"Small green factories producing valuable natural products"

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BASEL - A new study showed that genetic engineering, combined with a solid knowledge of plant metabolism, produced transgenic plants that more closely resembled the original species than those produced through conventional breeding.

One major concern of consumers is that genetically engineered plants could harm humans or the environment since they no longer correspond to the natural product, from which they are derived. The first safety step with transgenic plants is to see if they fit the standards of the principle of substantial equivalence. In general, this principle requires that genetically modified plants resemble their predecessors, or in some cases, conventional plants. To assess this, a set of standard laboratory tests is used. Further analysis includes toxicity and allergenicity tests.

Recently, Professor Soren Bak, from the Royal Veterinary and Agricultural University, Copenhagen (Denmark) and his team demonstrated that metabolic engineering offers the possibility to introduce new biosynthetic pathways into plants, which then allow them to manufacture a desired product. Through Dr. Bak's techniques, the product of interest will more strictly adhere to the principle of substantial equivalence than organisms generated by classical breeding techniques. Moreover, the scientist explain, in the February edition of PNAS, that the introduction of a complex pathway into the model plant Arabidopsis thaliana is possible with little to no side-effects on the physiology of the plant.

For their study, Dr. Bak and his team chose to use the dhurrin pathway, normally found in the crop Sorghum bicolor. Dhurrin is a cyanogenic glucoside derived from the amino acid tyrosine. The reason for choosing this pathway is that it, "Is unique in that only three cDNAs (copies of a gene) need to be introduced in order to build the pathway. Biosynthetic pathways for most other natural products such as alkaloids (plant synthesised organic compounds containing nitrogen), for example, require 10 genes or more, making the introduction of such pathways impractical," explained Dr. Bak.

Moreover, the dhurrin pathway is well studied so that genes involved are known, and the molecular tools to handle the pathway are commonly used. For example, it is well known that the end product, dhurrin, can be easily extracted with alcohol in order to obtain a pure product.

As Dr. Bak explained, "Our plants are small green factories turning the amino acid tyrosine into dhurrin. Maybe the use of GM crops in the fields at the moment has a hard time especially in Europe, but growing small green factories like our dhurrin plants for production of valuable natural products under glass may be more understandable to the society."

Industrial applications

When asked about what the interest in cyanogenic glucosides was, Dr Bak responded, "Dhurrin, like other cyanogenic glucosides, are toxic in that upon cellular disruption the glucosides are broken down and toxic HCN is released." In other words, plants use cyanogenic glucosides as a weapon against attacks by small animals and insects. When an insect bites a given plant, and thereby disrupts cells, the cyanogenic glucosides are cleaved and release cyanide (CN-).

Cyanides are strong toxins in that they block the respiratory pathway in living organisms, by inhibiting the synthesis of ATP in targeted cells - the cell's energy source. Cyanides is a so called inhibitors of the respiratory pathway, because they block the electron flow by tightly binding to certain cytochromes, thereby impeding the establishment of the proton motive force needed for ATP production.

Dr. Bak mentioned, "We have shown using flee beetles in preference feeding assays, that the presence of dhurrin repels the beetles. In that aspect, introduction of dhurrin in transgenic crops like rapeseed could be advantageous in that rapeseed fields are often attacked by flee beetles."

However, the main problem is not generating the plants, rather gaining their acceptance. "Many of our agricultural crops like rice, wheat, and barley are naturally producing cyanogenic glucosides, albeit at very low levels. The cassava plant on the other hand accumulates very high levels in its starchy tubers, and this is a health problem for millions of people in the tropics," said Dr. Bak.

If biosynthetic pathways can be built in such a way that toxic effects can be avoided, for example by metabolic cross talk as successfully shown by Dr. Bak and his team, and if the expression levels and place of expression are controlled in such a way that the accumulation of the end product (dhurrin) does not release toxic cyanides in unwanted places, transgenic plants may be produced having broad scale beneficial effects.

Looking into the near future, Dr. Bak frames the benefits of his research with the following perspective, "We have shown that natural products can be altered in transgenic plants and that very high levels of metabolites can be achieved without inadvertent effects. Our work thus paves the way for the use of transgenic plants for the production of natural products."

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