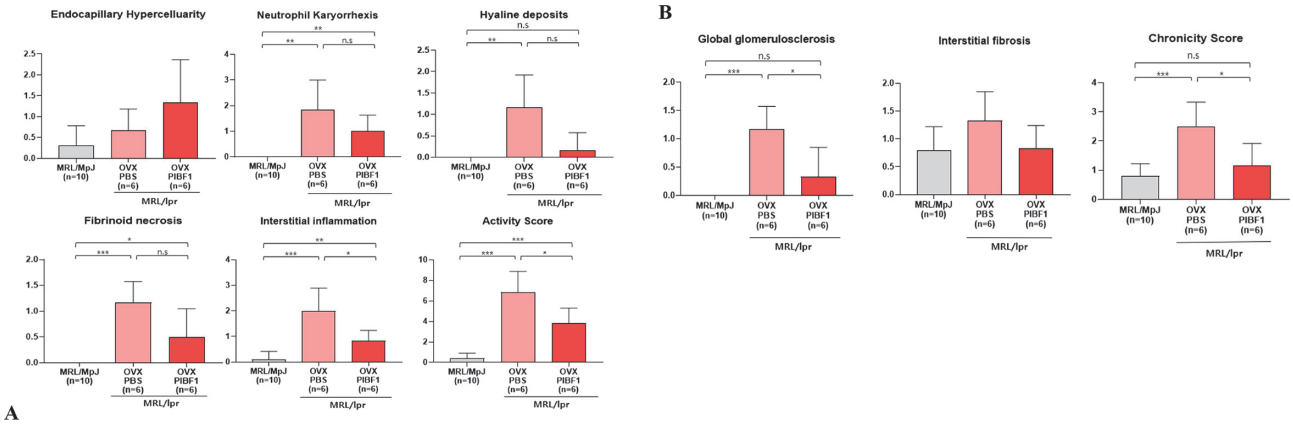

Abstract LSO-003 Figure 1 Kidney tissues of MRL/lpr mice at 26 weeks. (A) Activity index. (B) Chronicity index. OVX, ovariectomy, *p < 0.05, **p < 0.01, ***p < 0.001

PIBF1 treatment attenuated the increase in anti-dsDNA autoantibodies (statistical significance after 18 weeks, p <0.05). uACR at 26 weeks was significantly decreased in the PIBF1-treated ovariectomy group compared with the PIBF1-untreated ovariectomy group (p <0.05). Furthermore, interstitial inflammation, global glomerulosclerosis, total activity index, and chronicity index scores were significantly decreased in PIBF1-treated mice compared with non-treated mice (figure 1). Analysis of splenocytes revealed that B220+CD4-CD8- T cells were decreased in PIBF1-treated mice compared with non-treated mice (p <0.05). However, the levels of serum cytokines including IL-2, IL-10, and IL-21 were not different between the two groups.

Conclusions Administration of recombinant PIBF1 attenuated the laboratory and histologic scores of LN-prone mice. Therefore, PIBF1 may function as an immunomodulator in LN.

LSO-004 CGAS DEFICIENCY ENHANCES INFLAMMASOME ACTIVATION IN MACROPHAGES AND INFLAMMATORY PATHOLOGY IN PRISTANE-INDUCED LUPUS

[1,2]Sarinya Kumpunya*, [3]Arthid Thim-Uam, [4]Chisanu Thumarat, [5]Asada Leelahavanichkul, [1,2]Nuttiya Kalpongnukul, [1,6]Naphat Chantaravisoot, [1,7]Trairak Pisitkun, [4,8]Prapaporn Pisitkun. *[1]Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand., Center of Excellence in Systems Biology, Thailand; [2]Graduate School, Chulalongkorn University, Bangkok, Thailand., Interdisciplinary Program of Biomedical Sciences., Thailand; [3]School of Medical Sciences, University of Phayao, Phayao, Thailand., Division of Biochemistry, Thailand; [4]Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand., Program in Translational Medicine, Thailand; [5]Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand., Center of Excellence in Translational Research in Inflammation and Immunology (CETRII), Thailand; [6]Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, Bangkok., Program in Medical Biochemistry., Thailand; [7]National Institutes of Health, Bethesda, MD, USA., Epithelial Systems Biology Laboratory, National Heart, Lung and Blood Institute., USA; [8]Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok., Division of Allergy, Immunology, and Rheumatology., Thailand*

10.1136/lupus-2023-KCR.46

Background Type I interferon (IFN) plays a vital role in the pathogenesis of systemic lupus erythematosus. Cyclic GMP-AMP synthase (cGAS) is a cytosolic DNA sensor that recognizes dsDNA and creates cGAMP to activate STING-mediated type I IFN production. The activation of STING induces lupus disease in Fcgr2b deficient mice through the differentiation of dendritic cells. In contrast, Cgas deficient mice could be generated more autoantibody production and proteinuria in pristane-induced lupus (PIL). These data suggested that the other dsDNA sensors could be involved in lupus development mechanisms.

Methods This study aimed to identify the cGAS-mediated mechanisms contributing to lupus pathogenesis in PIL. The Cgas-deficient and WT mice were induced with lupus disease by pristane injection. The lung tissues were analyzed with the expression profiles by RT-PCR and western blot. The bone marrow-derived macrophages were stimulated with inflammasome activators and observed pyroptosis.

Results The Cgas-/- mice developed more severe pulmonary hemorrhage and autoantibody production than WT mice. The activated dendritic cells, IFN-g-, and IL-17a-producing T helper cells, and infiltrated macrophages in the lung were detected in Cgas-/- mice higher than in WT mice. We observed an increase in expression of Aim2, Casp11, and Ifi16 in the lung and serum IL-1a but IL-1b in pristane-injected Cgas-/- mice. The rise of Caspase-11 in the lung of pristane-injected Cgas-/- mice suggested noncanonical inflammasome activation. The activation of AIM2 and NLRP3 inflammasomes in bone marrow-derived macrophages (BMDMs) enhanced the number of dead cells in Cgas-/- mice compared with WT mice. Activation of the inflammasome significantly induced pyroptosis in Cgas-/- BMDMs. The dsDNA level, but not mitochondrial DNA, increased dramatically in pristane injected Cgas-/- mice suggesting the dsDNA could be a ligand activating inflammasomes. The cGAS agonist-induced BMDM

Conclusions These findings suggested that cGAS hampers the unusual noncanonical inflammasome activation through other DNA sensors.