

GREEN FORCE

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In Tours, France, Franck Michoux creates customized active ingredients for cosmetics by subjecting plants to brutal levels of stress. Time is of the essence: The first product must be launched on the market in November



Plants can't run away. They have to face their enemies and adapt their survival strategy as needed. If temperatures sink, some flowers flood their cells with a natural antifreeze agent. Other plants pump poison into their extremities when insects nibble on them or a fungus infests them. Evolution has equipped plants with these tools for successfully repelling attacks. Provoking the use of this arsenal and harnessing it for the benefit of human beings is the daily work of Franck Michoux, a 38-year-old entrepreneur with a doctorate in plant biology, and his team. "Plants are constantly under threat, whether it's from heat, cold, predators or parasites," he says. "For them it's a matter of life and death to produce a life-saving substance in the nick of time."

Some of these substances do more than just protect plants—they are also active ingredients in cosmetic products. Michoux and his colleagues have specialized in the production of these substances. His seven-person team cultivates plants that are unusually robust. To achieve this, they do not change the plants' genetic material. Instead, they alter the conditions under which the plants are cultivated.

Years of research have gone into this technology. The results of their work are very pure, highly concentrated, and natural active ingredients whose production requires significantly less water and less land. From the plants growing on one square meter in his lab, Michoux extracts the same amount of active ingredient as a conventional grower cultivating 400 square meters.

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BETWEEN THE BEAUTY GIANTS IN "COSMETIC VALLEY"

Tours lies in the midst of the picturesque Loire Valley. It's a quiet university town that is surrounded by lush vineyards and is renowned for its churches and cloisters. Few tourists wander into the nondescript industrial zone north of the town limits, where Michoux and his team have established their research center. It's a massive two-story laboratory with a dozen parking spaces in front. On the right is a noisy air conditioner, on the left a sun-dried yellow lawn. This is not a refuge for romantics, but it's a mecca for the cos-



Not a refuge for romantics: In an industrial zone on the outskirts of Tours, Franck Michoux and his team cultivate especially high-powered plants

metics industry. All of the giants in the beauty industry have production facilities in this region, which is popularly known as "Cosmetic Valley." So it's the perfect spot for Michoux. He founded his company, Alkion Biopharma, at a site near Paris in 2011. He had big plans, looked for a strong partner, and found Evonik. In 2016, after the company was acquired by Evonik, he moved it here.

Early this morning, the sun is already hot as Michoux opens the building's security doors. Today he's going to take us through operations at an accelerated pace: from the initial idea through years of research to the first market launch of an own product. "The next few weeks will be incredibly important. We've worked for years to reach this point," he says. The countdown has begun: In November the company will present its first own active ingredient, Neoplanta® Withania, in distant Bangkok. Its name is derived from the plant *Withania somnifera*, which is currently the center of attention at the lab. Practitioners of Ayurveda call it *ashwagandha*, and it's popularly known as Indian ginseng or winter cherry.

Michoux is standing in his laboratory and looking at metal racks full of rows of containers that represent the challenges to which he exposes his plants. There is an incubator with desert-like temperatures up to 40°C. Next to it, green seedlings are being cooled off to 7°C. An apparatus on the floor is swinging back and forth. Attached to it are six glass flasks in which a yellowish liquid sloshes around. The plants in the liquid are growing under the conditions created by rising water levels. In a corner, plastic tanks are standing under LED tubes that emit light of various wavelengths simulating different times of day, such as dusk or high noon. In between the few green plants languish others that are blackish brown. For them, the attacks mounted by Michoux's team were too brutal. Up to 40 different extreme conditions are being tested here simultaneously. Not all the seedlings survive.

"We change the light conditions, the pressure, the temperature, the composition of the nutrient medium, add chemicals or →

hormones, simulate attacks by fungi or insects, or do all of these things together. We really stress out the plants,” says Michoux, who also likes to test his limits in his private life after work. For a long time he did triathlons, but his greatest sports achievement was his completion of an Ultra-Trail four years ago. It’s an ultramarathon that runs for 60 hours over 170 kilometers at an altitude of 10,000 meters. “I’m always looking for solutions,” he says. “That’s why I can also adapt to every situation in extreme sports.” Through his attacks, he forces his plants to protect themselves by producing the desired substance. “The variety of these substances is incredible,” he enthuses. “We know of hundreds of thousands of chemicals that are produced by plants, but that’s only the tip of the iceberg.”

