

Q&A: Unlocking the potential of gamma delta T cell-based therapies

Presented by
Dr. Cheng Kang Zhang,
Associate Director, R&D,
Lonza Bioscience Solutions

Lonza continues to drive innovation in the immunotherapy space with the development of two advanced methods for expanding gamma delta ($\gamma\delta$) T cells using TheraPEAK® T-VIVO® Medium. These T cells, which do not require HLA antigen presentation, are well suited for a wide variety of treatments due to their reduced risk of graft-versus-host disease, enhancing their overall safety profile.

Dr. Zhang discusses two unique methods for clinical scale expansion of gamma delta T cells:

1. Zoledronic Acid Activation – Superior expansion of V 2 T cells, producing over 31 billion cells in just two weeks with potent anti-tumor activity.
2. Anti-CD3/CD28 Activation – Expands both V 1 and V 2 cells while maintaining high purity and functional integrity, achieving 80% transduction efficiency, making it ideal for large-scale clinical applications.

These methods offer unparalleled versatility and scalability, enabling the creation of therapeutic doses for personalized treatments. Lonza's innovative solutions enable researchers and clinicians to efficiently and reproducibly expand T cells, redefining the possibilities of advanced immunotherapy.



Q: How does Lonza's TheraPEAK® T-VIVO® Medium enhance T-cell expansion for clinical applications?

Lonza's TheraPEAK® T-VIVO® Medium is specifically formulated to support the efficient expansion of T cells without the need for serum, which makes it a suitable option for clinical-grade applications. The medium promotes the growth of both V 1 and V 2 T cell subsets, helping to ensure high purity and functional integrity of the expanded cells. Its formulation also helps maintain cell viability and supports efficient activation, making it an ideal choice for both small-scale research and large-scale clinical production, in compliance with GMP standards for clinical trials and therapeutic applications.

Q: How do activation methods influence the purity, functionality, and scalability of T cells?

The activation method used plays an important role in maintaining the purity and functionality of T cells. Anti-CD3/CD28 activation effectively preserves both V 1 and V 2 subsets, allowing for efficient expansion and genetic modification. This makes it well-suited for applications requiring diverse T-cell populations. In contrast, zoledronic acid predominantly expands V 2 cells, but it can also lead to contamination with NK and alpha-beta T cells. Both methods are scalable, but anti-CD3/CD28 activation offers more flexibility, which is beneficial for generating tailored T-cell therapies.

Q: Can T cells be cryopreserved, and how do fresh versus frozen PBMCs compare in terms of expansion?

Yes, T cells can be effectively cryopreserved using standard protocols, such as 10% DMSO, which helps ensure their viability for future use. While fresh PBMCs tend to yield better-quality T cells and higher expansion rates, frozen PBMCs are commonly used because of their convenience and the reproducibility they offer. The use of cryopreserved PBMCs removes the need for fresh sample collection, making it a more efficient and consistent approach for large-scale clinical applications.



Q: Is T-cell expansion consistent across different donors, and how do activation methods impact cell functionality?

There is some donor-to-donor variability in T-cell expansion, which is common with primary cells. However, TheraPEAK® T-VIVO® Medium has shown consistent results across multiple donors, helping to ensure reproducibility. Both zoledronic acid and anti-CD3/CD28 activation methods can effectively expand functional T cells. However, the proportions of V 1 and V 2 cells, which can vary depending on the activation method, may affect certain functional characteristics like cytotoxicity and memory marker expression. These methods are reliable for generating therapeutic-grade T cells for clinical applications.

Q: How can T-cell therapies be optimized for the treatment of cancer, and how do they compare to TCR-based T-cell therapies?

T cells offer a flexible and versatile approach for cancer immunotherapy, as they can recognize and target a wide range of tumor antigens in an MHC-independent manner, unlike TCR-based T-cell therapies. This flexibility makes T cells especially effective for targeting solid tumors, which can be difficult for traditional TCR-engineered T cells. Additionally, combining T cells with CAR-T technology further enhances their ability to target tumors, making them a promising option for cancer immunotherapy. Compared to TCR-based therapies, T cells provide broader applicability for a range of cancers, which may improve overall therapeutic outcomes.

Q: How long do activated T cells proliferate under different culture conditions, and how has their persistence been evaluated?

Activated T cells typically proliferate for 14–16 days under optimal small-scale culture conditions, with the potential to extend to 19 days under certain circumstances. In large-scale cultures, expansion is limited by factors like bioreactor capacity, with yields reaching 20–30 billion cells by day 14–16. Reactivation of expanded T cells with anti-CD3/anti-CD28 antibodies allows for continued proliferation, enabling a second round of expansion. This approach is scalable and helps ensure the production of large quantities of functional T cells for therapeutic use.

Q: Besides interleukin-2 (IL-2) and TransAct™, what other cytokines and reagents can be used to activate and expand T cells, particularly V 1 cells?

In addition to IL-2, cytokines such as IL-7 and IL-15 have been shown to enhance T-cell expansion. These cytokines, when combined with IL-2, can further optimize cell proliferation. For activation, TransAct™, which uses anti-CD3 and anti-CD28 antibodies, is commonly used. However, other reagents, such as Dynabeads™, can achieve similar activation. Additionally, antibodies targeting the TCR have been developed to specifically activate and expand V 1 cells, offering a more targeted approach for T-cell activation and expansion in therapeutic settings.

Transform your immunotherapy strategy with Lonza's advanced T-cell expansion methods in TheraPEAK® T-VIVO® Medium.



Contact us

North America

Customer Service: + 1 800 638 8174 (toll free)
order.us@lonza.com
Scientific Support: + 1 800 521 0390 (toll free)
scientific.support@lonza.com

Europe

Customer Service: + 32 87 321 611
order.europe@lonza.com
Scientific Support: + 49 221 99199 400
scientific.support.eu@lonza.com

International

Contact your local Lonza Distributor
Customer Service: + 1 301 898 7025
Fax: + 1 301 845 8291
scientific.support@lonza.com

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Lonza Walkersville, Inc. – Walkersville, MD 21793

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