Table of contents

Foreword

Sir Richard Roberts
biochemist and molecular biologist, 1993 Nobel Laureate in Physiology or Medicine

Judith Heimann's book *Using Nature's Shuttle* is a delightful account of the history of plant GMOs (genetically modified organisms) told in a very informal style through the eyes of the scientists working in Ghent, Belgium. Beginning with the discovery that certain bacteria could transfer their DNA into plants, Marc Van Montagu and Jeff Schell realized that this natural process could be used to transfer other DNA into plants, which could both speed up plant breeding and extend the traits that could be introduced. Seeing the great benefit this might bring to agriculture in the developing world, they spent their lives pursuing this goal, only to see it undermined by politically-driven anti-GMO groups. This denigration of what is probably the greatest advance in agricultural biotechnology since the invention of agriculture continues to this day, as described in a heartbreaking later chapter. To aficionados of biotechnology, this book offers new insight into the persona of the scientists who developed the GMO method and the ups and downs of their science and the impact it had on society.

Preface

I am guessing that most of what you first heard or read about genetically modified plants, seeds, or products came from news reports of popular protests against them. Perhaps it was one of the stories about the "March Against Monsanto" movement which began in early 2013 and was a mass movement by May of that year. The Associated Press, among media giants, reported on May 25th that there were hundreds of rallies that day across the USA and in more than fifty other countries[1]. The organizers of the "March Against Monsanto" claimed there were two million people worldwide who participated that day to draw attention to "the dangers posed by genetically modified food and the food giants who produce it." Non-partisan witnesses do not seriously doubt the numbers of protesters that day, nor their sincerity. One of the early organizers is quoted as saying: "We will continue until Monsanto complies with consumer demand. They are poisoning our children, poisoning our planet. If we don't act, who's going to?" Since then, the European Court of Justice has weighed in, in July 2018, against virtually the entire world scientific community, to reject all gene-edited crops, focusing their displeasure on the *process* of gene editing even when there is no discernible difference in the gene-edited product (the plant) from non-gene-edited plants.

Against this background, I am here to try to present to you the actual facts about genetically modified plants (widely known as GMOs): who first made them, how and why, and whether GM plants or products present any danger to people or to the environment. I operate from the principle that everybody is entitled to his/her opinion but not to the facts. I started looking into the facts about GM plants some months after the March Against Monsanto, but by then I already knew that Monsanto was a late-comer to the GMO story. By then I also knew that the GMO story had begun in Belgium, of all places, in the early 1970s, in a public university, in a lab headed and staffed by idealistic young scientists, most of whom were the first of their families to have received a higher education.

My story draws chiefly on my interviews of the scientists involved. And "in the interests of full disclosure," as the news reporters say on public radio, I want to tell you how I got into the act.

The idea for this book was first suggested to me in October 2013, months after the March Against Monsanto. I was sitting among a group of Belgian biotech plant scientists and next to geneticist Jeff Schell's widow, Betsy, having dinner under the dome of the Iowa state capitol building in Des Moines. We were there to witness a friend, Marc Van Montagu, a Belgian biochemist who was the scientific partner of the late Jeff Schell,

[1] The Associated Press: 25 May 2013 in *The Guardian,* "Millions march against GM crops."

receive the World Food Prize – along with two other scientists from different American labs (one of them Monsanto's). Marc was being given the prize for having, alongside Jeff, directed the Belgian lab that had discovered the initial facts and processes that led to the creation of GM plants.

The Belgian sitting next to me said, "You know, somebody should write up our discovery – how it happened, who did it, who helped, the mistakes, the bits of good luck, and all. It is a thrilling story. But we scientists haven't a clue how to write it so that ordinary non-scientists could understand it and enjoy learning about it. We need a book that gives the reader the sense of being there at the moment of discovery." And then he looked directly at me before saying, "Why don't YOU write it?"

I hesitated a moment, while the waiter cleared away the soup course. Science was not my subject and I had never written about it. The only assets I had that *might* help me were that I already had published other kinds of non-fiction books for a general audience; I know Belgium, having lived and worked there for many years as an American diplomat; and I have known several of the leading GM plant scientists for decades.

Then I thought: Maybe I could make a plus out of the fact that I know so little about science. My goal should be to learn from the scientists enough of what they did, and why and how they did it, so that I could explain it to people like me. That is what I have tried to do in writing this book.

Chapter One:

Preview

In April 1983, Jan Leemans, a young Flemish biochemist[2], casually dressed in this "Flower Power"[3] era, was enjoying working as a new "postdoc" in a brand-new biotech[4] lab at the National University of Mexico, when he got a phone call from overseas. It was Marc Van Montagu, who had been Jan's professor for his doctorate in biochemistry at the Flemish University of Brussels and was still Jan's scientific advisor and career patron – as he was for many others.

"Jan," said Marc, "can you hurry back briefly to Belgium?" Unsaid was that it would have to be without alerting the Belgian Army, for whom Jan would be breaking the rules of his public service in Mexico by leaving, however temporarily, before his two-year term was up in November 1984. (Two years of public service in a developing country was a permissible alternative to his otherwise obligatory one-year term of Belgian military service.) Marc wanted Jan to come back to make the plans, order the equipment, and initiate the plant research lab of Plant Genetic Systems (PGS) which was to be Europe's first biotech startup company.

