

Research Theme: Biochemistry / Synthetic Biology
Research Project Title: Quality control mechanisms of incomplete nascent proteins
Principal Investigator/Supervisor: Asst/ Prof Choe Young-Jun
Co-supervisor/ Collaborator(s) (if any): NA
Project Description a) Background: Ribosomes can stall during the translation for various reasons. A prominent example is translation of aberrant messenger RNAs that were truncated or chemically modified by UV or reactive oxygen species. The incomplete nascent proteins, being synthesized by stalled ribosomes, would be detrimental to cells. Eukaryotes have evolved an elaborate quality control pathway, RQC (ribosome-associated quality control), to get rid of stalled proteins by using the ubiquitin-proteasome system. The RQC complex assembles at stalled ribosomes and its E3 ligase component ubiquitylates nascent proteins for subsequent degradation by proteasomes. Complete knockout and hypomorphic mutation of RQC components in mice lead to embryonic lethality and a neurodegenerative disease, respectively, indicating the toxicity of stalled proteins. b) Proposed work: The RQC pathway comprises multiple steps, from recognition of stalled ribosomes to degradation of nascent proteins. Various gene products are expected to play roles in each step of the RQC pathway. We will carry out a genetic screening to identify new factors while characterizing previously reported RQC players. Newly identified RQC factors will be investigated by using methods of biochemistry / molecular biology / structural biology.
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