



Title of Project Brain Environment

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【Purpose of the Research Project】

The brain consists of many types of cells, such as neurons, glial cells, vascular cells, and immune cells. Neuronal health is maintained through the maintenance of a healthy environment by cells surrounding neurons. For many years, neurons have been the main focus of neuroscience research. In neurodegenerative disease research, such as in Alzheimer's and Parkinson's diseases, the primary research question was "Why are neurons dying?" To date, many important findings explaining neuronal death were made such as the accumulation of abnormal proteins and organelle dysfunction (mitochondria, endoplasmic reticulum, etc.).

However, recent unexpected new findings prompted us to recognize the importance of the extra-neural environment in disease. Glial cells are shown to play an important role in disease progression. Further, abnormal proteins released from damaged neurons trigger disease propagation in a spatial manner. These findings led us to explore the 'brain environment' in health and disease.

Therefore, our aim is to understand the 'brain environment' by creating a new innovative research area with a team of researchers from the fields of neurological and psychiatric diseases, basic neuroscience of development, regeneration, glial biology, neuroendocrinology, and molecular neuroimaging. Furthermore, we are promoting research elucidating the mechanisms of neuropsychiatric disease from the viewpoint of brain environment destruction.

【Content of the Research Project】

Our research team consists of three groups: (A01) "Mechanisms of neuronal dysfunction", (A02) "Extra-neural environment", and (A03) "Imaging".

The "Mechanisms of neuronal dysfunction" group aims to uncover the mechanisms of dysfunction within neurons, which leads to the destruction of brain environment, under neurological and psychiatric disease conditions. The "Extra-neural environment" group aims to elucidate the mechanisms of 1) maintenance and destruction of brain environment, and 2) propagation of brain environmental

deterioration, focusing on glia-neuron interaction, neuroinflammation, and neuroendocrine systems in health and disease.

The "Imaging" group aims to understand the brain environment by visualizing the elementary processes of maintenance and deterioration of brain environment using cutting-edge molecular imaging techniques including PET (Positron Emission Tomography) on laboratory animals and cell models.

【Expected Research Achievements and Scientific Significance】

A01: Elucidating 1) molecular mechanisms of neuronal death in neurodegenerative and psychiatric diseases, mainly from the viewpoint of intra-neuronal dysfunction, and 2) the mechanisms through which the damaged neurons release "toxic" signals such as abnormal proteins.

A02: Elucidating 1) mechanisms how extra-neuronal cells such as glial cells in the brain environment recognize and respond to toxic signals released from damaged neurons in brain diseases and trauma, and 2) mechanisms of propagation of disease when brain environment is deteriorated.

A03: Understanding brain environment through visualizing each elementary process in pathological disease conditions through the use of cutting-edge molecular imaging techniques (in vivo and cell models). Enhancing research activities of the team, and promoting collaborative research projects through application of imaging techniques.

【Key Words】

Brain Environment, Neurodegenerative Diseases, Glia, Molecular Imaging

【Term of Project】 FY 2011-2015

【Budget Allocation】 1,185,400 Thousand Yen

【Homepage Address and Other Contact Information】

<http://www.neurol.med.kyoto-u.ac.jp/brainenvironment/>