2019 Spring
Life Sciences & IBB Seminar

"From bacterial virulence factor to vaccine adjuvant and cancer immunotherapeutics: The story of flagellin"

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- **Date: 4:30PM/Mar. 29(Fri.)/2019**
- **Place: Auditorium(1F), Postech Biotech Center**
- **Inquiry: Prof. Sin-Hyeog Im (279-2356)**
- **Abstract:**

TLR ligands are considered attractive adjuvants for vaccines and immunotherapy. Flagellin is the cognate ligand for Toll-like receptor 5 (TLR5) of host cells. TLR stimulation leads to activation of innate immunity and subsequently modulates adaptive immune responses. In this presentation, we show that flagellin has a unique immunomodulating activity in the mucosal immune compartment. (1) Flagellin could be used as an adjuvant for mucosal vaccines. Mucosal co-administration of a V. vulnificus flagellin (FlaB) with microbial antigens induced significantly enhanced antigen-specific IgA responses in both mucosal and systemic compartments and IgG responses in the systemic compartment. Intranasally administered FlaB colocalized with CD11c as patches in DCs and caused an increase in the number of TLR5 expressing cells in draining lymph nodes. Further, we tested whether FlaB could serve as an effective mucosal adjuvant for an inactivated trivalent influenza vaccine (TIV), Streptococcus pneumonia antigen PspA, and Norovirus P domain antigens. In those vaccine formulations, flagellin exerted excellent adjuvanticity in combination with antigens. (2) Flagellin could serve an efficacious adjuvant for vaccines and immunotherapies against noninfectious intractable diseases in the mucosal compartments such as allergic asthma and cervical cancer. We found that therapeutic doses of flagellin together with allergens suppress allergic asthma by inhibiting pathogenic Th1/Th2/Th17 responses while generating regulatory DCs (DCreg) and Treg cells. Adoptive transfer of FlaB/allergen mixture-induced DCs effectively inhibited asthma. In the peripheral blood from allegic asthma patients, FlaB treatment induced DCreg, which subsequently induced allergen-specific Foxp3+ Treg cells in a lymphocyte co-culture while inhibiting Th1/Th2 responses in an IL-10-dependent manner. For cervical cancer, we examined whether flagellin can be used as an adjuvant for topical therapeutic cancer vaccine in a genital cancer model. Intravaginal co-administration of E6/E7 peptides with flagellin resulted in tumor suppression and long-term survival of the tumor bearing mice. IVAG immunization of E6/E7 peptide with flagellin induced accumulation of CD4+ or CD8+ cells and T cell activation in draining genital lymph nodes (gLNs). The co-administered flagellin elicited antigen-specific IFN-γ production in gLNs and spleen. The IVAG administered flagellin co-localzed with CD11c+ cells in the gLN T cell areas and enhanced TLR5 expression.

***This seminar will be given in English.**

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