MR1-restricted MAIT cells display ligand discrimination and pathogen selectivity through distinct T cell receptor usage.

*Mucosal-associated invariant T* (MAIT) cells express a semi-invariant T cell receptor (TCR) that detects microbial metabolites presented by the nonpolymorphic major histocompatibility complex (MHC)-like molecule MR1. The highly conserved nature of MR1 in conjunction with biased MAIT TCRα chain usage is widely thought to indicate limited ligand presentation and discrimination within a pattern-like recognition system. Here, we evaluated the TCR repertoire of MAIT cells responsive to three classes of microbes. Substantial diversity and heterogeneity were apparent across the functional MAIT cell repertoire as a whole, especially for TCRβ chain sequences. Moreover, different pathogen-specific responses were characterized by distinct TCR usage, both between and within individuals, suggesting that MAIT cell adaptation was a direct consequence of exposure to various exogenous MR1-restricted epitopes. In line with this interpretation, MAIT cell clones with distinct TCRs responded differentially to a riboflavin metabolite. These results suggest that MAIT cells can discriminate between pathogen-derived ligands in a clonotype-dependent manner, providing a basis for adaptive memory via recruitment of specific repertoires shaped by microbial exposure.

**General information**

Publication status: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Oregon Health and Science University, Cardiff University, University of Washington, Universidad Nacional de San Martin, Utrecht University
Number of pages: 10
Pages: 1601-1610
Publication date: 2014
Peer-reviewed: Yes

**Publication information**

Journal: Journal of Experimental Medicine
Volume: 211
Issue number: 8
ISSN (Print): 0022-1007
Ratings:
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 12.55 SJR 11.788 SNIP 2.754
Web of Science (2014): Impact factor 12.515
Web of Science (2014): Indexed yes
Original language: English
Keywords: Amino Acid Sequence, Antigens, Differentiation, B-Lymphocyte, Bacteria, Cell Line, Clone Cells, Complementarity Determining Regions, Gene Rearrangement, alpha-Chain T-Cell Antigen Receptor, Histocompatibility Antigens Class I, Histocompatibility Antigens Class II, Humans, Ligands, Molecular Sequence Data, Mucous Membrane, Receptors, Antigen, T-Cell, Receptors, Antigen, T-Cell, alpha-beta, Sequence Homology, Amino Acid, T-Lymphocytes, Vitamin B Complex, MR1 protein, human, invariant chain, 12001-76-2 Vitamin B Complex
DOIs:
10.1084/jem.20140507
URLs:
http://jem.rupress.org/content/211/8/1601.short
Source: FindIt
Source ID: 269410507
Research output: Contribution to journal › Journal article – Annual report year: 2014 › Research › peer-review