ACCELERATING ADENOVIRUS MANUFACTURING BY PERFUSION-BASED PROCESS OPTIMIZATION

Carina C D Joe, Jenner Institute, University of Oxford, Oxford, UK
Piergiuseppe Nestola, Sartorius Stedim Biotech GmbH, Goettingen, Germany
Nitin Chopra, Sartorius Stedim Biotech GmbH, Goettingen, Germany
Steffi Scholze, Sartorius Stedim Biotech GmbH, Goettingen, Germany
Julia Niemann, Sartorius Stedim Biotech GmbH, Goettingen, Germany
Yuanyuan Li, Jenner Institute, University of Oxford, Oxford, UK
Rameswara R Segireddy, Jenner Institute, University of Oxford, Oxford, UK
Alexander D Douglas, Jenner Institute, University of Oxford, Oxford, UK

Key Words: Chimpanzee adenovirus-vectored vaccine, perfusion, Ambr® 250, process intensification

Adenovirus vectors offer a rapidly adaptable and deployable platform with proven safety and efficacy. Properties such as suitability for refrigerated storage, ability of a single dose to achieve protection lasting months, and widespread manufacturing technology transfer make the platform particularly attractive in low- and middle-income countries.

In this presentation we optimized adenovirus vector manufacturing for rapid response, by minimizing time to clinical trial and first large-scale supply and maximizing the output from the available manufacturing footprint.

We described a new perfusion-based upstream production process, designed to maximize output while retaining simplicity and suitability for existing manufacturing facilities. This improves upstream volumetric productivity of ChAdOx1 nCoV-19 by around four-fold and remains compatible with the existing downstream process, yielding drug substance sufficient for 10000 doses from each liter of bioreactor capacity.

Here, we demonstrate that medium exchange using ATF can raise the cell density effect 150 barrier for production of ChAdOx1 nCov-19. Using the simplest possible perfusion manufacture conditions, we show that increasing viable cell density at infection to 6×10^6 cells/mL improves volumetric productivity by approximately four-fold, with no loss of cell-specific productivity. We also provided a workflow for rapid production of working virus seed to support our new process at global scale, enabling large-scale vaccine release within 100 days from pathogen sequence identification. Using a techno-economic model of the new method at large scale, we estimated the output from a typical facility, cost of goods, and the facility scale needed to produce 1 billion doses of a future vaccine within 130 days of genomic sequencing of a novel pathogen.

This accelerated manufacturing process, along with other advantages such as thermal stability, supports the ongoing value of adenovirus-vectored vaccines as a rapidly adaptable and deployable platform for emergency response.