Form 3

Report for Joint/usage program for Endocrine/Metabolism

Date: 2015/04/15

To:

Director of Institute for Molecular and Cellular Regulation

1. Program No. 13010
2. Research title:

   Role of OGR1 family GPCRs in inflammation

3. Objective of the research:

   Clarification of inflammatory regulation mechanism of protons and lipid signaling molecules by using knockout mice of OGR1 family GPCRs

4. Period

   From 2013/04/01 to 2014-03-31

5. Project organization

Name of Applicant: Dong-Soon Im

Position: Professor

Institution/department: College of Pharmacy, Pusan National University

Name of Co-applicant: Kyung-Pil Lee

Position: Graduate student

Institution/department: College of Pharmacy, Pusan National University

Name of Researcher in IMCR: Fumikazu Okajima

Position: Professor

6. Research plans:

In our previous study on this project, we found that extracellular proton inhibited lipopolysaccharide (LPS)-induced inflammatory cytokine release in microglia. Here, we will examine the role of MAPKs in the inhibitory actions of protons in the LPS signaling pathways using Western blot analysis and ELISA. Furthermore, we will show the involvement of TDAG8 by using TDAG8 KO mouse. We will further investigate the effect of extracellular proton and lipid signaling molecules in macrophage and neutrophils in the airway inflammation models.

7. Research results:

We found that LPS induced either proIL-1b and IL-1b protein production in cultured mouse microglia using Western blot analysis and ELISA. The change in cytokine protein level was associated with the change in IL-1b mRNA measured by quantitative real-time PCR (TaqMan). The LPS-induced actions were inhibited by extracellular acidic pH. In TDAG8-deficient microglia, the acidification-induced inhibitory action was partly attenuated. These results suggest that TDAG8 in involved, at least partly, in acidic pH-induced action. We also found that MAPKs, involving JNK and ERK, are involved in the LPS signaling pathways. Now we are investigating whether MAPKs are involved in TDAG8/acidic pH-induced inhibitory action. We also examined sphingosine 1-phosphate (S1P) actions in macrophages and found that S1P-induced M2 polarization of macrophages could be mediated via IL-4 signaling.

8. Publications and/or Presentations made through this collaboration

○ Jin Y, Sato K, Ayaka Tobo, Mogi C, Tobo M, Murata N, Ishii S, Im DS, and Okajima F: Inhibition of interleukin-1b production by extracellular acidification through the TDAG8/cAMP pathway in mouse microglia. J Neurochem 129:683-695 (2014)

○Park SJ, Lee KP, Kang S, Lee J, Sato K, Chung HY, Okajima F, and Im DS: Sphingosine 1-phosphate induced anti-atherogenic and atheroprotective M2 macrophage polarization through IL-4. Cellular Signalling 26:2249-2258 (2014)

(Please summarize the report in 2 pages)