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

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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 $(TLR4\text{-}MD\text{-}2)_2$ 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.

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