Article type: Editorial

Home Page URL: https://www.alliedacademies.org/immunology-case-reports/

CRISPR in parasite immunology: Editing our way to understanding.

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Received: *02-Aug-2025, Manuscript No. AAICR-25-171204;* ***Editor assigned:*** *03-Aug-2025, Pre QC No. AAICR-25-171204(PQ);* ***Reviewed:*** *18-Aug-2025, QC No. AAICR-25-171204;* ***Revised:*** *24-Aug-2025, Manuscript No. AAICR-25-171204(R);* ***Published:*** *30-Aug-2025, DOI: 10.35841/aaicr-8.3.204*

Introduction

Parasitic infections remain a major global health burden, affecting billions and contributing to chronic disease, developmental disorders, and mortality—particularly in low-resource settings. Despite decades of research, the immunological complexity of host-parasite interactions has hindered the development of effective vaccines and therapies. Enter CRISPR: the revolutionary genome-editing tool that is transforming parasite immunology by enabling precise genetic manipulation of parasites and host cells. With CRISPR, researchers are now able to dissect immune evasion strategies, identify virulence factors, and explore host immune responses with unprecedented clarity [1].

Parasites such as *Plasmodium* (malaria), *Trypanosoma* (Chagas disease and sleeping sickness), *Leishmania*, and *Schistosoma* have evolved sophisticated mechanisms to evade host immunity. These include antigenic variation, immune suppression, and manipulation of host signaling pathways. Traditional genetic tools have struggled to keep pace with the complexity of these organisms, many of which possess large, repetitive genomes and lack robust transfection systems. Understanding how parasites interact with the immune system—how they trigger, evade, or suppress responses—is essential for designing vaccines and immunotherapies. CRISPR-Cas systems offer a powerful solution to these challenges [2].

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) and its associated Cas enzymes, particularly Cas9, allow for targeted gene editing by creating double-strand breaks at specific genomic loci. This technology has been adapted for use in a wide range of parasites, enabling: These capabilities have opened new avenues for exploring parasite biology and host-pathogen interactions. Malaria research has benefited immensely from CRISPR. In *Plasmodium falciparum*, the most lethal malaria parasite, CRISPR has been used to: Identify genes involved in immune evasion, such as *PfEMP1*, which mediates antigenic variation and cytoadherence [3].

Trypanosomes are notorious for their ability to switch surface glycoproteins, evading antibody responses. CRISPR has enabled the deletion and modification of variant surface glycoprotein (VSG) genes, shedding light on the regulation of antigenic variation. In *Leishmania*, CRISPR has been used to study the role of lipophosphoglycan (LPG) and other surface molecules in modulating macrophage responses. By knocking out genes involved in immune suppression, researchers are identifying potential vaccine targets and understanding how the parasite persists in host tissues [4].

For example, CRISPR screens in macrophages have identified host genes required for *Leishmania* replication, offering new therapeutic targets. Genome-wide CRISPR screens are enabling systematic identification of genes involved in parasite-host interactions. These screens use libraries of guide RNAs to target thousands of genes simultaneously, revealing: Such approaches have been used to uncover host factors required for *Toxoplasma gondii* invasion and replication, providing a blueprint for similar studies in other parasites. Helminths such as *Schistosoma mansoni* have complex life cycles and large genomes, making genetic manipulation

Citation: Eard S. CRISPR in parasite immunology: Editing our way to understanding. Immunol Case Rep. 2025;8(3):204.

difficult. Recent advances have adapted CRISPR for use in schistosomes, allowing for: These studies are revealing how helminths shape immune responses to promote chronic infection and tolerance. CRISPR is not limited to parasites—it's also revolutionizing host immunology. By editing immune genes in host cells or animal models, researchers can: Study the role of cytokines, receptors, and transcription factors in parasite immunity [5].

Conclusion

CRISPR has ushered in a new era of parasite immunology, enabling researchers to edit their way to understanding. By dissecting the genetic basis of immune evasion, host response, and parasite survival, CRISPR is accelerating the development of vaccines, diagnostics, and therapies. As the technology continues to evolve, it promises to unlock the secrets of some of the world's most persistent and elusive pathogens—bringing us closer to controlling and eventually eradicating parasitic diseases.

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Citation: Eard S. CRISPR in parasite immunology: Editing our way to understanding. Immunol Case Rep. 2025;8(3):204.