

FUNDING PROGRAM FOR NEXT GENERATION WORLD-LEADING RESEARCHERS

Project Title: Development of *in vitro* culture technique for new neocortical neuronal progenitor cell (L1-INP cell) and clarification of its physiological function

Name: Koji OHIRA

Institution: Fujita Health University

1. Background of research

The mammalian neocortex is associated with higher brain functions such as awareness, thinking, consciousness, etc. Neurogenesis in the adult neocortex has been of particular interest to the field of neuroscience for over 100 years. Recently, in the neocortical layer 1 of adult rats, we have discovered neuronal progenitors, designated "Layer 1 Inhibitory Neuronal Progenitor cells (L1-INP cells)".

2. Research objectives

In this project, we will try to innovate a L1-INP cell culture method by which we can maintain and differentiate L1-INP cells *in vitro*. In addition, we will determine the physiological functions of newly-generated neurons from L1-INP cells.

3. Research characteristics (incl. originality and creativity)

Through this project, the precise nature of the biological basis for "novel therapy for brain damage and a part of psychiatric disorders such as major depression and schizophrenia by using L1-INP cells" will become clear. Moreover, we can open up a new field concerning neocortex in adult neurogenesis.

4. Anticipated effects and future applications of research

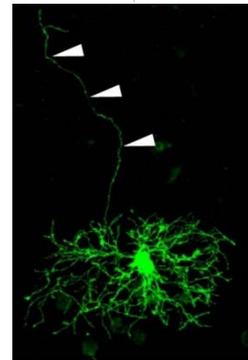
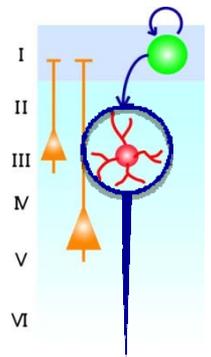
If we establish the culture method of L1-INP cells, the intra- and intracellular mechanisms of proliferation, maintenance, and differentiation of L1-INP cells will be investigated and further clarified. The possible outcome of researches about the mechanisms is essential as a resource for development of medicines, which allow revolutionary advance on oral drug therapy for brain damage and a part of psychiatric diseases.

Psychiatric and neurological disorder in Japan with the rapid advance of a dwindling birthrate and an aging population is a serious concern for the future of the Japanese economy and society

More than 80% of the newly-generated neurons from L1-INP cells contained **GABA** → Inhibition of neural activity

- 1) **Epilepsy** → Increased incidence of epilepsy after brain damage
Cognitive decline in epileptic patients and animals
- 2) **Psychiatric disorder** → Decrease in the number of **GABAergic neurons** in the neocortex of postmortem brains of patients with schizophrenia and major depression
- 3) **Neurodegenerative disorder** → Decrease in the amount of **GABA** in the neocortex of postmortem brains of patients with Alzheimer-type and senile dementias

L1-INP cells



GABAergic neurons

Control of proliferation and differentiation of L1-INP cells can realize a **novel cell therapy** with L1-INP cells



Fundamental study for establishment of "**New therapy with L1-INP cells**" for brain damage and psychiatric and neurological disorders, in which GABAergic neurons in the neocortex are involved

1. Innovation of L1-INP cell culture method

- *in vitro* assay system of homogeneous L1-INP cells
- It is possible to investigate **the inter- and intracellular mechanisms of proliferation, maintenance, and differentiation of L1-INP cells**



Development of medicines: revolutionary advance on **oral drug therapy** for brain damage and a part of psychiatric diseases

2. Elucidation of the physiological functions of newly-generated neurons from L1-INP cells

- Functional significance of neurogenesis by L1-INP cells



- Essential study for the therapy with L1-INP cells
- Opening up **a new area concerning neocortex in adult neurogenesis**
- **Academically and clinically high developability of L1-INP cells**