LOW-COST CELL-BASED PRODUCTION PLATFORM FOR SEASONAL AND PANDEMIC INFLUENZA VACCINES

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Influenza-related illnesses have caused an estimated over million cases of severe illness, and it has about hundred thousands of deaths worldwide annually. Traditionally these vaccines are produced in embryonated chicken eggs. However, in the case of a pandemic outbreak, this egg-based production system may not be quickly enough to meet the surging demand. The efficacy associated with egg-based vaccines are low in recently years. The raising concerns with egg-derived vaccines is resulting in the spurred exploration of alternatives. MDCK cells are becoming as an alternative host to embryonated eggs for influenza virus propagation. Although MDCK cells were considered to be a suitable host for the virus production, their inability to grow in suspension still limits the process of scale-up and their production capability.

Table 1. Virus titers of pandemic and seasonal influenza vaccine strains grown in sMDCK cells.

Virus	Source	HA unit/50 µL	
		received	adapted
A/Vietnam/1194/2004 (H5N1)	NIBSC	512	989
A/Anhui/1/2013 (H7N9)	Egg-derived	256	996
A/Singapore/GP2050/2015 (H3N2)	VIDRL	n.a	n.a.
B/Brisbane/63/2014 (Victoria)	Cell-derived	1337.2	1708.8
B/Brisbane/9/2014 (Yamagata)		838.2	1552.9

In this study, NHRI, Taiwan and Irvine Scientific, USA has developed a suspension MDCK cell line and proprietary medium (BalanCD simple MDCK). The cell concentration of the suspension MDCK (sMDCK) cells up to 2×10^6 cells/ml after 96 hrs was obtained, and the doubling time of 30-35 hrs was found very similar to the adhesion MDCK (aMDCK)cells cultivated on microcarriers (5g/L). In addition, no fresh medium replacement was necessary in the sMDCK cell culture during the cell growth stage. The H7N9 candidate vaccine virus (NIBRG-268 which was derived from A/Anhui/1/2013) was used and infected both sMDCK and aMDCK cells with a low multiplicity of infection. The harvest of viruses was collected on day three post infection. The HA titers in sMDCK and aMDCK cells were reached to 996 and 574 HA units/50ul, respectively. The results show that the HA titers from both pandemic and seasonal vaccine strains cultured in sMDCK cells are high (see table 1). A similar finding was found in the small-scale bioreactor. The animal study also showed higher immunogenic response over the antigen produced from the aMDCK cell culture. Based on the overall recovery yield (30%) and the consumable cost from medium usage, the production cost is similar to the egg process.

In summary, a new adapted sMDCK cell line was developed. This sMDCK cultured using chemical-define (CD) medium can remain the similar growth rates as aMDCK cells but showed higher viral titers in both pandemic and seasonal influenza strains. Thus, this new combined technology of sMDCK with specifically-optimized CD medium could provide a low-cost vaccine production to the bottlenecks for establishing a large-scale cell culture using adherent MDCK cells.