Form 2

Dissertation Abstract

Report no.	(Course-based) No.1230	Name	Fang Qi (ファン チー)
Dissertation title	Functional studies of mammalian HEMK1 and its interactors in mitochondrial translation and metabolism (ミトコンドリアの翻訳と代謝における哺乳類 HEMK1 とそのインタラクターの機能解析)		

Abstract

Protein translation is highly conserved in all species. At the final step of protein translation (or translation termination), stop codons at the P-site are read by peptide release factors, facilitating the release of nascent polypeptides. Glutamine methylation on the GGQ motif of prokaryote peptide release factors is essential for their function. Enzymes that mediate glutamine methylation on peptide release factors have divergently evolved beyond the prokaryote lineage and split into two homologous proteins in mammals, namely HEMK1 and HEMK2. HEMK2 dimerized with a multifunctional methyltransferase subunit 112, TRM112, serves as an active methyltransferase complex for the glutamine methylation on eukaryote release factor 1 in the cytosol. In mitochondria, HEMK1 is the putative methyltransferase for mitochondrial release factors. There are four putative mitochondrial release factors (mtRFs) containing the universal GGQ motif in mammals, namely MTRF1, MTRF1L, MRPL58, and MTRFR. I demonstrated that HEMK1 indeed confers methylations at Q252 of MTRF1L, Q313 of MTRF1, Q90 of MRPL58, and Q73 of MTRFR. Although I have examined the cell physiology of *HEMK1* KO cells, disruption of the *HEMK1* gene showed no significant impacts on the overall cell growth, mtDNA copy number, mitochondrial membrane protein level, and mitochondrial membrane potential. Furthermore, nascent mitochondrial protein synthesis was not affected in *HEMK1* KO cells. These results suggest that HEMK1 mediates the GGQ methylation of all four mtRFs in human cells; however, this methylation is likely to be dispensable in cell growth and mitochondrial protein homeostasis.

Coincidently, PreY, a TRM112 domain-containing protein from vertebrates, was found located in mitochondria. I hypothesized that HEMK1 may require PreY to function as a methyltransferase, like as HEMK2 requires TRMT112 for its enzymatic activity. Although both HEMK1 and PreY localized in mitochondria, I failed to demonstrate the HEMK1-PreY interaction by immunoprecipitation. Future studies will be needed for above issue.