Feverfew genes yield anticancer compounds

3 December 2013, by Hj (Harro) Bouwmeester

The tobacco-like plant Nicotiana benthamiana can be used to produce potential anti-cancer drugs. Researchers of Wageningen UR (University & Research centre) discovered which genes in the herb feverfew are responsible for the production of bioactive ingredients that are used in various types of medication. They expressed these genes in N. benthamiana and successfully produced the medicinal substance.

Water-soluble, bioactive compounds

"Apart from the bioactive compound parthenolide, which we were aiming to produce, we found that N. benthamiana also produces slightly modified compounds. These are more water-soluble and can therefore be absorbed better by patients. That is very promising for application in medicine", says Qing Liu, who is going to defend the findings of his PhD research on Monday, 2 December 2013.

Advantages of genetic modification of tobacco

Taking the genes out of feverfew and expressing them in a tobacco plant has various advantages. "Feverfew is not easy to cultivate. To ensure a continuous production of medicinal compounds with a stable quality, it is important to work with plants that can be kept in a controlled environment", explains Ric de Vos of Wageningen UR Plant Research International. Professor Harro Bouwmeester of Wageningen University adds: "The concentrations of parthenolide in Feverfew are pretty low. N. benthamiana, which grows fast, has the potential to produce much larger amounts of it. Plus it makes better water-soluble variants of parthenolide."

Higher concentrations

PhD candidate Liu: "To increase the parthenolide production we will probably have to use a few more genes. Parthenolide is produced in four steps. The first step produces something that is used by the second step, and so on. We probably need to do something before step one to increase the output of the pathway." Bouwmeester: "Producing high concentrations of parthenolide would be fatal to the plant. That is why it converts it into the better water-soluble variants. At first that seemed to be a problem as we lost parthenolide. Now it turns out that the water-soluble variants also have advantages."

Competition to be the first to find the genes

Liu's main objective during his PhD research, part of the EU-project TERPMED, was to find the genes in feverfew that are involved in producing the medicinal parthenolide. "The first gene we already had in hand when I started my research but an article about the second gene by a competing group was published while I was studying which parts of the feverfew contain the highest concentrations of parthenolide", he says. "Studying the physiology of the plant was necessary to know where to look for the genes", he explains.

Publication of the first two genes helped to identify the other genes involved, but it also meant there was competition with other researchers around the world. Liu: "I found the third gene, but on the day I wanted to submit my article, a Canadian group published the same finding." Liu's discovery of the fourth gene is so recent, that it hasn't been published yet. Nervously: "We have submitted a paper to a high-impact scientific journal and are hoping it will be accepted. I hope we beat the competing group this time."

Provided by Wageningen University