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Short Commentary OMICS International

Toll-Like Receptor 11: Role in Post-Transplantation Renal Infections

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Abstract

Uropathogenic microorganisms interact with the intestinal tract mucosa, which activate immune cell responses through the Toll-like receptors (TLRs). TLRs are single, membrane-spanning, non-catalytic proteins and it has significant role in the innate immune system. Recent studies have demonstrated that TLRs expressed in sentinel cells such as dendritic and macrophages cells that recognize structurally conserved molecules derived from microorganisms. Interestingly, the massive infection of the kidney observed in the TLR11 knockout mice, which indicate the hypothesis that TLR11 provides a barrier that prevents uropathogenic bacteria from infecting specifically the post-transplantation kidneys.

Keywords: Toll-like receptors; TLR11; Uropathogenic bacteria; Post-transplantation Infection

Introduction

There are several types of the toll-like receptors (TLRs) have been identified namely; TLR1, TLR2, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, TLR11, TLR12, and TLR13 [1]. TLRs proteins sequences have maximum homology with the protein coded by the toll gene, which is identified in *Drosophila* [2]. TLRs comprise a family of type I transmembrane proteins, each with an N-terminal ectodomain consisting of multiple leucine-rich repeat (LRR) domains involved in ligand binding extracellular, as well as a C-terminal cytosolic region containing a Toll/interleukin-1 receptor (TIR) domain that mediates recruitment of signaling components [3]. Based on existing structures of TLR ectodomains, the activated, ligand-bound state appears to be a dimer [4-7]. Most of the TLRs use common signaling adaptor molecules, MyD88 (myeloid differentiation primary response gene 88) and/or TRIF (TIR domain-containing adaptor inducing interferon-b), to initiate signaling [3].

In humans, both innate and adaptive immune responses have developed as defensive system against contagious microbes. TLRs have a significant role in the detection of invading microbes. They have been identified as the first receptors, which detect infectious microorganisms and induce the immune response. Furthermore, TLRs play a vital association between the innate and adaptive immune responses [8,9]. TLRs play crucial roles in the innate immune system by recognizing pathogen-associated molecular patterns (PAMPS) derived from numerous microbes. TLRs signal through the recruitment of specific adaptor molecules, leading to activation of the transcription factors nuclear factor of kappa-light-chain-enhancer of activated B cells (NF-κB) and interferon regulatory factors (IRFs), which dictate the result of innate immune responses. TLR signaling appears to be divergent and to play important roles in many aspects of the innate immune responses to given pathogens [8].

Among the most common post-transplantation infectious diseases, urinary tract infections (UTIs), including asymptomatic bacteriuria, cystitis and pyelonephritis, are a major cause of human morbidity and mortality [10,11]. UTIs are also the most common form of bacterial infection in renal transplant recipients [12,13]. It is generally agreed that post-transplant UTIs are caused by exposure to pathogens as a result of surgical procedures (i.e., urethral and ureteral stent catheters) and long-term immunosuppressive therapy [13,14]. The massive infection of the kidney observed in the TLR11 knockout mice supports the hypothesis that TLR11 provides a barrier that prevents uropathogenic bacteria from infecting the kidneys [15]. TLR11 is abundantly expressed in the bladder, where it probably shares the burden of responding to uropathogenic *Escherichia coli* (UPECs) with TLR4, but in the kidney, TLR11 alone appears to be responsible for mounting innate immune responses.

The studies on TLR11 assume significance in the wake of its association with binding of specific ligand present on *Salmonella typhi* as demonstated by Mathur et al. [16]. They have further shown that TLR11 knockout mice were significantly infected with *S. typhi*. Moreover, *S. typhi* is a human pathogen and causes typhoid fever. As data indicated that due to typhoid fever, more than 20 million people are affected globally, in which 220 thousand deaths occur per year. Therefore, it is necessary to carry out further studies on mechanism of action of TLR11 and association with *Salmonella* and other human pathogens.

Based on the sequence of the human genome in the NCBI-GenBank and the genomic sequence of some human cell lines, it appears that humans might not express full-length TLR11 protein. It is possible that the stop codons in the ORF of human TLR11 might represent a form of genetic polymorphism, similar to the situation observed for TLR5 in which a stop codon within the ORF of human TLR5 in many individuals makes them incapable of responding adequately to flagellated bacterium [17]. The presence or absence of TLR11 from the human population or only from a subpopulation can be done by systematic analysis of TLR11 sequences. However, it is tempting to speculate that one of the reasons humans are particularly susceptible to UTIs is because the absence of TLR11 has removed a defense pathway with the unique ability to specifically recognize UPECs [15].

Conclusion

Elucidation of role of TLR 11 in kidney should eventually allow us to manipulate them in strategies to treat various post-transplantation renal infections, which are reaching dangerous proportions due to increasing diabetic-associated renal failure globally. It could be target for drug design to prevent the post-transplantation kidney infections as well as other human infections like typhoid fever caused by *S. typhi* and other such infections affecting large human populations.

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