Journal of Clinical and Cellular Immunology

OPEN ACCESS Freely available online

Perspective

Harnessing MAIT Cells for Antimicrobial Immunotherapy

Jia Jun*

Department of Immunology, Tsinghua University, Beijing, China

DESCRIPTION

Mucosal-Associated Invariant T (MAIT) cells are an unconventional subset of T lymphocytes that bridge innate and adaptive immunity. Characterized by a semi-invariant T-Cell Receptor (TCR) that recognizes microbial-derived vitamin B metabolites presented by the MR1 molecule, MAIT cells are abundant in mucosal tissues, liver, and blood. They rapidly respond to bacterial and fungal infections by producing pro-inflammatory cytokines such as interferon-gamma, tumor necrosis factor-alpha, and interleukin-17 (IL-17), as well as by exerting cytotoxic functions granzyme B and perforin. Their unique antigen recognition, tissue residency, and effector versatility make MAIT cells promising candidates for antimicrobial immunotherapy, especially in the context of multidrug-resistant infections and immunocompromised patients. Recent advances in immunology have highlighted strategies to harness MAIT cells therapeutically, offering a novel avenue for precision immunomodulation.

MAIT cells in antimicrobial defense

MAIT cells play a critical role in the host defense against a broad spectrum of bacterial and fungal pathogens. Unlike conventional T cells, MAIT cells detect microbial vitamin B2 metabolites through the MR1 molecule, allowing them to rapidly respond to microbial invasion without the need for classical peptide antigens. Upon activation, MAIT cells secrete IFN-γ and TNF-α, which activate macrophages and dendritic cells, enhancing pathogen clearance. Simultaneously, the production of IL-17 recruits neutrophils to the site of infection, promoting rapid containment of bacterial growth.

In addition to cytokine secretion, MAIT cells exert direct cytotoxicity. They express perforin, granzyme B, and granulysin, which enable them to kill infected epithelial or immune cells, limiting pathogen replication. Their strategic localization at mucosal barriers such as the lungs, gut, and liver ensures that MAIT cells are among the first responders to microbial entry, forming an essential component of the early immune defense. Studies in both humans and animal models demonstrate that MAIT cell deficiency or dysfunction correlates with increased susceptibility to bacterial infections, highlighting their protective role and making them an attractive target for immunotherapeutic strategies.

MAIT cells also respond to inflammatory cytokines, including IL-12 and IL-18, in a TCR-independent manner, allowing them to contribute to antiviral responses and enhance the overall immune reaction. This dual sensing ability through both MR1-mediated antigen recognition and cytokine-driven activation positions MAIT cells as versatile effectors capable of orchestrating rapid and robust antimicrobial immunity.

Strategies for harnessing MAIT cells in immunotherapy

The therapeutic potential of MAIT cells lies in their ability to be selectively activated or expanded to enhance antimicrobial immunity. One approach involves using synthetic MR1 ligands that mimic microbial vitamin B metabolites. These ligands can selectively stimulate MAIT cells, boosting cytokine production and cytotoxic activity without triggering widespread systemic inflammation. Preclinical studies have demonstrated that administration of MR1 ligands can enhance MAIT-mediated protection against bacterial infections, suggesting a viable strategy for prophylactic or adjunctive therapy in high-risk patients.

Adoptive cellular therapy represents another promising approach. Similar to strategies used with Chimeric Antigen Receptor (CAR) T cells, MAIT cells can be isolated, and reintroduced into patients to augment antimicrobial immunity. This strategy is particularly relevant for immunocompromised individuals, such as those undergoing hematopoietic stem cell transplantation or chemotherapy, are at heightened risk of severe infections. Engineering MAIT cells to enhance tissue homing, cytotoxicity, or cytokine production could further optimize their therapeutic potential.

Additionally, MAIT cells can be leveraged as adjuvants in vaccine development. Their rapid cytokine release and interaction with antigen-presenting cells make them effective enhancers of adaptive immune responses. Incorporating MAIT cell-activating ligands into vaccine formulations may accelerate

Correspondence to: Jia Jun, Department of Immunology, Tsinghua University, Beijing, China, Email: jun@gmail.com

Received: 20-Aug-2025, Manuscript No.JCCI-25-39130; **Editor assigned:** 22-Aug-2025, PreQC No.JCCI-25-39130 (PQ); **Reviewed:** 05-Sep-2025, QC No.JCCI-25-39130; **Revised:** 12-Sep-2025, Manuscript No.JCCI-25-39130 (R); **Published:** 19-Sep-2025, DOI: 10.35248/2155-9899.25.16.766

Citation: Jun J (2025). Harnessing MAIT Cells for Antimicrobial Immunotherapy. J Clin Cell Immunol. 16:766

protective immunity against bacterial and fungal pathogens, offering a complementary strategy to traditional vaccination approaches.

Challenges remain in translating MAIT cell-based therapies to the clinic. Overactivation of MAIT cells could lead to excessive inflammation and tissue damage, while chronic infection or immune exhaustion can impair their function. Understanding the balance between activation and regulation is therefore critical. Moreover, interindividual variation in MAIT cell frequency and functionality necessitates personalized approaches to optimize therapeutic outcomes.

CONCLUSION

MAIT cells represent a unique and highly adaptable component of the immune system, capable of rapid antimicrobial defense through both cytokine-mediated activation and direct cytotoxicity. Their ability to recognize microbial vitamin B metabolites, respond to inflammatory cytokines, and reside strategically at mucosal barriers makes them promising candidates for innovative immunotherapies. Strategies to harness MAIT cells including synthetic MR1 ligands, adoptive cellular therapy, and vaccine adjuvants offer new avenues to combat bacterial and fungal infections, particularly in the era of antibiotic resistance. Continued research into the biology, regulation, and therapeutic modulation of MAIT cells will be essential to fully realize their potential, paving the way for next-generation antimicrobial immunotherapies that are both targeted and robust.