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REGULATORY ROLES OF NLRC4 IN EOSINOPHILIC FUNCTIONS

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The immune response is so dynamic that its intensity and nature change over time. The cells of the innate immune system signal through cytokines that coordinate and shape the characteristics of adaptive immunity. Nucleotide oligomerization domain (NOD)-like receptors (NLRs) is an intracellular receptor family with 22 members in human and 34 members in mice. Although they are mostly considered as the components of innate immunity, they have been reported to set a gate between innate and adaptive immunity by countless research. Of all the NLRs that have been discovered to date, AIM2, NLRP1, NLRP3 and NLRC4 are known to form an inflammasome complex. A typical inflammasome complex is a multiple protein complex that is composed of ASC (Apoptosis associated speck-like protein containing a CARD) adaptor protein, caspase-1 enzyme and the NLR protein. Following inflammasome activation, IL1B and IL18 are cleaved by caspase-1 and released to the extracellular environment. In this study, we examined how NLRC4, a member of NLR family, regulates the immune responses. The preliminary data from in vivo suggested a role for NLRC4 in eosinofilic functions during asthma and allergy. Based on these preliminary data, we characterized NLRC4 further in vitro as the number of eosinophils are significantly increased during asthma, allergic diseases and parasitic infections in healthy individuals or wild type mice. In our case, we observed a significant reduction in eosinophils of NLRC4 deficient mice. Then we went ahead and studied NLRC4 in a human cell line of eosinophils called EoL-1 for mechanistical studies. Even though, NLRC4 is known to form an inflammasome complex, our preliminary data suggest no change in ASC adaptor molecule, but induction of IL1B, therefore, NLRC4 in eosinofils may not be interacting with ASC, but most likely be interacting with caspase-1 or caspase-8, since we were able to induce IL1B after NLRC4 ligand treatment in EoL-1 cells, an eosinofilic cell line. We plan to expand these experiments to primary human eosinofils and investigate the eosinophilic functions in the context of NLRC4. Our findings might be an important asset to treat the severe clinical symptoms deriving from eosinophilia.

Biography

Ceren Ciraci has completed her PhD from Iowa State University and Postdoctoral Studies from University of Iowa Inflammation Program. She is currently serving as a Junior Faculty at Istanbul Technical University.

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