

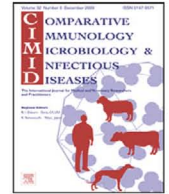


ELSEVIER

Contents lists available at ScienceDirect

Comparative Immunology, Microbiology and Infectious Diseases

journal homepage: www.elsevier.com/locate/cimid



Cetacean Toll-like receptor 4 and myeloid differentiation factor 2, and possible cetacean-specific responses against Gram-negative bacteria

Reiko Shishido^{a,b}, Kazue Ohishi^{a,*}, Rintaro Suzuki^c, Kiyotaka Takishita^a, Dai Ohtsu^d, Kenji Okutsu^d, Koji Tokutake^d, Etsuko Katsumata^e, Takeharu Bando^f, Yoshihiro Fujise^f, Tsukasa Murayama^g, Tadashi Maruyama^{a,b}

^a Japan Agency for Marine–Earth Science and Technology (JAMSTEC), Yokosuka, Kanagawa 247–0061, Japan

^b School of Marine Science and Technology, Tokyo Marine Science University, Minato-ku 108–8477, Japan

^c Protein Research Unit, National Institute of Agrobiological Sciences, Tsukuba, Ibaraki 305–8602, Japan

^d Yokohama Hakkeijima Sea Paradise, Yokohama, Kanagawa 236–0006, Japan

^e Kamogawa Sea World, Kamogawa, Chiba 296–0041, Japan

^f Institute of Cetacean Research, Tokyo 104–0055, Japan

^g School of Marine Science and Technology, Tokai University, Shizuoka 424–8610, Japan

ARTICLE INFO

Article history:

Received 21 January 2010

Accepted 30 March 2010

Keywords:

Whale

Dolphin

Cetacean

Toll-like receptor 4

Myeloid differentiation factor 2

Lipopolysaccharide

Innate immunity

ABSTRACT

Toll-like receptor 4 (TLR4) and myeloid differentiation factor 2 (MD-2) are essential for recognizing the lipopolysaccharides (LPS) of Gram-negative bacteria. We determined the sequences of cDNAs encoding TLR4 and MD-2 from cetaceans and generated three-dimensional (3D) models for a better understanding of their modes of interaction and LPS recognition. The 3D reconstructions showed that cetacean TLR4 and MD-2 formed a horseshoe-like structure comprised of parallel β -strands and a β -cup structure consisting of two anti-parallel β -sheets, respectively. The (TLR4–MD-2)₂ duplex-heterodimer was shown to form a symmetrical structure. Comparison with the interfaces of the complexes in other mammals revealed that cetacean TLR4s have some amino acid residue substitutions involved in duplex-heterodimer formation and in species variation for LPS recognition. These substitutions in the changed amino acid residues may alter the interaction among TLR4, MD-2, and LPS and modify the TLR4/MD-2 immunological responses.

© 2010 Elsevier Ltd. All rights reserved.