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PII: S0717-3458(18)30009-5
DOI: doi:10.1016/j.ejbt.2018.03.004
Reference: EJBT 312

To appear in:

Received date: 17 July 2017
Accepted date: 1 March 2018

Please cite this article as: Raúl Espinosa Pérez, José García Suárez, Emilio Narciandi Diaz, Ricardo Silva Rodríguez, Evelin Caballero Menéndez, Héctor Díaz Balaguer, Alexis Musacchio Lasa , Scaling-up fermentation of Escherichia coli for production of recombinant P64k protein from Neisseria meningitidis. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Ejbt(2018), doi:10.1016/j.ejbt.2018.03.004

Espinoza R, Garcia J, Narciandi E, et al. Scaling-up fermentation of *Escherichia coli* for production of recombinant P64k protein from *Neisseria meningitidis*. Electron J Biotechnol (2018), https://doi.org/XXXXXX

Electronic Journal of Biotechnology
EJBT-D-17-00110
Original research article
Received: July 17, 2017
Accepted: March 1, 2018
Areas: Biotechnology Industry; Process Biotechnology;

Scaling-up fermentation of *Escherichia coli* for production of recombinant P64k protein from *Neisseria meningitidis*

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Abstract

Background: P64k is a *Neisseria meningitidis* high molecular weight protein present in meningococcal vaccine preparations. The *lpdA* gene, which encodes for this protein, was cloned in *Escherichia coli* and the P64k recombinant protein was expressed in *E. coli* K12 GC366 cells under the control of a tryptophan promoter. P64k was expressed as an intracellular soluble protein about 28% of the total cellular protein. Several scale-up criteria of fermentation processes were studied to obtain the recombinant P64k protein at the pilot production scale.

Results: The best operational conditions at a larger scale production of P64k recombinant protein were studied and compared using the four following criteria: Constant Reynold's number (Re constant), Constant impeller tip speed (n di constant), Constant power consumption per unit liquid volume (P/V constant) and Constant volumetric oxygen transfer coefficients (KLa/k constant). The highest production of the recombinant protein was achieved based on the constant KLa/k scale-up fermentation criterion, calculating the aeration rate (Q) and the impeller agitation speed (n) by iterative process, keeping constant the KLa/k value from bench scale. The P64k protein total production at the 50 l culture scale was 546 mg l-1 in comparison with the 284 mg l-1 obtained at 1.5 l bench scale.