-2010/6 Assistant Professor at Department of Biophysics and Biochemistry,  
Graduate School of Science, The University of Tokyo

2010/7-2012/3 Project Assistant Professor at Laboratory of Structural Biology,  
Graduate School of Science, The University of Tokyo

2012/4-2013/3 Research scientist at Systems and Structural Biology Research Team,  
RIKEN Systems and Structural Biology Center

2013/4-2018/3 Unit Leader at Translation Factors Structural Biology Unit, RIKEN  
Center for Life Science Technologies

2018/4-2019/3 Unit Leader at Laboratory for Translation Structural Biology, RIKEN  
Center for Biosystems Dynamics Research

2019/4-present Team Leader at Laboratory for Translation Structural Biology, RIKEN  
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## Publication:

### Original Papers

1. Chen, M., Asanuma, M., Takahashi, M., Shichino, Y., Mito, M., Fujiwara, K., Saito, H., Floor, S.N., Ingolia, N.T., Sodeoka, M., Dodo, K., **Ito, T.** and Iwasaki, S.\* Dual targeting of DDX3 and eIF4A by the translation inhibitor rocaglamide A. *Cell Chem Biol*, published online. DOI: 10.1016/j.chembiol.2020.11.008
2. Zyryanova, A.F.<sup>#</sup>, Kashiwagi, K.<sup>#</sup>, Rato, C., Harding, H.P., Crespillo-Casado, A., Perera, L.A., Sakamoto, A., Nishimoto, M., Yonemochi, M., Shirouzu, M., **Ito, T.\*** and Ron, D.\* (2021) ISRIB blunts the integrated stress response by allosterically antagonising the inhibitory effect of phosphorylated eIF2 on eIF2B. *Mol Cell*, **81**, 88-103. DOI: 10.1016/j.molcel.2020.10.031 (<sup>#</sup> equally contributed) (\* co-corresponding authors)
3. Hayashi, M., Haruna, K., Sato, H., Ito, K., Makino, C., **Ito, T.** and Sakamoto, K.\* (2021) Incorporation of halogenated amino acids into antibody fragments at multiple specific sites enhances antigen binding. *ChemBioChem*, **22**, 120-123. DOI: 10.1002/cbic.202000429
4. Terumitsu-Tsujita, M.\*, Kitaura, H., Miura, I., Kiyama, Y., Goto, G., Muraki, Y., Ominato, S., Hara, N., Simankova, A., Bizen, N., Kashiwagi, K., **Ito, T.**, Toyoshima, Y., Kakita, A., Manabe, T., Wakana, S., Takebayashi, H.\* and Igarashi, H. (2020) Glial pathology in a novel spontaneous mutant mouse of the *Eif2b5* gene: a vanishing white matter disease model. *J Neurochem*, **154**, 25-40. DOI: 10.1111/jnc.14887
5. Yokoyama, T.<sup>#</sup>, Machida, K.<sup>#</sup>, Iwasaki, W.<sup>#</sup>, Shigeta, T., Nishimoto, M., Takahashi, M., Sakamoto, A., Yonemochi, M., Harada, Y., Shigematsu, H., Shirouzu, M., Tadakuma, H.\*, Imataka, H.\* and **Ito, T.\*** (2019) HCV IRES captures an actively translating 80S ribosome. *Mol Cell*, **74**, 1205-1214. DOI: 10.1016/j.molcel.2019.04.022 (<sup>#</sup> equally contributed) (\* co-corresponding authors)
6. Kashiwagi, K., Yokoyama, T., Nishimoto, M., Takahashi, M., Sakamoto, A., Yonemochi, M., Shirouzu, M. and **Ito, T.\*** (2019) Structural basis for eIF2B inhibition in integrated stress response. *Science*, **364**, 495-499. DOI: 10.1126/science.aaw4104
7. Iwasaki, S.\*, Iwasaki, W.<sup>#</sup>, Takahashi, M.<sup>#</sup>, Sakamoto, A., Watanabe, C., Shichino, Y., Floor, S.N., Fujiwara, K., Mito, M., Dodo, K., Sodeoka, M., Imataka, H., Honma, T., Fukuzawa, K., **Ito, T.\*** and Ingolia, N.T.\* (2019) The translation inhibitor Rocaglamide targets a bimolecular cavity between eIF4A and polypurine

