SIMPLE AND ROBUST DOWNSTREAM PURIFICATION PROCESS FOR CELL-DERIVED INFLUENZA VACCINES

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New emerging influenza viruses with pandemic potentials were occurred in recent years, e.g. H5N1 in 1997, H1N1 in 2009, and H7N9 in 2013. The demand of producing pandemic influenza vaccines for human use with quick supply is high. For the cell-based pandemic influenza vaccines, we proposed a flow-through chromatography purification process. This process has only involved few purification steps and is easy to operate. Vero- and MDCK- cell derived avian influenza viruses including H5N1 and H7N9 were purified efficiently by the process proposed.

The presented purification process consisted of clarification, inactivation, concentration, anion exchange chromatography (Capto Q), size exclusion and adsorption chromatography (Capto Core 700), diafiltration and sterile filtration. In the chromatography steps, cell DNA and protein were removed remarkably, and the virus were flowed through these columns. The flow rate was set as fast as 250 cm/min. The loading volume of virus solution was up to 50 times of column volume (CV).The DNA was removed over 90% after using Capto Q column, and was further removed by Capto Core 700 column. The overall removal rate of cellular DNA was more than 99%. The HA recovery rates of H5N1 and H7N9 influenza virus from Vero and MDCK cells were 20 to 40%. The DNA concentration of all purified bulks met the regulatory requirement of 10ng per dose. The developed purification process is simple and efficient, and it is suitable for purification of various influenza virus strains and can be used for the pandemic influenza vaccine production.