Innovating for the future: Accelerating the arrival of immuno-oncology 2.0

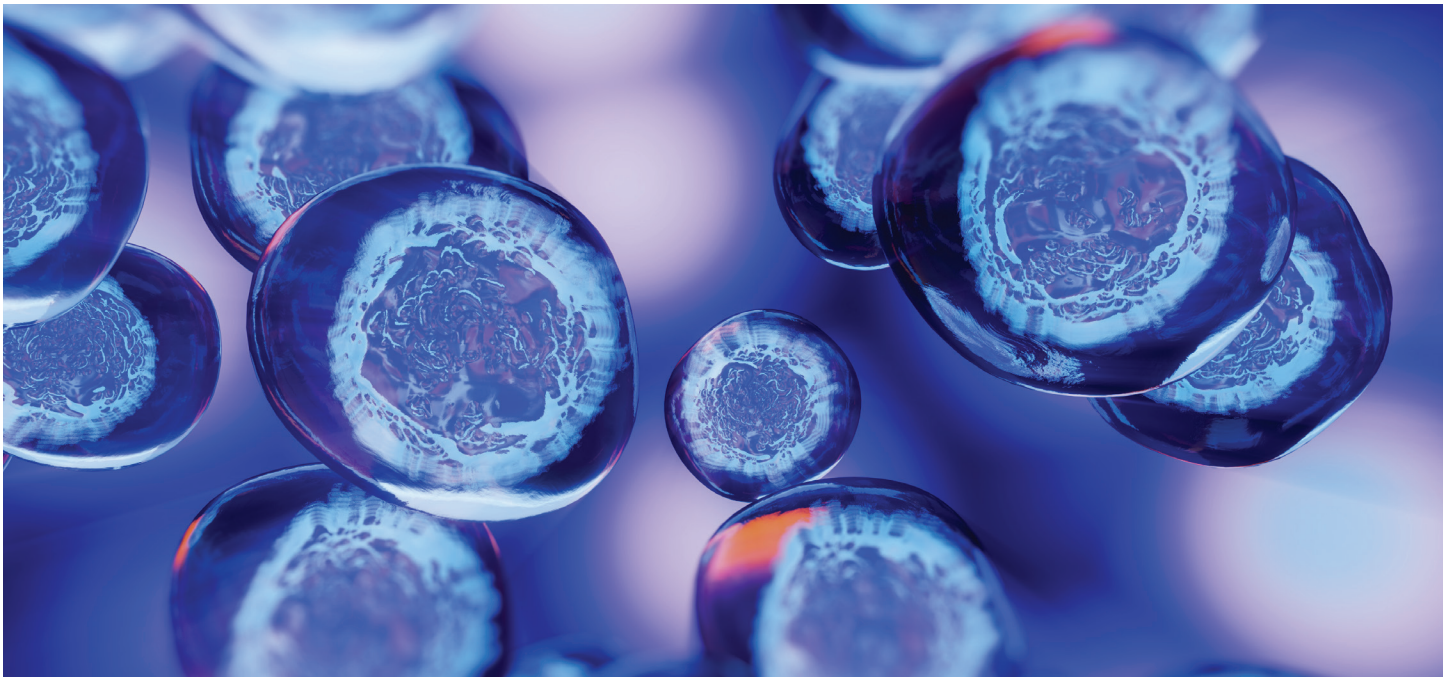
There is little doubt that immuno-oncology has become one of the most exciting and dynamic fields in modern medicine, particularly following the regulatory approval of the first chimeric antigen receptor (CAR) T cell therapies—Kymriah® from Novartis, Yescarta® from Kite Pharma, and, most recently, Breyanzi© from Bristol-Myers Squibb.

In addition, there are several next-generation therapeutics on the horizon, and many technical achievements such as improvements in CAR engineering that have led to increased efficacy.

Alongside these developments is a growing interest in a proposed new era of optimized cell therapy manufacturing —referred to as “immuno-oncology 2.0”.

However, before further progress is made, there remain several challenges facing the development of optimized manufacturing processes. There are also still many hotly debated questions surrounding the overall future direction of the industry. These range from deciding on the best automation strategy to the choice of pursuing either autologous or allogeneic platforms when innovating new treatments.

To overcome these challenges and begin answering these questions, there are three key areas where development and collaboration are needed: innovation of analytical equipment, automation of processes, and scalability of manufacturing. By enabling the delivery of solutions in these areas, the new era of manufacturing can begin, and the next generation of cell-based immunotherapies can reach patients.



