Enhanced Production of Plant-based Pharmaceuticals

Enhanced production of proteins, including pharmaceuti- cals in plants, has been demonstrated by an up-to-50-fold increase in the expression of the gene encoding the human lysosomal enzyme a-L-iduronidase (IDUA) in tobacco leaves (Figs. 1 and 2). This enzyme is involved in the degradation of glycosaminoglycans, and its deficiency leads to a genetic disease causing death in early childhood.

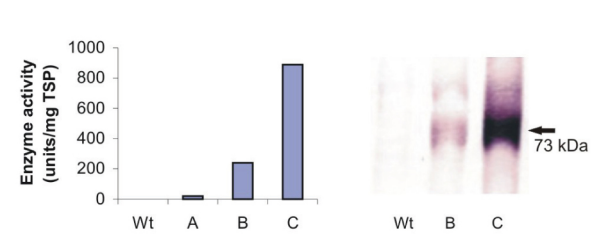

Fig. 1 (left). Activity of human enzyme in tobacco leaves co-transformed with the human-protein-encoding gene construct and the activator construct (**B**); the enhancement effect of hormone is shown in **C**. Wt = untransformed control; **A** = tobacco leaves transformed with human-protein-encoding gene construct alone. **Fig. 2 (right).** Western blot of Figure 1 extracts showing enhancement in human protein accumulation.

The invention is based on the expression of a gene construct containing 5' and 3' regulatory sequences that normally yield high-level expression of the protein of interest, in this case human IDUA, in plant seeds. Co-expression of a second gene construct ('the activator') switches on high- level synthesis of the therapeutic protein in other parts of the plant, and this synthesis is further enhanced by a natural plant hormone (Figs. 1 and 2).

This technology could be applied to other therapeutics, for example, to increase the yield of human insulin for diabetes management and serum albumin for blood volume replacement in surgery and severe burns therapy.

The Problem

Conventional commercial protein production from microbial fermentation and mammalian cell lines has limitations of cost, scalability and potential contamination with animal pathogens.[1,2]

The Need

Plants offer a more economical and safer system compared with the traditional methods for production of recombinant proteins (Table 1). However, production of plant-based pharma-ceuticals is hampered by low yields of the protein of interest[2]. There is a need for increased protein expression in plants to achieve commercial-scale production.
Enhanced production of plant pharmaceutical proteins will meet the growing demand, which the current methods are unable to fulfill, and it will also make these products afford- able to everyone who needs them. For instance, the annual demand for human serum albumin is over 500 tons.

System	Overall Cost	Scale-up Capacity	Contamination Risks
Bacteria	Low	High	Endotoxins
Mammalian cell culture	High	Very low	Viruses, prions and oncogenic DNA
Plant cell culture	Medium	Medium	Low
Transgenic plants	Very low	Very high	Low

Table 1. Comparison of production systems for recombinant human pharmaceutical proteins.[2]

The Benefits

This technology can be extended to enhance the expression of other recombinant therapeutic proteins in other plant hosts and tissues.

Partnering Opportunity

Looking for partners to develop the technology:

Research collaboration

- Provide cDNA vectors that express protein of interest
- Pilot manufacturing of plant cell cultures o Purification of protein
- Pre-clinical trials

Industry collaboration

- Provide guidance on regulatory strategy
- Assess manufacturing capability of plant cell cultures
- Ascertain market and regional size.

Contact

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