

Structural insights into cardiolipin bound to mouse CD1d receptor on T-cells that are involved in immune surveillance during infections

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INTRODUCTION

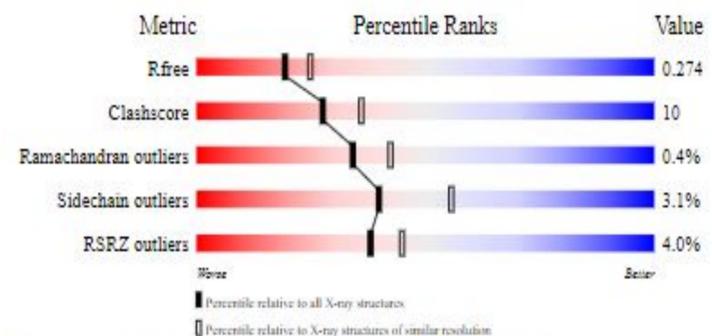
In mammalian cells, and plant cells, cardiolipin (CL) is found almost exclusively in the inner mitochondrial membrane, where it is essential for the optimal function of numerous enzymes that are involved in mitochondrial energy. Cardiolipin (CL), a major phospholipid in bacterial cell walls, is sequestered from the immune system in mammalian mitochondria and is, therefore, a potential danger signal. Based on growing evidence that phospholipids constitute natural ligands for CD1 and that CD1d-restricted T cells recognize phospholipids.

HYPOTHESIS

In this study we hypothesized that CD1d binds and presents CL and that T cells in the normal immune repertoire respond to CL in a CD1d1-restricted manner. We furthermore demonstrate the functional stimulatory activity of CL, showing that splenic and hepatic $\gamma\delta$ T cells from healthy mice proliferate in vitro in response to mammalian or bacterial CL in a dose-dependent and CD1d-restricted manner, rapidly secreting the cytokines IFN- γ

EXPERIMENTALS

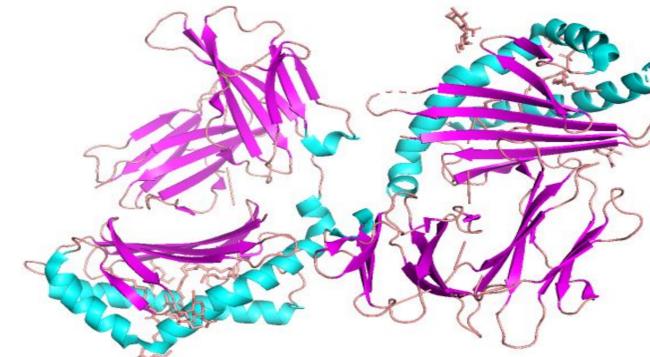
In order to understand the overall organization of the ligands and CD1d1, 3-dimensional analysis of its structure was performed using Computational biology tools. structure was downloaded from the protein data bank(PDB ID: 3MA7). The analysis includes evaluation of the secondary structure (alpha helices and beta strands) followed by hydrogen bonding analysis using PYMOL software.



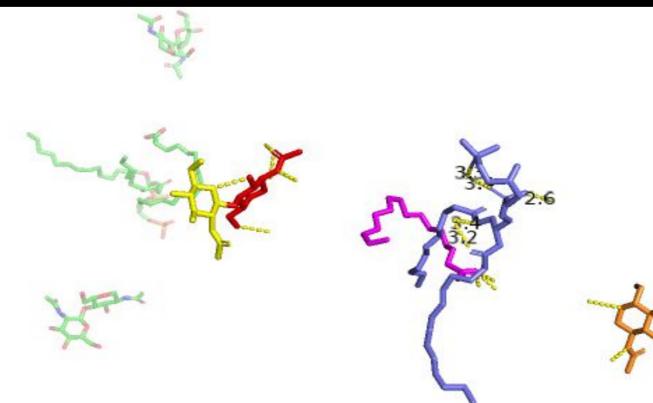
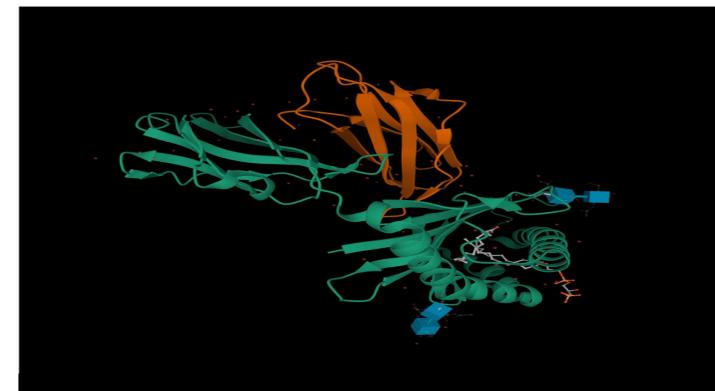
X-ray source:	SSRL BEAMLINE BL7-1		
R-values:	R	R _{work}	R _{free}
	0.234	0.232	0.273

Expression system: *Spodoptera frugiperda*

R Free - R Work = 0.041
(< 5%)



structure downloaded from PYMOL



structure downloaded from PYMOL

RESULTS & DISCUSSION

The structure of 3MA7 is a dimer and contains 6 alpha helices and 6 beta strands.(Fig.2) The ligand CD4 is attached to the CD1d1 restricted T cells by forming 5 hydrogen bonds in which 3 of them binds with water molecules remaining two binds with threonine at 156 position of CD1d1. Out of this five one H2 bond is strong. (Bond length <3Å). (Fig.4)

MACROMOLECULES:

T-cell surface glycoprotein CD1d1
Beta-2 microglobulin
OLIGOSACCHARIDES

SMALL MOLECULES:

PALMITIC ACID (PLM), CD4, NAG

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Cardiolipin binds to CD1d and stimulates CD1d-restricted $\gamma\delta$ T cells in the normal murine repertoire.

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Luoma AM1, Castro CD2, Mayassi T3, Bembister LA2, Bai L4, Picard D5, Anderson B6, Scharf L2, Kung JE2, Sibener LV2, Savage PB6, Jabri B3, Bendelac A7, Adams EJ1

Natural Killer T Cells and Mucosal-Associated Invariant T Cells in Lung Infections.

Trottein F1, Paget C2