EuroSciCon

EuroSciCon conference on

Protein, Proteomics and Computational Biology

December 06-07, 2018
Amsterdam, Netherlands

Zajonc, Biochem Mol biol J Volume:4
DOI: 10.21767/2471-8084-C5-019

MODULATING IMMUNE RESPONSES WITH DESIGNED GLYCOLIPID ANTIGENS THAT TARGET NATURAL KILLER T CELLS USING A STRUCTURAL-FUNCTIONAL APPROACH

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Natural Killer T (NKT) cells are a unique T cell population characterized by features of both the innate and adaptive immune response. Two main classes of NKT cells (Type I and II) exist that express different antigen receptors (TCRs) and respond to different glycolipids presented by the shared antigen-presenting molecule CD1d. Type I NKT cells respond rapidly to the prototypical antigen -galactosylceramide (-GalCer) and can secrete both pro- and anti-inflammatory cytokines, while Type II NKT cells recognize the self-glycolipid sulfatide and are thought to be controlling autoimmunity. The cytokine profile of Type I NKT cells can be altered using modified synthetic glycolipids to produce the cytokine response of choice. Through biophysical TCR binding affinity measurements, as well as crystallographic studies of how the TCR engages different CD1d-presented glycolipids, we and others have identified the structural basis of glycolipid recognition by NKT cells. The TCR of Type I NKT cells binds to CD1d with a conserved footprint, while inducing structural changes in both CD1d and the glycolipid antigens. This conserved TCR binding mode allows for the design of glycolipid antigens, predominantly analogs of -GalCer in an attempt to obtain glycolipids that elicit a particular cytokine profile. We are especially interested in identifying novel antigens that elicit pro-inflammatory cytokines, since they have great potential as vaccine adjuvants. I will present our ongoing work on characterizing novel CD1d-restricted antigens, which led us to a surprising discovery.

Biography

Prof. Zajonc obtained his Ph.D. in Biology from the Friedrich Alexander University in Erlangen, Germany in 2001, working on fatty acid elongation and sphingolipid metabolism in yeast. For his postdoctoral work, he joined the laboratory of Ian A. Wilson at the Scripps Research Institute in La Jolla, California, where he worked on the structural basis of glycolipid presentation by the CD1 family. At that time, he made seminal findings of how glycolipids can be recognized by T cells. In 2006, he started his own lab at the La Jolla Institute for Immunology, where he continued to work on microbial antigen recognition by T cells, antibody recognition of viral antigens, as well as viral interference with immune recognition. He has published over 90 peer-review papers in top tier journals including Science, Nature Immunology, Journal of Experimental Medicine, Immunity and PNAS.

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