ImmunoTools IT-Box-Cy55M-Award 2013

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Functional and therapeutical implications of ligand recognition by scavenger-like receptors

The lymphocyte surface receptors CD5 and CD6 are highly homologous members of the Scavenger Receptor Cysteine-Rich superfamily (SRCR-SF), sharing similar protein structure, function and tissue expression pattern. They are mainly expressed in thymocytes, mature peripheral T cells, a subset of B cells called B1a cells and in some dendritic cells (DC). Physically, they are associated with the antigen-specific receptors present on both T- and B-cells (TCR and BCR), modulating their intracytoplasmic signals. As far as is known, they are involved in thymocyte selection, lymphocyte survival and homeostasis.

During recent years it has been reported that both lymphocyte receptors could bind to not only endogenous but also exogenous structures of microbial origin not present in mammalian cells, namely pathogen-associated molecular patterns (PAMPs). In fact, our laboratory previously reported that CD6 binds to both Gram- and Gram+ bacteria through recognition of LPS, PGN and LTA. Furthermore, our group also reported that CD5 binds to fungal but not bacterial cell wall components through recognition of β-glucans present on zymosan, a fungal cell wall derivative from the yeast *Saccharomyces cerevisiae*. Besides, focusing on clinical application, the administration of a recombinant and soluble protein form of both CD6 and CD5, rsCD6 and rsCD5, significantly improved mice survival in an LPS- or zymosan- induced septic shock-like model, respectively. Given this data, it might position CD5/CD6 as key elements in the fine tuning of adaptive immune responses to infections.

In order to study further this hypothesis, our laboratory has recently obtained a CD5-deficient murine line. So far, we have found differences in some clinical parameters (i.e. weight loss and survival) and significant changes in cytokine concentrations during the inflammation caused by zymosan induced septic shock-like syndrome in CD5-deficient mice as compared with wild type mice. The IT-Box Cy55M from ImmunoTools would help us to study further how these differences in cytokines can relate to the divergence in the final clinical outcome. Since differentiation of CD4 T cells to T helper 1, T helper 2, or T helper 17 determinates the outcome of fungal and bacterial infections, it is necessary to know whether its differentiation is directly affected by the ligation of CD5 to zymosan. Accordingly, our first approach would be to differentiate *ex vivo* CD4 T cells from wild type and CD5/-deficient mice into Th1 (rmIFNg+rmIL-2), Th2 (rmIL4+rmIL2) and Th17 (rmIL6) in presence of zymosan. As DC and macrophages are key cells in the linkage of innate and adaptative immune response and in some conditions can express CD5 we will also study this cells in and *ex vivo* controlled experiments (e.g. culture myeloid cells in presence of cytokines as rmGM-CSF and rmIL-4 to obtain DC and macrophages to further study).