- RNA. *Mol Cell*, **73**, 738-748. DOI: 10.1016/j.molcel.2018.11.026 (# equally contributed) (\* co-corresponding authors)
8. Machida, K., Shigeta, T., Yamamoto, Y., **Ito, T.**, Svitkin, Y., Sonenberg, N. and Imataka, H. (2018) Dynamic interaction of poly(A)-binding protein with the ribosome. *Sci Rep*, **8**, 17435. DOI: 10.1038/s41598-018-35753-1
  9. Handoko, L., Kaczkowski, B., Hon, C.-C., Lizio, M., Wakamori, M., Matsuda, T., **Ito, T.**, Jeyamohan, P., Sato, Y., Sakamoto, K., Yokoyama, S., Kimura, H., Minoda, A. and Umehara, T. (2018) JQ1 affects BRD2-dependent and independent transcription regulation without disrupting H4-hyperacetylated chromatin states. *Epigenetics*, **13**, 410-431. DOI: 10.1080/15592294.2018.1469891
  10. Teramoto, H., Amano, Y., Iraha, F., Kojima, K., **Ito, T.** and Sakamoto, K. (2018) Genetic Code Expansion of the Silkworm *Bombyx mori* to Functionalize Silk Fiber. *ACS Synth Biol*, **7**, 801-806. DOI: 10.1021/acssynbio.7b00437
  11. Matsuda, T.<sup>#</sup>, **Ito, T.**<sup>#</sup>, Takemoto, C., Katsura, K., Ikeda, M., Wakiyama, M., Kukimoto-Niino, M., Yokoayama, S., Kurosawa, Y. and Shirouzu, M. (2018) Cell-free synthesis of functional antibody fragments to provide a structural basis for antibody - antigen interaction. *PLoS One*, **13**, e0193158. DOI: 10.1371/journal.pone.0193158 (# equally contributed)
  12. Kuwasako, K., Nameki, N., Tsuda, K., Takahashi, M., Sato, A., Tochio, N., Inoue, M., Terada, T., Kigawa, T., Kobayashi, N., Shirouzu, M., **Ito, T.**, Sakamoto, T., Wakamatsu, K., Güntert, P., Takahashi, S., Yokoyama, S. and Muto, Y. (2017) Solution structure of the first RNA recognition motif domain of human spliceosomal protein SF3b49 and its mode of interaction with a SF3b145 fragment. *Protein Sci*, **26**, 280-291. DOI: 10.1002/pro.3080
  13. Christian, T., Sakaguchi, R., Perlinska, A.P., Lahoud, G., **Ito, T.**, Taylor, E.A., Yokoyama, S., Sulkowska, J.I. and Hou, Y.-M. (2016) Methyl transfer by substrate signaling from a knotted protein fold. *Nat Struct Mol Biol*, **23**, 941-948. DOI:10.1038/nsmb.3282
  14. Kashiwagi, K., Shigeta, T., Imataka, H., **Ito, T.**\* and Yokoyama, S.\* (2016) Expression, purification, and crystallization of *Schizosaccharomyces pombe* eIF2B. *J Struct Funct Genomics*, **17**, 33-38. DOI: 10.1007/s10969-016-9203-3 (\* co-corresponding authors)
  15. Kashiwagi, K., Takahashi, M., Nishimoto, M., Hiyama, T.B., Higo, T., Umehara, T., Sakamoto, K., **Ito, T.**\* and Yokoyama, S.\* (2016) Crystal structure of eukaryotic translation initiation factor 2B. *Nature*, **531**, 122-125. DOI: 10.1038/nature16991 (\* co-corresponding authors)