Based in Ghent, in Flanders (the northern, Dutch-speaking half of Belgium) PGS had just been founded by two newly famous Belgian scientists, geneticist Jeff Schell and biochemist Marc Van Montagu, in concert with some European investors and an American plant biotech startup company (the world's first) where Marc and Jeff had been its scientific advisors.

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[2] Biochemistry, sometimes called biological chemistry, is the study of chemical processes within and relating to living organism. By controlling information flow through biochemical signaling and the flow of chemical energy through metabolism, biochemical processes give rise to the complexity of life. Over the last decades of the 20th century, biochemistry became so successful at explaining living processes that now almost all areas of the life sciences from botany to medicine to genetics are engaged in biochemical research. Today, the main focus of pure biochemistry is on understanding how biological molecules give rise to the processes that occur within living cells which in turn relates greatly to the study and understanding of tissues, organs, and whole organisms – that is, all of biology. Biochemistry is closely related to molecular biology (see Glossary), the study of the molecular mechanisms by which genetic information encoded in DNA is able to result in the processes of life. Depending on the exact definition of the terms used, molecular biology can be thought of as a branch of biochemistry, or biochemistry as a tool with which to investigate and study molecular biology.

[3] See page 24.

[4] Biotechnology (or biotech) is the use of living systems and organisms to develop or make products, or any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use.

Marc, who had been assembling the PGS team, had been counting on Jan to join it once his two-year term in Mexico was over, but Jan was needed now, sooner than had been planned. The race to develop useful applications of the newly invented method to genetically engineer plants was in full swing. There was no time to lose.

Jan knew the story of all the scientific history that had led to this moment. He called the Mexican lab director and started packing as soon as he had put down the phone.

Beginning in the 1960s, Jeff Schell and Marc Van Montagu, both Flemings, had started out in basic research at the public, non-religiously-affiliated University of Ghent. By 1968, at Jeff's urging, they had focused their respective genetic and cell biology labs on trying to answer an old question: How and why do some strains of a common soil bacterium known as *Agrobacterium tumefaciens* (Latin for tumor-inducing soil bacterium) induce tumors, known as *crown galls,* in a number of plants, such as sunflowers and some varieties of valuable fruit trees? (A crown gall is a tumor-like growth on the infected plant, often at the junction between the root and the shoot.)

Jeff and Marc were not the first to attack this problem. In 1907, plant pathologists Erwin Smith and Charles Townsend of the U.S. Department of Agriculture had tried – and failed – to find the cause of crown gall tumors in a variety of plants, though Smith was sure that the *Agrobacterium* was somehow to blame.

Forty years later, Armin Braun, a plant biologist at the Rockefeller Institute for Medical Research[5] in New York City, decided there was something odd about the connection between this particular soil bacterium and the growth of crown galls on plants. No other bacterium was known to be able to do such a thing *without being present in the plant*. Strange as it seemed, when Braun made cultures of cells from these tumors, he found they could grow – for decades – without any agrobacteria being present in the cultures. And the tumors could thrive on a diet of salts and sugars without the additional growth hormones that normal plant cells need to remain healthy when cut off from the leaves and roots of the rest of the plant.

Braun had concluded that merely infecting plants for a brief period of time with the strain of *Agrobacterium tumefaciens* (sometimes written as *A. tumefaciens*) altered the plant so that the resulting crown gall cells could grow indefinitely without the help of any hormones. He reasoned that this bacterium probably gives the plant tumor cells something that keeps the tumors alive *in vitro* (i.e. growing in a test tube, culture dish, or elsewhere outside a living organism). And whatever it gives them must replicate, because these tumor cells were stably inherited when they divided to make new tumors. He called

[5] Situated in New York City, it is now known as Rockefeller University.

whatever the something was – a chemical maybe, or protein, gene, or infectious material – a "tumor-inducing principle." The phrase "tumor-inducing principle" became famous in the field to describe this unexplained phenomenon in this one bacterium and came to be abbreviated as TIP.

Further research in the late 1960s conducted by a lab outside of Paris encouraged one of that lab's young French scientists to dare to suggest in 1970 that the crown gall tumor could be the result of a transfer of genes (DNA) from the bacterium to the plant during the tumor induction process.

However, the scientific community in 1970 was for the most part unready to accept the notion of a bacterial gene getting into a plant cell and functioning there. Such an event had never been found anywhere before. A more likely cause was a chemical reaction of some kind, or maybe even infection by a phage (i.e. a virus that attacks bacteria).

Jeff Schell, by 1970 Belgium's youngest ever full professor, had done his doctoral work in microbiology in a Ghent University lab that had a collection of more than a hundred live samples of *Agrobacterium*, and he now wanted to examine these bacterial strains at the molecular level and try to identify the "tumor-inducing property" that some strains had, and perhaps figure out how it worked its transformation of plants. Marc also believed it should be approached at the molecular level.

