European Respiratory Society
Annual Congress 2012

Abstract Number: 1132
Publication Number: P3409

Abstract Group: 3.2. Airway Cell Biology and Immunopathology
Keyword 1: Physiology **Keyword 2:** Nitric oxide **Keyword 3:** Cell biology

Title: TLR4 signaling potentiates airway secretion from the swine submucosal gland via NO/cGMP/cGK pathway

Mr. Koji 10558 Murakami k-mura@rm.med.tohoku.ac.jp MD [1], Dr. Tsutomu 10559 Tamada tamada@rm.med.tohoku.ac.jp MD [1], Dr. Masayuki 10560 Nara nara@hosp.tohoku.ac.jp MD [2], Mr. Soshi 10561 Muramatsu 99mb1091-thk@umin.ac.jp MD [1], Dr. Toshiaki 10562 Kikuchi kikuchi@idac.tohoku.ac.jp MD [1], Mr. Masahiko 10563 Kanehira kanehira@idac.tohoku.ac.jp [1] and Dr. Masahito 10564 Ebina ebinam@idac.tohoku.ac.jp MD [1]. [1] Department of Respiratory Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan and [2] Department of Comprehensive Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan .

Body: [RATIONALE] Airway secretion plays an important role in the airway defense as a part of innate immunity. A major fraction of the airway fluids appears to be derived from submucosal gland in response to ACh. Toll-like receptor 4 (TLR4) recognizes gram-negative bacteria and activates the innate immune systems. However, the biological role of TLR4 in the airway secretion is not well understood. [METHODS] Freshly isolated swine tracheal submucosal gland cells were investigated their secretory activities as ionic currents by applying a patch-clamp technique. LPS was used as a potent TLR4 ligand. The expression of TLR4 was estimated by both the immunofluorescent staining and RT-PCR. The involvement of NO/cGMP/cGMP-dependent protein kinase (cGK) pathway was investigated by applying both the NOS and cGK inhibitors. The synthesis of endogenous NO was estimated by an intracellular NO indicator, DAF-2DA. [RESULTS] LPS significantly potentiated the ACh-evoked ionic currents. This potentiating effect was completely abolished by the pretreatment of anti-TLR4 antibody or TLR4 antagonist. The immunofluorescent staining and RT-PCR revealed the abundant expression of TLR4 on tracheal submucosal glands. Two different inhibitors of each NOS and cGK completely abolished the LPS-induced potentiating effect, respectively. LPS further increased the ACh-induced synthesis of NO. [CONCLUSIONS] Our studies revealed that TLR4 signaling could potentiate the electrolyte and water secretions from tracheal submucosal glands via the activation of NO/cGMP/cGK pathway. These findings suggest that TLR4 takes part in the airway mucosal innate immune systems as one of important pathogen-specific secretagogue.