【Grant-in-Aid for Scientific Research (S)】

Biological Sciences (Medicine, Dentistry, and Pharmacy)

Title of Project： Generation of neural network repair medicine

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Research Area：　Medicine, dentistry, and pharmacy
Keyword：　Neuroscience, neuronal network

【Purpose and Background of the Research】

Neurological disorders such as cerebrovascular disease, focal and central nervous system disorders from traumatic brain and spinal cord injury, higher brain dysfunction, and neuropathic pain, form their pathology and bring about spatiotemporal changes in the biological system which is made up not only of the nervous system but the immune system, the vascular system, and various organs. In this study, we analyze central neural circuit disorders and the subsequent restoration process from the viewpoint of the functional network of the biological system, and attempt to reveal in an integrated manner the control mechanism for the series of processes using the spatiotemporal dynamics of the biological system. The research particularly aims to uncover the control mechanism based on the linkage between the nervous system and each organ (Figure 1). We approach the process of central neural circuit disorders and functional recovery as the dynamics of the entire biological system and analyze the linkage between the nervous system and each system in an integrated manner to clarify the working principles of the living body with regard to central neural circuit disorders.

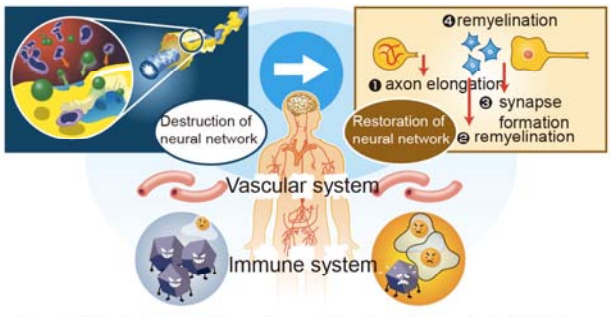

Figure 1 Biological systems that regulate rewiring of neural network after CNS injury

【Research Methods】

Unilateral cerebral cortex injury, local encephalomyelitis (EAE), and ADHD model mice are used. Using these pathological models, we analyze the dynamics of various organ cell groups and the spatiotemporal changes in gene expression. Furthermore, we continue analysis of the mechanisms of how immune cells, vascular cells, and organs control damage and repair of neural circuits. Along with these findings, we reveal the neural circuit repair mechanisms caused by activation of each cell group, and elucidate the working principles of the reactions of the living body.

【Expected Research Achievements and Scientific Significance】

Previous research has tended to identify the central nervous system as an independent organ and clarified the linkage between neural cells. Research that considers the central nervous system as an organ of the biological system and asks how the whole biological system is involved in the damage and repair of neural circuits is still in its early stages. We are generating research that understands neural circuit damage and the subsequent repair process reaction of living organisms as a 'scrap-and-build' strategy to reveal the mechanisms of this series of reactions and their significance, and we anticipate that this will create a new trend in life science research.

【Publications Relevant to the Project】

・Fujita, Y., Masuda, K., Nakato, R., Katou, Y., Tanaka, T., Nakayama, M., Takao, K., Miyakawa, T., Shirahige, K. and **Yamashita, T.** (2017) Cohesin regulates formation of neuronal networks in the brain. **J. Exp. Med.** 214, 1431-1452.
・Fujitani, M., Zhang, S., Fujiki, R., Fujihara, Y. and **Yamashita, T.** (2017) A chromosome 16p13.11 microduplication causes hyperactivity through dysregulation of miR-484/protocadherin-19 signaling. **Mol. Psychiatry** 22, 364-374.

【Term of Project】 FY2017-2021
【Budget Allocation】 158,600 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.med.osaka-u.ac.jp/pub/molneu/index.html