Cultivation of E. coli carrying a plasmid-based Measles vaccine constructs (4.2 kbp pcDNA3F) employing medium optimisation and pH-temperature induction techniques

Abstract

Background

Plasmid-based measles vaccines offer great promises over the conventional fertilised egg method such as ease of manufacture and mimic wild-type intracellular antigen expression. The increasing number of clinical trials on plasmid-based measles vaccines has triggered the need to make more in less time.

Results

In this work, we investigated the process variables necessary to improve the volumetric and specific yields of a model plasmid-based measles vaccine (pcDNA3F) harboured in *E. coli* DH5*a*. Results from growth medium optimisation in 500 mL shake flasks by response surface methodology (RSM) generated a maximum volumetric yield of 13.65 mg/L which was 1.75 folds higher than that of the base medium. A controlled fed-batch fermentation employing strategic glycerol feeding and optimised growth conditions resulted in a remarkable pcDNA3F volumetric yield of 110 mg/L and a specific yield of 14 mg/g. In addition, growth pH modification and temperature fluctuation between 35 and 45°C were successfully employed to improve plasmid production.

Conclusion

Production of a high copy number plasmid DNA containing a foreign gene of interest is often hampered by the low plasmid volumetric yield which results from the over expression of foreign proteins and metabolic repressors. In this work, a simple bioprocess framework was employed and successfully improved the production of pcDNA3F