CD48 on mast cells: a master regulator of allergic inflammation.

מרצה: הדס פחימה

מנחה: פרופ' פרנצ'סקה לוי שפר

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בזום:

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שם התלמידה: הדס פחימה Student name: Hadas Pahima

שם המדריכה : פרופסור פרנצ'סקה לוי-שפר Principal investigator: Prof. Francesca Levi-Schaffer

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Abstract:

MCs and Eos are the key cellular players in allergic diseases such as asthma, atopic dermatitis (AD), allergic rhinitis and food allergy. Both cells contain prominent cytoplasmic granules and derive from the CD34+ progenitor. In allergic/atopic individuals, the allergen exposure induces the production of IgE antibodies, through a mechanism regulated by T helper (Th) 2 and/or ILC-2 cells. The IgE antibody binds to its high affinity receptor FCεRI located on the surface of MCs. During subsequent exposures, the allergen binds to the IgE bound to FCεRI and the coupling of the receptors triggers the activation of MCs and thus the initiation of the early phase of the allergic reaction. This phase is characterized by MC degranulation and by production and release of lipid mediators and cytokines. A few hours later the late phase of the reaction begins, characterized by infiltration of immune cells with Eos as the most prominent cells. A pro-inflammatory soluble mediator and physical crosstalk between MCs and Eos named the "Allergic Effector Unit" (AEU) is pivotal component of allergy. CD48-2B4 interaction is a main component of the AEU and important for the initiation and continuation of the allergic reaction. CD48 is a glycosylphosphatidylinositol (GpI) receptor belongs to the SLAM family and is expressed on most of the hematopoietic cells. As several GpI receptors do, also CD48 exists as both a membrane bound (mCD48) and a soluble (sCD48) form. Being a GpI anchored receptor lacking an intracellular domain molecule, CD48 is considered as a co-activating receptor rather than a bona fide AR. The known high affinity ligand for CD48 is 2B4, and vice versa. Our group found that CD48 expressed by human cord blood MCs (CBMCs), bind *S. aureus*, which is known to be the most important bacterium involved in allergic

diseases. Moreover, binding of S. aureus or its exotoxins [i.e., SEB, Protein A (PtA) and Peptidoglycan (PGN)] to CD48 causes the release of TNF-α and IL-8 from eosinophils. In a peritonitis model induced by SEB intraperitoneal injection an increase in sCD48 was found in the peritoneal cavity indicating that the presence of sCD48 is an event elicited by S. aureus toxins also in an *in vivo* setting. As for function, sCD48 was found to be a decoy receptor both when injected in the SEB peritonitis model and in vitro when Eos were activated with SEB or with anti-2B4 mAb. Therefore, in this study we proposed: A. to dissect the role of CD48 as expressed on MCs and on Eos in allergic inflammation. B. to discover small molecules targeting the binding site of CD48 to 2B4 and SEB. C. To understand whether CD48 can directly bind allergens and in consequence activate MCs and/or Eos.