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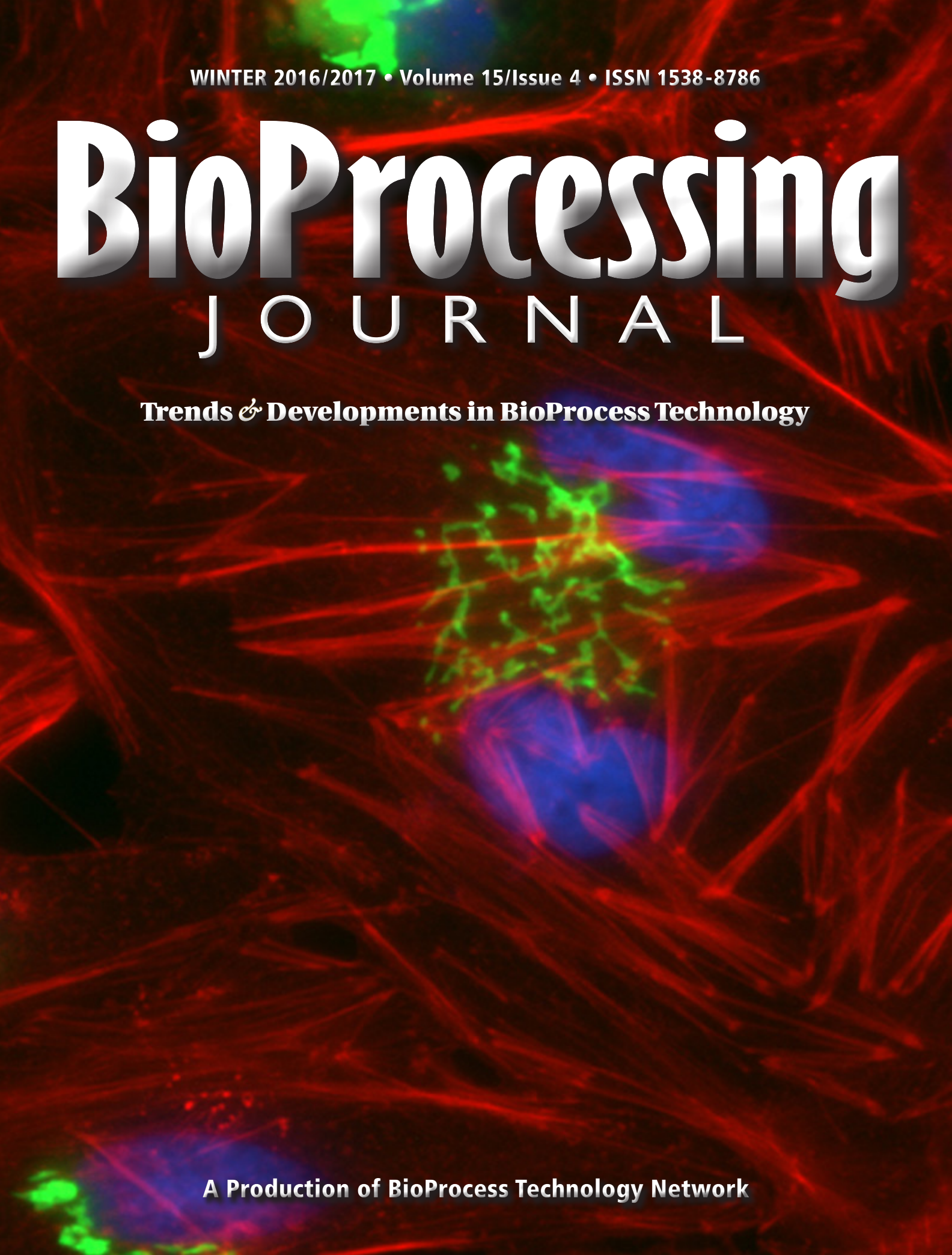
BioProcessing JOURNAL

Trends & Developments in BioProcess Technology

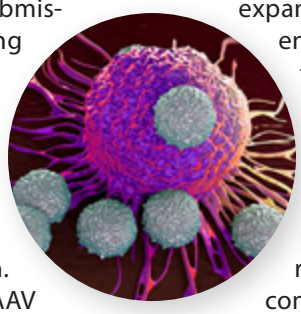


A Production of BioProcess Technology Network

From The Editor-In-Chief:

There are so many exciting things happening in the biotech industry. As we have all seen, antibody products are being approved for more and more cancer applications, in addition to those for auto-immune diseases, which used to dominate how they were being used. And of course, these applications are in addition to the many which use antibodies conjugated to chemotherapeutic drugs and imaging agents—where the antibody acts as a targeting mechanism. Then there are the hundreds of monoclonal and polyclonal antibody applications that have dominated diagnostic testing for decades.

But what really demands my attention are the advancements we are seeing with viral gene vectors, cellular and regenerative tissue therapies, and sub-unit vaccines. Apparently, the FDA is being flooded with submissions for potential AAV applications involving a number of serotypes (AAV2, 8, 9, *etc.*), as well as processes that result in both higher yields and fewer empty capsids. And we're no longer limited to transient transfection techniques with the development of an increasing number of stable, transfected cell lines for both AAV and lentivirus production. Then to make matters even more interesting, AAV production is still split between the use of human cell lines (*e.g.*, HEK-293 and PER.C6), and baculovirus expression in insect cells.



And some incredibly hot applications are those in which lentiviruses are being used to transfect a patient's cells for chimeric antigen receptor (CAR) T-cell therapies. These applications have become so prevalent and successful that the early developers are being considered for a Nobel Prize, and lentiviral vectors, primarily HIV-1, are second only to AAV in the Investigational New Drug (IND) submissions for viral vectors. Then lentivirus production has progressed to impressive yields in anchorage dependent HEK-293T cells that are being propagated in multi-plate devices such as Nunc's™ (Thermo Fisher Scientific) Cell Factory™ and Corning's® CellCube®, as well as a number of packed-bed systems, including the iCELLis® bioreactor now available through Pall Life Sciences. In addition, advancements are being made in adapting the HEK-293T cells to suspension with serum-free media, and formulations have been developed that can keep lentiviral vectors stable without the use of serum.

Characterization techniques have become ever more powerful for viral vectors, and this is making it far easier to compare production lots, evaluate transfection efficiency, and establish potency. And another field which is becoming more controllable and quantitative is the gene editing that is done to quantitate expression and eliminate replication competency of the vectors used for transfection.

Then for cellular therapies, products are becoming more and more effective, but they are still dominated by autologous applications which involve the patient's own cells, and limited success with cryopreservation restricts these applications to each treatment being a new batch. Costs remain extremely high, and patients are often left in a highly vulnerable condition as they wait for their cells to be expanded and transfected. So these already weakened patients must be further stressed to receive these treatments, and early-stage clinical trials are made that much more difficult.

And finally, the production facilities are becoming more and more flexible so that product changeover is becoming faster, and product containment is becoming more reliable. Then single-use process systems and components are dominant for almost all product types. However, air handling remains a challenge for viral applications where most processing suites are being designed for single-pass air, which is very expensive to operate. But at a minimum, air can be recirculated within a processing suite where a small percentage of make-up air is brought in from the outside.

Therefore, many of the toughest biological products are becoming easier to produce at higher volumes with increased yields and transfection efficiency. And advances in analytical techniques are making product characterization and comparison much faster and easier. But improvements are still needed in cryopreservation so that cellular therapies aren't so limited to autologous applications, and multiple treatments can result from a single patient extraction.

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