

Lactate morbidostat: A novel approach in ALE to improve lactate resistance of LAB

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Abstract

End-product inhibition by lactic acid is the major limiting factor in the production of lactic acid bacteria (LAB) for starter cultures. Despite applying pH-control, lactic acid inhibits bacterial growth, resulting in decreased biomass productivity, titer and yield. Neither the mechanism of inhibition by lactic acid, nor the strategy of LAB to grow under lactic acid stress is well described. Adaptive laboratory evolution (ALE) provides a top-down approach to overcome this knowledge gap. In this project, we apply a novel ALE technology which we coined the lactate morbidostat. This technology expands the use of chemostat in ALE from increasing substrate affinity to improving resistance towards end-product inhibition. In contrast to the classical chemostat, there is no substrate limitation in the lactate morbidostat. Instead, a constant inhibitory concentration of lactic acid is applied. During the fermentation, the lactic acid concentration increases *in situ* through LAB fermentation in contrast to the external input applied in a drug resistance morbidostat. Using this system, we aim to create LAB mutant(s) with improved lactic acid resistance and to gain more insight into the resistance mechanism(s) against lactic acid stress.

ABSTRACT BOOK

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