

An LDHa single allele CHO cell mutant exhibits altered metabolic state and enhanced culture performance

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BACKGROUND: Reducing lactate production in animal cell cultures has been reported to improve cell culture performance and productivity of recombinant protein. A novel genome editing tool, CRISPR/Cas, has been used widely to induce double-strand breaks in the genome and introduce targeted mutations efficiently. **RESULTS:** In the present work, we used a publicly available human-codon optimized CRISPR/Cas system to introduce mutations in one of the LDHa gene copies to obtain an LDHa single-allele knockout Chinese hamster ovary (CHO) cell clone to analyze its effect over cell metabolism. Fed-batch cultures were conducted in order to evaluate the culture performance of mutant cells. Results show that cell growth was reduced and metabolism was modified by the LDHa single-allele knockout, whereas specific protein rate and volumetric production were greatly enhanced. Additionally, the first in-depth analysis of the metabolic effects of LDHa single allele knock