But unlike the USDA men decades earlier, Jeff and Marc did not approach this project as agronomists seeking to rid the world of crown galls. Rather, they, like a number of other scientists since the early 20th century, hoped that finding out how tumors in plants are induced by these soil bacteria would reveal something new and fundamental – ideally, something that could help them find how cancer occurs in humans, but at the least more about the inner workings of bacteria and/or plants, about which little was known at the molecular level.

The double helix structure of DNA had been found in the early '50s by James Watson and Francis Crick across the Channel, at Cambridge University, using electron microscopes and high magnification x-ray machines, new tools that were making the micro-world of bacteria, genes, and even DNA molecules visible to scientists for the very first time.

In Jeff's Ghent lab, beginning in 1971, and working around the clock for more than a year, a Flemish lab engineer whom Marc had recruited found one night in March 1972, after many hours of running the Ghent lab's ultra-centrifuge for days at very high speeds, what might be the "tumor-inducing principle" floating as a narrow fluorescent band near the bottom of his test tube.

Ten years of sustained effort were set off by that potential discovery. Finally, in late 1982, thanks to an international team of committed young scientists and technicians, initiated by Jeff to deal with the *Agrobacterium* problem, and assembled and led by both Jeff and Marc, their joint labs (now including one run by Jeff in Cologne, West Germany) having meanwhile confirmed the precise location of the "tumor-inducing principle" inside the *Agrobacterium tumefaciens* had (helped by colleagues in Europe, Australia, and the USA) also figured out how to use *A. tumefaciens*'s DNA transfer mechanisms as a way to ferry desirable new genes into plants, where they were stably implanted. The new genes were passed on to future generations of the transformed plant the way the crown galls had been.

In early January 1983, Jeff and Marc and some of the other key scientists involved in this research submitted a patent application for this novel method of transferring genes between the bacterial and the plant kingdom. That was the official beginning of genetic engineering.

But Marc's and Jeff's labs and their outside colleagues were not alone in having come this far. Partly thanks to the free flow of information then customary in basic scientific research, Jeff's and Marc's teams had important rivals who had arrived by late 1982 with virtually the same information at almost the same time. Marc's and Jeff's teams saw their chief rival as Mary-Dell Chilton, a brilliant, driven American scientist and the star of a small but prestigious lab at the University of Washington in Seattle, who was now at Washington University in St. Louis, Missouri, down the road from the new plant genetics lab at Monsanto, a long-established chemical agrobusiness.

Monsanto had come much more recently to bio-engineering than the others but, with many years of leadership in creating and marketing chemicals for crop protection, it was on its way to becoming the world's biggest commercial source of genetically engineered plant seeds. In this accomplishment, it was helped by expertise provided, sometimes for free and sometimes as Monsanto consultants, by the commercially naïve Jeff, Marc, and Mary-Dell.

Now, in April 1983, Marc had just explained to Jan over the phone that Jan was needed to come back to Ghent to work on a project to protect plants against insects. Jan later said, "That project" to create insect-resistant tobacco plants, by transferring and expressing a gene that encoded for an insecticidal protein from a well-known bacterium that had long been authorized to be used as an insecticide spray to control caterpillars, "was PGS's first technological breakthrough [in 1985] and was crucial to getting PGS going."

The project had a rocky beginning. A private company had agreed to supply PGS with the gene that encodes for the bacterial insecticide PGS needed to use, but in fact it supplied PGS with the wrong gene. So the PGS team in Ghent had decided to start all over and clone the needed gene from scratch. It drew on all that the labs' scientists working under Jeff and Marc in Brussels and Ghent and Cologne and colleagues elsewhere had discovered or learned to do to implant new properties into plants by genetic modification.

Jan remembers that, for a long time, after they had started the project to make tobacco plants resistant to insects, "we never had enough expression of the insecticide in the plants to kill the insects." They tried many ways in their efforts to obtain sufficient expression of the gene to kill insects feeding on these plants. And then they waited.[6]

December 6th is the Feast of Saint Nicolas, and they had a party that night they called the St. Nicolas party. It was held in the apartment of a Finnish couple; the husband was working in the Ghent University lab and his wife at PGS. There were some other Scandinavians at the party, and the Mexicans and, as Jan recalls "a lot of booze." And there was a Belgian PhD student of Jan's with them on the project.

Late in the party, the student goes back to the lab to check on the new plants that were being tested. And at 2 AM he comes back with big eyes and says, "It's unbelievable! They're dead." And I said, "The plants?"

"No, the bugs."

It was the first time they had killed the bugs. That night or the next morning, Jan had one of those rare moments "when I felt I was seeing something nobody has ever seen before: healthy plants that protected themselves from insects. It put us on the map. We had beaten the competitors in getting this technology to work for the first time."

[6] Jan explains that they learned to use only half the Bt gene, the active part, and to fuse it with an additional antibiotic gene and, by that means, they could select the plants with a higher expression of the insecticidal Bt gene.

Chapter Five:
The *Agrobacterium* puzzle

Jeff proposed focusing his and Marc's lab on finding out how some strains of *Agrobacterium* induced tumors in plants. As already noted, he and Marc would not be the first to attack this problem. Armin Braun had called whatever it was – a chemical maybe, or protein, gene, or infectious material – a "tumor-inducing principle." The phrase "tumor-inducing principle" became famous in the field to describe this unexplained phenomenon and came to be abbreviated as TIP.

