Report for Joint Research Programs 2017, Institute of Advanced Medical Sciences, Tokushima University

I. Joint Research

B-8. Division of Molecular Biology (Professor Seiichi Oyadomari)

II. Personal information

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III. Proposed research

1) Title

Role of GTPBP1/2 during ER stress

2) Aspect (choose one from Joint Usage A1-A4 and Joint Research B1-B17)

B-8. Division of Molecular Biology (Professor Seiichi Oyadomari)

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4) Research background

During cellular stress, it is often advantageous to inhibit protein synthesis. Phosphorylation of eIF2α impairs initiation of the translation of most mRNAs; however, a few mRNAs are translated more efficiently under such conditions. The best characterized encodes the transcription factor ATF4. Unpublished results from my group indicate that Drosophila ATF4 drivesthe expression of GTPBP1 and GTPBP2. These poorly characterized proteins are homologous to translation elongation factor EF1A, but have been implicated in mRNA degradation and in the disassembly of stalled polysomes.

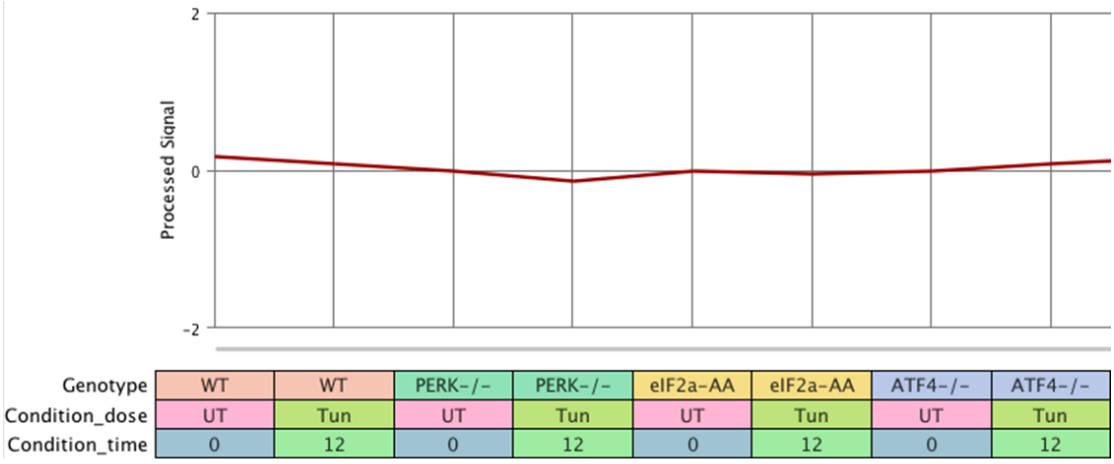
5) Hypothesis

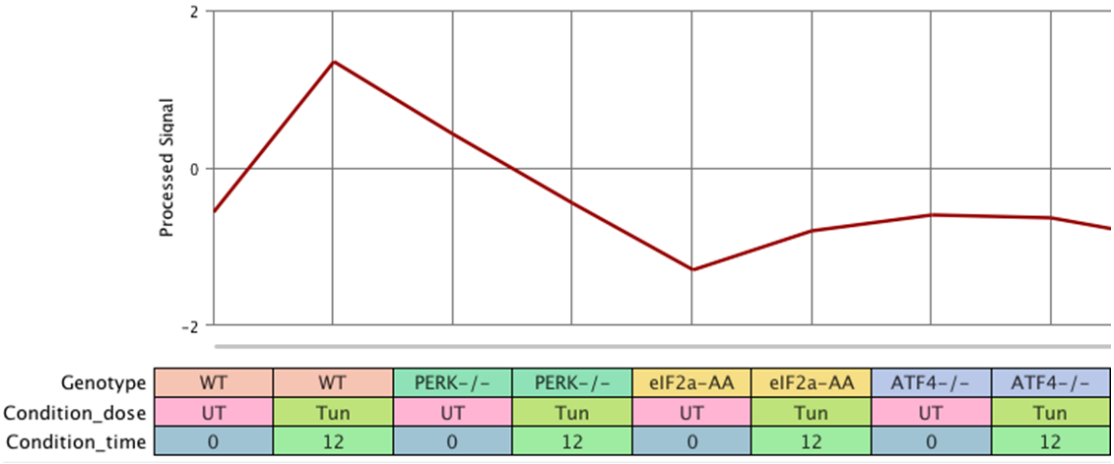
We hypothesize that GTPBP1/2 are play a role in modulating protein synthesis during ER stress via one or more of (i) degradation of mRNA, (ii) disassembly of existing polysomes, or (iii) biasing translation to ISR-target proteins.

6) Progress

We have tested these hypotheses by harnessing multiple OMICS platforms available at the Institute of Advanced Medical Sciences, Tokushima University. Drosophila S2 cells in the presence or absence of ER stress were treated with interfering RNA targeting GTPBP1 and GTPBP2,and then be analyzed by OMICS platforms.

(i) RNAseq
RNA microarray data show it's GTPBP2 and not GTPBP1 that is an ISR target in mammalian cells.





(ii) Polysome profiling
The profiling is still on-going in the University of Cambridge.

(iii) Proteomics
Newly synthesized proteins will be purified by Bioorthogonal Noncanonical Amino Acid Tagging (BONCAT) followed by mass spectrometry.GTPBP1 and GTPBP2 bound to different proteins from each other and GTPBP2 to co-purify with eIF4G and ataxin-2.