Geminivirus-Based Replicons for Co-Expression of Multiple Proteins in Plants

AzTE Case # M08-086L

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Invention Description

The global market for therapeutic monoclonal antibodies (mAbs) is approaching $50 billion and growing at a brisk pace. Stiff competition in drug discovery efforts will favor companies that can move quickly from antibody discovery into preclinical and clinical trials. Antibody production in tobacco has a major advantage – once the genes encoding antibodies are introduced into a plant viral expression cassette, gram quantities of mAbs can be produced in days rather than months. Highly complex proteins, such as secretory immunoglobulin A, can be produced in tobacco. Because each plant is a production unit, scale up of production is simple, especially as compared to fermentation. In addition, tobacco genetic selection has provided plants with human-like glycosylation; published studies have shown capability of producing MAbs with homogenous mammalian glycosylation. Very uniform mAbs may correspond to enhanced pharmacokinetic properties as compared to existing drugs and thus be an important step in developing improved versions of currently approved biopharmaceuticals ("biobetters").

For mAb manufacturing process development, key issues are maintaining cost effectiveness and desired quality attributes while reducing time to market with manufacturing flexibility. Plant-based mAb production began two decades ago with transgenic plants, but speed and flexibility have more recently come with transient viral-based vectors. A challenge to efficient transient expression of hetero-oligomeric proteins is the need for a different viral expressions system for each protein.

Researchers at Arizona State University's Biodesign Institute have developed a single vector that contains two non-competing replicons for coordinate expression of two proteins in transgenic plants. This system advances plant expression technology by eliminating the need for non-competing viruses. This feature enhances time to market in commercial application of newly discovered mAbs.

Potential Applications

- GMP production of a wide variety of therapeutic proteins for research and commercial use

Benefits and Advantages

- Transient expression or stable transgenic plants
- High yield of hetero-oligomeric proteins (e.g. fully assembled tetrameric functional IgG)
    - E.g. Production of IgG mAb against Ebola virus GP1 within 2 days post infiltration (dpi) and peaking at 0.4-0.5 mg/g LFW within 4 days dpi
- Simple expression vector – eliminates the need to identify non-competing viruses and the need for co-infection of multiple expression modules
- Plant based systems do not require animal or human-derived nutrients, minimizing the risk of contamination with animal or human pathogens and toxins
- Appropriate post-translational modifications of recombinant proteins are enabled with this plant based system

Intellectual Property Status:
US Granted Patent (US 8,513,397 B2)

Patents Pending in: US, Japan, Israel, EPO, Canada & Australia

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