The 17th Global and Local Infectious Diseases Research Seminar

RCGLID
OITA UNIVERSITY

September 26th , 2023
16:00-17:00

Scan here to register
https://forms.gle/LAMY8czBNYt9w5mU8

Presenter : Prof. Tanapat Palaga, PhD

Department of Microbiology, Faculty of Science, Center of Excellence in Immunology and Immune-mediated Diseases, Chulalongkorn University

The Roles of a DNA Repair Enzyme O6-Methylguanine DNA Methyltransferase in Inflammation, Infection, and Innate Immune Memory in Macrophages

O6-methylguanine DNA methyltransferase (MGMT) is an enzyme responsible for DNA repair of lesion induced by alkylating agents. Loss of MGMT predisposes mice to alkylating agent-induced tumorigenesis and aberration in MGMT expression is reported in various tumor types. However, the involvement of MGMT in innate immunity is completely unknown. MGMT was uncovered in our screening to identify enzymes that regulate trained immunity in macrophages. *MGMT* KO macrophages exhibited dampened response to activation by TLR3 agonist, poly I:C, but the response to other TLRs was not altered. Loss of MGMT induced activation of AMP-activated protein kinase (AMPK) and spontaneous autophagy. Colocalization of mitochondria and autophagosome was detected, an indication of mitophagy. When Salmonella infection was performed, increased colocalization of bacteria and autophagosomes was found with enhanced bacterial killing. In β-glucan-induced trained immunity, targeted deletion of *MGMT* in macrophages resulted in reduction of the trained responses both *in vitro* and *in vivo* models. The transcriptomic analysis revealed that the dampening trained immunity in MGMT KO macrophages is partially mediated by farnesoid X receptor (FXR)/AMPK and mTOR/HIF1 pathways and the reduction in glycolysis function. In a high fat diet-induced obesity model, reduction in liver lipid deposition was observed in *MGMT* KO mice. Taken together, a failure to resolve DNA damage may have consequences for inflammation, infection and innate immune memory.

Manager Takashi Kobayashi
(Professor, Department of infectious disease control,Faculty of Medicine)

Seminar Contact
Research Center for Glocal and Local Infectious Diseases（5444）
TEL 097（586）5444 E-mail glocal@oita-u.ac.jp