



## Increased tolerance towards serine obtained by adaptive laboratory evolution

Mundhada, Hemanshu; Seoane, Jose Miguel; Koza, Anna; Herrgard, Markus; Feist, Adam; Nielsen, Alex Toftgaard

*Published in:*  
Proceedings of SIMB Annual meeting 2014

*Publication date:*  
2014

*Document Version*  
Publisher's PDF, also known as Version of record

[Link back to DTU Orbit](#)

*Citation (APA):*  
Mundhada, H., Seoane, J. M., Koza, A., Herrgard, M., Feist, A., & Nielsen, A. T. (2014). Increased tolerance towards serine obtained by adaptive laboratory evolution. In *Proceedings of SIMB Annual meeting 2014* Article P57 <https://sim.confex.com/sim/2014/webprogram/Paper27691.html>

---

### General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Title

Increased tolerance towards serine obtained by adaptive laboratory evolution

Authors:

Hemanshu Mundhada<sup>1</sup>, Jose Seone Miguel<sup>1</sup>, Anna Koza<sup>1</sup>, Markus Herrgard<sup>1</sup>, Adam Feist<sup>2</sup> and Alex Nielsen\*<sup>1</sup>

Affiliations:

<sup>1</sup> Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark, Hørsholm 2970, Denmark

<sup>2</sup> Bioengineering, University of California, San Diego, La Jolla, CA

Journal:

Abstract Book – SIMB Annual meeting 2014 — 2014

Proceedings:

SIMB Annual meeting 2014

Type:

Article

Publisher:

Technical University of Denmark

Language:

Eng

Abstract:

The amino acid serine has previously been identified as one of the top 30 candidates of value added chemicals, making the production of serine from glucose attractive. Production of serine have previously been attempted in *E. coli* and *C. glutamicum*, however, titers sufficient for commercial applications have not yet been achieved. This is partly due to the fact that the key serine degradation pathway (serine to glycine), encoded by *glyA*, has not yet been successfully deleted in *E. coli* or *C. glutamicum*. So far, the most successful attempts of serine production have been achieved using a *C. glutamicum* auxotroph for the cofactor of *glyA*, however, this requires the use of rich fermentation media or the addition of folic acid.

Here, we demonstrate that the two major pathways for degradation of serine can be deleted in *E. coli* MG1655. In addition to the conversion of serine to glycine (encoded by *glyA*), the conversion of serine to pyruvate (encoded by *sdaA*, *sdaB* and *tdcG*) was also deleted. As expected, the resulting strain turned out to be susceptible to even low concentrations of serine in the media. In order to improve the tolerance of the strain towards serine, adaptive laboratory evolution was implemented using a state of the art robotics platform. The strain was grown under inhibiting concentrations of serine in minimal media and was periodically transferred to new media during mid log phase. After achieving a desired increase in growth rate, the concentration of serine was gradually increased. During the evolution experiment, the serine tolerance was increased substantially. Genome re-sequencing was subsequently used to analyze the genotype of a number of selected strains. These results reveal insights towards the adaptation process as well as the mechanism of serine tolerance.