DATE: 3, Aug, 2018

SUMMARY of

2017 RESEARCH RESULTS REPORT

For International Collaborative Research with IPR, Osaka University

Research Title		**Computer simulations reveal ribosomal rolling motion during programmed frameshifting**
Applicant	**Name**	**Lee-Wei Yang**
	Affiliation	**Institute of Bioinformatics and Structural Biology, National Tsing Hua Univ., Taiwan**
	Present Title	**Professor**
Research Collaborator (Host PI)		**Akira Shinohara**

Summary

Prof Lee-Wei Yang's IPR, U Osaka visit (3/23-3/29; on campus from 3/26 to 3/29) was a downsized version of International Collaborative Research project proposed in early 2017. In the proposal, Dr Yang proposed the mechanism of program ribosomal frameshifting (PRF), utilized by many viruses to encode ≥2 functional/structural protein products using a single mRNA template. The computer simulations suggested the counter forces generated during ribosome's unwinding of specific structured mRNA (pseudoknots, or PKs) make ribosome undergo a 'rolling' motion. The motion transiently compresses tRNAs (supported by earlier cryo-EM evidence at low resolution), which in turn causes the weakening of tRNA-mRNA base pairing. All-atom simulations then revealed that under such condition, A/P site tRNA either dissociates from the mRNA or slides one base backward toward the P-site by exactly one base but no further because the dissociated P/E-site tRNA poses a stable hindrance. It will be very nice if this prediction can be further assessed by the new cryo-EM facilities in IPR; hence one of the reasons for Lee's one-week visit in March 2018 is to seek collaboration and discuss in finer details with **Prof Kenji Iwasaki**'s team in order to jointly work on this project. Serving as the second purpose is to learn from **Prof Akira Shinohara** standing puzzles on homologous recombination. Lee would assess his possible contribution to these issues providing his past simulation experience in dsDNA kinking, RNA unwinding and protein/RNA/ssDNA interactions.

After a detailed discussion with Prof Iwasaki, he and his team members decided to work on this project. Our current goal is to resolve the cryo-EM images for PK-stalled and -free prokaryotic ribosome particles in <8Å resolution, or, high enough to distinguish different sub-population of conformational states in the presence of PK from that in PK's absence. With a good prediction, the conformational states should be distributed along the "rolling" direction.

The PK-stalled and PK-free ribosome samples will be prepared locally from Prof Iwasaki's lab with the protocol suggested by Prof Yang and his Taiwanese collaborators, Prof Jin-Der Wen.