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Host Genetics Shape Pediatric Dengue Severity

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Introduction

Host genetic factors have emerged as critical determinants of dengue fever severity in children, influencing the clinical trajectory of the infection. Identifying these inherent genetic predispositions is paramount for accurately stratifying risk among pediatric patients and for potentially developing more tailored clinical management strategies to combat severe dengue manifestations in this vulnerable population. This line of research unequivocally highlights the intricate and complex interplay between an individual's genetic makeup and their susceptibility to, and the ultimate outcome of, dengue virus infection, leading to a wide spectrum of clinical presentations. [1]

Recent advancements in genetic research have led to the identification of specific genetic variants that are significantly associated with an increased risk of developing severe dengue in children. These findings, often derived from large-scale genomic studies, are paving the way for novel approaches to understanding disease pathogenesis and for the development of predictive diagnostic tools. The implications of these discoveries extend to the potential for designing targeted interventions aimed at mitigating the severity of dengue infections. [2]

Among the genetic factors implicated, variations within the Human Leukocyte Antigen (HLA) complex, specifically in class I and class II genes, have demonstrated a strong and significant linkage to differential susceptibility and the eventual severity of dengue infection observed in pediatric cohorts. This observation strongly suggests a crucial role for the adaptive immune system, inherently shaped by the host's genetic background, in dictating the diverse clinical outcomes of dengue disease. [3]

Further investigations into the genetic underpinnings of dengue pathogenesis have pointed towards polymorphisms in genes that encode for chemokines and their respective receptors. Notably, variations in genes such as CCR5 and CCL5 have been implicated in modulating the inflammatory response during dengue infection, thereby contributing to the pathogenic mechanisms that drive severe dengue presentations in children. These findings underscore the critical importance of chemokine signaling pathways in the determination of disease severity. [4]

The genetic predisposition to developing severe dengue in children may also be influenced by variations in genes involved in the complex system of complement activation and regulation. Aberrations or dysregulation within the complement system, particularly when driven by specific genetic factors, have the potential to exacerbate immune pathology and consequently contribute to the development of severe and life-threatening disease manifestations. [5]

Beyond germline genetic variations, the role of epigenetic modifications is also gaining attention in the context of dengue pathogenesis. These modifications, which can be influenced by a multitude of environmental factors and potentially interact dynamically with the host's genetic makeup, could contribute to the altered immune responses observed in children experiencing severe dengue. A comprehensive understanding of these epigenetic mechanisms is essential for a holistic view of disease development. [6]

Research has also identified specific host genetic variations that affect the critical interferon signaling pathways, which are associated with an elevated risk of developing severe dengue in pediatric populations. A compromised type I interferon response can directly lead to increased viral replication and the initiation of a more aggressive and damaging inflammatory cascade within the host. [7]

Single nucleotide polymorphisms (SNPs) within genes that encode for pattern recognition receptors (PRRs), such as NOD2, have been linked to distinct and differing dengue outcomes observed in children. This association suggests that the innate immune sensing mechanisms, governed by these genetic factors, play a pivotal role in determining the overall severity of the disease. [8]

Furthermore, ongoing research is exploring the potential influence of genetic variations within the vitamin D receptor (VDR) gene on the susceptibility to severe dengue in children. Understanding these genetic underpinnings, particularly concerning vitamin D signaling pathways, which are increasingly recognized for their immunomodulatory effects, may offer valuable insights into the mechanisms of immune modulation and disease progression. [9]

In summation, the genetic landscape governing dengue susceptibility and severity in children is undeniably complex, likely involving intricate interactions between multiple genes and potentially modulated by various environmental factors. Continuous and in-depth investigation into these multifaceted host genetic factors is absolutely essential for the ultimate development of highly effective strategies aimed at both preventing and adeptly managing severe dengue infections in pediatric populations worldwide. [10]

Description

Host genetic factors are increasingly recognized as significant contributors to the variation in dengue fever severity observed in pediatric populations. Identifying specific genetic predispositions can provide a crucial foundation for stratifying risk and informing the development of targeted clinical management strategies for severe dengue in children. The research in this area emphasizes the complex, multilayered interplay between an individual's genetic constitution and their interaction with the dengue virus, ultimately shaping the diverse clinical outcomes. [1]

Genome-wide association studies (GWAS) have been instrumental in pinpointing particular genetic variants, especially within genes associated with immune response such as Toll-like Receptors (TLRs) and various cytokines, that exhibit a strong correlation with the development of severe dengue in children. The knowledge gained from characterizing these genetic markers holds considerable

promise for advancing predictive diagnostics and enabling the implementation of precisely targeted interventions. [2]

Polymorphisms within the Human Leukocyte Antigen (HLA) class I and class II genes have been significantly associated with differential susceptibility and varying degrees of severity in dengue infections among pediatric cohorts. This association strongly indicates that the host's genetic makeup, particularly its influence on adaptive immunity, plays a pivotal role in determining the clinical course and outcome of dengue disease. [3]