Innovation of analytical equipment

Currently, the biggest technological gaps in the immuno-oncology field are related to the lack of tools to enable detailed analysis of cells, especially in terms of characterization during early development. These are particularly vital since being able to connect characterization with functionality at the earliest possible stages can enable further development in other areas such as manufacturing efficiency and automation.

The limitations in this area have mainly resulted from a past imbalance of innovation. Primarily, the overall industry has been focused on developing equipment to enable more efficient processing of cells rather than robust characterization. The lasting impact of this is that many current assays are designed for academia rather than commercial manufacture. This means they are low-throughput and require technical knowledge and thus incur a significant time cost and need a skilled team of scientists to successfully operate.

These technology gaps have been further exacerbated by the limited cooperation between pharmaceutical companies and instrumentation developers when it comes to identifying industry needs. In the immuno-oncology field, there has been a widespread tendency for pharmaceutical companies to overcome their inability to patent therapies by instead focusing on protecting their process. This greatly limits the communication of their precise instrumentation needs, which in turn limits the ability of developers to meet the overall needs of the entire industry.

The insular nature of cell therapy manufacturing within pharmaceutical companies also has led to a lack of standardization, which itself presents challenges. This is because when collaboration does occur, it is usually in the form of intensive one-to-one relationships, resulting in the development of highly process-specific equipment rather than technological advancements that are beneficial to the wider industry.

Automation of processes

Another area where innovation is needed, with respect to both analysis and manufacture, is automation. There are many industry-wide advantages to implementing automation within workflows, including improved consistency and efficiency. There are also more specific benefits, such as overcoming the shortage of experienced specialists within the cell and gene therapy field.

When it comes to automating the manufacture of immuno-oncology therapeutics, there are two distinct approaches—single-unit and modular—each with their own advantages and disadvantages.

Utilizing a single-unit approach allows for the design of an integrated closed system with a validated workflow, which can greatly increase efficiency and reduce long-term costs while minimizing risk for single-dose autologous cell therapies. However, in many cases this involves relying on one piece of equipment and one vendor for the entire process, so even a single technical or supply chain issue can be tremendously disruptive. By taking a modular approach instead, nonfunctional units can be easily swapped, increasing robustness as well as providing an increased capacity for dynamic evolution over time.

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For many, the optimal automation strategy may appear to depend on the current stage of development. For example, it may be beneficial to start with a modular approach during process optimization and then migrate to a single-unit approach once the process is more defined. However, recently it has become more apparent that it may in fact be more dependent on the type of therapy.

This is due to the changing perspective around the ultimate uses of autologous and allogeneic platforms. As autologous therapies become increasingly individualized, they are likely to be produced using an exact workflow provided at the point of care.

Scalability of manufacturing

The divergence of industry needs, depending on whether an autologous or allogeneic platform is used, can also be seen in terms of the scalability required within the manufacturing process itself.

While there is, of course, always a need to scale up from the initial R&D stages to a commercial manufacturing platform, individualized autologous treatments are likely to be permanently manufactured in relatively small volumes. In addition, there is the growing opportunity to use the human body itself for cell expansion, meaning that only the upstream processes—such as isolation, activation, and vector transduction—need to be carried out *ex vivo*. Overall, this means that the manufacturing time of autologous drugs will most likely become shorter, resulting in lower cost of goods.

On the other hand, true scalability is going to be essential for future allogeneic therapies—not only to enable initial cell expansion, but also to enable large-scale bioproduction with volumes entering the hundreds, if not thousands, of liters while maintaining efficacy and quality. Due to the current lack of specific technologies for this, automated equipment for allogeneic therapy manufacture is one of the solutions in the highest demand within the field. There is also high demand for innovative media for use in manufacture that promote strong T cell proliferation, maintain the central memory phenotype, and allow for higher production of interferon-gamma with healthy donor cells.

It is also critical to consider the logistics of storing allogeneic CAR T cell therapies and, crucially, transporting them from manufacturing facilities to the desired patients or sites. As this involves a complex cold chain, the expansion of infrastructure to facilitate this is vital to support large-scale manufacture.

Innovating for the future

Overall, it is clear that the future of immuno-oncology is bright, and that many exciting developments will continue to emerge. However, the wait before they are translated into licensed therapeutics that are available to patients in the clinic remains uncertain.

It is not simply enough for innovation in the areas of analytics, automation, and scalability to continue. To enable true efficiency in this process there is also a vital need for enhanced collaboration between stakeholders across the entire industry. Only by working together can precise industry needs be identified, best-in-class solutions be developed, and, crucially, the arrival of immuno-oncology 2.0 be accelerated.

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