

Japan-U.S. Brain Research Cooperation Program
Researchers Dispatched to the U.S. Program FY2021: Report

Field: Cellular/ Molecular

1. Researcher

Name: Takafumi Kawai

Title: Assistant Professor, Dept of Medicine, Osaka university

Affiliation: Yamada-oka 2-2, Suita, Osaka, Japan

2. Research Title: Function of calcium-activated ion channels in medial habenula neurons

3. U.S. Joint Researchers/Institutes

Please give the name, title and affiliation.

Name of Institute: Department of Neurobiology, Duke University Medical Center

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Host Researcher: Huanghe Yang

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4. Research Period, from/to (yyyy/mm/dd):

2021/6/1-2021/10/1

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

Medial habenula (MHb) neurons highly express diverse types of nicotinic acetylcholine receptors (nAChRs) and play substantial roles in nicotine addiction, withdrawal and nicotine aversion. Previous studies suggest that MHb neurons also show the high expression level of two different types of Ca^{2+} -activated ion channels; K^{+} channels (BK) and Cl^{-} channels (CaCCs). In the present study, we revealed that strong nicotine stimulation of MHb neurons induce long-lasting plateau potentials that significantly suppress the neural firings. We found that these plateau potentials are regulated by the above-mentioned Ca^{2+} -activated ion channels. Inhibiting or manipulating CaCC activities alter the appearance of plateau potential and our results indicated that CaCC positively regulate the plateau potentials. On the other hand, pharmacological inhibition or genetic activation of BK channels experiments suggested that BK channels negatively regulate the plateau potentials. Furthermore, two different types of high threshold voltage-gated Ca^{2+} channels (VGCCs) functionally coupled with the CaCC activities and play important role in maintaining the plateau potentials. We also found that milder nicotinic stimulation of MHb neurons could still induce the long-lasting plateau phase depending on the excited states of the neurons. The present study proposes the novel model about the nicotinic regulation of firing activities in MHb neurons that could potentially involve the nicotine aversive behavior.

6. Other (Research-related concerns, particular points to note):

First I visited Huanghe Yang lab to study the functional significance of the potential TMEM16B regulation by $\text{PI}(4,5)\text{P}_2$. However, I found that there seems to be no regulation of TMEM16B by $\text{PI}(4,5)\text{P}_2$. So, we changed the research topic to another Ca^{2+} -activated Cl^{-} channel, TMEM16A.

*Please attach any reference materials as necessary.