

Expression of proteins via a two-vector based inducible System

Expression of proteins, virus-like particles (VLPs) and other bio-nanoparticles is one of the most important task in the production and value chain of bio-pharmaceuticals for human and animal treatment. Insect cells in combination with the baculovirus expression system is a very promising platform. Genetic modification is established, propagation is easy and safe.

BACKGROUND

Products, such as proteins, VLPs and other nanoparticles are often produced in insect cells using the baculovirus system. However, purification of the final product is difficult and requires several tedious steps, because the baculovirus particles are present as a DNA containing contaminant in the supernatant. Therefore, strategies have been tested to abolish baculovirus secretion during the protein production process. Usually, a gene that is essential for virus budding, is deleted from the baculovirus genome, and a helper cell line providing the missing gene is generated, that allows propagation of this virus. However, these helper cell lines suffer from instability and poor virus production. Antisense-RNA based strategies have been established in insect cells, usually targeting cellular genes. Most of these approaches are not efficient. The technology requires cell specific polymerase 1 promoters for exact transcription of the guide RNA. For identification of such promoters, the whole genome sequence must be available.

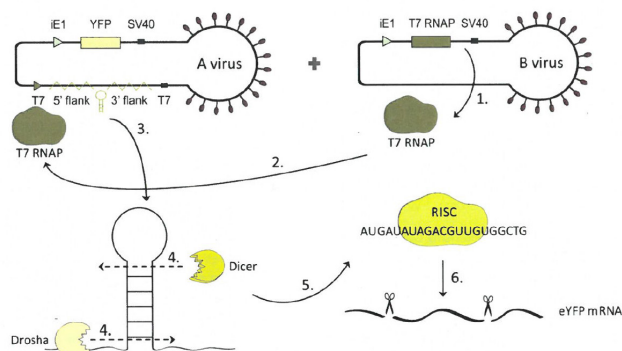


Figure: Mechanism of the inducible silencing System

TECHNOLOGY

The invention provides a baculovirus based expression system for targeted downregulation of any gene on the baculovirus genome or the cellular genome. By antisense RNA or CRISPR/Cas9 technology, genes that are essential for baculovirus budding are being downregulated during the time of protein production, thereby avoiding baculovirus particles to be present in the final product. The downregulation mechanism is induced only when a combination of two different baculovirus species is present (dual vector system) and is regulated by the bacterial T7-System, which allows universal use in all insect cells as well as mammalian cells (no cell specific Polymerase 1 promoter required). The baculovirus species can be produced individually to high titers, only in combination, baculovirus production is hampered or abolished.

BENEFITS

- Inducible expression in insect cells without the use of helper cell lines
- Suitable for downregulation of essential genes on the baculoviruses genome
- Downregulation mechanism can be used in insect and mammalian cells
- Baculovirus free protein production

REFERENCE:
2018 -17

AVAILABLE FOR:
 ■ License Agreement
 ■ Cooperation

APPLICATION:
Improved production of high quality protein based products such as proteins, VPLs and bio-nanoparticles

KEYWORDS:
Protein expression,
Baculovirus system,
Antisense-RNA,
CRISPR/Cas 9 system,
Two vector system

DEVELOPMENT STATUS:
Proof of Concept

IPR:
PCT filed

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