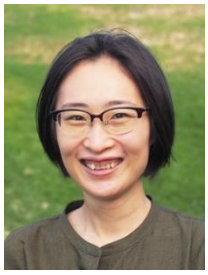
【Grant-in-Aid for Transformative Research Areas（B）】

Section III



Title of Project： **Pressio neuro-brain science: principle for brain function development through compressive stresses under physiological or pathological condition**

TANAKA Keiko (NONOMURA Keiko)
(National Institute for Basic Biology, Division of Embryology, Assistant Professor)

Number of Research Area：21B302　Researcher Number：70799246

【Purpose of the Research Project】

The brain, which exerts centralized control over organs in our body, is surrounded by the cerebrospinal fluid within a confined space inside the skull. Thus, the brain tissue inevitably suffers compressive stress (brain pressure). Given that mechanobiological research over a quarter century has successfully identified a variety of "mechanosensor" molecules in various types of cultured cells, mechanosensing and subsequent cellular responses (mechanoresponses) may be involved in functions of eventually all organs including the brain. In this Research Project, we aim at revealing how compressive stress is detected by brain cells and regulates brain tissue function. To this end, we organize a close collaboration team of young, talented researchers with different backgrounds of biology, physics and engineering.

【Content of the Research Project】

This Research Project focuses on cellular mechanosensing and mechanoresponse in the brain tissue suffering compressive stress. Particularly, we ask 1) what type and magnitude of mechanical stresses the brain cells suffer, 2) how the cells detect these stresses, 3) what cellular responses downstream of the mechanosensing are, and 4) what the roles of cellular mechanoresponses in brain development, function and pathogenesis are. We tackle these points in the following 5 specific research subjects (Fig. 1).

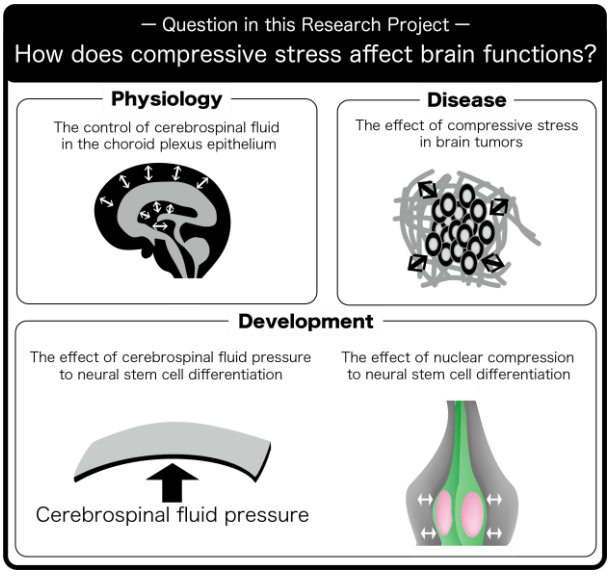


Fig. 1. Question and goal in this Research Project.

I. Revealing the mechanical feedback mechanism for the control of cerebrospinal fluid production in the choroid plexus epithelium.
II. Revealing neural stem cell responses against cerebrospinal fluid pressure-induced extension of the neuroepithelium during brain development.
III. Revealing how neural stem cell differentiation is affected by nucleus compression in a crowded environment.
IV. Revealing the effect of compressive stress in brain tumors on tumor cell proliferation
V. Developing new probes to visualize compressive stress and novel methods for quantitatively manipulating compressive stress.

The researchers in this Research Project are expertized in development of novel tools for mechanical stimulation of cells/tissues, development/application of biosensor probes, molecular biological/genetical analyses of brain tissues, and/or time-lapse imaging of biomolecules/cells/tissues. Thus, with active and close collaboration between our members, we can address the above subjects.

【Expected Research Achievements and Scientific Significance】

It has been suggested that brain functions are influenced by brain pressure. However, the actual role of compressive stress in brain functions and the underlying molecular mechanisms remain unsolved, due to a lack of experimental methodology to address them. Our mechanobiological approaches will overcome this limitation and unveil molecular mechanism(s) for sensing compressive stress and roles of cellular responses against compressive stress in development, functions, and pathogenesis of the brain.

【Key Words】

Mechanosensing: to detect a mechanical stimulus to a cell using a mechanosensor molecule(s)
Mechanoresponse: a cellular response(s) occurred downstream of mechanosensing

【Term of Project】 FY2021-2025

【Budget Allocation】 104,800 Thousand Yen

【Homepage Address and Other Contact Information】

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