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Increased tolerance towards serine obtained by adaptive laboratory evolution

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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 was 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.