

Spring 5-9-2016

Purification of a hepatitis C vaccine candidate: Comparison between multi- column chromatographic processes operated in positive and negative mode

Ricardo Silva
iBET, rsilva@ibet.pt

Alex Xenopoulos
EMD Millipore

Paula Alves
iBET

Manuel Carrondo
iBET

Cristina Peixoto
iBET

Follow this and additional works at: http://dc.engconfintl.org/cellculture_xv

 Part of the [Biomedical Engineering and Bioengineering Commons](#)

Recommended Citation

Ricardo Silva, Alex Xenopoulos, Paula Alves, Manuel Carrondo, and Cristina Peixoto, "Purification of a hepatitis C vaccine candidate: Comparison between multi- column chromatographic processes operated in positive and negative mode" in "Cell Culture Engineering XV", Robert Kiss, Genentech Sarah Harcum, Clemson University Jeff Chalmers, Ohio State University Eds, ECI Symposium Series, (2016). http://dc.engconfintl.org/cellculture_xv/18

This Abstract is brought to you for free and open access by the Proceedings at ECI Digital Archives. It has been accepted for inclusion in Cell Culture Engineering XV by an authorized administrator of ECI Digital Archives. For more information, please contact franco@bepress.com.

PURIFICATION OF A HEPATITIS C VACCINE CANDIDATE: COMPARISON BETWEEN MULTI-COLUMN CHROMATOGRAPHIC PROCESSES OPERATED IN POSITIVE AND NEGATIVE MODE

Ricardo Silva, iBET

rsilva@ibet.pt

Alex Xenopoulos, EMD Millipore

Paula Alves, ITQB-UNL/iBET

Manuel Carrondo, FCT-UNL/ITQB-UNL/iBET

Cristina Peixoto, ITQB-UNL/iBET

Key Words: Continuous Chromatography, Multi-Column Processes, Virus-Like Particles, Vaccines.

Given the increasing efficiencies in bioreaction and growing interest on complex biopharmaceutical products such as virus-like particles (VLPs), downstream processing (DSP) is becoming ever more relevant. Therefore, the biopharmaceutical industry is looking for alternative downstream strategies capable of improving purification yields whilst improving product quality and lowering costs. One of most promising improvements to DSP is to replace single-column batch operation by continuous, or semi-continuous, multi-column chromatography.

We report on the development and comparison of two types of multi-column chromatographic systems aimed at the purification of Hepatitis C VLPs, produced using insect cell-based expression with recombinant baculovirus. The first process described herein is based on direct product capture using an anion exchange chromatographic media and subsequent elution with the modulation of ionic strength. By using a multi-column approach, one is able to overcome the limits of dynamic binding capacity characteristic of single-column batch processes, thus increasing the media capacity utilization. The second process reported is based on negative chromatographic purification. In this approach elution conditions are such that impurities should adsorb on the chromatographic media whereas the product of interest flows through the column. Both process approaches are subjected to a temporal arrangement of operations steps suchlike column equilibration, product application, production and regeneration. Volumetric productivity thus depends not only on the optimal scheduling of the referred steps, but also upon factors such as media capacity for the product and related impurities, operational flow-rates, and mechanical limitations of the systems used.

The proposed analysis compares volumetric productivity, resin capacity utilization, equipment footprint and skid complexity for both purification strategies. Also we will demonstrate that the optimal design is a balance between the manufacturing scale, complexity and imposed product quality requirements.