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QUIESCENT CELLS (Q-CELLS)

Summary

Developed in the laboratory of Dr David Summers (Department of Genetics), Q-cells provide a key process innovation for the low cost manufacture of products in recombinant *E.coli.* The technology enables biomass to be accumulated then switched from growth to product production using an ultra-low cost chemical switch

Key features/advantages

- Indole induced cessation of cell division and growth
- Cell resources are directed towards product production, rather than unwanted biomass.
- Q-Cells remain capable of de novo transcription and translation
- Glycolytic pathway remains highly active
- Efficient conversion of C-source to product
- Easily applied to existing production strains
- Temperature independent
- Effective in a variety of production growth media
- System particularly suitable for metabolite production (biorefining)
- Reduced production costs

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Background

Q-Cells are non-growing, but metabolically active *E. coli*. They remain capable of *de novo* transcription and translation. As a novel bacterial cell factory they offer a solution to the problem of maintaining productivity in the absence of cell growth and division. By separating the product production phase from the accumulation of unwanted biomass they offer an efficient conversion of resource (e.g. growth medium C source) to product.

Technology

In the original formulation of the Q-Cell system, expression of a regulatory RNA was used to stimulate indole production in the production strain (ref 1).

Second generation Q-Cells have been designed for much greater ease of use. A specific *hns* mutation is introduced into the client's preferred *E.coli* production strain that can then be switched to quiescence simply by the addition of indole (2-3 mM) to the growth medium (ref 2).

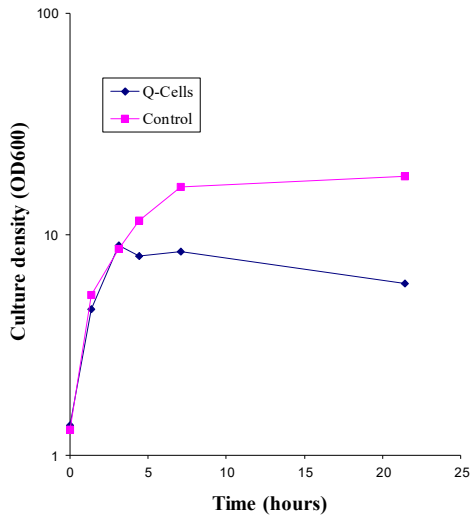
In proof-of-principle experiments 3-hydroxybutyric acid has been produced at 26g.l^{-1} in non-optimised fed-batch Q-Cell cultures. This is a twofold increase in 3-HB yield over the optimized conventional production process (ref 3).

The Market

Q-Cells technology is ideally suited to biorefining and other manufacturing processes that must operate at low cost of goods sold.

Further Developmental Work

The technology has been validated in shake flask culture and small scale fermenters for a variety of metabolite and protein products. The next stage is validation for commercial production targets at process scale.



References

1. Mukherjee, K.J., et al., Studies of Single-Chain Antibody Expression in Quiescent Escherichia coli. Appl. Environ. Microbiol., 2004. 70(5): p. 3005-3012.

2. Chen, C. C., R. Walia, K. J. Mukherjee and D. K. Summers (2014) A novel method for the generation of a quiescent E. coli cell factory. *Manuscript in preparation. Preprint available upon request.*

3. Liu, Q., et al., Microbial production of R-3- hydroxybutyric acid by recombinant E. coli harboring genes of phbA, phbB, and tesB. Applied microbiology and biotechnology, 2007. 76 (4): p. 811-8.

Commercialisation

The Q-Cells system is protected by pending and granted patents derived from PCT/GB2006/004751 also published as WO 2007/071959 A1.

Cambridge Enterprise is seeking licensees interested in deploying Q-Cells in established production processes. We are also interested in collaborative development of entirely new biorefining processes