

## INTEGRATED SCALABLE CYTO-TECHNOLOGY FOR RECOMBINANT PROTEIN BIOPROCESSING

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Biological knowledge of infectious diseases and other diseases for which vaccines may provide therapeutic benefits, such as cancer, is growing at an accelerated pace. The implications of this knowledge are improved stratification of diseases, possibilities for personalized treatments, and explicit understanding of protective immune responses to be elicited by vaccines. With this knowledge, it is becoming increasingly feasible to engineer vaccines for specific responses rather than relying on empirical development. Despite this potential, the challenge of routine, low-cost manufacturing of vaccines creates a barrier to transforming health care in both high- and low-resource countries. Vaccines today do not benefit from well-defined, platform-like processes for manufacturing, and concepts such as continuous bioprocessing remain largely within the realm of biopharmaceutical products.

The InSCyT platform is an advanced prototype manufacturing system that provides integrated and automated production and purification of multiple protein therapeutics. The system allows end-to-end manufacturing of 100's to 10,000's of doses of recombinant protein drugs in days. It uses a state-of-the-art approach to process design and implementation that takes advantage of a fast-growing, tractable microbial host (*Pichia pastoris*) and continuous processing for automated, hands-free purification through simple 2- or 3-stage chromatographic processes. The platform design is highly modular, allowing facile process development and process deployment for multiple products. This feature emerges from the predictable behavior of the fermentation and cell culture fluids, and rapid cloning of new molecules, that together facilitate fast development of entirely new processes in weeks. To date, this system has been used to reproducibly manufacture high-quality human growth hormone (hGH), granulocyte-colony stimulating factor (G-CSF), and interferon- $\alpha$ 2b (IFN- $\alpha$ 2b) in an integrated, automated manner. The speed of production using the InSCyT prototype allows volumetric productivities that compare favorably to those for mammalian-based production.

This talk will outline the design and capabilities of the InSCyT system, demonstrate the quality of biologic drugs made to date on the system, and outline opportunities for advancing the platform to provide new capabilities in manufacturing recombinant proteins for use in vaccines. As part of a Gates Foundation-funded Grand Challenge called ULTRA, we have begun to assess the feasibility of manufacturing millions of doses of a trivalent recombinant rotavirus vaccine annually on a small-scale production system like InSCyT. Integrated bioprocessing enabled by systems such as these could offer potential advantages for routine production in local regions with minimal infrastructure, and for democratization of manufacturing capacity for new vaccine concepts and personalized treatments in cancer.