

Prediction of Epitope and Host Organism for Generation of Antibodies against Human Toll-Like Receptor 5 Protein

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Abstract

Toll-like receptors (TLRs) are transmembrane proteins that help in the recognition of pathogen-associated molecular patterns (PAMPs) expressed on infectious agents and mediate the activation of signaling pathways invoking immune and inflammatory responses for their destruction. These receptors are highly conserved in eukaryotes and share similarities at structural and functional levels. Among TLRs, TLR5 is the receptor for flagellin, a major constituent of bacterial flagella and a virulence factor.

Methods and Findings: Accurately locating epitopes plays an important role in antibody production, vaccine design and immunodiagnostic tests. The present study thus aimed at *in silico* prediction of various properties of human TLR5 amino acid residues including epitope linearity, β -turn, antigenicity, flexibility, hydrophilicity and surface accessibility of amino acid residues. The peptides of TLR5 possessing all the properties to qualify being an epitope were selected and used for the prediction of a suitable host organism, which could serve as a potential source for the commercial production of antibodies against human TLR5.

Conclusions: To our knowledge, this is for the first time that variations in TLR5s from human, *Gallus gallus* and *Cirrhinus mrigala* have been reported and it is suggested that these two host organisms may be used for the production of human TLR5-specific antibodies, which could be exploited for research purposes. Thus, *in silico* methods have high potential for efficient, cost-effective and large-scale epitope prediction of antigens consequently expediting the process of antibody production.

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Introduction

Toll-like receptors (TLRs) are key components of the innate immune system, which play role in the recognition of specific microbial components in certain groups of microbes and activate adaptive immunity [1]. For example, TLR2 recognizes bacterial lipoproteins and lipoteichoic acid, TLR3 recognizes viral double-stranded RNA, TLR4 recognizes lipopolysaccharides and TLR5 is the receptor for flagellin [2,3].

Flagellin is the major constituent of bacterial flagella and a virulence factor for Gram-negative and Gram-positive bacteria. The structure of bacterial flagellins is highly conserved and hence TLR5 can detect a wide array of flagellated bacteria including

Legionella, *Listeria*, *Pseudomonas* and *Salmonella* [2,3]. Flagellins are expressed by bacteria, particularly pathogenic bacteria, in the lungs and gut and activate epithelial TLR5 signaling. The presence of flagellin thus gives an alarm signal indicating subepithelial invasion and/or disruption of the epithelial barrier function [3]. Upon binding to TLR5 receptor, flagellin triggers activation of MyD88 adaptor protein-dependent signaling pathway and nuclear translocation of NF- κ B. Further, MAP kinases are activated, which ultimately induces the maturation of antigen-presenting cells and secretion of proinflammatory chemokines and cytokines, such as tumor necrosis factor- α , necessary for the development of effective immunity [2,4-9]. TLR5 can generate a proinflammatory signal as a homodimer, which suggests it to be the only TLR participating in flagellin recognition [2]. However,