01.ALBUMIN INTERIM CASE STUDY

High quality vaccine ingredients for the many, not the few

In the realm of global health, cost often limits access to life-saving vaccines, especially in low and middle-income countries (LMIC). For years a key ingredient for vaccine manufacturing, recombinant albumin, has kept high-quality formulations of these preventative medicines out of reach for millions of people, due to its high price and limited availability.

As of now, recombinant proteins are being sold to premium markets at high prices because - rightly or wrongly - existing suppliers are protecting their manufacturing know-how and letting market dynamics do the rest.

Problem

Restricted access to high quality albumin is not just a threat to the lives of children in LMICs. Cell and gene therapy (C&GT) - which is widely considered to be critical in the future of medicine - depends on high quality cell culture media, many of which contain albumin.

More immediately, an albumin bottleneck also threatens to drive up the cost of biosimilars that require it for their manufacture or formulation, deterring competition on both price and quality.

For those who care about equitable healthcare, the stakes are therefore high.

Solution

Phenotypeca's goal, supported by the Bill & Melinda Gates Foundation, is to optimise strains of *Saccharomyces cerevisiae* (baker's yeast) to produce animal-free, high-quality recombinant albumin at commercial scale using methods adapted to manufacturing in developing countries. This approach is designed to ensure maximum quality and net yield, thereby reducing supply costs.

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Approach

The approach taken was to:

- Use *Saccharomyces cerevisiae* strains with genomes that can be optimised for specific manufacturing processes - which is not realistically feasible for mammalian and prokaryotic expression hosts, such as CHO and *E. coli.*
- Generate a genetically diverse library of around one billion progeny strains, all containing specific engineering to improve albumin production.
- Select individual progeny with new properties (called phenotypes) advantageous for manufacturing in developing countries.
- Identify the underlying genetic improvements, providing IP protection for the new processes.

Outcomes

The first phase of the project has already been a resounding success.

New approach

Protected know-how has been avoided. We've developed a reliable strain development process that:

- Identified additional phenotypes valuable for robust, sustainable manufacturing in LMICs.
- Provides strains for manufacturing recombinant human albumin (rHA) at commercial scale.
- Develops strains with improved performance during fermentation at elevated temperatures, cell harvesting and downstream processing.

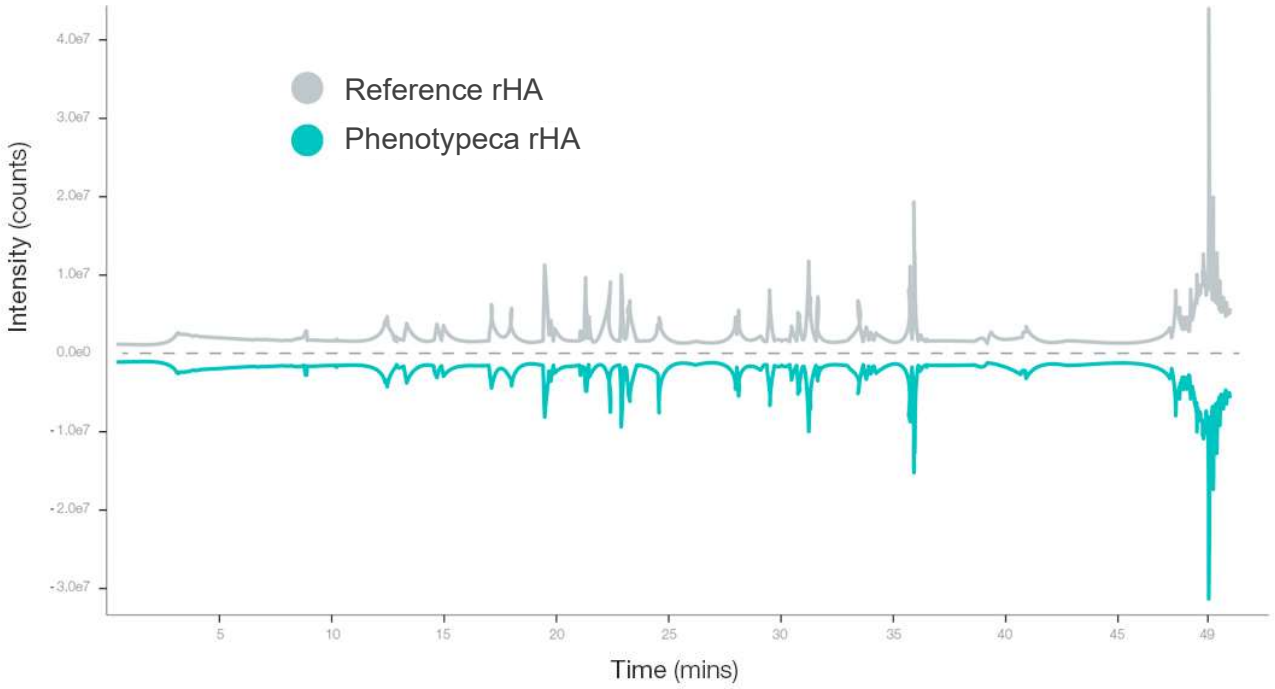
Better yield

Strains have been established to secrete recombinant albumin at 5-10 times higher levels compared to the initial strains.

High quality

High-sensitivity mass spectrometry analysis has indicated that our purified recombinant albumin from yeast is:

- Superior to human plasma-derived albumin.
- Equivalent to the recombinant control standard.
- Matching the highest quality recombinant albumin on the market - vital for stabilising childhood vaccines.



The figure above shows a total ion chromatogram for Phenotypeca's recombinant albumin indicating its identity and high quality compared to the quality reference standard albumin. Data was generated using an LC-MS Sciex ZenoTOF 7600 MS with an upstream Waters Acquity HPLC.*

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Benefits

Turning innovative science into lifesaving vaccines on the ground requires more than laboratory work. The Bill & Melinda Gates Foundation is also playing a key role in helping to identify manufacturing partners who are equipped to produce commercial quantities of albumin for use in LMIC vaccines such as measles and rubella.

The successful outcomes of this project have demonstrated the power of collaboration in advancing global health. The project also highlights how Phenotypeca's QTL technology can provide cost-effective technical solutions at commercial scale where existing methods fall short. This is especially true for biosimilars and novel therapeutics where optimised manufacturing is key for market success.

Phenotypeca adds value by improving process yields and downstream product recovery. It reduces the investment needed to meet market demand - and generates valuable IP to protect your market lead.

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** Mass spectrometry was performed by David J Boocock and Clare Coveney at the John van Geest Cancer Research Centre, Research Centre for Systems Health and Integrated Metabolic Research (SHiMR), Nottingham Trent University, NG11 8NS.*

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