NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

Seminar Announcement

Immunosenescence-related gene Zizimin2 (Dock 11) and its family

Date: 26 October 2015 Monday

Time: 3:30pm to 4:30pm

Venue: SBS Classroom 1 (SBS-01n-33)

Host: Asst/Prof Su I-Hsin

Speaker: **Professor Mitsuo Maruyama**
Deputy Director,
Department head of Mechanism of Aging, Research Institute, National Center for Geriatrics and Gerontology (NCGG)

Abstract

We have cloned and identified murine Zizimin2 (Ziz2; Dock11) that is highly expressed in germinal center B cells after T cell-dependent antigen stimulation. It has been demonstrated that Ziz2 is a guanine nucleotide exchange factor for Cdc42, one of the major Rho GTPases, and promotes filopodia formation. Since its expression levels in immune tissues are reduced in aged mice, Ziz2 may be associated with immunosenescence. However, the function of Ziz2 had not been fully examined *in vivo*. In this study, we tried to elucidate the function of Ziz2 *in vivo* by using Ziz2 knock out (KO) or structurally-related Zizimin3 (Ziz3; Dock10) KO mice.

To gain insights into the mechanisms underlying immunosenescence, we generated Ziz2 KO mice and examined the in vivo functions of Ziz2 in B cell development and immune responses. The results revealed that Ziz2 KO mice had a higher percentage of early bone marrow B cells (Fraction A), but a reduced fraction of marginal zone (MZ) B cells. In addition, an examination of B cell-specific Ziz2 KO mice revealed that Ziz2 was intrinsically required for MZ B cell development, but not for mature follicular B cells. However, immune responses against NP-CGG (T cell-dependent), TNP-LPS (T cell-independent, TI, type I), and TNP-Ficoll (TI, type II) were not altered in KO mice. We finally demonstrated that the MZ B cell region outside CD169-positive marginal metallophilic macrophages (MMM) was narrowed in Ziz2 KO mice. Furthermore, MMM morphology appeared to be altered in Ziz2 KO mice. This study also indicated that aging maybe induce delocalization of splenic MZ B cells.

In conclusion, we herein showed that Ziz2 was associated with early bone marrow B cell development, MZ B cell formation and/or localization around MZ, and MMM morphology which may explain in part the mechanism underlying high susceptibility to infectious diseases in the elderly.