Form 3

Report for Joint/usage program for Endocrine/Metabolism

Date 2014/April/15

To: Fumikazu Okajima

Director of Institute for Molecular and Cellular Regulation

Name of Principal Researcher: Dong-Soon Im
Affiliation/Position: Professor
E mail: imds@pusan.ac.kr

（Program No: 13010 ）

1. Research title	Role of OGR1 family GPCRs in inflammation			
2. Objective of the research	Clarification of inflammatory regulation mechanism of protons and lipid signaling molecules by using knockout mice of OGR1 family GPCRs			
3. Period	2013/April/1 ～ 2014/March/31			
4. Project organization				
Name	Affiliation	Position		
Dong-Soon Im	College of Pharmacy, Pusan National University	Professor		
Kyung-Pil Lee	College of Pharmacy, Pusan National University	Graduate student		
5. Name of Researcher in IMCR	Laboratory	Signal Transduction	Name	Fumikazu Okajima

※ Please summarize items 1-5 in 1 page.

（Program No.　13010　）

6. Research plans:

We will characterize immune regulatory responses and signal transduction mechanisms of protons through TDAG8 and OGR1 in microglia by using TDAG8 and OGR1 knockout mice. We also try to clarify effects of extracellular proton and lipid molecules in the cells involved in airway inflammation. To this end, we will test the effect of extracellular proton on lipopolysaccharide (LPS)-induced inflammatory cytokine release by Western blot and ELISA of IL-1・ in microglia in central nervous system. The role of TDAG8 will be examined by using TDAG8 KO mouse. Moreover, we will investigate the effect of extracellular proton and lipid signaling molecules on M1/M2 macrophage transition by RT-PCR and Western blot in peritoneal macrophages.

7. Research results:

We found that extracellular proton inhibited lipopolysaccharide (LPS)-induced production of IL-1b, an inflammatory cytokine, in mouse microglia. The inhibitory cytokine production was associated with the inhibition of pro-IL-1b and IL-1b mRNA expression. These inhibitory actions of extracellular acidification were attenuated in the TDAG8-deficient microglia, suggesting the involvement of proton-sensing TDAG8 in the acidic pH effects. In future study, we need to characterize the signaling mechanism of proton/TDAG8 in the inhibitory cytokine production. In the M1/M2 transition experiments, we observed that acidification caused the inhibition of the expression of M1 markers and, on the contrary, enhancement of M2 expression. We are now investigating the signal transduction mechanism of the phenotype changes by acidic pH.

8. Publications and/or Presentations made through this collaboration

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

2. Park SJ, Lee KP, Kang S, Chung HY, Bae YS, Okajima F, and Im DS.: Lysophosphatidylethanolamine utilizes LPA1 and CD97 in MDA-MB-231 breast cancer cells. ***Cellular Signalling*** 25: 2147-2154 (2013).

※ Please summarize items 6-8 in page