Automated plant factory for the prodution of vaccines

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Professor Vidadi Yusibov and Professor Andre Sharon (from left to right) in the fully automated plant factory. Credit: Dirk Mahler/Fraunhofer

Molecular farming is an easy, fast, and safe method for producing vaccines and therapeutic proteins in plants. Now a team of Fraunhofer researchers from the USA has built up a Good Manufacturing Practices (GMP) compliant plant factory.

The vaccine shortage during the swine flu pandemic in 2009 showed that although chicken-egg production is a reliable method, in a global emergency, it takes too long and does not yield enough vaccine. What is required are alternative methods with shorter production times and larger capacity, such as the production of vaccines and therapeutic agents in plants for example. Molecular farming, as this method is known in the trade, is easy, fast, and safe: the genetic information needed for target protein production is introduced into the plant via virus vectors that are harmless to humans. Moreover, plants have protein synthesis machinery similar to that of humans and can accommodate complex proteins.

"We use tobacco plants because they multiply and maintain our virus vectors very well. In addition, they grow fast yielding, large quantities of biomass in a short period of time," says Vidadi Yusibov from the Fraunhofer Center for Molecular Biotechnology (CMB). It has already been demonstrated in the laboratory that the method works well. But can this approach be scaled for mass production? The researchers have already cleared the first hurdles: they have developed a fully integrated, automated, GMP facility – a fundamental prerequisite for the production of biopharmaceuticals. In recognition of this achievement, one of this year's Joseph von Fraunhofer prizes is being awarded to two Fraunhofer researchers from the United States: Prof. Dr. Andre Sharon from the Fraunhofer Center for Manufacturing Innovation (partner institute of the Fraunhofer Institute for Production Technology IPT) and Prof. Dr. Vidadi Yusibov from the Fraunhofer Center for Molecular Biotechnology (partner institute of the Fraunhofer Institute for Molecular Biology and Applied Ecology IME).

Plants with predictable quality – any time, any place

The decisive moment was receiving a contract from the U.S. government's Defense Advanced Research Projects Agency (DARPA), which was looking for vaccine production alternatives. "Once some initial difficulties in understanding each other were overcome, our teams of biologists and engineers succeeded in building up our automated plant-based vaccine production factory. Now we have plants that consistently grow and make proteins to the same predictable quality, time after time whenever and wherever we like – crazy as that might sound!" says Andre Sharon from Fraunhofer CMI and Professor of Engineering at Boston University.

The plants grow in trays with hydroponic cultures of mineral wool as opposed to soil, in specially designed growth modules. Light, water, and nutrients are precisely dosed and distributed. Specially developed robots bring the plants from station to station to carry out the various steps – from inserting the tiny seeds and vacuum infiltration, to harvesting and extraction.

The plants grow for four weeks before the vector is introduced by means of vacuum infiltration. This process goes as follows: A robot picks up a tray with plants, turns it upside down, and submerges the tobacco plants headfirst into water. "This water holds the vector (biological carrier) containing the genetic information that tells the plants which protein they should produce. Then a vacuum is applied by drawing the air from the water and the plants. As soon as we switch off the vacuum, the plants suck in the water together with the vector. This takes just a few seconds," explains Sharon. Then the plants are put back in the growth module to grow further. In about a week they have produced the proteins. Once harvested, the leaves are cut into small pieces and homogenized in fully automated processes. This produces a liquid, from which the proteins are extracted. The end product is a clear liquid.

The pilot facility is capable of producing up to 300 kilograms of biomass a month, which roughly corresponds to 2.5 million units of vaccine.

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