SMARt CoMBo
Stable Multistage Axenic Regulated Continuous Microbial Bioprocessing

In the last century, the petrochemical industry has enabled the manufacturing of ubiquitous products that form the backbone of modern society - ranging from pharmaceuticals to everyday household goods. Petroleum-based processes, however, are unsustainable and contribute to global climate change. Biomanufacturing of renewable alternatives has largely not been able to compete on price, as the underlying production process, batch fermentation, has not changed in decades. Replacing the common batch and fed-batch bioreactor systems with a continuous-flow bioreactor would minimize equipment downtime, increase volumetric productivity, and reduce operational cost. However, continuous flow bioreactors are currently considered unreliable and are rarely used in biomanufacturing processes owing to the contamination and strain stability problems.

The project team envisions a process that overcomes genetic drift and contamination, the major challenges of continuous fermentation. We solve these two problems by combining three emerging technologies that will enable an efficient novel bioprocess: (1) the introduction of a highly controllable and economical genetic switch technology that minimizes genetic drift and enables efficient decoupling of growth from production, and (2) an economical biocide/biocide-resistant system to prevent biological contamination during prolonged continuous fermentation, using (3) a novel fermentation process. The above process will be first implemented in Visolis' patented mevalonolactone (MVL) production system. Visolis' current MVL fed-batch production process is economical for higher-value applications such as 3MPD, but for low margin markets such as isoprene or fuels, the cost of production has to be reduced. This can be accomplished with Capex reduction and productivity boost (to >2g/L/hour) by the proposed bioprocess.

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