GENES PROVIDE THE BLUEPRINT

Many genes in a plant’s genome only become active when danger looms. The rest of the time they are not read. But if a fungus infests the stem, an alarm is triggered. Receptor cells, which exist in every cell, identify the attacker. The plant’s genes then deliver the blueprint for a fungicide. Finally, the plant uses this antifungal substance to combat the pest. The more varied the threats faced by the plant in its daily life, the greater is its defense potential.

At the beginning of the work with *Withania somnifera*, the herbal active substance was not the only focus of attention. Its marketing potential also seemed promising. “In order to effectively advertise the finished product, there has to be an exciting story behind it. ‘Indian ginseng’ sounds mystical and powerful,” says Michoux. Another special feature of the work was Michoux’s intention to extract the cosmetic active ingredients from ginseng roots.

The person responsible for the plants until their roots grow is Ruben Mallon, a 38-year-old botanist with a doctorate in plant biology. Two weeks ago he cleaned the ginseng seeds with ultra-pure water and alcohol and put them in a plastic box. The nutrient medium in the box is a gelatinous liquid full of vitamins, sugar, hormones, and other secret ingredients. It contains everything the seeds need to live. “In this way we grow many young plants as fast as possible under ideal conditions,” says Mallon.



Seedlings are now sprouting in the box. Mallon now selects tiny leaves from the seedlings and treats them so that they will grow roots. He’s sitting in a glass cubicle behind a metal table. In front of him is a white honeycombed membrane wall from which filtered air is hissing in order to blow away unwanted particles. Mallon is wearing a hairnet, purple rubber gloves, and a white lab coat. When he speaks, he turns his head sideways so as not to contaminate the Petri dish in front of him. “We have to work in sterile conditions, because we’re cultivating the roots in a special nutrient medium. Bacteria would enjoy growing there as well.”

Mallon’s fifteen years of experience in plant research help him decide which leaves will grow roots and which ones will wither. His scalpel slices through the tender green leaves, and he uses tweezers to place the tiny leaves in a Petri dish. After they start to sprout, they will be transferred from the Petri dish to glass vessels called bioreactors. There the roots will grow for two months in a dark cultivation room.

Patricia Corral will be watching over them. Now she presses the light switch and fills the cultivation room with green light. Along the walls are rows of bioreactors with condensation water running down their glass walls. From each bioreac-



The botanists let ginseng seeds sprout in plastic boxes with a nutrient medium under the best possible conditions (left) and then select the plants that are to form roots (top)

“The research I do here is much more creative than what I did at the university”

PATRICIA CORRAL, PLANT BIOLOGIST AT EVONIK ADVANCED BOTANICALS

tor’s cover emerges a plastic tube for regulating the pressure within. “Plants can’t perceive green light, so for them it’s always still dark here,” she says. Her sentences have a staccato rhythm. Just now she spoke to her colleagues in Spanish, then French, and now she’s speaking English. All the members of this team can communicate in several languages. Corral has a doctorate in plant biology from the University of Santiago de Compostela. She worked there for ten years as a research associate, collecting and protecting endangered plant species. She used to work with Ruben Mallon there, and he recruited her for Franck Michoux’s team. “The work I do now brings me a new challenge every day. The research I do here is much more creative than what I did at the university,” she says.

But she also needs a lot of patience. It took Corral and her team a whole year to find out the optimal conditions under which the tiny leaves of *Withania somnifera* would form roots. And it took them →

an additional year to find out how the roots could be forced to produce even more of the active ingredient. In the process, the ginseng plants were subjected to countless tests under various conditions and different kinds of stress. The process ended with a “final protocol.” This is the definitive blueprint that shows the composition of the nutrient medium, the light, the temperature, and the maturation period. In short, it shows all the conditions under which *Withania somnifera* will produce the desired active ingredients. It’s one of the well over 70 final protocols for various species that Corral has already worked with.