16. **Ito, T.**, Masuda, I., Yoshida, K., Goto-Ito, S., Sekine, S., Suh, S.W., Hou, Y.-M. and Yokoyama, S. (2015) Structural Basis for methyl-donor-dependent and sequence-specific binding to tRNA substrates by knotted methyltransferase TrmD. *Proc Natl Acad Sci U S A*, **112**, E4197-E4205. DOI: 10.1073/pnas.1422981112
17. Ehara, H., Makino, M., Kodama, K., **Ito, T.**, Sekine, S., Fukuzawa, S., Yokoyama, S. and Tachibana, K. (2015) Crystal Structure of okadaic acid binding protein 2.1: a sponge protein implicated in cytotoxin accumulation. *ChemBioChem*, **16**, 1435-1439. DOI: 10.1002/cbic.201500141
18. Kanamori, T., Ohzeki, H., Masaki, Y., Ohkubo, A., Takahashi, M., Tsuda, K., **Ito, T.**, Shirouzu, M., Kuwasako, K., Muto, Y., Sekine, M. and Seio, K. (2015) Controlling the fluorescence of benzofuran-modified uracil residues in oligonucleotides by triple-helix formation. *ChemBioChem*, **16**, 167-76. DOI: 10.1002/cbic.201402346
19. Kuwasako, K.<sup>#</sup>, Takahashi, M.<sup>#</sup>, Unzai, S., Tsuda, K., Yoshikawa, S., He, F., Kobayashi, N., Guntert, P., Shirouzu, M., **Ito, T.**, Tanaka, A., Yokoyama, S., Hagiwara, M., Kuroyanagi, H. and Muto, Y. (2014) RBFOX and SUP-12 sandwich a G base to cooperatively regulate tissue-specific splicing. *Nat Struct Mol Biol*, **21**, 778-86. DOI: 10.1038/nsmb.2870 (<sup>#</sup> equally contributed)
20. Kashiwagi, K., **Ito, T.** and Yokoyama, S. (2014) Crystal structure of the eukaryotic translation initiation factor 2A from *Schizosaccharomyces pombe*. *J Struct Funct Genomics*, **15**, 125-130. DOI: 10.1007/s10969-014-9177-y (Epub 2014 Feb 26)
21. Nakagawa, H., Kuratani, M., Goto-Ito, S., **Ito, T.**, Katsura, K., Terada, T., Shirouzu, M., Sekine, S., Shigi, N. and Yokoyama, S. (2013) Crystallographic and mutational studies on the tRNA thiouridine synthetase TtuA. *Proteins*, **81**, 1232-44. DOI: 10.1002/prot.24273
22. Hanawa-Suetsugu, K., Kukimoto-Niino, M., Mishima-Tsumagari, C., Akasaka, R., Ohsawa, N., Sekine, S.-I., **Ito, T.**, Tochio, N., Koshihara, S., Kigawa, T., Terada, T., Shirouzu, M., Nishikimi, A., Uruno, T., Katakai, T., Kinashi, T., Kohda, D., Fukui, Y. and Yokoyama, S. (2012) Structural basis for mutual relief of the Rac guanine nucleotide exchange factor DOCK2 and its partner ELMO1 from their autoinhibited forms. *Proc Natl Acad Sci U S A*, **109**, 3305-10. DOI: 10.1073/pnas.1113512109
23. Georges, L., Goto-Ito, S., Yoshida, K., **Ito, T.**, Yokoyama, S. and Hou, Y.-M. (2011) Differentiating analogous tRNA methyltransferases by fragments of the methyl donor. *RNA*, **17**, 1236-1246. DOI: 10.1261/rna.2706011
24. Ito, T.\* , **Ito, T.\*** and Yokoyama, S. (2011) Plasma-assisted biological

