Form 1-5-2

Japan-U.S. Brain Research Cooperation Program
Report of Researchers Dispatched to the U.S. for the 2010 Fiscal Year

Field: (4) Others

1. Name/Title/Affiliation:

Miho Watanabe
Project assistant professor
Division of Homeostatic Development, Department of Developmental Physiology, National Institute of Physiological Sciences

2. Project Title:

The role of excitatory GABA action in synchronized activity of GnRH neurons.

3. U.S. host researcher's Name, Title, and Affiliation:

Dr.Suzan Wray
Senior Investigator
Cellular and Developmental Neurobiology Section, National Institute of Neurological Disorders

4. Term of Research: From 2010 Yr. 9 Mo. 25 Day to 2010 Yr. 10 Mo. 24 Day (1 mo.)

5. Abstract, Results, and Research Significance (300 Words):

Gonadotropin-releasing hormone (GnRH) neurons form the final common pathway for the central regulation of reproduction. Although the hypothalamus contains a relatively small number of GnRH neurons that are diffusely scattered, the mechanisms enabling GnRH neurons to synchronize their activity to generate pulsatile and cyclic GnRH release to induce luteinizing hormone surge for ovulation remain unknown. We showed that GABA, the main inhibitory neurotransmitter in the adult brain, exerts an excitatory action in GnRH neurons from adult rats. In neurons at early stages of development, GABA acts excitatory and shows spontaneous activity, $[Ca^{2+}]_i$ oscillations and synchronized patterns of activity. GnRH neurons also show spontaneous activity and $[Ca^{2+}]_i$ oscillations. Therefore, the excitatory action of GABA in GnRH neurons may contribute to synchronous activity to generate discrete episode of GnRH and increase the firing activity.

Because GnRH neurons lack any specific identifying morphology, and due to their diffuse location, it is difficult to directly study the cellular and molecular mechanisms in functional GnRH neurons. To overcome these barriers, Dr. Susan Wray laboratory developed slice culture of nasal explant from embryo containing many GnRH neurons before migrating to the hypothalamus from the olfactory placode. I learned the techniques of nasal explant culture and recording the spontaneous $[Ca^{2+}]_i$ oscillations using Ca^{2+} imaging and the data analysis. Furthermore, we examined the role of somatostatin in $[Ca^{2+}]_i$ oscillation of GnRH neurons using these techniques. Our results suggested that somatostatin inhibited the frequency of $[Ca^{2+}]_i$ oscillations via the somatostatin 2 receptors by activating the voltage-gated K^+ channels. I will examine the role of excitatory action of GABA in synchronized GnRH neuronal activity by recording the synchronized Ca^{2+} oscillation of GnRH neurons using nasal explant slice culture containing GnRH neurons.

6. Other (Any concerns regarding the research or special instructions):

(Please attach reference materials.)