



Technology Commercialization Opportunity

Method to Produce Recombinant Proteins in Large Yields without Acetate Contamination

UGARF Case: 1181

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Intellectual Property Status: Patent Pending

Introduction

Recombinant proteins are used in therapeutics, industrial enzymes and as diagnostics, and comprise a market of over \$20 billion. *Escherichia coli* is the most commonly used microorganism for the production of recombinant proteins. A problem with *E. coli* grown at high growth rate, however, is the production of acetic acid (acetate) as an undesirable by-product. Over the last twenty years, much research has focused on the inhibition of cell growth and protein production by acetate, with the general conclusion that acetate production is to be avoided.

One way to prevent acetate is to grow *E. coli* at a reduced growth rate by limiting the supply of growth nutrients. An obvious consequence of this approach is that the rate of protein production is also reduced. Therefore, the currently used approach to preventing acetate formation is ultimately to limit the rate of protein production.

If a particular company seeks to produce a protein at a specific target annual production to meet market demands, limiting the rate of protein production in this way means that the capacity necessary to meet the target is increased (i.e., one needs a larger fermenter to produce the same quantity of material in a given amount of time).

UGA investigators have addressed this drawback and developed a means to simultaneously increase protein production at least two-fold and completely eliminate the contamination by acetate. Consequently, production is maximized while the need for purification of the end-product is largely reduced.

Technology Summary

Our patent-pending technology, based on simple and stable genetic modifications of *E. coli*, substantially reduces the formation of acetate with a concomitant increase in the production of a recombinant protein. Zero-level contamination by acetate has been achieved by this method.

Results from recently completed studies involving recombinant protein production in our engineered strains, are shown below. In this study, all strains were grown in batch culture with 10 g/L initial glucose concentration.

	Target protein generated (kU/L)	Acetate generated (g/L)
Wild type	26.8	1.21
Standard 1	30.0	0.63
Standard 2	34.8	0.68
Our strain	59.5	0.00

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