PLANT-BASED SYNTHESIS PRODUCTS

BACKGROUND OF THE INVENTION

[0001] Recombinant protein manufacturing describes the science of producing proteins within another structure other than their original organism. A gene of the protein of interest is inserted into a new organism with the ability of being multiplied. After this expression process, the recombinant proteins are extracted and purified. This technology has been implemented on a commercial scale since the early 1980s and is widely used today to produce a wide range of proteins from enzymes dedicated to the textile industry, to therapeutics, antibodies or growth factors commonly used in science.

[0002] Different expression systems have been developed over the years. Using yeast, bacteria, animal cells or human cells, they rely on similar production steps. Plant molecular farming is the green revolution of recombinant proteins manufacturing, offering an animal-free solution, efficient yield, high flexibility, and easy production scale-up path. Plant technology allows an exceptional flexibility with a production system costing 40 times less than our current cell-ag. competitors, and a scale-up potential meeting the requirements of the clean-meat sector. Plant molecular farming presents a solution to this problem. However, up to 80% of the production cost with plant molecular farming was linked to high particle burden of primary extracts, plant secondary metabolites, pigments and phenols. These additional clarification steps (extraction process) increase costs significantly. Thus, there is a need for more efficient systems for plant molecular farming.

SUMMARY

[0002a] In one aspect, provided herein is a plant cell, wherein the plant cell comprises a vector comprising: (i) a polynucleotide sequence encoding for a heterologous protease inhibitor or a functional variant thereof; and (ii) a polynucleotide sequence encoding for a mammalian protein or a functional variant thereof, wherein the mammalian protein is a mammalian growth factor protein selected from the group consisting of mammalian fibroblast growth factor 2 (FGF-2), mammalian insulin-like growth factor 1 (IGF-1), and mammalian vascular endothelial growth factor (VEGF).

[0002b] In another aspect, provided herein is a method of manufacturing a mammalian protein, comprising: (i) culturing a plurality of plant cells , each of the plurality of plant cells comprising a vector comprising: (a) a polynucleotide sequence encoding for a heterologous protease inhibitor or a functional variant thereof, and (b) a polynucleotide sequence encoding for a mammalian protein or a functional variant thereof; and (ii) extracting soluble proteins from a harvested plurality of plant

cells, thereby generating an extraction product comprising the mammalian protein or a functional variant thereof, wherein the mammalian protein is a mammalian growth factor protein selected from the group consisting of mammalian fibroblast growth factor 2 (FGF-2), mammalian insulin-like growth factor 1 (IGF-1), and mammalian vascular endothelial growth factor (VEGF).

[0003] Provided herein are plant cells comprising a polynucleotide sequence encoding for a heterologous protease inhibitor gene or a functional variant thereof; and a polynucleotide sequence encoding for a mammalian gene or a functional variant thereof. Further provided herein are plant cells, wherein the polynucleotide sequence encoding for a heterologous protease inhibitor gene or a functional variant thereof and the polynucleotide sequence encoding for a mammalian gene or a functional variant thereof are within a bacterial or viral vector. Further provided herein are plant cells, wherein the bacterial vector is an Agrobacterium species. Further provided herein are plants cells, wherein the viral vector is Tobacco Mosaic Virus. Further provided herein are plants cells, wherein the mammalian gene is selected from the group consisting of TGF-β, IGF-1, IGF-2, human FGF-2, Activin A, BMP-4 and VEGF. Further provided herein are plants cells, wherein the heterologous protease inhibitor gene is SICYS8. Further provided herein are plants cells, wherein the