

OPTIMIZATION OF HYALURONIC ACID SYNTHESIS BY A GENETICALLY MODIFIED STRAIN OF *STREPTOCOCCUS ZOOEPIDEMICUS*

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Hyaluronic acid (HA) is a linear glycosaminoglycan composed of alternating units of D-glucuronic acid and N-acetylglucosamine linked by β -1,3 and β -1,4 glycosidic bonds. Due to its biocompatibility, viscoelasticity, and high water-retention capacity, HA is widely used in biomedicine, cosmetology, and pharmaceuticals, which has led to a constant increase in market demand. *Streptococcus zooepidemicus* is the main industrial producer of HA with the highest yield, but its production is associated with high costs and difficulties in controlling molecular weight (MW) [1].

A review of the literature shows that regulation of HA MW requires the development of a production strain capable of precisely controlling this parameter. It was found that the transcription level of *hasE*, which links two HA synthesis precursors, positively correlates with HA molecular weight. Based on this finding, a recombinant strain of *S. zooepidemicus* (SE3) was constructed from the wild-type strain S12 (ATCC 39920). First, a markerless knockout of the *hasE* gene (encoding phosphoglucose isomerase) was performed to obtain the intermediate strain SE0, which disrupted precursor balance and reduced HA molecular weight. Then, *hasE* was reintroduced into SE0 under the control of the endogenous sucrose-inducible promoter *scrA-scrR* by cloning into the plasmid pDL278 followed by electroporation, resulting in the engineered strain SE3 [2].

To evaluate production performance, fed-batch fermentation of the modified SE3 strain was conducted in HA fermentation medium (FSB) at 37 °C, with aeration of 1.5 vvm and pH maintained at 6.8. In the FSB medium containing 20 g/L fructose, sucrose was exponentially fed for 8 hours. Under this mixed-carbon source condition, SE3 achieved the highest HA yield of 4.38 g/L, while sucrose induction at 3–10 g/L resulted in HA molecular weights ranging from 0.78 to 1.77 MDa, respectively [2].

Thus, based on the literature analysis, one of the strategies for obtaining a productive strain was proposed, demonstrating the efficiency of an inducible system for tunable HA biosynthesis in a simplified single-stage fermentation process. This approach enables direct production of low-molecular-weight HA, which has significant potential for biomedical applications. The obtained results confirm the feasibility of precise polymer structure regulation through inducible expression systems.

References:

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