

INTEGRATED MANUFACTURING WITH MICROBIAL HOSTS FOR FAST PROCESS DEVELOPMENT AND PRODUCTION

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Integrated and continuously operating processes for recombinant protein drugs that rely on non-mammalian hosts offer potential advantages compared to CHO-based platforms for the rapid production of high-quality biopharmaceuticals. This talk will describe insights and technical advances related to the realization of microbial-based production of proteins gained over the past four years in developing a small prototype system for on-demand production of biologics (Figure).

Key learnings discussed will include: 1) how deep ‘-omic level’ understanding of a minimal yeast genome can inform both strain engineering and defined media formulation for enhanced production; 2) new platformable approaches for rapid *in silico* identification of downstream processes that provide highly orthogonal host-related impurity selectivity between individual chromatographic steps; and 3) examples of integration of these elements to enable hands-free production over days with only minor system changes required to accommodate multiple products.

In total, holistic design principles and integration of knowledge together facilitate rapid process development and speed to production at scales relevant for a variety of use cases. These examples highlight the opportunities for employing well-defined alternative hosts with tractable genomes in efficient integrated processes for agile manufacturing. Such strategies should complement on-going and existing efforts to convert CHO-based platforms into continuous operations.

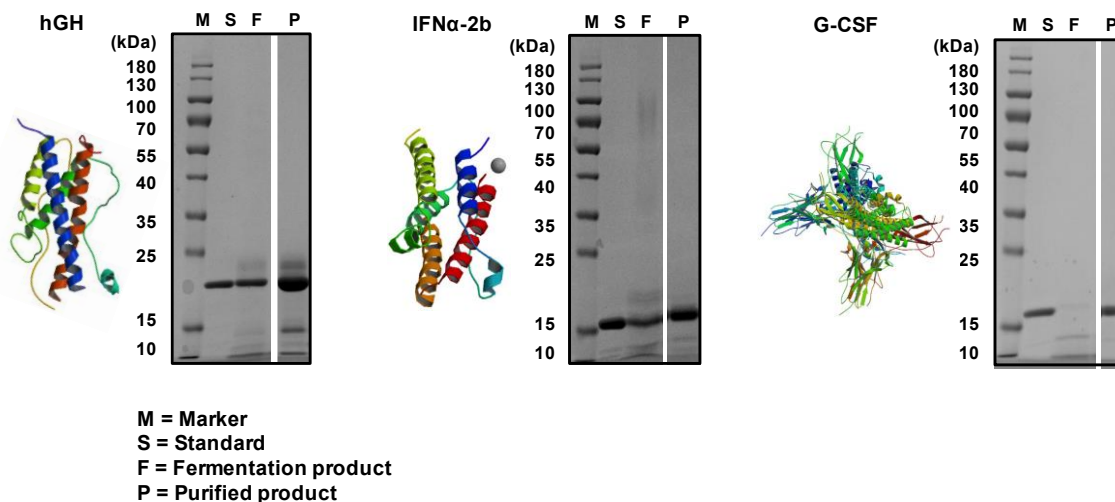


Figure. Non-platformed protein drugs produced by integrated manufacturing with microbial hosts. Examples of three non-platform products produced by *Pichia pastoris* and purified using new approaches determined for purification using *in silico* methods.