Proposal for ENS-Lyon / Univ. Tokyo Internship Program

Project Title: RNA Processing Research - Function, Structure and Regulation

The project will be conducted at: RNA Processing Research Group, Biomedical Research Institute, National Institute of Advanced Industrial Sciences and Technology (AIST), Tsukuba, Ibaraki 305-8566, Japan (http://www.tomita-lab.net).

Project period: Sep. to Dec., 2014 or Feb. to May., 2015

Internship supervisors: Kozo Tomita (Research Group Leader at AIST; Adjunct Professor at Tokyo Univ. kozo-tomita@aist.go.jp)

Key words: RNA processing, quality control, molecular cell biology, structural biology

Background and summary of the project:

The main interest in our lab is the structures and functions of RNA processing machinery. In particular, we have investigated the mechanisms of synthesis, maturation and degradation of RNAs. RNA processing, which includes maturation process of functional RNAs and metabolism of RNAs, is important step for the gene regulation in cells. RNA processing dysregulations are often associated with the human diseases. In the last decades, by structural and functional analysis of RNA processing enzymes, such as template-independent RNA polymerases, and viral RNA polymerases, we have contributed to solving classical and important problems in the RNA enzymology. More recently, we have focused on the regulatory mechanism of biogenesis of RNAs in human cell by employing biochemistry, molecular cell biology, and structural approaches in complementary manner. Our studies would provide the molecular basis for the development of drags against human diseases such as cancer. In the internship program, we will study the molecular mechanism of degradation of dysfunctional small RNAs in human cells using molecular cell biology and biochemistry.

Techniques used: molecular cell biology, structural biology, biochemistry

Related publications from our laboratory:

 Yamashita S, Takeshita D & *<u>Tomita K</u> Translocation and rotation of tRNA during template-independent RNA polymerizaion by tRNA nucleotidyltransferase. *Structure* Vol. 22, No 2, pp315-325, **2014** Takeshita D, Yamashita S & *<u>Tomita K</u> Mechanism for template-independent terminal adenylation activity of Qβ replicase. *Structure* Vol. 20, No 10, pp1661-1669, **2012** Takeshita D, *<u>Tomita K</u> Molecular basis for RNA polymerization by Qβ replicase. *Nature Structural & Molecular Biology* Vol.19, No2, pp229-237, **2012** Toh Y, Takeshita D, Nagaike T, Numata T, *<u>Tomita K</u> Mechanism for the alternation of the substrate specificities of template-independent RNA polymerases. *Structure* Vol.19, No 2, pp232-243, **2011** Takeshita D, *<u>Tomita K</u> Assembly of Qβ viral RNA polymerase with host translational elongation factors EF-Tu and -Ts. *Proc Natl Acad Sci U S A*. Vol. 107, No 36, pp15733-15738, **2010**

6. Toh Y, Takeshita D, Numata T, Fukai S, Nureki O, * Tomita K

Mechanism for the definition of elongation and termination by the class II CCA-adding enzyme. *EMBO J.* vol. 28, No 21, pp3353-3365, 2009

7. Toh Y, Numata T, Watanabe K, Takeshita D, Nureki O, * Tomita K

Molecular basis for maintenance of fidelity during the CCA-adding reaction by a CCA-adding enzyme. *EMBO J.* Vol. 27, No 14, pp1944-1952, **2008**

8. Watanabe K, Toh Y, Suto K, Shimizu Y, Oka N, Wada T, * Tomita K

Protein-based peptide-bond formation by aminoacyl-tRNA protein transferase. *Nature*. Vol.449, No 7164, pp867-871, **2007**

9. Suto K, Shimizu Y, Watanabe K, Ueda T, Fukai S, Nureki O, *Tomita K

Crystal structures of leucyl/phenylalanyl-tRNA-protein transferase and its complex with an aminoacyl-tRNA analog.

EMBO J. Vol.25, No 24, pp5942-50, **2006**

10. * Tomita K, Ishitani R, Fukai S, Nureki O.

Complete crystallographic analysis of the dynamics of CCA sequence addition. *Nature*. Vol. 443, No 7114, 956-960, **2006**