Usage Report for Fiscal Year 2021

Project Title:

Deciphering the brain by translating ribosome profiling

Name:

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1. Background and purpose of the project, relationship of the project with other projects

Translation in axons and dendrites has been known to play an important role in the development and function of neurons. Messenger RNAs (mRNAs) are transported to and locally translated in axon terminals and synapses. However, the distribution and homeostasis of translation machineries, i.e., ribosomes and transfer RNAs (tRNAs), in these distal sites have been largely remained unexplored.

Recent studies have found that the synthesis and incorporation of some ribosomal proteins in neurons was altered between the subcellular compartments and changed by the environmental changes. This suggests a scenario that tRNAs may also differentially distribute and respond to environmental changes within neurons. tRNAs are essential molecules in translation, which transport their cognate amino acids to the ribosome for the following aminoacylation reactions and nascent peptide elongation. Defects in tRNA biogenesis processes impair the stability and functions of tRNA, which have been known to impede mRNA translation and cause various neurological diseases. Therefore, it is critical to have a detailed and completed study of the temporal and spatial control of all neuronal tRNAs

2. Specific usage status of the system and calculation method

There were two major calculation methods I am using on the RIKEN HBW system. For the analysis of tRNA species and modification, the mim-tRNAseq pipeline was used as a conda environment. The second method is the uORF-tools also as a conda environment. The usage of the HBW started from December, 2021, therefore, most of the time was spent to setup and test of the calculation methods.

3. Result

I have analyzed the ribosome profiling data using the uORF-Tools to discover the presence of novel ORF from mouse brains, mainly the Fmr1KO mice and also the mice under chronic social defeat stress (CSDS). I also tried to analyse the differential expression of these novel ORFs, and found the candidates genes with potential regulation on gene expression via the control of uORF.

4. Conclusion

Although the experiments still needed to be modified and repeated, the preliminary results demonstrate the ability of the calculating from HBW is well suitable for my research purpose.

5. Schedule and prospect for the future

I will continue to setup the analyzing pipeline for tRNA-seq data in the near future. The expected tRNA sequencing data will soon be available. These data will analyzed by the newly established tRNA-seq pipeline. The modified CSDS mice sequencing data will also be available on early May, and probably the repeated experiments on July. These data will be used for uORF analysis by the uORF-Tools on the HBW.

6. If no job was executed, specify the reason.