World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:11, No:09, 2017

Production of Recombinant Human Serum Albumin in Escherichia coli: A Crucial Biomolecule for Biotechnological and Healthcare Applications

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Abstract : Human Serum Albumin (HSA) is one of the most demanded therapeutic protein with immense biotechnological applications. The current source of HSA is human blood plasma. Blood is a limited and an unsafe source as it possesses the risk of contamination by various blood derived pathogens. This issue led to exploitation of various hosts with the aim to obtain an alternative source for the production of the rHSA. But, till now no host has been proven to be effective commercially for rHSA production because of their respective limitations. Thus, there exists an indispensable need to promote non-animal derived rHSA production. Of all the host systems, Escherichia coli is one of the most convenient hosts which has contributed in the production of more than 30% of the FDA approved recombinant pharmaceuticals. E. coli grows rapidly and its culture reaches high cell density using inexpensive and simple substrates. The fermentation batch turnaround number for E. coli culture is 300 per year, which is far greater than any of the host systems available. Therefore, E. coli derived recombinant products have more economical potential as fermentation processes are cheaper compared to the other expression hosts available. Despite of all the mentioned advantages, E. coli had not been successfully adopted as a host for rHSA production. The major bottleneck in exploiting E. coli as a host for rHSA production was aggregation i.e. majority of the expressed recombinant protein was forming inclusion bodies (more than 90% of the total expressed rHSA) in the E. coli cytosol. Recovery of functional rHSA form inclusion body is not preferred because it is tedious, time consuming, laborious and expensive. Because of this limitation, E. coli host system was neglected for rHSA production for last few decades. Considering the advantages of E. coli as a host, the present work has targeted E. coli as an alternate host for rHSA production through resolving the major issue of inclusion body formation associated with it. In the present study, we have developed a novel and innovative method for enhanced soluble and functional production of rHSA in E.coli (~60% of the total expressed rHSA in the soluble fraction) through modulation of the cellular growth, folding and environmental parameters, thereby leading to significantly improved and enhanced -expression levels as well as the functional and soluble proportion of the total expressed rHSA in the cytosolic fraction of the host. Therefore, in the present case we have filled in the gap in the literature, by exploiting the most well studied host system Escherichia coli which is of low cost, fast growing, scalable and ‘yet neglected’, for the enhancement of functional production of HSA- one of the most crucial biomolecule for clinical and biotechnological applications.

Keywords : enhanced functional production of rHSA in E. coli, recombinant human serum albumin, recombinant protein expression, recombinant protein processing
Conference Title : ICBB 2017 : International Conference on Biophysics and Bioengineering
Conference Location : Zurich, Switzerland
Conference Dates : September 15-16, 2017