Stress and the Brain: A Proteomics Approach into Investigating Neurodegenerative Disorders and Stress Stimuli

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Proteomics, a systematic study of proteins present in a cell, tissue, organ, or organism at a particular moment during the life cycle, is one of the key research areas in the functional genomics era. Although DNA-based microarray technology has become an increasingly popular research field for profiling genome-wide expression of genes at the mRNA level, it is “proteins not genes” that are directly responsible for the cell functions and phenotype. Moreover, these powerful genomic tools do not provide any direct information on protein levels and their state of modification mainly due to post-translational regulation, which results in a lack of correlation between mRNA and protein abundance. This difference is just one of the examples of many types of information, such as the total number of genes in a given genome, protein function, localization and compartmentalization, and protein-protein interactions, which we cannot obtain from the study of genes alone. Other than the vast wealth of genomic data available to the proteomics researcher, a series of tremendous technological developments in immobilized pH gradient (IPG) based two-dimensional gel electrophoresis (2-DGE), mass spectrometry (MS), staining and scanning methods, chromatography, bioinformatics, and protein chips, have all fuelled a proteomics revolution in yeast, humans and even plants.

Our present research involves rats treated with neurotoxins as animal models for psychiatric & neurological disorders and stress stimuli. Why we use animal models? Animal models are genetically homogenous, and their environment can be easily controlled allowing for more interventions as opposed to the clinical cases. Why not mice? We use rats over mice because of a larger brain size for experimental analysis in rats. Moreover, rats treated with various drugs have been used as animal models for important psychiatric disorders such as the attention-deficit hyperactivity disorder (ADHD), one of the developmental disorders. We will present some results of the proteomics analysis of the Wiggling-Wistar King Aptekman/Hokkaido (WKAH) rats (Wig) that were designated from a strain of the Long-Evans Cinnamon (LEC) as a new rat model of ADHD in Hokkaido University. Moreover, we are also studying the effects of radiation on the brain in particular looking at how gamma radiation affects the rat brain proteome. Finally, we have selected three examples for investigating stress responses in rat (brains), such as treatment with water (fear), continuous light (disturbance in circadian rhythm), and immobility (physical).

We believe that a systematic proteomic analysis of brain/brain regions may help to understand the complexity, to investigate disorders of the central nervous system and under stress factors, and to search for corresponding early biomarkers, one of our goals.