scientists like Šorm and Wichterle were placed on a renewable contract for employment, ranging from a few months to three years depending on an assessment by the party. They were prohibited from publishing, travelling and reading foreign books or journals.

The previously liberal atmosphere quickly evaporated and was replaced with sullen management, countless restrictions and exasperating regulations. The one-sided orientation toward Soviet science that had prevailed in the 1950s was back. The wrath of the government against a scientific institution that harbored reformers and dissidents was vicious. Eventually, the Academy was placed under the control of the Government and the Party. The budgets of the Institute were drastically reduced, foreign travel and participation in scientific congresses became severely restricted.

For Antonín Holý, the humiliation of his mentor came as a grave shock. He vowed he would do everything to restore the honor of the man he so admired. His first priority was to preserve Šorm’s creation, the IOCB. When equipment of the laboratories became painfully scarce, Holý was most creative. All the skills he had learned in his father’s workshop were called upon to blow glass canisters and to weld his own tools. He was no longer allowed to make trips abroad with his wife and children, but he would bring home extensive slide shows from each of his foreign visits. The whole family would share and analyze his observations.

Holý was not to be subdued. Encouraged by the recognition he had gained abroad through his publications, he concentrated on his scientific work. The making of phosphonates was becoming his trade mark. He was aware that the leaders of the Academy had been admonished by the government and the communist party to make the institution economically productive and that chemistry was considered as something that could be useful for industry. Just about every one of his achievements, like those of other practitioners of the natural sciences, was placed under patent in the hope that they could be sold abroad to gain badly-needed hard currency

The Institute of Genetics, on the other hand, was viewed by the new leadership as totally unproductive. Hašek had been expelled from the Party and demoted from all his functions in the Academy. The famous immunogenetic school he had built was reduced to a shadow of its former self. More than twenty-four of his young scientists fled and dispersed to
various countries around the world where they were to make a considerable impact in the field of immunology.

The return to dogmatic communism and its gray strictures was presented by the authorities as “normalization.” Tens of thousands of people emigrated, leaving family and once-flourishing companies behind. People learned to keep their mouths shut in front of some communist zealots and those who were suspected of being secret police informers. After 1969, the Party blacklisted most of the country’s best movie Directors, but simultaneously wanted film production to continue and be perceived as successful. Living in such contradictions sapped the morale of a nation during the seventies, and Czechoslovakia entered a period of paralysis.

In other parts of the world, the upheavals of 1968 meant something very different from the Prague Spring. Student protesters in Paris were calling for leftist governing regimes that if put in practice would be even more oppressive than those of Eastern Europe.

In Berlin, student riots broke out over the killing of a leftist student leader, Rudi Dutschke.

In Leuven, the student rebellion coincided with growing linguistic tensions in the centuries-old bilingual university. It also had an element of reaction against organized religion. The Catholic Church’s clergy and hierarchy exerted a tight grip on Flemish villages where many students and professors of Leuven had originated.

In the United States, in 1968 Martin Luther King and Robert Kennedy were both assassinated. Riots erupted in more than a hundred cities and merged with protests against the Vietnam war.
Chapter V
Enzymes: the secret of life
as chemistry

*Nothing is sacred in science; you give up the old when you find something new that is better.*
— Thomas Rivers

**At Stanford, a new world opens up**

It seemed the whole village of Hamme had come to the airport to wave the newly-wedded couple goodbye as they embarked on their trip to San Francisco. Friends and family were very proud of Erik De Clercq, the bright young medical doctor, but also of his lovely bride, Lili, who had grown up in the village apothecary just around the corner from Erik’s family home. Lili herself was an accomplished pharmacist. It was a marriage made in heaven, bathed in an aura of chemistry. The honeymoon kicked off to a thrilling start. Neither Erik nor Lili were experienced travelers and flying in a plane was an absolute novelty. The last leg of the trip, from San Francisco airport to Palo Alto by helicopter, filled their stomach with butterflies. Gazing down at the verdant landscape, they were totally overwhelmed by the beauty of the hills undulating like the Tuscan countryside in Italian renaissance paintings.

De Clercq had received a fellowship to come to the Stanford Medical Center in 1968 and work in the laboratory of the Infectious Diseases division.¹ The Director was the quick-witted Tom Merigan, one of the youngest professors at Stanford at that time and only a few years older than his postdoctoral fellow. Merigan and his wife could not have been more welcoming as they helped the honeymooners settle into their new home in the California hills. The balmy weather, the sun burning off the fog that rolled in from the Pacific Ocean, a house surrounded by exotic flowers
and a swimming pool made it seem like paradise.

Stanford University was more sedate than Berkeley, which just across the Oakland Bridge had become the epicenter of student protests against the Vietnam War. The flower power movement and hippies in nearby San Francisco seemed far away. Erik De Clercq was consumed by his research and the task of absorbing new knowledge. His bride was almost as passionate as he was, transcribing during the night with an old fashioned typewriter the notes he had made during the day.

Merigan and De Clercq were fascinated by the startling news that had just come out of the Merck laboratory. Maurice Hilleman had found that certain nucleic acids could induce interferon both in cell cultures and in laboratory animals on a much larger scale than was ever thought possible. This had an immediate effect on just about every laboratory that was investigating viral diseases. A decade after the discovery of interferon, most scientists were eager to work on the induction of interferon, which became the new wave in research. The ultimate goal was to find clusters of nucleic acids or polynucleotides that could be used as drugs in humans.

