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C5A RECEPTOR SIGNALLING IN PEYER'S PATCH DENDRITIC CELLS ENHANCES THE ANTIGEN-SPECIFIC CD8+ T CELL RESPONSE IN DENGUE MUCOSAL VACCINE MODEL

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Chemoattractant complement 5a receptor (C5aR) is associated with mucosal immunity. Although C5aR is expressed in several cell types including macrophages, monocytes, and neutrophils, its expression is controversial in mucosal dendritic cell (DC) subsets. In this study, we found that $CD11c^{+}CD11b^{-}CD8^{-}$ Peyer's patch (PP) DCs located in subepithelial dome expressed the C5aR where stimulation of C5aR with its cognate ligand, C5a, or a specific peptide (Co1) effectively induced antigen-specific IFN-γ^{+} Th1 cells through the induction of pro-inflammatory cytokines. Based on the previous observation that Co1 peptide has an M cell-targeting ability and its moiety is homologous to C5aR agonist, EP67, which is capable of inducing $CD8^{+}$ cells, we assumed that oral administration of Co1 peptide-conjugated antigen may induce the antigen-specific Th1 and/or CD8 response through both M cell antigen-targeting and the induction of pro-inflammatory cytokines via C5aR signalling in systemic and mucosa immune compartments. To this end, a model antigen, partial-nonstructural 3 (NS3) protein of dengue virus serotype 2 (DENV-2) was conjugated with Co1 peptide (p-NS3-Co1) and M cell-targeting of the antigen and co-localization with C5aR on M cells were confirmed. As we assumed, oral prime and boost immunization with p-NS3-Co1 effectively induced the NS3-specific IFN-γ^{+} effector $CD8^{+}$ T cells. In addition, challenge with DENV-2 at 4 weeks post immunization with p-NS3-Co1 induced not only the functional restimulation of memory effector $CD8^{+}$ T cells but also proliferation of $CD107a^{+}$ cytolytic effector $CD8^{+}$ T cells in mucosal and systemic compartments. Collectively, we concluded that C5aR plays a role as mucosal immune modulator in PPs and Co1 peptide ligand-mediated C5aR activation contributes to develop the $CD8^{+}$ T cell immune response induction.

Biography

Yong-Suk Jang has completed his PhD from Northwestern University, Chicago, IL, USA in 1993 and Postdoctoral study at Cancer Research Institute of Seoul National University Medical School, Seoul Korea. He is a Professor and Chairman in the Department of Molecular Biology, College of Natural Science, Chonbuk National University, Republic of Korea. He has published more than 150 papers in reputed journals including the *Journal of Immunology, Biomaterials, European Journal of Immunology,* and *Scientific Reports*. He will serve as a President of the Korean Association of Immunologists for 2019. His current research is mainly on Mucosal Immune Regulation and Mucosal Vaccine Development.

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