NOVEL AVIAN DuckCeltTM-T17 CELL LINE FOR PRODUCTION OF VIRAL VACCINES: APPLICATION TO INFLUENZA VIRUSES PRODUCTION

Emma Petiot , VirPath Laboratory EA4610, Université Claude Bernard Lyon 1, Lyon, France
emma.petiot@univ-lyon1.fr
Anais Proust , VirPath Laboratory EA4610, Université Claude Bernard Lyon 1, Lyon, France
Aurélien Traversier, VirPath Laboratory EA4610, Université Claude Bernard Lyon 1, Lyon, France
Manuel Rosa-Calatrava, VirPath Laboratory EA4610, Université Claude Bernard Lyon 1, Lyon, France
Jean-Marc Balloul, Research & Development Department, Transgene, 400 Boulevard Gonthier d'Andernach, France

Key Words: Influenza vaccine, Viral production processes, Avian cells, Process optimization.

For the last 15 years, the viral vaccine manufacturing sector is looking for new producer cell lines, easily scalable, highly permissive to various viruses, and more effective in term of viral productivity. One critical characteristic for such cell lines is their ability to grow in suspension in serum free conditions at high cell densities. Regarding the pathogens under focus, influenza virus causing severe epidemics both in human and veterinary field is an important threat for world healthcare. The manufacturing sector is still demanding effective production processes to replace/supplement embryonated egg-based process and to provide efficient response to such threats. Cell-based production, with a focus on avian cell lines, is one of the promising solutions. Indeed, three avian cell lines ; namely duck EB66®cells (Vivalis), duck AGE.CR® cells (Probiogen) and quail QOR/2E11 cells (Baxter), are now competing with traditional mammalian cell platforms used for influenza vaccine productions (Vero and MDCK cells) and are currently at advance stage of commercial development for the manufacture of vaccine and biologicals [1].

The DuckCeltTM-T17 derived line presented here is a novel avian cell line developed by Transgene SA[2]. To generate immortalized duck cell lines, Transgene has used its proprietary DuckCelT technology which consisted in constitutively expressing the duck telomerase reverse transcriptase (dTERT) in primary embryo duck cells from spf eggs.

DuckCeltTM-T17 cells were able to grow in batch suspension cultures and serum-free conditions up to 7 x 106 cell/ml and such growth was easily scalable in bioreactors up to 3L. Permissivity for different viruses including influenza has been evaluated. In the present study, DuckCeltTM-T17 cell line was tested for its abilities to produce various influenza strains from different origins; human, avian and porcine. All strains were satisfyingly produced with titres higher than 5.8 log TCID50/ml. H1N1 human strains and H5N2 and H7N1 avian strains were the most efficiently produced with highest titres reached of 8 log TCID50/ml. Porcine strains were also greatly rescued with titres of 4 to 7 log TCID50/ml depending of the subtypes. Interestingly, maximal titres are reached at 24h post-infection, allowing to have early harvest time.
Process optimization on H1N1 2009 Human Pandemic strain allowed to identify best operating conditions for production (MOI, trypsin concentration, medium and density at infection) allowing to improve the production level by 2 log.

1. Meyer H-P, Scmidhalter DR: Industrial Scale Suspension Culture of Living Cells. 2014.
2. Balloul Jean-Marc, Duck cell line dedicated to the production of virus-based vaccines and therapeutic products BioProduction Optimization Workshop, September 22 & 23 2010 Frankfurt Germany