SUDDENLY, 80 PROSPECTIVE BUYERS

For Michoux, all of this began in London. While he was studying at Imperial College, he came up with the idea of extracting complex chemical substances from plants. He wanted to come up with herbal active ingredients with a very high degree of purity—active ingredients that did not yet exist on the market. However, this happened during the recession of 2008, and he couldn’t find any investors. So he founded Alkion Biopharma on his own and continued doing his research right through the economic crisis.

He also did research with plant stem cells—the primordial cells that can develop into every other type of cell. Back then, only a handful of companies were conducting research in this area. The breakthrough came suddenly in Paris in 2012. Michoux had just presented a few of his research results at a conference—and he suddenly had 80 prospective buyers including L’Oréal, Chanel, Dior, and Clarins, the grandes of the cosmetics industry.

All of them were eager to benefit from plant stem cells. “Back then they were hoping that plant stem cells could work in the same way as human stem cells and thus rejuvenate human skin,” Michoux recalls. They followed up their interest with lucrative orders. Michoux successfully entered a sector he had never considered before—through the back door, so to speak.



Only two years later, all of his orders were coming from cosmetics companies, and Michoux and his colleagues were concentrating on research and development. In order to ride the trend toward natural cosmetics, the producers were seeking the team’s expertise. The cosmetics companies would come to Alkion with a plant, and Michoux’s team would coax out its active ingredients or reduce its toxic substances. And

everyone benefited. The young company, which is now called Evonik Advanced Botanicals (EAB), established itself and grew, while its customers received quick results thanks to its cutting-edge technology. These customized preparations, which are often provided exclusively to certain companies for years, are still EAB’s core business.

However, Michoux has so far not had a catalogue of active ingredients derived from various plants that customers can freely choose from. That will soon change. For a young company, launching its own products on the market is a big step, and it’s connected with considerable financial risks. Now EAB is taking this step with Neoplanta® *Withania*. “We entered the right market at the right time with the right technology. But we also had some luck,” says Michoux, who has a realistic perspective on his own success story.

His company has been owned by Evonik since May 2016. With Evonik backing him up, Michoux could finally undertake the market launch of his company’s own products, which are being sold to several producers.

A GREATLY EXPANDED PORTFOLIO

The hard work, the long waiting periods—all of it hones in on this moment: the harvest. The ginseng roots, which have been growing in the dark for two months, have developed into a damp nest with a total weight of 25.48 grams. That doesn’t sound like much, but the roots have precisely followed the blueprint. They are full of the active ingredient.

And the result will never fluctuate, in contrast to conventionally cultivated plants, which suffer from hot summers, environmental pollution or contamination by chemical sprays. However, this high degree of reliability requires a big investment of energy. One day this energy may be provided by solar panels covering an area of 600 square meters.

After the harvest, the roots are freeze-dried and crushed to produce a very fine odorless brown powder. The powder is dissolved and distilled in glycerol until the result is highly concentrated. Michoux now uses a pipette to fill a testing flask with this concentrate. Next, he places the flask in a high-performance liquid chromatograph, or HPLC. This device identifies all of the active ingredients in a product and indicates their concentrations. The result rises and falls in a curve on the monitor, looking very much like an irregular heartbeat. The researchers have subjected more than 70 plant species to this procedure, and only two of them produced no results—the line of their HPLC “heartbeat” stayed flat. Today Michoux points to two spikes in the profile. They represent the desired active ingredients. When Neoplanta® *Withania* is admixed in face creams and shampoos later on, it will account for only one percent or even less of the total volume.

But *Withania somnifera* is only the beginning. In the years ahead, EAB plans to greatly expand its portfolio of own active ingredients with 14 other plant extracts. “In the past, our company was known in four countries,” says Franck Michoux and pauses for a short, almost solemn, moment. “Today it’s known in 100 countries.”

“We entered the right market at the right time”

FRANK MICHOUX, HEAD OF
EVONIK ADVANCED BOTANICALS

Company founder Franck Michoux and his team have stringent criteria for the selection of plants (left). Tours in the Loire Valley, the “Cosmetic Valley” of France (bottom)

