Form 1-5-2

Japan-U.S. Brain Research Cooperation Program
Researchers Dispatched to the U.S. Program FY2018: Report

Field:1,2, and 4

1. Researcher

Name: Lena Iwai
Title: JSPS RPD
Affiliation: National Institute of Genetics, Brain Function lab

2. Research Title: Wnt signaling in regulation of RPE-retinal ganglion cell interactions in the albino retina

3. U.S. Joint Researchers/Institutes
Department of Pathology and Cell Biology, Neuroscience, and Ophthalmology
Mortimer B. Zuckerman Mind Brain Behavior Institute, Columbia University
Dr. Carol Mason, PhD

4. Research Period, from/to (mm/dd/yyyy):
02/24/2019-03/08/2019

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

In mammalian albinism, disrupted melanogenesis in the retinal pigment epithelium (RPE) is associated with fewer retinal ganglion cells (RGCs) projecting ipsilaterally to the brain. A reduced ipsilateral RGC projection in albinism results in numerous abnormalities in the retina and visual pathway, especially binocular vision. How melanin deficiency in the RPE regulates the ipsi-contralateral RGC projection is not understood. To further understand the molecular link between disrupted RPE and a reduced ipsilateral RGC projection in albinism and in normal pigmented animals, we compared gene expression in the embryonic albino and pigmented mouse RPE by microarray analysis.

We found that the Wnt pathway, which directs peripheral retinal differentiation and, generally, cell proliferation, is dysregulated in the albino RPE. Wnt2b expression is expanded in the albino RPE compared with the pigmented RPE, and the expanded region adjoins the site of ipsilateral RGC neurogenesis and settling. Pharmacological activation of Wnt signaling in pigmented mice by lithium (Li+) treatment in vivo reduces the number of Zic2-positive RGCs, which are normally fated to project ipsilaterally, to numbers observed in the albino retina. These results implicate Wnt signaling from the RPE to neural retina as a potential factor in the regulation of ipsilateral RGC production, and thus the albino phenotype.

In addition to complete this study, we started a collaborative study to analyze temporal progression of RGC subtypes and whether it is changed in the albino mouse retina compared with pigmented retina. Preliminary, we found that a number of intrinsically photosensitive RGCs, which are related to regulation of the circadian rhythms, is reduced in albino retina. We will further analyze details including numbers of other major RGC subtypes. Identifying molecular signals regulating RGC diversity is critical for driving stem cells into RGCs for replacement therapy and directing axon regeneration in injured and degenerating visual pathways.

6. Other (Research concerns, particular points of note):

*Please attach any reference materials as necessary.