A young Frenchman, Jacques Tempé, and other co-workers in Georges Morel's lab at the Institut National de Recherche Agronomique in Versailles (near Paris) found, by inoculating hundreds of plants with various *Agrobacterium* strains in the late 1960s, that different agrobacterial strains induced tumors that contained new organic compounds (known as metabolites[35]), that Tempé called *opines*. These opines had never been found before in plants. The crown gall tumors all contained one of two different sorts of opines: octopine and nopaline. (Nopaline is a chemical compound derived from the amino acids glutamic acid and arginine, whereas octopine is derived from the amino acids arginine and alanine.)

What the French lab knew then was that, upon inoculation in a plant, certain *A. tumefaciens* strains would elicit the development of a plant tumor containing either octopine or nopaline, never both. It was not until a bit later that it was recognized that these opines are used by the bacterium as an important source of nitrogen and energy.

By 1969 the French scientists knew that each *A. tumefaciens* strain could degrade (i.e. eat) only the kind of opine that it had caused plants to produce.

Furthermore, Jacques and his team hypothesized in a 1970 paper[36] that such a connection between the bacterium and the plant tumor could be the result of a transfer of genes (DNA) encoding opine synthesis from the bacterium to the plant during the tumor induction process.

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[35] Metabolites are any of various organic compounds produced by metabolism, the processes involved in the maintenance of life in an organism (see Glossary).

[36] Petit, A, Delhaye, S, Tempé, J and Morel, G (1970) "Recherches sur les guanidines des tissus de crown gall. Mises en évidence d'une relation biochimique spécifique entre les souches d'*Agrobacterium* et les tumeurs qu'elles induisent," *Physiol. Veg.*, Vol. 8, pp. 205-213.

However, the scientific community in 1970 was, for the most part, far from ready to accept the notion[37] of a bacterial gene getting into a plant cell and functioning there. A more likely explanation, most felt, for converting normal plant cells into tumor cells would involve the injection of chemicals into the plant, or less likely, but faintly possible, a *phage* getting into the plant and creating tumors in its new home. It was reasoned that injections of chemicals, or the presence of a phage could awaken silent plant genes that produced opines and cause the plant cells to divide without any kind of control, the way a cancer would.

Citing these possible alternative explanations[38], the scientific community challenged Jacques' group's hypothesis of DNA transfer from bacteria to plants. Some of the challenging scientists claimed (wrongly, as it turned out) to have found octopine in normal plant material.

Jeff, who had done his doctoral work in a lab that had a collection of more than a hundred live samples of *Agrobacterium*, wanted to examine these samples at the molecular level and try to locate the tumor-inducing property that some samples had, and perhaps figure out how it worked. Marc was also intrigued by the problem. Both men hoped that finding out how tumors are induced by some agrobacteria in plants would reveal something new and fundamental – if not about how cancer occurs in humans, at least more about the inner workings of bacteria and/or plants.

Jeff and Marc by the late '60s had focused their teams' attention on learning more about phages. Based on the evidence at the time, it seemed to them a reasonable hypothesis that the TIP would be a *lysogenic* phage, meaning a phage that could do one of two things after it attacks a bacterium. In some cases, the phage starts to replicate immediately as part of its effort to make many copies of itself before its host is killed. In other cases, the phage shuts down nearly all of its genes and lies dormant for many, many bacterial lifetimes, like a sleeping volcano. However, if it does not wake up on its own, you can

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[37] Currently, scientists working in Strasbourg under molecular biologist Léon Otten (who had worked under Jeff in Cologne and earlier under Rob Schilperoort in Leiden) are studying a soil bacterium now known as *Rhizobium rhizogenes* (formerly called *Agrobacterium rhizogenes)* that is a close relative of *Agrobacterium tumefaciens* but produces hairy roots in plants instead of crown galls. In many other respects, it behaves similarly to its better-known cousin and might even have been used to genetically modify plants if the capabilities of *A. tumefaciens* had not been exploited first. Work done in Jacques Tempé's lab showing that these hairy roots were able to regenerate plants was reported, with Mary-Dell Chilton as first author, in (1982) "Transfer of Foreign Genes into Plants," *Nature,* Vol. 295, No. 3848, Feb. 4-10 issue.

[38] As explained by Mary-Dell Chilton, then a young American scientist who was working on the same problem in Gene Nester's lab at the University of Washington, a rival group to Ghent's, in "Agrobacterium. A Memoir," p.8 (published by www.plant.org, copyright 2001, American Society of Plant Biologists, downloaded from www.plantphysiol.org).

wake up the dormant lysogenic phage by adding certain DNA-damaging elements to the bacterium's culture medium, and make it virulent again, replicating rapidly. At some point in the course of replicating inside the bacterium's genome, this reawakened phage multiplies as a circular DNA molecule or forms a supercoiled structure. (To approximate its supercoiled shape, take a rubber band and fold it upon itself so that it ceases being a circle or an oval, but becomes supercoiled, making it more compact.)