- macromolecular crystallization. *Applied Physics Express*, **4**, 026201. DOI: 10.1143/APEX.4.026201 (\* equally contributed)
25. **Ito, T.** and Yokoyama, S. (2010) Two enzymes bound to one transfer RNA assume alternative conformations for consecutive reactions. *Nature*, **467**, 612-616. DOI: 10.1038/nature09411
  26. Kuratani, M., Hirano, M., Goto-Ito, S., Itoh, Y., Hikida, Y., Nishimoto, M., Sekine, SI., Bessho, Y., **Ito, T.**, Grosjean, H. and Yokoyama, S. (2010) Crystal Structure of *Methanocaldococcus jannaschii* Trm4 complexed with sinefungin. *J Mol Biol*, **401**, 323-333. DOI: 10.1016/j.jmb.2010.06.046
  27. **Ito, T.**, Kiyasu, N., Matsunaga, R., Takahashi, S. and Yokoyama, S. (2010) Crystal structure of nondiscriminating glutamyl-tRNA synthetase from *Thermotoga maritima*. *Acta Crystallogr D Biol Crystallogr*, **66**, 813-820. DOI: 10.1107/S0907444910019086
  28. Goto-Ito, S., **Ito, T.**, Kuratani, M., Bessho, Y. and Yokoyama, S. (2009) Tertiary structure checkpoint at anticodon loop modification in tRNA functional maturation. *Nat Struct Mol Biol*, **16**, 1109-1115. DOI: 10.1038/nsmb.1653
  29. Hiyama, T.B., **Ito, T.**, Imataka, H. and Yokoyama, S. (2009) Crystal Structure of the alpha subunit of human translation initiation factor 2B. *J Mol Biol*, **392**, 937-951. DOI: 10.1016/j.jmb.2009.07.054
  30. Goto-Ito, S., **Ito, T.**, Ishii, R., Muto, Y., Bessho, Y. and Yokoyama, S. (2008) Crystal Structure of Archaeal tRNA (m1G37) methyltransferase aTRM5. *Proteins*, **72**, 1274-1289. DOI: 10.1002/prot.22019
  31. Goto-Ito, S., Ishii, R., **Ito, T.**, Shibata, R., Fusatomi E., Sekine, S., Bessho, Y. and Yokoyama, S. (2007) Structure of an archaeal TYW1, the enzyme catalyzing the second step of wye-base biosynthesis. *Acta Crystallogr D Biol Crystallogr*, **63**, 1059-1068. DOI: 10.1107/S0907444907040668
  32. **Ito, T.** and Wagner, G. (2007) Resonance assignments of the  $\alpha\beta$  subunit of human eukaryotic initiation factor 2 (heIF2 $\alpha\beta$ ). *J Biomol NMR*, **38**, 173. DOI: 10.1007/s10858-006-9099-5
  33. Gelev, V., Aktas, H., Marintchev, A., **Ito, T.**, Frueh, D., Hemond, M., Rovnyak, D., Debus, M., Hyberts, S., Usheva, A., Halperin, J. and Wagner, G. (2006) Mapping of the Auto-Inhibitory Interactions of Protein Kinase R by Nuclear Magnetic Resonance. *J Mol Biol*, **364**, 352-363. DOI: 10.1016/j.jmb.2006.08.077
  34. Frueh, D.P., **Ito, T.**, Li, J.-S., Wagner, G., Glaser, S.J., and Khaneja, N. (2005) Sensitivity enhancement in NMR of macromolecules by application of optimal control theory. *J Biomol NMR*, **32**, 23-30. DOI: 10.1007/s10858-005-3592-0

