CONTINUOUS BIOPROCESSING for BIOLOGICS MANUFACTURING

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Various strategies are explored for continuous bioprocessing for manufacturing of recombinant proteins and monoclonal antibodies: 1. continuous perfusion culture plus batch product capture; 2. continuous perfusion culture plus semi-continuous product capture; 3. continuous perfusion culture plus continuous product capture (Figure 1). Our main focus has been on the several initial unit operations: high cell concentration perfusion cell cultures and early product capture steps, in order to realize its potentials of being flexible, improving product quality and lowering costs. These initial unit operations require large volumes and represent the most important part of this processing platform, where we can deliver the largest benefits.

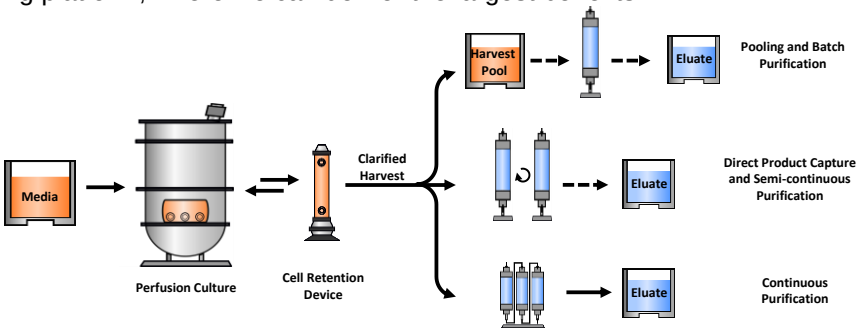

Figure 1 – Strategies for Continuous Bioprocessing

This presentation will focus on two case studies to illustrate these strategies. The first case study focuses on direct scale-up of an ATF (Alternating Tangential Flow) based high cell concentration perfusion culture, from 2L scale coupled with ATF2 to large single use bioreactors of 150-1000L scale coupled with ATF6 or ATF10. Appropriate considerations of agitation and aeration rates, ATF operation parameters as well as bioreactor processing conditions resulted in successful scale-up of more than 100 folds, with highly consistent process performance, productivity and quality of directly captured products.

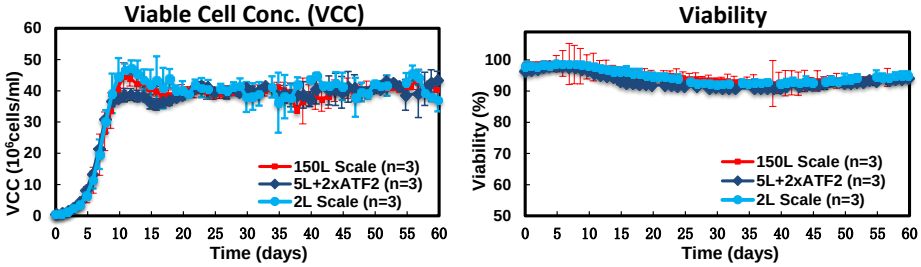

Figure 2 – Consistent Performance between Scale-Up and Scale-Down Models

The second case study involves development of high cell concentration and volumetric productivity perfusion cultures and continuous direct product capture. We will discuss our efforts towards intensified cell culture processes by culture parameter and media optimization, and a continuous direct product capture steps using multiple column chromatography systems. Challenges in connecting these two continuous unit operations will be discussed as well.

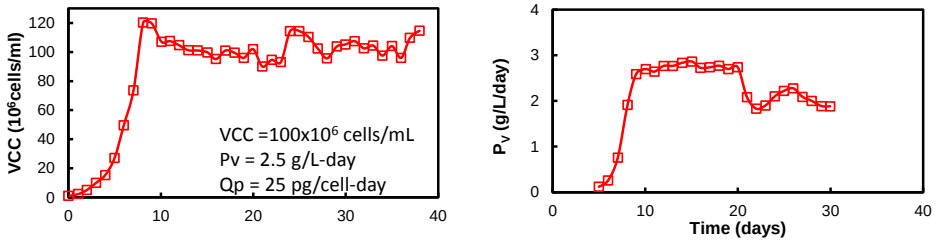

Figure 3 – High VCC and Productivity Perfusion Culture