Jeff and Marc found that suggesting that what they learned might lead to new discoveries in human cancer research proved a fruitful way of obtaining funding. Thanks to their skill at finding research money, the number of doctoral students, postdocs, technical engineers, and lab technicians working on the fifth floor – already about 20 people working under either Marc or Jeff – began to grow.

Jeff's first recruit to his Ghent lab as a doctoral candidate was a young Fleming, Marcelle Holsters, who had been the best undergraduate in biology of her year. (She got her *licence* in 1969, at age 20.) Jeff helped her get a grant to do her PhD research on the discovery and description of phages inside *A. tumefaciens*.

Another of the lab's new recruits, found by Marc in early 1971, was a skilled technical (now called *industrial*) engineer named Ivo Zaenen. Ivo was a Fleming in his early twenties who had graduated from the Higher Institute for Nuclear Energy, the technical school in Mol that Marc had helped to set up.

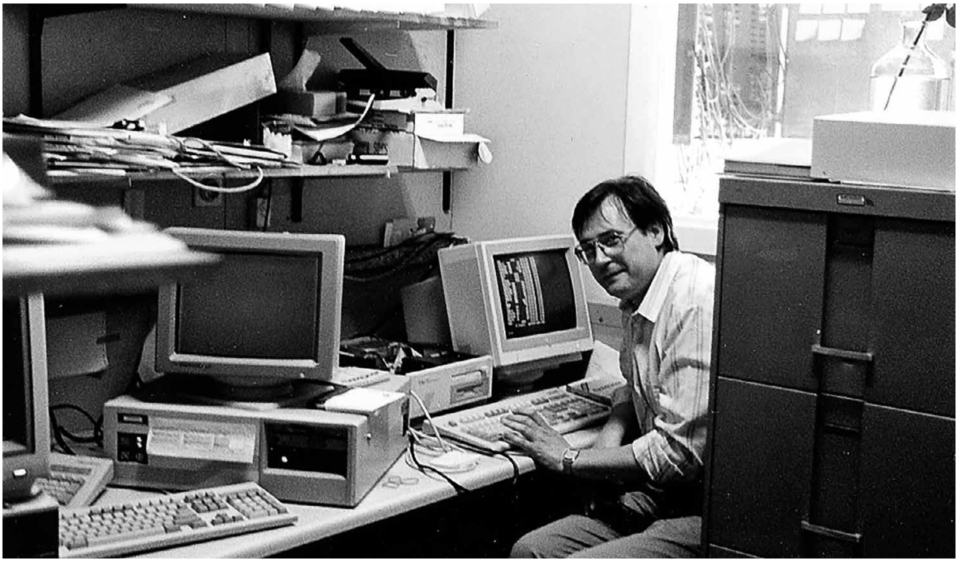
Jeff Schell and Marcelle Holsters in Ghent in 1978.

Ivo came from a small Limburg mining town. He said, “Everything was owned by the coal mining company: the school, the shops, the hospital.” His father, a Flemish Socialist, was a mine employee responsible for safety in the coal mines. Ivo’s mother was Catholic, and she taught at the local primary school but was obliged by the school’s rules to quit teaching when she was expecting her first child. Ivo and his siblings had been raised Catholic but Ivo and his sister Annie stopped going to church when they were old enough to decide for themselves.

Ivo started to work in the Ghent lab in early 1971, after completing his military service as an Army truck driver, and after working for a short period as a schoolteacher. Jeff wanted him to examine whether certain forms of a particular lysogenic phage (known as PS8) could be found in tumor-making *Agrobacterium*.

Ivo said that Jeff had hoped that this phage in its supercoiled phase would turn out to be what causes tumors in plants. And Ivo was the kind of guy who, when set a problem to solve, goes after it like a terrier looking for a buried bone.

Gilbert Engler, also a Fleming from Limburg, arrived at the lab less than a year later than Ivo, in the fall of 1971. Unlike Ivo, Gilbert had been educated at the University of Ghent and was pursuing his studies for a *licence* in plant biology under Jeff Schell, with Marcelle Holsters as his *licence* thesis advisor.



Ivo Zaenen in the Ghent lab in the 1970s.

At a 1978 farewell party for Jeff and Betsy given by Ivo Zaenen's sister, Annie Zaenen (who after her Ghent University studies had gone on to become a pioneer in computational linguistics in the USA), it was clear to all at that party that Jeff felt real regret at lessening his close connection with the Ghent lab and was anxious to maintain his collaboration with Marc and the others. He was not at all convinced he would be comfortable working in a German environment. Therefore, when he started in Cologne in September 1978, his mother (who was now part of his household), his wife, and his two boys stayed in Brussels for the next three years, until September 1981.

For Jeff, becoming a director of a Max Planck Institute offered a chance to spend more time and effort on basic scientific aspects[70] of what his and Marc's Belgian labs had found out in the years following the appearance of the Ti plasmid.

