

GENETIC POLYMORPHISMS OF TOLL-LIKE RECEPTOR 4 IN CHILDREN WITH RECURRENT URINARY TRACT INFECTIONS

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Abstract

Recurrent urinary tract infections (rUTIs) remain one of the most common bacterial diseases in pediatric practice and are associated with renal scarring, hypertension, and chronic kidney disease. Recent advances in molecular immunology have demonstrated that host genetic factors significantly influence susceptibility to recurrent infections. Among these factors, polymorphisms of the Toll-like receptor 4 (TLR4) gene have attracted considerable attention because of their role in innate immune recognition of Gram-negative bacteria. This review summarizes current evidence regarding the biological role of TLR4 polymorphisms in pediatric recurrent urinary tract infections and discusses their potential clinical application in early diagnosis, risk prediction, and personalized treatment strategies.

Keywords: recurrent urinary tract infection, TLR4, polymorphism, children, innate immunity, genetics.

Introduction

Urinary tract infections affect millions of children worldwide and continue to represent a major public health concern. Although most children recover after appropriate antimicrobial therapy, approximately 30% experience recurrent episodes that increase the risk of permanent renal damage. Clinical observations indicate that recurrence cannot be explained solely by anatomical abnormalities or bacterial virulence. Therefore, increasing attention has been directed toward host genetic susceptibility.

Innate immunity constitutes the first line of defense against uropathogenic microorganisms. Pattern-recognition receptors, particularly Toll-like receptors, play an essential role in recognizing bacterial components and initiating inflammatory responses. Among these receptors, TLR4 is considered one of the most important molecules involved in host defense against *Escherichia coli*, the predominant causative pathogen of pediatric urinary tract infections.

Main Discussion

TLR4 recognizes lipopolysaccharide (LPS), the major component of the outer membrane of Gram-negative bacteria. Activation of TLR4 triggers intracellular signaling pathways involving MyD88 and NF- κ B, leading to the production of pro-inflammatory cytokines including IL-6, IL-8, and TNF- α . These cytokines recruit neutrophils to the site of infection and facilitate bacterial clearance.

Genetic polymorphisms within the TLR4 gene may alter receptor expression or signaling efficiency. Functional variants such as Asp299Gly (rs4986790) and Thr399Ile (rs4986791) have been extensively investigated because they reduce cellular responsiveness to bacterial endotoxins. Consequently, impaired bacterial recognition may contribute to persistent infection and recurrent disease.

Recent systematic reviews and meta-analyses have demonstrated a significant association between TLR4 polymorphisms and susceptibility to recurrent urinary tract infections in several populations. However, the strength of this association varies according to ethnicity, environmental factors, and genetic background. Data from Central Asian pediatric populations remain extremely limited, highlighting the need for regional molecular epidemiological studies.

The identification of TLR4 polymorphisms has important clinical implications. Genetic screening may help identify children at increased risk of recurrent infections before irreversible renal damage develops. Integration of molecular genetic markers with laboratory findings and imaging studies may improve individualized risk stratification and optimize long-term follow-up strategies.

Furthermore, advances in precision medicine suggest that combining genetic biomarkers with artificial intelligence algorithms may significantly improve prediction models for recurrent urinary tract infections. Such approaches could contribute to personalized prevention programs and rational antimicrobial therapy.

Conclusion

TLR4 gene polymorphisms represent promising genetic biomarkers for predicting susceptibility to recurrent urinary tract infections in children. Their identification may facilitate early diagnosis, individualized monitoring, and personalized therapeutic interventions. Future large-scale multicenter studies involving Central Asian populations are required to validate these findings and establish clinically applicable genetic risk models.

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