USE OF STABLE CHO POOLS AND CHO TGE TO ACCELERATE SARS-COV-2 VACCINE DEVELOPMENT

Yves Durocher, National Research Council of Canada and University of Montreal
Yves.durocher@nrc.gc.ca
Matthew Stuible, National Research Council of Canada
Simon Lord-Dufour, National Research Council of Canada
Simon Joubert, National Research Council of Canada
Sergio Alpuche, National Research Council of Canada
Zalma Vanesa Sanchez Martinez, University of Montreal
Louis Bisson, National Research Council of Canada
Denis L'Abbé, National Research Council of Canada
Joseph Schrag, National Research Council of Canada
Majida El Bakkouri, National Research Council of Canada
Mauro Acchione, National Research Council of Canada
Jason Baardsnes, National Research Council of Canada
Janelle Sauvageau, National Research Council of Canada

Key Words: Quality attributes, trimeric SARS-CoV-2 spike, SARS-CoV-2 eVLPs

Chinese Hamster Ovary (CHO) cells are the workhorse expression host for manufacturing glycoprotein-based therapeutics. Expression from stably transfected CHO clones is the standard method of recombinant protein manufacturing since lower productivity and longstanding regulatory guidelines have restricted the use of alternative approaches such as non-clonal stable pools and transient gene expression (TGE). The performance of stable CHO pool and TGE methods have improved dramatically in recent years, making them viable options for the rapid production of drug substances for GLP-toxicology and early-phase clinical trials. The current pandemic has clearly contributed to a wider acceptance of these approaches by the regulatory authorities in order to accelerate clinical evaluation of potentially life-saving drugs (e.g. mostly SARS-CoV-2 neutralizing antibodies). Using our cumate-inducible stable CHO pool generation platform, we have been able to produce SARS-CoV-2 spike protein variants at 100-1000 mg/L levels. Using a robust generic 3-step chromatographic process, we obtained >95% pure trimeric spike proteins with an overall recovery of >40%. We have shown that these trimeric spike proteins are highly immunogenic in mouse and effectively protect Golden Syrian hamsters against viral challenges. We also demonstrated that quality attributes of spike protein produced from stable CHO pool are very similar to that obtained from stable CHO clones. This antigen thus shows very strong manufacturability potential compared to many licensed COVID19 vaccines or other candidates under development. We also demonstrate that CHO cells represent an efficient platform for the production of SARS-CoV-2 eVLP that are highly immunogenic in mouse and hamster models.

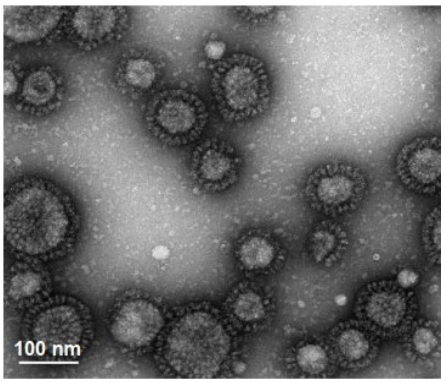

Figure 1. Purified SARS-CoV-2 VLPs produced by CHO cells