By the early '80s, Jeff saw the results of the previous decade's work as opening "the way to broad range exploitation of T-DNA in plant transformation, physiology, and genetics." The potential to extend the scope of emerging molecular genetic studies to plants was fully recognized by Prof. Reimar Lüst, the president of the Max Planck Society in 1972-84, who had in 1977 been the one to invite Jeff to take the Cologne directorship. He gave Jeff a free hand and strong personal support to realize this important goal, which made the Cologne institute one of the first world centers of this new research field, providing know-how and tools to hundreds of industrial and plant-breeding partners (including Monsanto) to develop new agricultural applications.

At this time, Marc's and Jeff's labs were in a race against Chilton's lab and others to develop new uses, including commercial applications, using *Agrobacterium*'s T-DNA as a vector that could transform plants. At the same time, Jeff recognized that to advance the application of new molecular technologies, he would need to rally significant political interest and support. Thus, he made the Max Planck Institute in Cologne a place often visited by high ranking people such as the German State President Richard von Weizsäcker and the Belgian King, Baudouin, heads of research-funding agencies and science foundations, EU representatives, and CEOs of major companies.

The institute also became a training center for scientists from Western and Eastern Europe. Drawing upon such scientific exchange programs as the German Grant Agency DFG (Deutsche Forschungsgemeinschaft), the number of these exchanges was enormous. Between 1982 and the year 2000, some 300 researchers just from Hungary alone spent time at Max Planck Cologne.

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[70] See Schell, J, and Koncz, C (2000) "The Ti plasmid and Plant Molecular Biology," In *Discoveries in Plant Biology*, Vol. III. eds. Kung, S-H, and Yang, S-F (Singapore: World Scientific Publishing Co. Ltd.) pp. 393-409; quotes are from pp. 402 and 393.

Jeff and Betsy Schell with Professor Josef Straub, Jeff's predecessor as director at Max Planck Cologne, and other German scientists in Cologne in 1979.

A few years later, in a world where patents were making many scientists cautious about sharing what they knew, Cologne strove to remain a place of free scientific exchange. Thus, when Pope John Paul II asked[71] Jeff whether he could explain to him the essence and future of the new discoveries, Jeff wrote an extensive review for the "Study Week on Modern Biological Experimentation", which appeared eventually in the Vatican journal *Pontificiae Academiae Scientiarum Scripta Varia*. Jeff followed up with a visit to the Pope at the Vatican in 1981 to explain to him in person some details of the new discoveries, with mixed results.

In the years 1987-1990, Jeff himself became one of the best-known personalities of Cologne. At one point, his life-size image appeared on posters on the city's streets as one of a handful of distinguished foreigners who were enhancing Cologne's reputation as a world center of the arts and sciences.

[71] Schell, J (1984) "Gene transfers into plants as a natural and experimental phenomenon" in: "Study Week on: Modern Biological Experimentation," (*Pontificiae Academiae Scientiarum Scripta Varia*, no. 51) Chagas, C (ed.), Citta del Vaticano, Pontificia Academia Scientiarum, pp. 107-115.

In the early 1990s, on behalf of the European Commission, Jeff and Richard Flavell, whose name is associated with the creation of a major plant molecular biology institute at the John Innes Centre in Norwich, UK, together with other scientific colleagues and friends, organized and launched the first coordinated European plant molecular biology project AMICA. The purpose of this organization was to promote plant molecular genetics for an environmentally compatible agriculture. AMICA was involved, among other things, in creating a more transparent and open system of dispensing government and institutional grants for scientific research in this new field.

Jeff with Pope John Paul II at the Vatican in 1981.

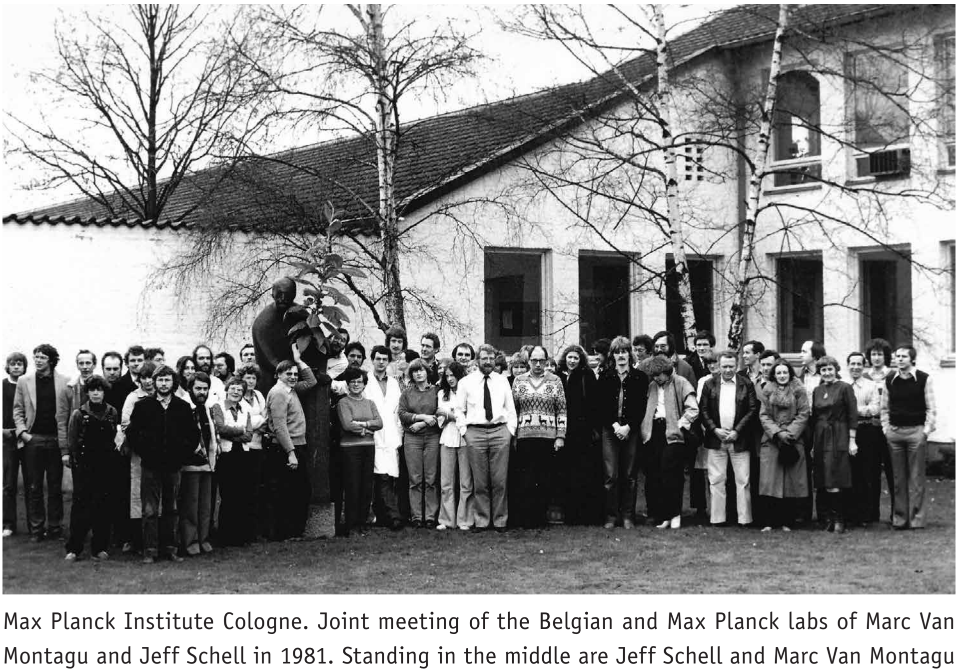
The fact that the Max Planck Institute in Cologne became so well-known under Jeff's directorship had its risks. Despite its not being directly involved in industrial production of GMOs, in 1985 his Cologne institute was the target of a bomb attack by the terror organization Rote Zora in recognition of its leading role in the development of plant genetic engineering technologies. The bomb exploded in the cellar of a brand new empty lab building across the way from the lab where Jeff worked. It caused serious damage to the building and a water reservoir but nobody was hurt. The perpetrator was never found.

