Enhanced protein and biochemical production using CRISPRi-based growth switches - DTU Orbit (30/05/2019)

Enhanced protein and biochemical production using CRISPRi-based growth switches

Production of proteins and biochemicals in microbial cell factories is often limited by carbon and energy spent on excess biomass formation. To address this issue, we developed several genetic growth switches based on CRISPR interference technology. We demonstrate that growth of Escherichia coli can be controlled by repressing the DNA replication machinery, by targeting dnaA and oriC, or by blocking nucleotide synthesis through pyrF or thyA. This way, total GFP-protein production could be increased by up to 2.2-fold. Single-cell dynamic tracking in microfluidic systems was used to confirm functionality of the growth switches. Decoupling of growth from production of biochemicals was demonstrated for mevalonate, a precursor for isoprenoid compounds. Mass yield of mevalonate was increased by 41%, and production was maintained for more than 45 h after activation of the pyrF-based growth switch. The developed methods represent a promising approach for increasing production yield and titer for proteins and biochemicals.

General information
Publication status: Published
Organisations: Novo Nordisk Foundation Center for Biosustainability, Research Groups, Jülich Research Centre
Number of pages: 11
Pages: 274-284
Publication date: 2016
Peer-reviewed: Yes

Publication information
Journal: Metabolic Engineering
Volume: 38
ISSN (Print): 1096-7176
Ratings:
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 8.33 SJR 3.626 SNIP 1.865
Web of Science (2016): Impact factor 8.142
Web of Science (2016): Indexed yes
Original language: English
Keywords: CRISPRi, Growth switch, Metabolic engineering, Mevalonate production, Protein production
DOIs:
10.1016/j.ymben.2016.09.003
Source: FindIt
Source-ID: 2345080909
Research output: Contribution to journal › Journal article – Annual report year: 2016 › Research › peer-review