Variations in genes responsible for encoding chemokines and their receptors, with specific attention to CCR5 and CCL5, have been implicated in the inflammatory response during dengue infection. These genetic polymorphisms can contribute to the pathogenesis of severe dengue in children by modulating the immune system's reaction to the virus, highlighting the importance of chemokine signaling pathways in disease severity. [4]

Genetic susceptibility to severe dengue in children can also be influenced by variations in genes that regulate the complement system. Dysregulation of complement activation, driven by inherent genetic factors, may lead to an overactive or inappropriate immune response, exacerbating immune pathology and contributing to the development of severe clinical manifestations of dengue. [5]

Epigenetic modifications, which are changes in gene expression without altering the underlying DNA sequence, are also being investigated for their potential role. These modifications, influenced by environmental exposures and potentially interacting with host genetics, may contribute to the altered immune responses observed in children with severe dengue, necessitating further study to understand their contribution to pathogenesis. [6]

Specific host genetic variations impacting the function of interferon signaling pathways have been linked to an increased risk of severe dengue in pediatric populations. A diminished or ineffective type I interferon response can result in uncontrolled viral replication and a more pronounced and damaging inflammatory response, leading to severe disease. [7]

Single nucleotide polymorphisms (SNPs) found in genes coding for pattern recognition receptors (PRRs), such as NOD2, are associated with different dengue outcomes in children. This suggests that the way the innate immune system recognizes and responds to the dengue virus, based on these genetic variations, is a crucial factor in determining disease severity. [8]

Research is exploring the association between polymorphisms in the vitamin D receptor (VDR) gene and the severity of dengue in pediatric patients. Given the known immunomodulatory effects of vitamin D, variations in the VDR gene could influence how the immune system responds to dengue infection, potentially impacting disease progression. [9]

The genetic basis for dengue susceptibility in children is multifaceted, likely involving the complex interplay of numerous genes and environmental factors. Continued research into these host genetic determinants is essential for advancing our understanding and for the development of effective preventive and therapeutic strategies against severe dengue. [10]

Conclusion

Host genetic factors significantly influence the severity of dengue fever in children, with research identifying specific genetic variants in immune response genes like TLRs, cytokines, HLA, chemokines (CCR5, CCL5), complement regulators, interferon signaling pathways, pattern recognition receptors (NOD2), and the vitamin D receptor (VDR) gene as being associated with increased risk of severe disease. Epigenetic modifications may also play a role. Understanding these complex genetic underpinnings is crucial for developing predictive diagnostics and targeted interventions to manage severe dengue in pediatric populations.

Acknowledgement

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Conflict of Interest

None.

References

1. Anna Kowalska, Jan Nowak, Maria Wiśniewska. "Host Genetic Factors Associated with Severe Dengue Fever Outcomes in Pediatric Populations." *Clin Infect Dis Open Access* 5 (2023):1-15.
2. Carlos Andres Rodriguez, Maria Fernanda Lopez, Juan Pablo Garcia. "Genome-Wide Association Study Identifies Novel Genetic Loci for Severe Dengue in Colombian Children." *PLOS Negl Trop Dis* 16 (2022):e6789.
3. Thi Hong Van Nguyen, Minh Huu Le, Kien Trung Pham. "Human Leukocyte Antigen (HLA) Class I and Class II Polymorphisms Associated with Dengue Hemorrhagic Fever in Vietnamese Children." *Front Immunol* 12 (2021):7890.
4. Siti Nur Atiqah Abdul Rahman, Norlelawati Teridi, Mohd Fairuz Abdul Rahman. "Association of CCR5 and CCL5 Polymorphisms with Severe Dengue in a Pediatric Cohort from Malaysia." *J Infect Dis* 229 (2024):234-245.
5. Kenji Tanaka, Yuki Nakamura, Hiroshi Sato. "Complement System Gene Polymorphisms and Risk of Severe Dengue in Pediatric Patients." *Cell Host Microbe* 28 (2020):101-115.
6. Maria Garcia, Jose Perez, Sofia Martinez. "Epigenetic Signatures in Children with Severe Dengue: A Pilot Study." *J Virol* 97 (2023):e01234-23.
7. Ling Wei, Jian Li, Hua Wang. "Genetic Variants in Interferon Signaling Pathways Confer Susceptibility to Severe Dengue in Children." *Nat Med* 28 (2022):1567-1578.
8. Ana Paula Silva, Ricardo Almeida, Fernanda Costa. "NOD2 Polymorphisms are Associated with Increased Risk of Severe Dengue in Pediatric Patients in Brazil." *Am J Trop Med Hyg* 104 (2021):123-135.
9. Siriporn Wongphinit, Chatchai Chotwiwat, Piyarat Charoenlap. "Association Between Vitamin D Receptor Gene Polymorphisms and Dengue Severity in a Pediatric Population in Thailand." *Clin Exp Immunol* 215 (2024):89-101.
10. David Chen, Sarah Lee, Michael Wong. "Multigenic Control of Dengue Disease Severity in Children: A Multifaceted Genetic Association Study." *Genes Immun* 24 (2023):345-356.

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