Flashback

The Roots of Genetic Engineering

The notion that genetic engineering is mankind's invention is misguided: even the bacterium *A. tumefaciens* has mastered the technique of genetic manipulation. Jeff Schell and his colleagues at the Max Planck Institute for Plant Breeding Research in Cologne were the first to attempt to harness this talent of nature.

Once again, the debate centered on genetic engineering and plants. And once again, it was perceived as a threat, rather than an opportunity. Two thousand delegates from 150 countries recently met at a UN conference in Bonn to discuss how genetic engineering in the agricultural sector could be used to combat the threat to biological diversity. Genetically modified crops such as soybeans, corn, rapeseed and cotton were cultivated in 23 countries worldwide last year on a total area of 114 million hectares. German authorities have thus far approved only the commercial cultivation of genetically modified corn – approximately 4,000 hectares in 2008 – plus field tests with potatoes and cereals. The participants at the Bonn-based negotiations agreed that countries could demand compensation from companies if genetically modified seeds caused environmental or other damage.

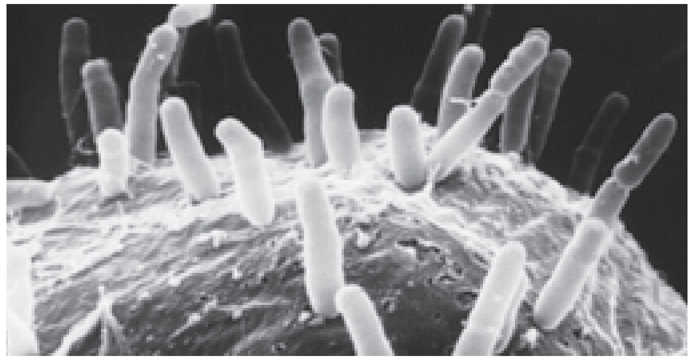
Most of the conference participants were probably unaware that agricultural genetic engineering was discovered and first tested near the meeting venue, at the Max Planck Institute for Plant Breeding Research in Cologne-Vogelsang. Jeff (Joszef) Schell, a trailblazing pioneer in this field, carried out research there for 22 years.

Schell, born in Antwerp in 1935, earned his doctorate at the University of Ghent where, after working in London and Toronto, he headed a research group in the genetic laboratory. There he discovered that a form of genetic engineering exists in nature. Some plant diseases, such as crown gall disease, are the result of genetic manipulation by bacteria. Crown gall disease, a plant cancer, is found in flowers and fruit trees, and results in tumors at the meeting point between roots and stem. It is caused by *Agrobacterium tumefaciens*, which normally lives in the soil. If plants are damaged very close to the soil, the Agrobacteria penetrate the wounds and quickly trigger the growth of tumors.

Even if the bacteria are killed off by an antibiotic the day after the infection, the cancer continues to grow. It appears that the cells already carry the instruction for uncontrolled growth at that stage, and pass this on to their daughter cells. When the researchers examined the crown gall disease cells more closely, they discovered that these cells contained opines that met the bacterial parasites' requirements for nitrogen, carbon and energy. It appeared that they forced the plants to produce these substances – in other words, they were able to alter the plants' metabolism to produce bacteria-specific nutrients, in effect subjecting the genes to a kind of conscription.

The mechanism that turns a normal cell into a tumorous one remained a mystery for some time until the research groups led by Jeff Schell and his colleague Marc van Montagu discovered large quantities of plasmids, ring-shaped DNA sections usually found only in the cell nucleus, in the bacteria responsible for the tumors. Such plasmids contain the genetic information that controls some of the cell processes, and can leave their original cells and enter into other cells.

Pioneer of genetic engineering: Jeff Schell (second from left) with his colleagues at the Max Planck Institute for Plant Breeding Research.



The researchers in Cologne used the micro organism *Agrobacterium tumefaciens* as genetic engineering tool for potatoes, tobacco and wheat.

Photos: MPI for Plant Breeding Research (2)

The scientists suspected that the *Agrobacterium tumefaciens* plasmids were causing the tumors, as part of the DNA is integrated into the genome of the host plant. This idea was received with skepticism at the time, but was later confirmed. The plant tumor cells do, in fact, contain part of the bacteria DNA. The microbes therefore genetically change the plant cells into tumor cells, meaning that genetic engineering is nature's invention. This is what makes gene exchange possible between two unrelated species.

