EXTENSIVE UTILIZATION OF CELL CULTURE BASED VACCINES IN THE MODERN SCENARIO

JAINTH, S.² AND GUPTA, M.

Department of Scientific Research, Mahatma Jyoti Rao Phoole University, Jaipur,

E. mail: rubyharshita@gmail.com

Received: August, 14, 2014;

Abstract: Hopes of growing poliovirus in the lab without the use of live animals drove many of the researchers in the 1930s and 1940s. Cell cultures involve growing cells in a culture dish, often with a supportive growth medium like collagen. They offer a level of control that was unavailable using live animals, and can also support large-scale virus production. (For more about cell cultures and cell lines, as well as cell lines made using human cells, see our article “Human Cell Strains in Vaccine Development.”) Early efforts to grow poliovirus in culture, however, repeatedly ended in failure. In 1936, Albert Sabin and Peter Olitsky at the Rockefeller Institute successfully grew poliovirus in a culture of brain tissue from a human embryo. The virus grew quickly, which was promising, but Sabin and Olitsky were concerned about using this as starting material for a vaccine, fearing nervous system damage for vaccine recipients. They tried to grow poliovirus in cultures using tissue that had been taken from other sources, but were unsuccessful. Today, many different animal cell strains are available for use in scientific research and development. Several vaccines currently available in the United States were developed using the Vero cell line, started from African green monkey kidney cells: Rotavirus vaccines (Rotarix/GlaxoSmithKline, RotaTeq/Merck), Polio (IPOL/Sanofi Pasteur). Smallpox (ACAM2000/Sanofi Pasteur – Used only for selected military personnel). Japanese encephalitis (Ixiaro/Intercell – Used only for those traveling to areas with known outbreaks of disease). Future U.S. vaccines may use other animal cell strains, including the Madin Darby Canine Kidney (MDCK) line, which was started in 1958 with kidney cells from a cocker spaniel. (Some European vaccines are already made using MDCK.)

Key words: Cell cultures based vaccines

Cell culture-based vaccines have been developed in order to address concerns about the limitations of egg-grown influenza vaccines. It was recognized that in the event of a pandemic, the available egg-grown influenza vaccine would be insufficient to meet global demand and that supplies of vaccine, traditionally grown in hens’ eggs would be threatened if birds were also vulnerable to infection from the pandemic virus strain (as is the case with H5N1 (avian flu)). Additionally, increasing demand for seasonal influenza vaccines have also increased the need...
to explore new methods of influenza vaccine production [1].

**METHODOLGY**

In order to make cell culture-based influenza vaccines, frozen, preserved cells are taken from storage and grown in an incubator at 37°C. The cells are first grown in a small volume of culture medium. As the cells grow and multiply they are transferred to successively larger containers. On reaching a certain volume, influenza seed virus, obtained from the World Health Organization, is added to the cell-containing bioreactor (container) where the virus then infects the cells and multiplies, making more virus particles [2,3]. After several days the influenza virus has infected and destroyed all the cells in the bioreactor. The virus is then harvested by removing the debris made by the cells and made non-infectious, before being further purified. This purified, non-infectious solution is then blended, concentrated and filled into syringes or vials ready for use.

**RESULT AND DISCUSSION**

Leading manufacturers of vaccines and antiviral drugs are working hard to develop new and novel methods of preparing seasonal influenza vaccines, as well as pandemic vaccine candidates [4]. Until recently, most efforts have been focused on improving currently licensed egg-based vaccines. Manufacturers have been racing to increase production capacities and automate portions of largely manual steps in egg-based vaccine technology to meet the demands of the next seasonal campaign and to generate prototypes of pandemic vaccines for clinical trials. At least 30 clinical trials of avian pandemic prototype vaccines are in progress, and manufacturers are working with international agencies, such as the World Health Organization, European Medicines Agency, and the National Institutes of Health, on the development, licensing, and production of pandemic vaccines on a global scale. Currently, about 25 of these projects are based on classical egg-based technology, and six are based on cell-culture systems (Chiron has one cell-culture vaccine in the final stages of development and approval by regulatory agencies). Cell-culture technologies may offer distinct advantages over egg-based manufacturing methods. They eliminate the need for embryonated chicken eggs from managed, biosecure flocks. They combine and automate upstream and downstream processes. They reduce the potential for contamination by viable and nonviable particulates [5].

They eliminate the four- to six-month lead times for the organization of egg supplies. They have faster, high-volume start-up times for production. They have higher initial purity. They could supplement seasonal vaccine supplies when multiple strain changes are necessary. They would substantially increase global stockpiles of pandemic influenza vaccines.

**CONCLUSION**

Cell-culture-based technology is robust and reliable and could become a practical alternative for the pharmaceutical industry in vaccine production. Once the virus is propagated and harvested, the downstream processing parameters for purification, filling, and packaging of the vaccine are similar to current pharmaceutical methodologies and egg-based methodologies. However, there are no lead times involved, because typical cell-culture processes use cell lines; once a cell line is infected with the seed virus in a fermenter, the process can begin. The critical step is the availability of the seed virus. The substrates or media for cell-line propagation are not susceptible to virulent virus strains as embryonated chicken eggs are. The cell-culture vaccine process is suitable for large-scale manufacture, and the process parameters can be ramped up and run routinely and cost effectively.

The typical cell-culture production process can be run in batch sizes of practical scale, sufficient to provide vaccine quantities for interpandemic periods and pandemics. However, to date, no vaccines have been licensed using this technology. Chiron has already submitted “mock-
up” dossiers to European Union (EU) regulatory authorities for review and approval of an avian influenza vaccine (currently in clinical trials) and a license application for a cell-culture-based vaccine. This paper is focused on the cell-culture vaccine manufacturing process used by Chiron, as well as the use of adjuvants to enhance immunogenicity and reduce dosage size [6].

REFERENCES


