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## Recommended Citation

[1] Tiainen et al., End-to-end continuous production of complex recombinant proteins – integration of perfusion cultivation and automated multi-step purification [Abstract presented at Integrated Continuous Biomanufacturing I, Barcelona, Oct 2013] [2]  
Åkesson et al., Integrated continuous production - a bench-top factory framework for rapid preclinical supply of fragile proteins [Abstract presented at Cell Culture Engineering XIV, Quebec City, May 2014]

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## **INTEGRATED CONTINUOUS BIOPROCESSING – A GOLD MINE FOR CELL CULTURE PROCESS UNDERSTANDING?**

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We have developed an integrated continuous processing framework for end-to-end production of complex fragile proteins based on perfusion cultivation and automated multi-step purification [1,2]. Upstream, the integrated system consists of a stirred tank bioreactor with an ATF cell retention system. The clarified harvest directly enters an off-the-shelf ÄKTA chromatography system converted into a continuous purification unit. Two alternating capture columns precede a multi-step purification train with full flexibility and control of individual columns.

The integrated set-up enables compact automated bench-top factories converting cell culture media to purified protein in an efficient manner without intermediate storage. It provides monitoring of the production progress allowing for “just-enough” production and better use of resources. Importantly, the integrated approach also enables continuous monitoring of product quality attributes. This aspect is obviously relevant in a manufacturing setting but perhaps even more so during process development to aid deciphering the relation between cell culture performance and product quality.

Case studies from production of fragile proteins for pre-clinical supply will be presented. As an example of process intensification, the combination of the integrated continuous framework with a novel perfusion platform enabled laboratory-scale equipment to produce amounts that previously would have required pilot-scale resources. Examples with disturbances and/or deliberate changes and/or in the cell culture process during integrated processing will be given to illustrate the monitoring benefits from an upstream perspective.

### **References**

[1] Tiainen et al., End-to-end continuous production of complex recombinant proteins – integration of perfusion cultivation and automated multi-step purification [Abstract presented at Integrated Continuous Biomanufacturing I, Barcelona, Oct 2013]

[2] Åkesson et al., Integrated continuous production - a bench-top factory framework for rapid preclinical supply of fragile proteins [Abstract presented at Cell Culture Engineering XIV, Quebec City, May 2014]