Proof of this mechanism is found in the fact that *Agrobacterium tumefaciens* without plasmids does not cause tumors. However, if the kind of DNA rings that cause tumors are injected into the plasmid-free bacteria, the microbe starts to cause cancer once again. This is how the scientists came up with the term tumor-inducing plasmid, or Ti plasmid for short. From then on, Schell's *Agrobacterium tumefaciens* was affectionately known as the MPI plant geneticists' pet. The plant test objects they used were predominantly the easy-to-propagate tropical Kalanchoe, but they also used potatoes and tobacco – as well as various species of grains later on. In subsequent years, the scientist analyzed the Ti DNA in greater detail to find out which genes were coded by the DNA and what function each of the genes performed in the tumors.

After being appointed director at the Max Planck Institute for Plant Breeding Research in 1978, Jeff Schell put into practice an idea that he had discussed with Marc von Montagu in Ghent. He believed it was possible to localize the genes of the cancer-causing bacteria in the plant tumor cells and to replace them with others using *Agrobacterium*. Using this technique, the researchers wanted to produce plants with new properties. Schell's idea was to improve agriculture by breeding new plant species – plants that are more productive, more resistant and better able to adapt to different environmental conditions could help solve the world's food problems. Many scientists are working on this even today, and *Agrobacterium* is still used as a gene ferry.

Schell took the first successful step toward making his idea a reality in 1983: for the first time, he used the bacteria to transfer individual genes to the cells of higher plants, creating plants that could reproduce. He initially managed to create transgenic plants that were resistant to antibiotics. Some time later, plant geneticists from across the globe achieved further successes: they altered plants such that they were protected against herbicides, fungal infestation or viral diseases. Genetically modified plants were later trialed in field tests.

Schell said that there was no risk that these kinds of experiments would have unforeseen environmental consequences, a view now shared by most experts. Individual genes are also sometimes transferred to a plant in nature, even across species types. Schell also opposed the view that plants that are cultivated using genetic engineering and that are resistant to chemicals could foster uncontrolled use of herbicides. In fact, the method would enable the development of environmentally friendly herbicides that specifically harm only plant organs and break down in the soil into completely harmless products.

"Die Welt" on May 15, 1990

The one thing Professor Joszef Stefaan Schell hopes to see is "objectivity with regard to research into genetic engineering" [...] The reaction yesterday in Cologne to the field test with genetically modified petunias is a prime example of the ignorance shown toward the highly differentiated field of genetic engineering in the Federal Republic of Germany.

Jeff Schell's discovery of *Agrobacterium tumefaciens* makes him one of the pioneers of green genetic engineering. He has received various prestigious awards. He attained major scientific recognition when he was awarded the highly regarded Japan Prize in 1998. However, that year was marked not only by celebration, as a scandal came to light in the Cologne-based institute, sparking outrage in the research community. One of the technical assistants in Schell's department had been falsifying results for several years.

Many of these studies had been published in leading scientific journals, and Schell was often cited as the co-author, but it was later shown to be merely the customary honorary authorship. A committee set up by the Max Planck Society to examine the case found that Schell was blameless in all of the cases of falsification. The assistant and her group leader left the institute. Jeff Schell retired in July 2000 to pursue his hobby of sailing. However, he had little opportunity to do so, as he fell ill with a neurodegenerative disease and died in April 2003.

Lothar Willmitzer, Director at the Max Planck Institute of Molecular Plant Physiology in Golm, recently explained science's position on agricultural genetic engineering in view of the global food crisis in an interview with Berlin's Tagesspiegel. Traditional production methods yield low returns. More must be produced. In order to do so, plants must be better equipped to cope with dryness and salt and to make better use of phosphate and nitrogen.

There are many examples from India and China where small farmers have increased their harvest with genetically modified plants, improving their situation economically and ecologically. The danger of dependence on companies that have protected their innovations through patents does not exist in many third-world countries, as these companies have not registered their patents there. Willmitzer accepted the concerns of some critics that the genes of genetically modified plants could spread to other plants if they were plants that normally pollinated. To prevent this from occurring, there are specified distances between genetically engineered and conventionally cultivated crops. A distance of 30 meters is sufficient for corn fields.

Hybridization with related wild plants is also possible in principle. However, corn has no such relatives in Germany, and neither do potatoes, tomatoes or soybeans. This may not be the case for rapeseed and sugar beet. Willmitzer does not believe that authorized genetically modified products pose any particular health risk. He said they are the most thoroughly examined plants, so any risk was actually likely to be lower than with plants produced using traditional methods.

Michael Globig