ADDRESSING THE CHALLENGES OF INFLUENZA VIRUS-LIKE PARTICLES PURIFICATION

Cristina Peixoto, iBET; Instituto de Tecnologia Química e Biológica António Xavier, Universidade Nova de Lisboa, Portugal
peixoto@ibet.pt
Sofia B. Carvalho, iBET; Instituto de Tecnologia Química e Biológica António Xavier, Universidade Nova de Lisboa, Portugal
A. Raquel Fortuna, Max Planck Institute for Dynamics of Complex Technical Systems, Germany
Michael Wolff, Max Planck Institute for Dynamics of Complex Technical Systems; Institute of Bioprocess Engineering and Pharmaceutical Technology, University of Applied Sciences Mittelhessen, Germany
Udo Reichl, Max Planck Institute for Dynamics of Complex Technical Systems, Otto von Guericke University Magdeburg, Germany
Paula M. Alves, iBET; Instituto de Tecnologia Química e Biológica António Xavier, Universidade Nova de Lisboa, Portugal
Manuel J.T. Carrondo, iBET; Departamento de Química, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal

Key Words: downstream processing; membrane adsorption chromatography; vaccine production; virus-like particle.

Virus-like particles (VLPs) have been widely used in vaccine development over the last decades [1]. In fact, there are already several approved human vaccines against viruses that use recombinant VLPs as antigen, e.g. for hepatitis B virus and human papillomavirus [2]. Vaccination remains the most effective way to prevent infection with influenza viruses. However, their constant antigenic drift requires an annual update of the seasonal vaccine to prevent influenza epidemics [3-4]. To use the full potential of VLPs as vaccines efficient upstream processing as well as downstream processing (DSP) trains need to be established. The latter is of particular importance as it often accounts for the major biomanufacturing costs. Here we describe the establishment of an improved DSP unit train platform, adapted from virus particles to influenza VLPs, using pseudo-affinity sulfated cellulose membrane adsorbers (SCMA) [5]. An initial clarification step prepares the bulk for the subsequent purification steps. SCMA performance was optimized using a design of experiments (DoE) approach. More than 80% of the product was recovered with removal of host cell protein and DNA above 89% and 80%, respectively. This represents a significant improvement in performance compared to the traditional use of ion exchangers commercially available. Using this SCMA platform for influenza virus particles purification we were able to speed up the process by decreasing the number of DSP steps, to improve the scale-up and to reduce costs due to the removal of other chromatographic steps.

References

[1] L. Lua, et al., Biotechnology and Bioengineering, 111(3): p. 425-440 (2014).
[2] Q. Zhao, et al., Trends in Biotechnology, 31(11): p. 654-663 (2013).
[3] D. Smith, et al., Science, 305(5682): p. 371-376 (2004).
[4] C. Thompson, et al., Virology Journal, 10 (2013).
[5]M. Wolff, and U. Reichl, Expert Review of Vaccines, 10(10): p. 1451-1475 (2011).