OMB No. 0925-0001 and 0925-0002 (Rev. 10/15 Approved Through 10/31/2018)

BIOGRAPHICAL SKETCH

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NAME: Maehigashi, Tatsuya

eRA COMMONS USER NAME (credential, e.g., agency login): TMAEHI

POSITION TITLE: Research Associate

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

| INSTITUTION AND LOCATION | DEGREE  (if applicable) | Completion Date  MM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| Utah State University, Logan, UT | B.S | 5/2002 | Biochemistry |
| Georgia Institute of Technology, Atlanta, GA | Ph.D. | 5/2009 | Structural Biology |
| Emory University, Atlanta, GA | Postdoctoral | 2/2015 | Structural Biology |
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**A. Personal Statement**

I have the expertise in macromolecule preparations, including challenging protein purifications, large complexes (bacterial ribosomes), as well as *in vitro* transcribed RNA and structured RNAs (tRNAs). My training as an X-ray crystallographer began during my Ph.D. studies with Dr. Loren D. Williams at Georgia Tech, where I worked on DNA and DNA-drug complexes at ultra-high resolution. I started my postdoctoral training with Dr. Christine Dunham at Emory in 2009, and I have since then completed variety of crystallographic challenges including toxin-antitoxin protein-protein complexes and several 70S ribosome complexes. Through my postdoctoral training, I also had the opportunities to collaborate with researchers from other groups, and produced several peer-reviewed publications. These projects involve careful and often difficult biomolecule preparations, as well as complex instrumentations and data analyses. This expertise will help in determining the structure of the HIV-1 RT bound to mismatch primer (Aim 2) to contribute to the mechanistic understanding of its uniquely efficient mismatch extension capability.

**B. Positions and Honors**

**Positions and Employment**

**2014-2015 Research Associate, Department of Biochemistry, Emory University, Atlanta, GA**

**2015- Research Associate, Department of Pediatrics, Emory University, Atlanta, GA**

**Other Experience and Professional memberships**

**2014- Member, RNA Society**

**2007 “Chem 1310 2007-2008 Laboratory Manual” (Author), Houghton Mifflin.**

**Honors**

**2003 Graduate Teaching Assistant Award, Department of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA**

**2004 CETL/BP Outstanding Teaching Assistant Award, Center for Enhancement of Teaching and Learning, Georgia Institute of Technology, Atlanta, GA**

**2005 Graduate Honoree, Colloege of Sciences, Georgia Institute of Technology, Atlanta, GA**

**C. Contribution to Science**

**Complete List of Published Work in MyBibliography**

[**http://www.ncbi.nlm.nih.gov/sites/myncbi/10SlcYpeBay54/bibliography/47860155/public/?sort=date&direction=ascending**](http://www.ncbi.nlm.nih.gov/sites/myncbi/10SlcYpeBay54/bibliography/47860155/public/?sort=date&direction=ascending)**.**

**1.** During my Ph.D. studies, I have determined several high resolution structures of DNA in the presence of biologically relevant counter-ion. While the basic structure of DNA itself in general has been known for over the decays, increasingly accurate X-ray structures offer highly detailed characterization of conformation, hydration and counter-ion interactions. These work revealed that the new high-resolution structure of DNA with extended A-tracts differs significantly from a previous structure in both conformation and hydration (**ref. a**), and DNA with uniquely tethered cation in the major groove influences DNA deformation and the distribution of the counter-ion (**ref. b**). The high-resolution sub-atomic data obtained by improved methods allowed more accurate modeling of the DNA, revealing polymorphism of the DNA atomic positions, conformation and hydration, and is the first observation of full base pair positional heterogeneity observed by X-ray diffraction of DNA (**ref. c**).

* 1. [Woods, K.K., **Maehigashi, T.**, Howerton, S.B., Sines, C.C., Tannenbaum, S., Williams, L.D.](http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Search&db=PubMed&term=Woods+Maehigashi+Howerton+Sines+Tannenbaum+Williams+), “High-resolution structure of an extended A-tract: [d(CGCAAATTTGCG)]2”.*J.Am.Chem.Soc.* , **126**, pp. 15330 - 15331, 2004. PMID: 15563130.
  2. Moulaei, T., **Maehigashi, T.**, Lountos, G., Komeda, S., Watkins, D., Stone, M., Marky, L., Li, J., Gold, B., Williams, L.D., “Structure of B-DNA with Cations Tethered in the Major Groove”, *Biochemistry*, **44**, pp. 7458 - 7468, 2005. PMID:15895989
  3. **Maehigashi, T.**, Hsiao, C., Woods, K. K., Moulaei, T., Hud, N. V. and Williams, L. D., “B-DNA structure is intrinsically polymorphic: even at the level of base pair positions”, *Nucleic Acids Res.*, **40**, pp. 3714-3722, 2012. PMID: 22180536.

2. During my postdoctoral training, my primary research goals were directed toward mechanistic understanding of translational controls in bacteria through ribosome crystallography. During this time, my projects involved elucidating the mechanism of long known phenomena of how ribosomal ambiguity mutations (ram) promotes miscoding event (**ref. a**) and structural insights into how suppressor tRNA induce +1 frameshifting to understand the role played by the ribosome in maintaining the correct translational reading frame (**ref. b and c**).

