



Bacteria Modified to Secrete Biologically Active Protein for Large-Scale Production

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WARF: P100362US02

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing bacteria modified to secrete biologically active, recombinant protein needed for bioenergy production, therapeutic biologics, research tools and other applications.

Overview

E. coli is the most common prokaryote used to produce protein. The expressed protein generally accumulates in the cytoplasm. While this approach is useful for some proteins, not all proteins can be accumulated in the cytoplasm in an active state. When the desired protein is produced at high levels, it may be toxic to the host cell or accumulate as an insoluble particle known as an inclusion body, making it difficult to recover in an active form.

One option is to engineer protein so it is secreted from the cell, but *E. coli* and other Gram-negative bacteria generally are considered poor hosts for secreted protein production. No well-understood secretory pathways in *E. coli* to transport heterologous proteins to the extracellular environment currently exist. The recent discovery of YebF-mediated secretion is the first report of a native *E. coli* system capable of secreting both the native protein YebF and translational fusions to YebF. However, the expression level of YebF fusion proteins typically is low.

The Invention

UW–Madison researchers have discovered *E. coli* mutations that substantially increase the amount of biologically active, recombinant protein secreted from cells. The mutations disrupt genes in a YebF-mediated protein secretion pathway. Bacteria modified to contain these mutations are useful for the production of secreted proteins. They can be used to produce proteins that might otherwise not be expressed due to toxicity or folding errors. They also can be used to produce secreted complexes of enzymes such as cellulases and xylanases for the manufacture of cellulosic biofuels.

Applications

- Manufacturing proteins for bioenergy production, therapeutic biologics and research tools
- Rapid, high throughput production of proteins on a commercial scale

Key Benefits

- Enables the production of proteins that might not otherwise be expressed due to toxicity or folding errors
- Substantially increases the amount of biologically active, heterologous protein that can be secreted from *E. coli* and other bacteria
- Suitable for *Shigella*, *Yersinia*, *Salmonella* and *Escherichia* sp. bacteria
- May be readily employed in automated systems
- Mutations do not affect bacterial growth.

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- Because proteins are exported, the levels of contamination, endotoxin, host cell proteins and nucleic acids are significantly lower, making purification easier and thus lowering production cost and time.

Additional Information

Related Intellectual Property

- [View Divisional Patent in PDF format.](#)

Tech Fields

- [Clean Technology : Biobased & renewable chemicals & fuels](#)
- [Research Tools : Other research tools](#)

For current licensing status, please contact Jennifer Gottwald at jennifer@warf.org or 608-960-9854

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