35. **Ito, T.**, Marintchev, A. and Wagner, G. (2004) Solution structure of human initiation factor eIF2  $\square$  reveals homology to the elongation factor eEF1B. *Structure*, **12**, 1693-1704. DOI: 10.1016/j.str.2004.07.010
36. Kato, M., **Ito, T.**, Wagner, G. and Ellenberger, T. (2004) A molecular handoff between bacteriophage T7 DNA primase and T7 DNA polymerase initiates DNA synthesis. *J Biol Chem*, **279**, 30554-62. DOI: 10.1074/jbc.M403485200
37. **Ito, T.** and Wagner, G. (2004) Using codon optimization, chaperone co-expression, and rational mutagenesis for production and NMR assignments of human eIF2  $\square$ . *J Biomol NMR*, **28**, 357-367. DOI: 10.1023/B:JNMR.0000015405.62261.cb
38. Kato, M., **Ito, T.**, Wagner, G., Richardson, C.C. and Ellenberger, T. (2003) Modular architecture of the bacteriophage T7 primase couples RNA primer synthesis to DNA synthesis. *Mol Cell*, **11**, 1349-1360. DOI: 10.1016/S1097-2765(03)00195-3
39. Kitamura, A., Muto, Y., Watanabe, S., Kim, I., **Ito, T.**, Nishiya, Y., Sakamoto, K., Ohtsuki, T., Kawai, G., Watanabe, K., Hosono, K., Takaku, H., Katoh, E., Yamazaki, T., Inoue, T. and Yokoyama, S. (2002) Solution structure of an RNA fragment with the P7/P9.0 region and the 3'-terminal guanosine of the tetrahymena group I intron. *RNA*, **8**, 440-451. DOI: 10.1017.S1355838202026043
40. **Ito, T.**, Muto, Y., Green, M.R. and Yokoyama, S. (1999) Solution structures of the first and second RNA-binding domains of human U2 small nuclear ribonucleoprotein particle auxiliary factor (U2AF<sup>65</sup>). *EMBO J*, **18**, 4523-4534. DOI: 10.1093/emboj/18.16.4523

### Proceedings

1. Kitamura, A., Muto, Y., Watanabe, S., Kim, I., **Ito, T.**, Nishiya, Y., Ohtsuki, T., Kawai, G., Watanabe, K., Hosono, K., Takaku, H., Katoh, E., Yamazaki, T., Inoue, T. and Yokoyama, S. (1999) The guanosine binding mechanism of the Tetrahymena group I intron. *Nucleic Acids Symp Ser*, **42**, 191-192.

### Review in English

1. Marintchev, A.\* and **Ito, T.\*** (2020) eIF2B and the integrated stress response: a structural and mechanistic view. *Biochemistry*, **59**, 1299-1308. DOI: 10.1021/acs.biochem.0c00132
2. Kashiwagi, K., **Ito, T.** and Yokoyama, S. (2017) Crystal structure of eukaryotic translation initiation factor 2B. *Spring-8/SACLA Research Frontiers 2016*, 22-23.

3. Goto-Ito, S., **Ito, T.**\* and Yokoyama, S.\* (2017) Trm5 and TrmD: two enzymes from distinct origins catalyze the identical tRNA modification, m<sup>1</sup>G37. *Biomolecules*, **7**, E32. DOI:10.3390/biom7010032 (\* co-corresponding authors)
4. Kashiwagi, K., **Ito, T.**\* and Yokoyama, S.\* (2017) Crystal structure of eIF2B and insights into eIF2-eIF2B interactions. *FEBS J*, **284**, 868-874. DOI:10.1111/febs.13896 (\* co-corresponding authors)
5. **Ito, T.** and Yokoyama, S. (2011) Crystal structure of glutamine transamidosome: two enzymes bond to one transfer RNA function cooperatively for consecutive reactions. *Photon Factory Activity Report 2010*, **28**, 48-49.
6. **Ito, T.** and Yokoyama, S. (2011) Crystal structure of glutamine transamidosome reveals how two enzymes bound to one tRNA assume alternative conformations for consecutive reactions. *Spring-8 Research Frontiers 2010*, 20-21.