Jeff Schell showing Belgian King Baudouin and German President Richard von Weizsäcker around the Max Planck lab in 1989.

In December 1987 scientists at the Cologne lab announced in *Nature* that they had created a petunia blossom in a new color, thanks to the plants' genetic transformation using a gene from a maize plant. Two years later, in 1989, a field trial of the new petunias was demolished by someone (never identified) who knew precisely which plants to destroy.

Now that Jeff had two labs, each in a different country, it was a delicate matter to see that both labs felt they had Jeff's full backing and support. Léon Otten, a Dutch molecular biologist who had done his doctorate in Schilperoort's Leiden lab before becoming in 1979 an early member of Jeff's Max Planck lab in Cologne, recalls that Jeff and Marc made it quite clear that each lab had different topics and specializations. "Everybody had his own territory and worked in his/her own field, and there were people coming from Ghent and Brussels to Cologne and vice versa [of which Léon was one]." Léon went to Brussels to see Jean-Pierre Hernalsteens and his student Henri De Grève,; "I was received very well. They would tell me everything I needed to know; there was no barrier."

That Léon was a native Dutch speaker who also spoke flawless English helped. By contrast, the brilliant Max Planck Cologne scientist, Csaba Koncz, who spoke a Hungarian-flavored German and English, was not so well-understood by others; less because of the language barrier, per se, than because of Csaba's habit of speaking as if he had marbles in his mouth, in a very low register. He also would often turn his head away when he had something important to say – which he often had. Allan Caplan was one of those in Ghent who very much enjoyed chances to learn from Csaba, and Jeff, a great



Max Planck Institute Cologne. Joint meeting of the Belgian and Max Planck labs of Marc Van Montagu and Jeff Schell in 1981. Standing in the middle are Jeff Schell and Marc Van Montagu with their labs' scientists, technicians, and other staff around them. For example, Jean-Pierre Hernalsteens (of their VUB lab in Brussels) is 3rd from the left in the last row and Marc De Beuckeleer from the Ghent lab is 7th from the right in the front row. The face of Csaba Koncz of the Cologne lab is visible just behind and to the left of Jeff's.

Chapter Sixteen:
GM plants, their enemies and their friends

How GM plants came to be invented is the story I set out to tell in this book. It is told mostly from the Ghent lab point of view because that is how I first learned of it and where I knew the most scientists. (An illustration showing a timeline with the most relevant discoveries is shown on the inside of the cover of this book.) But you readers know that the story has continued since then to produce new developments, many of them less uplifting.

Monsanto, the last of the three crucial pioneers in the making of GM plants, was the one best suited to take commercial advantage of GM techniques. Roundup's[114] principal ingredient, glyphosate, at the time of its initial use by Monsanto customers, was the safest herbicide around, and the least likely to cause damage to other living things – aside from the weeds standing in the way of crop production. It was also the most efficient weed-killer of its day. In cotton, in the Mississippi hill country and in Alabama, cotton farmers who had sprayed eight times in 1995 – for budworm and bollworm using insecticidal sprays – now that they were planting Bt cotton, used insecticidal sprays on average only 1.5 times in 1996. A few years later, when they had a combined BT/Roundup Ready cotton seed, Monsanto had produced a near-perfect pair: Roundup herbicide and Roundup Ready plant seeds (that grew into the only plants that could withstand Roundup's weed-killing ingredient), and Bt plants that carried their own insecticide. The St. Louis company had thereby carved a path to an immense fortune in a new branch – biotechnology – of what had been an agro-chemical business.

Yet, advancing from the late 1970s into the early 1990s, at about the same pace as the final refinements prior to the use on farms of GM plant seeds, was non-scientist-led opposition to biotechnology in agriculture. The early opposition consisted of "people with disparate, sometimes idiosyncratic objections to biotechnology[115] [who] found their way to each other, forming a recognizable political force.... They saw genetic engineering as a perilous intrusion into the natural world, and they nurtured a visceral skepticism of the motives and trustworthiness of the large companies that were doing most of the intruding." To oppose GM plants was also a short-hand way to express nostalgia for pre-World War II iconic family farms, now largely replaced by crops production on an industrial scale. The opposition to GM products has snowballed since GM products began to be marketed.