1. Fagan, C. E., Dunkle, J. A., **Maehigashi, T.**, Dang, M. N., Miles, S. J., Qin, D., Fredrick, K. and Dunham, C. M., “Reorganization of an intersubunit bridge induced by disparate 16S ribosomal ambiguity mutations mimics an EF-Tu- bound state”. *Proc. Natl. Acad. Sci. U S A.*, **110(24),** pp. 9716-9721, 2013. PMID: 23630274.
2. **Maehigashi\*, T.**, Dunkle\*, J. A., Miles, S. J. and Dunham, C. M., “Structural insights into +1 frameshifting promoted by expanded or modification-deficient anticodon stem-loops”. *Proc. Natl. Acad. Sci. U S A.*, **111(35)**, pp. 12740-12745, 2014. PMID: 25128388.

[\*These authors contributed equally]

1. Fagan, C. E., **Maehigashi, T.**, Dunkle, J. A., Miles, S. J. and Dunham, C. M., “Structural insights into translational recoding by frameshift suppressor tRNASufJ”. *RNA,* **20(12)**, pp. 1944-1954, 2014. PMID: 25352689.

3. Bacterial toxin-antitoxin (TA) systems regulate key cellular processes to promote cell survival during periods of stress. Among known TA systems, Type II TA operons encode small antitoxin and toxin protein that under normal growth conditions form a tight, nontoxic complex. These complexes transcriptionally autorepress by binding at operator sequences in their promoter region. Upon stress, the antitoxin is degraded by proteases, allowing the toxin to target key cellular processes, including translation (eg. ribosome-bound mRNA). We have solved x-ray crystal structures of the ribosome-dependent TA systems; *proteus volgaris* HigBA (**ref. a**) and *E. coli* DinJ-YafQ TA complexes (**ref. b**). We further biochemically analyzed how ribosome-dependent toxin YafQ mediates recognition of both the ribosome and the mRNA substrate (**ref. c**).

* 1. Schureck, M. A., **Maehigashi, T.**, Miles, S. J., Marquez, J., Ei Cho, S., Erdman, R. and Dunham, C. M., “Structure of the P vulgaris HigB-(HigA)2-HigB toxin-antitoxin complex”. *J. Biol. Chem.*, **289(2)**, pp. 1060-1070, 2014**.** PMID: 24257752.
  2. Ruangprasert\*, A., **Maehigashi\*, T.**, Miles, J. M., Giridharan, N., Liu, J. X. and Dunham, C. M., “Mechanisms of toxin inhibition and transcriptional repression by *E. coli* DinJ-YafQ”. *J. Biol. Chem.*, **289(30)**, pp. 20559-20569, 2014. PMID: 24898247.

[\*These authors contributed equally]

* 1. **Maehigashi\*, T**., Ruangprasert\*, A., Miles, S. J., Dunham, C. M., “Molecular Basis of ribosome recognition and mRNA hydrolysis by the E. coli YafQ toxin”. *Nucleic Acids Res.* 2015. PMID 26261214. [Epub ahead of print] [\*These authors contributed equally]

3. In collaboration with Dr. Charles Moran group, we have determined the structure of the basal components of a bacterial transporter SpoIIQ and SpoIIIAH. These proteins interact through two membranes to connect the forespore and the mother cell during endospore development in the bacterium *Bacillus subtilis* (**ref. a**). The predicted ring-forming motif of SpoIIIAH and other evidence led to the model that SpoIIQ and SpoIIIAH form the core components of a channel or transporter through which the mother cell nurtures forespore development, which we simulated through molecular modeling using the determined crystal structure of these proteins. In collaboration with Dr. Nancy Woychik group, we have provided the molecular modeling evidence to support their biochemical finding of how Doc toxin from bacteriophage P1 inactivates elongation factor Tu by phosphorylating a single amino acid, which leads to the protein synthesis and thereby arrests cell growth (**ref. b**). This work and others further demonstrated the diverse function of toxin-antitoxin systems. In other collaborative work with Woychik group, we also showed how growth-regulating Mycobacterium tuberculosis VapC-mt4 toxin is an isoacceptor-specific tRNase by providing how VapC potentially interact with the target tRNAs through molecular modeling (**ref. c**).

1. Meisner\*, J., **Maehigashi\*, T.**, Andre, I., Dunham, C. M., Moran Jr., C. P., “Structure of the basal components of a novel bacterial transporter”. *Proc. Natil. Acad. Sci. U S A.* , **109,** pp. 5446-5451, 2012. PMID: 22431613

[\*These authors contributed equally]

1. Cruz\*, J. W., Rothenbacher\*, F. P., **Maehigashi, T.**, Lane, W. S., Dunham, C. M. and Woychik, N. A., “Doc toxin is a kinase that inactivates elongation factor tu”. *J. Biol. Chem.*, **289(11)**, pp. 7788-7798, 2014. PMID: 24448800.

[\*These authors contributed equally]

1. Cruz\*, J. W., Sharp\*, J. D., Hoffer, E. D., **Maehigashi, T.**, Vvedenskaya, I. O., Konkimalla, A., Husson, R. N., Nickels, B. E., Dunham, C. M., and Woychik, N. A. “Growth-regulating Mycobacterium tuberculosis VapC-mt4 toxin is an isoacceptor-specific tRNase”. *Nature communications,* **6**, 7480. 2015. PMID: 26158745.

[\*These authors contributed equally]

**D. Research Support**

**Ongoing Research Support**

**Completed Research Support**