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A Transformed Insect Cell Protein Expression System

» Reference Number

032.4

» Background

A unique process for the large scale production of valuable recombinant proteins for research, clinical and veterinary applications has been developed by researchers at The University of Calgary as an alternative to baculovirus and mammalian cell expression systems. Lepidopteran insect cells are genetically engineered to continuously express a desired protein in vitro at high levels and secrete it into the cell culture supernatant for easy purification. High expression levels result from the transcriptional stimulation of a strong cellular promoter (the silkworm *Bombyx mori* cytoplasmic actin gene) which drives expression of foreign gene sequences. This promoter is mediated by an enhancer element and a transcriptional activator protein which stimulate expression of the foreign gene greater than 1,000 fold. The same technology is used to generate cell lines expressing specific receptors on their surface or nuclei, for use in new drug discovery screening programs.

» Areas of Application

- Large scale expression, secretion and purification of foreign proteins including cytokines, cytoplasmic and nuclear factors in protein free medium.
- Generation of cell lines continuously expressing receptors on their surface or nuclei for research and drug screening programs.
- Powerful transient expression for biological analysis – rapid generation of all classes of recombinant proteins just 2 days post-transfection. Can be scaled-up.

» Competitive Advantages

- Continuous expression of foreign proteins from cloned cDNAs and intron-containing genes in a variety of Lepidopteran cell lines; re-infection is not required.
- Significantly higher expression levels than baculovirus or mammalian cell expression systems. For example a silkworm cell line overexpressing the secreted glycoprotein Juvenile Hormone Esterase (JHE) produced approximately 190 mg/L in batch suspension cultures versus a baculovirus cell line (AcNPV) expressing the same gene under control of the p10 promoter of AcNPV which produced only 4 mg/L of active JHE. Similarly, a transformed silkworm cell line over-expressing human tissue plasminogen activator (tPA) produced approximately 150 mg/L tPA as opposed to 2.5 mg/L that was produced by a recombinant AcNPV in Sf9 cells.
- Post-translational modifications, such as glycosylation, can be faithfully and consistently performed.
- Secretion of nuclear and cytoplasmic factors and expression of membrane receptors is possible.

» Stage of Development

- Proven large-scale production in bioreactors.
- Assessments of protein expression levels and biological activity for a wide variety of cytokines, other secreted proteins, membrane and nuclear receptors, and other cytoplasmic proteins are being done.

» Intellectual Property Status

Issued: US Patent No's 5,759,809; 5,989,541; 6,037,150; 6,221,632, Additional Canadian and US patent

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