

Synthetic sRNA-Based Engineering of *Escherichia coli* for Enhanced Production of Full-Length Immunoglobulin G

Jinhua Zhang, Yanshu Zhao, Yingxiu Cao, Zhenpeng Yu, Guoping Wang, Yiqun Li, Xiaoqiong Ye, Congfa Li, Xue Lin, Hao Song

First published: 08 February 2020

<https://doi.org/10.1002/biot.201900363>

Abstract

Production of monoclonal antibodies (mAbs) receives considerable attention in the pharmaceutical industry. There has been an increasing interest in the expression of mAbs in *Escherichia coli* for analytical and therapeutic applications in recent years. Here, a modular synthetic biology approach is developed to rationally engineer *E. coli* by designing three functional modules to facilitate high-titer production of immunoglobulin G (IgG). First, a bicistronic expression system is constructed and the expression of the key genes in the pyruvate metabolism is tuned by the technologies of synthetic sRNA translational repression and gene overexpression, thus enhancing the cellular material and energy metabolism of *E. coli* for IgG biosynthesis (module 1). Second, to prevent the IgG biodegradation by proteases, the expression of a number of key proteases is identified and inhibited via synthetic sRNAs (module 2). Third, molecular chaperones are co-expressed to promote the secretion and folding of IgG (module 3). Synergistic integration of the three modules into the resulting recombinant *E. coli* results in a yield of the full-length IgG $\approx 150 \text{ mg L}^{-1}$ in a 5L fed-batch bioreactor. The modular synthetic biology approach could be of general use in the production of recombinant mAbs.