



GRADUATE SCHOOL OF BIOMEDICAL SCIENCES

INTERDISCIPLINARY GRADUATE PROGRAM

Ph.D. THESIS DEFENSE

HSIN-JUNG CHOU

MENTOR: Oliver Rando, MD/PhD
THURSDAY, 12/21/2017 1:00 p.m.
LRB Room 816

"Transcriptome-wide analysis of roles for tRNA modifications in translational regulation"

Covalent nucleotide modifications in RNAs affect numerous biological processes, and novel functions are continually being revealed even for well-known modifications. Among all RNA species, transfer RNAs (tRNAs) are highly enriched with diverse modifications, which are known to play roles in decoding and tRNA stability, charging, and cellular trafficking. However, studies of tRNA modifications have been limited in a small scale and performed by groups with different methodologies. To systematically compare the functions of a large set of noncoding RNA modifications in translational regulation, I carried out ribosome profiling in 57 budding yeast mutants lacking nonessential genes involved in tRNA modifications. Deletion mutants with enzymes known to modify the anticodon loop or non-tRNA substrates such as rRNA exhibited the most dramatic translational perturbations, including altered dwell time of ribosomes on relevant codons, and altered ribosome density in protein-coding regions or untranslated regions of specific genes. Several mutants that loss tRNA modifications in the locations away from the anticodon loop also exhibited altered dwell time of ribosomes on relevant codons. Translational upregulation of the nutrient-responsive transcription factor Gcn4 was observed in roughly half of the mutants, consistent with the previous studies of Gcn4 in response to numerous tRNA perturbations. This work also discovered unexpected roles for tRNA modifying enzymes in rRNA 2'-O-methylation, and in transcriptional regulation of TY retroelements. Taken together, this work revealed the importance and novel functions of tRNA modifications, and provides a rich resource for discovery of additional links between tRNA modifications and gene regulation.

Mentor(s)

Oliver Rando, MD/PhD

Dissertation Exam Committee

Allan Jacobson, PhD (Chair)
Marian Walhout, PhD
Andrei Korostelev, PhD
Paul Kaufman, PhD
Peter Dedon, MD/PhD