

Next-Gen Cell Therapy Starts with the Right T Cells

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Sophie He, Vice President, Cell Therapy at Bracco, explores why selecting the right CD8+ T-cell populations and adopting gentler, more precise separation technologies could improve cell fitness, manufacturing efficiency and therapeutic outcomes.



As cell therapies advance towards greater clinical sophistication and commercial scale, the focus is shifting from simply achieving high cell purity and yield to identifying immune cells with the right functional and therapeutic characteristics. **In an interaction with BioSpectrum Asia, Sophie He, Vice President, Cell Therapy at Bracco,** discusses the potential of CD8+ T cells, the limitations of conventional magnetic bead and flow cytometry-based separation, and how emerging microbubble-based technologies could simplify manufacturing while preserving cell quality. She also outlines why the next phase of cell therapy innovation will increasingly centre on selecting the **right cells, not simply more cells**

CD8+ T cells are often described as the immune system's "executioners". What advantages do they offer over CD3+ T cells in the development of next-generation cell therapies?

CD3+ T cells have been used successfully as starting material for first-generation commercial CAR-T cell therapies. However, there are multiple CD3+ subpopulations that each function differently. These include CD8+ T cells, which are responsible for directly recognizing and killing diseased or tumor cells, as well as other subsets that can suppress antitumor immune responses.

Several CD3+ T cell subtypes may be suited for different therapeutic strategies. The specific selection and activation of CD8+ T cells may increase the likelihood of mounting an effective tumor-killing response, making them attractive for next-generation cell therapies.

As the executioners, the selection and activation of CD8+ T cells may increase the likelihood of mounting an effective tumor-killing response, as they are responsible for directly recognizing and killing diseased or tumor cells. This makes them particularly attractive for next-generation cell therapies, as they have the potential to support a more targeted and

potent therapeutic product.

CD3+ cells do not offer the same level of specificity. However, CD8+ and CD3+ cells may each be suited for different therapeutic strategies. The industry is increasingly exploring ways to maximize efficacy, durability and safety across these and other cell therapy types.

Despite their therapeutic potential, many developers continue to rely on CD3+ cells. What are the biggest scientific and operational barriers preventing broader adoption of CD8+ T cells?

Isolating CD8+ T cells using traditional, magnetic bead-based techniques adds extra separation steps, increasing manufacturing costs and making it more difficult to remain within the therapeutic window.

One approach is positive selection, using antibodies that bind specifically to CD8. This can lead to the inclusion of unwanted, non-T cells that also express CD8. At the same time, CD8+ T cells expand and survive better in the presence of certain additional subtypes, while others can have the opposite effect. Finally, positive selection can unintentionally activate CD8+ T cells, leading to poor expansion or exhaustion.

Ultimately, the additional manufacturing steps used today to mitigate these downstream issues have negative impacts on manufacturing time, scalability, reproducibility, cost efficiency, or all of these.

One scientific barrier is that not all CD8+ cells have the same therapeutic potential, as CD8+ cells exist in a range of cell states. For example, exhausted CD8+ cells may still respond to traditional selection markers but have low therapeutic value. Another scientific barrier is that CD8+ therapies may not achieve optimal *in vivo* persistence without support from CD4+ helper T cells. These are two reasons why many developers continue to rely on CD3+ cells.

From a manufacturing point of view, this means developers need to focus on isolating the right CD8+ cells, as not all CD8+ cells are equal. Donor variability further complicates starting material challenges as two donors with the same purity and yield percentages can have vastly different makeups of various CD8+ cell subpopulations, and therefore vastly different therapeutic benefits.

The field should focus on developing manufacturing processes that can consistently deliver the most therapeutically relevant CD8+ subsets while maintaining scalability, reproducibility, and cost efficiency.

Traditional cell separation methods such as magnetic beads and flow cytometry remain widely used. How do these approaches affect cell viability, functionality and manufacturing outcomes, particularly for CD8+ cells?

Traditional methods require multiple steps such as antibody labeling and bead attachment and removal, extending the processing time needed. Use of standard platforms like magnetic columns and centrifuges can introduce mechanical stresses that may reduce cell viability or lead to batch failure.

Additionally, these approaches increase manufacturing complexity, cost, and processing duration, which can limit scalability and narrow the available therapeutic window. Until now, developers and manufacturers have largely accepted these limitations as unavoidable, but emerging technologies aim to sidestep these shortcomings by preserving cell quality while improving manufacturing efficiency.

Microbubble-based cell separation is emerging as an alternative. Could you explain how this technology differs from conventional methods, and what advantages it offers for cell therapy developers?

The microbubble-based cell selection approach differs from conventional methods by offering a gentler technology that helps maintain high cell purity and viability. It is an open platform and highly flexible technology that can be applied to almost any type of cell therapy workflow and does not require dedicated hardware to work. In addition, cell selection and activation can be achieved in a single step, further simplifying the overall workflow. By reducing processing steps and manufacturing complexity, it provides a more cost-effective alternative to conventional cell separation techniques while helping preserve cell quality for downstream therapeutic applications.

As the industry moves towards commercial-scale manufacturing, what role will improved cell separation technologies play in enhancing process efficiency, product consistency and patient outcomes?

Commercial viability for cell therapy products hinges on better cost and quality control, both achievable through streamlining processes.

By simplifying workflows and significantly reducing the number of processing steps, these approaches can help limit variability, lower the risk of manufacturing delays or failures, and support more reproducible final products. Starting with healthier, more relevant cell populations can also improve downstream expansion and functionality, ultimately helping developers produce therapies that are more consistent, scalable, and better positioned to deliver meaningful benefit to patients.

Looking ahead, what innovations do you believe will have the greatest impact on immune cell isolation over the next five years, and how should therapy developers prepare for this transition?

To date, much of cell therapy development has focused on purity and yield. Over the next few years, the field will need to move beyond simply isolating more cells and toward isolating the right cells — defined by function, phenotype, and therapeutic potential. As we better understand how specific immune cell states drive efficacy, it will no longer be sufficient to deliver a highly pure population if those cells lack the characteristics needed for durable clinical benefit. Technologies that can selectively enrich for therapeutically relevant subsets, such as central memory cells, while preserving cell fitness and functionality, will be critical to the next generation of cell therapies.