

## Molecular Parasitology

Principal Investigator Kiong Ho

E-mail.address [kiongho@md.tsukuba.ac.jp](mailto:kiongho@md.tsukuba.ac.jp)

URL [http://www.md.tsukuba.ac.jp/basic-med/kiongho/Ho\\_Lab/Welcome.html](http://www.md.tsukuba.ac.jp/basic-med/kiongho/Ho_Lab/Welcome.html)



### Major Scientific Interests of the Group

Our primary research interest is to understand the gene expression of eukaryotic parasites with a goal in identifying parasite-specific processes that can be exploited as targets for novel therapeutic interventions. We have focused on how messenger RNA acquire 5' cap in the protozoan parasites that responsible for malaria and sleeping sickness. The structure and mechanism of protozoan capping enzyme is completely different from human host, and thus, capping is an attractive target for anti-protozoal drug discovery. We are also investigating how RNAs are repair and recombination. RNA ligase is the key enzyme that joins the broken RNAs together. We have characterized three separate types of RNA ligases from various species and our immediate goal is to define how these ligases recognize the breaks in the RNA and to identify what types of RNA are repaired in the cell.

### Projects for Regular Students in Doctoral or Master's Programs

- 1) Dissecting the mechanism of hypermethylated cap 4 synthesis in Trypanosome brucei.
- 2) Characterization of T.brucei capping enzyme complex with transcription and processing factors.
- 3) Defining the physiological targets for RNA ligase through genome wide screening.

### Study Programs for Short Stay Students (one week – one trimester)

- 1) Screening of small molecule inhibitor against malaria and sleeping sickness.
- 2) Regulation of gene expression by cytoplasmic mRNA recapping.
- 3) Defining the optimal RNA substrates for RNA ligase.

### Selected Publications

- 1) Yoshinari S, Liu Y, Gollnick PG and Ho CK. (2017) Cleavage of 3'-terminal adenosine by archaeal ATP-dependent RNA ligase. *Scientific Reports* 7:11662.
- 2) Gu H, Yoshinari S, Ghosh R, Murakami KS, Ignatochkina AV, Gollnick P and Ho CK. (2016) Structural and Mutational Analysis of Archaeal ATP-dependent RNA ligase Identifies Amino Acid Required for RNA Binding and Catalysis. *Nucleic Acid Res.* 44: 2337 - 2347.
- 3) Smith P, Ho CK, Takagi Y, Djaballah H, and Shuman S. (2016) Nanomolar Inhibitors of Trypanosoma brucei RNA Triphosphatase. *mBIO* 7: e000058-16
- 4) Ignatochkina AV, Takagi Y, Liu Y, Nagata K, and Ho CK. (2015) The Messenger RNA Decapping and Recapping Pathway in Trypanosoma. *Proc. Natl. Acad. Sci. USA*
- 5) Torchea C, Takagi Y and Ho CK. Archaea RNA Ligase is a Homodimeric Protein that Catalyzes Intramolecular Ligation of Single-Stranded RNA and DNA. (2008) *Nucleic Acid Res.* 36: 6218 - 6227.
- 6) Takagi Y, Sindkar S, Ekonomidis D, Hall MP and Ho CK. (2007) Trypanosoma brucei Encodes a Bifunctional Capping Enzyme Essential for Cap 4 Formation on the Spliced Leader RNA. *J. Biol. Chem.* 282: 15995-16005.
- 7) Pfeffer S, Sewer A, Lagos-Quintana M, Sheridan R, Sander C, Grässer FA, van Dyk LF, Shuman S, Ho CK, Chien M, Russo JJ, Ju J, Randall G, Lindenbach BD, Rice CM, Simon V, Ho DD, Zavolan M, and Tuschl T. Identification of the MicroRNAs of the Herpesvirus Family. *Nature Method* 2005; 2: 269-276.