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[114] Charles, D, *Lords of the Harvest*, pp. 174-175. While a blessing to farmers and the environment, Roundup's and Bt's effectiveness were a serious rival to companies selling insecticides and the crop dusters who spray such chemicals on the fields.

[115] Charles, D, *Lords of the Harvest,* p. 92-93. 167.

Monsanto was the biggest single target of the anti-GMOers. Monsanto, the agrochemical giant in St. Louis (which was absorbed by Bayer in 2018), had already made a bad name for itself with these people for some of its products over the years, most recently for its easy-to-hate BGH (bovine growth hormone). Launched in 1994, BGH was an injectable biotechnological product that could greatly increase the amount of milk a cow produced. Although the FDA eventually confirmed Monsanto's claim that milk produced with the help of BGH was in no way different from milk produced without it, Monsanto's reputation with the general public took a hit from BGH it could not afford to take right then.

Also in 1994, Calgene, a small American competitor to Monsanto in genetically modified plants, launched the first GMO food for human consumption on the market: the Flavr Savr tomato. Calgene claimed its new tomato had been modified so that – unlike other commercially traded tomatoes that were picked green – it could be left to ripen on the vine without compromising its shelf life. Moreover, the Flavr Savr tomato carried an FDA statement that it was "as safe as tomatoes bred by conventional means." The FDA had never – and has never – declared *any* food "safe," so this was as near to an endorsement of food safety as it could deliver.

Calgene, however, was new to the food business, and some claimed it was less savvy at developing a product that could compete with the best traditional tomatoes on taste and texture than it was on shelf-life. Delays in deliveries and crop disasters compounded the company's troubles. Calgene's Flavr Savr was bought by Monsanto in 1995; by 1997 it was the main ingredient in a tomato paste that outsold the conventional variety in Britain. But, by late the following year, sales were down, and soon thereafter the Flavr Savr tomato disappeared from the world market.

Bad timing continued to plague efforts to market GM plants in Europe – in part through unrelated developments. For example, in 1989, the Soviet wall fell and the Soviet Union collapsed, leaving Eastern European countries ready to consider entry into the European Union, bringing along their agricultural sectors totally committed to agrochemical fertilizers, herbicides, and insecticides. And then, in March 1996, "five short days after Europe voted to accept Roundup Ready soybeans, British Prime Minister John Major announced to an incredulous, tumultuous House of Commons that ten people had died from a human form of 'mad cow disease'"[116] transmitted by eating British beef. The beef cattle had allegedly caught the disease from (non-GMO) animal food containing fats from the corpses of other livestock that had been infected by scrapie, a disease related to mad cow, but occurring among sheep.

[116] Charles, D, *Lords of the Harvest*, p. 179.

About the author

Judith M. Heimann, a New Yorker by birth, and a Harvard graduate in English literature, comes from a family of writers, mostly journalists. She has lived much of her adult life in Europe, Asia, and Africa as an American diplomat and diplomat's wife; their two children were born abroad. She worked more than twenty years as a diplomat in Benelux countries. She speaks French, Dutch, and Indonesian/Malay.

Heimann's three previous full-length books, all nonfiction, tackle disparate topics. Her best-known book, *The airmen and the headhunters* (Harcourt Publishers, 2007) was made into a Hugo award-winning TV documentary she helped write that was nominated for an Emmy. Based on Heimann's interviews of all the surviving airmen and headhunters, the book relates how generous and courteous Borneo headhunters could be to helpless American airmen shot down over Borneo's tribal land during the last year of World War II.

Heimann's first book, *The most offending soul alive: Tom Harrisson and his remarkable life* (University of Hawaii Press, 1999; Aurum Press, 2nd edition, 2002) was also made into a TV documentary, for the BBC, presented by Sir David Attenborough. Via some two hundred interviews on four continents, the book relates how many different fields of learning in different parts of the world a single imaginative Englishman could contribute meaningfully to, despite his frequent bouts of heavy drinking and mischief-making.

Heimann's most recent book, *Paying calls in Shangri-La: scenes from a woman's life in American diplomacy* (Ohio University Press, 2016) was nominated for the American Academy of Diplomacy's annual prize for the best book on the art of diplomacy. In addition to giving the flavor of life in the Cold War days of American diplomacy in Europe, Asia, and Africa, it shows how crucial to the successful advancement of a nation's diplomatic priorities are the unpublicized efforts of low-level diplomats who know how to find and exploit opportunities where both sides can come away feeling they have won.

All four of her books have in common, aside from their overturning of various accepted popular misconceptions regarding their subjects, Heimann's intense focus on getting the people she interviews to think hard about their past. Inviting them to remember what they saw, did, and felt when they were young and the world was new, she gets them to recall for her fascinating, revealing, and relevant stories.

In *Using nature's shuttle* (Wageningen Academic Publishers, 2018), Heimann's dozens of scientist informants tell her what it was like for them when they were first exploring the newly visible worlds of molecular and microbiology.

Heimann brings to the history of these young scientists' challenges, triumphs, surprises, and setbacks a sense of you-are-there immediacy. Her hope is that reading this book will not only clarify what the motives were of these pioneers in a new field about which there is currently much debate, but will also encourage adventurous, imaginative young people to opt for careers in the life sciences.