Special Seminar

共催：医学セミナー　第72回 免疫学セミナー

"Inhibit activation or activate inhibition of mast cells and eosinophils: Which weapon is better to fight allergic diseases?"

Tue. July 10

16:00-17:30

Health and Medicine Science Innovation Bldg.
8th-floor Auditorium
健康医科学イノベーション棟
8階講堂医学学群棟

Guest Speaker

Dr. Francesca Levi-Schaffer
Institute for Drug Research
School of Pharmacy, Faculty of Medicine
The Hebrew University of Jerusalem, Israel

Abstract

Mast cells (MCs) and eosinophils are the key effector cells of allergic inflammatory diseases such as asthma, allergic rhinitis, atopic dermatitis (AD), etc. Drugs are available to downregulate the symptoms of allergy such as antihistamines or limit the ongoing inflammation and tissue/organ damage such as corticosteroids. While mild/moderate forms of allergy are well controlled by a combination of these approaches, severe asthma and AD remain unmet clinical needs. In the last decades monoclonal antibodies (mAb) therapies especially for autoimmune diseases and cancer have made tremendous progress. In allergy anti-IgE antibodies are already on the market and useful for some forms of asthma. However a global approach suitable for most patients and with minimal side effects is warranted. We have taken a different approach following the discovery of the novel activating receptor (AR) CD48 and of the inhibitory receptors (IRs) CD300a and Siglec-7 on both MCs and eosinophils. We reasoned that blocking ARs and stimulating IRs with specific mAbs will inhibit these cell functions and hence allergy. We have fully characterized these receptors on mouse and human MCs (bone narrow and cord blood derived) and eosinophils (bone marrow derived and peripheral blood isolated) by assessing their expression and signal transduction. For down or upregulating CD48 or Siglec-7 commercially available blocking or activating mAbs were used, while for CD300a we synthesized bi-specific Abs to target specifically MCs and eosinophils. We have tested the anti-inflammatory/anti-allergic properties of the Abs in mouse models of asthma, PCA, allergic peritonitis and AD.

In vitro we demonstrated that our approach significantly inhibited MC and eosinophil functions such as degranulation, cytokine production, chemotaxis and in vivo it downregulated the allergic responses. Therefore mAbs for ARs or IRs specifically expressed on MCs and eosinophils can be a better pharmacological tool than existing drugs for the treatment of allergy.

This seminar is hosted by:
Ph.D. Program in Human Biology
School of Interactive and Global Majors (SIGMA)
Email: sigma@un.tsukuba.ac.jp ext.: 7085