Ribosome profiling analysis reveals the roles of DDX41 in translational regulation
（リボソームプロファイリングによる翻訳制御における DDX41 の役割の解明）

Background and Purpose: DDX41 gene mutation has previously been observed in myeloid malignancies including myelodysplastic syndromes and acute myeloid leukemia, but the underlying causative mechanisms of these diseases have not been fully elucidated. The DDX41 protein is an ATP-dependent RNA helicase and supposedly plays a role in RNA metabolism. Our laboratory previously showed that DDX41 was involved in ribosome biogenesis by promoting the processing of newly transcribed pre-rRNA. Because of these findings, in this study we investigated the involvement of DDX41 in translation, by taking advantage of ribosome profiling technology.

Methods: In this study, we performed comprehensive translational analysis by taking advantage of ribosome profiling; in this assay, only mRNA that are being translated (i.e., those incorporated into ribosome) are selectively purified and are sequenced by next generation sequencer. We introduced shRNA targeting DDX41 in K562 leukemia cells, and the translation of the cells was compared with that of control K562 cells. In addition, RNA-sequencing (RNA-seq) data was obtained from the same set of the cells and dissected the transcriptional changes and translational changes separately.

Results: DDX41 knockdown resulted in both translationally increased and decreased transcripts. Both gene set enrichment analysis and gene ontology analysis indicated that ribosome-associated genes were translationally promoted after DDX41 knockdown, in part because these transcripts had significantly shorter transcript length and higher transcriptional and translational levels. In addition, we found that transcripts with 5'-terminal oligopyrimidine motifs tended to be translationally upregulated when the DDX41 level was low.

Conclusions: Our data suggest that a translationally regulated feedback mechanism involving DDX41 may exist for ribosome biogenesis.