Merigan had abandoned his production of fibroblast interferon in order to jump on the inducer bandwagon. Chemists in his wide network of contacts sent him all kinds of compounds to be tested in his lab. De Clercq seized the case like a detective on a hunt. During one of his lab tests, he found that the compounds made by Fritz Eckstein at the Max Planck Institute in Göttingen were surprisingly powerful inducers. The discovery was published by De Clercq, Eckstein and Merigan in *Science* and in the *Chemical and Engineering Magazine* which won them instant acclaim.

A patent for these interferon inducers was not far behind and preparations were made for the legal paperwork to be signed together with Fritz Eckstein. In the legal labyrinth at Stanford, Erik’s name as co-inventor on the patent had been left out and was only reinstated after Eckstein’s insistence. But the compound never became a drug. It never went further than a hot and uncomfortably humid visit to Philadelphia to meet with Wyeth, the company which bought the license but never produced the drug. The frustrating effort had nevertheless yielded one blessing: Erik had acquired a new friend, Fritz Eckstein, who introduced him a few years later to chemists who would open new doors in his professional life.

In Tom Merigan’s lab, De Clercq not only learned to protect his patent
rights but also acquired the all-important habit among scientists to “pub-
lish or perish.” For Tom, each and every one of De Clercq’s findings was 
worthy of publication. If an editor was slow in responding, Merigan would 
urge Erik to reach out to a more prestigious journal. Not surprisingly, two 
years at Stanford yielded twenty-five of De Clercq’s publications, each of 
them appearing in distinguished scientific journals.

Stanford harbored many other delights. Thanks to his fanatical work 
schedule, working at night and on weekends, Erik earned unfettered 
access to the scintillation counters in the laboratory. In his free time, he 
would attend lectures given by some of the giants in molecular biology, al-
most on a daily basis. Arthur Kornberg’s lectures left a deep impression.7

Borrowing from his experience as a ship doctor and a nutritionist at 
NIH, Kornberg sprinkled his lectures with philosophical insights but al-
ways circled back to enzymes. The yeast cell, which is responsible for the 
birth of modern biochemistry, can convert sugar or starch into wine or 
beer. The ways it gives champagne its sparkle and bread its leavening ef-
fect have led biochemists toward a deeper understanding of the molecu-
lar basis of cellular behavior.

Kornberg taught his students that enzyme is Greek for yeast,

You have to know the actors in order to understand the plot. And the 
actors are the enzymes. They are the mini-chemists, the devices by 
which a biological phenomenon takes place, whether it is the legendary 
question of alcohol fermentation or how a firefly comes to luminesce. 
In naming each of the thousand and more enzymes that have been dis-
covered, the suffix ‘-ase’ has usually been added to the chemical pro-
cess it catalyzes.8

By studying enzymes, Kornberg unraveled the complex chemistry of DNA 
replication:

DNA is simply the construction manual that directs the assembly of the 
cell’s proteins. It also serves as a template for replication in order that 
the DNA of two daughter cells will be identical to that of the parent.

He was awarded a Nobel Prize in 1959 for his discovery of DNA polymerase,
the enzyme that makes DNA. He was quoted as saying that “DNA itself is lifeless; what gives the cell its life and personality are enzymes.” Later, he synthesized DNA which possessed the genetic activity that created “life in a test tube,” as coined by the press, and opened the way for his postdoctoral fellow, Paul Berg, to develop recombinant DNA.

Kornberg created a congenial atmosphere both in his laboratory and in the lecture hall. He was kind, witty, and adored by all his students, some of whom he launched into illustrious careers. With his very didactic, almost poetic skills, he proved that teaching and exquisite research can go hand in hand and even reinforce one another. He had a decisive influence on Erik De Clercq’s understanding of biochemistry and his love of teaching.9

Tom Merigan offered Erik the possibility to stay at Stanford and become the head of a new clinical virology department. It was an offer he would have loved to accept. Piet De Somer, however, visited the United States regularly and kept a close watch on his postdoctoral fellows, like the Argus giant with one hundred eyes. He was all too aware of the very attractive conditions they were working in, particularly those in Stanford. Erik De Clercq was reminded of his contract; the time at Stanford was up. He recounted it as a Faustian pact with the devil. He was left with no choice but to come back to Belgium.

Erik and Lili left Stanford with a heavy heart. They were allowed to delay their return as De Clercq had been invited to give lectures on the East Coast in the DuPont experimental station in Wilmington, Delaware, at Johns Hopkins in Baltimore, Maryland and at the NIH near Washington, DC. He made many new friends, some of whom became his future co-workers.

The Rega Institute cuts corporate ties and goes its own way

Back in Belgium, Erik found that things had changed rather drastically. The search for a worldwide distribution of RIT’s rubella vaccine had attracted the attention of a major pharma company, Smith Kline and French.10 The small and dynamic RIT was now becoming part of the SKF empire.11 The new pharma giant was not interested in the Rega Institute’s research into interferon and subsequently cut ties with the Rega Institute.
On a political level, the fracturing of the six hundred year-old Catholic University in Leuven left a deep scar. It unleashed a nationalist fervor for an independent Flanders that began to mount as the Flemish community grew wealthier and stronger. The by-product was a diminished role for the Catholic Church in the management of the university. It reinforced the University’s historical independence of scientific thought. One of its proudest achievements—paradoxical for a Catholic university—was the development of the “Big Bang theory” in the 1930s by the Leuven priest Georges Lemaître.

Piet De Somer was entrusted with a new role as the president of the Flemish university. As the quintessential figurehead representing both the old tradition and the new wave of secularization, he was at the peak of his fame. The charisma, the vitality, the sheer energy that radiated from him electrified any room he entered. In the Rega Institute, his presence was felt even when he was not physically there.

But somehow, things were not the same. Several French speaking researchers had been hired away by RT/ST/ or moved on to other universities. Erik was assigned to an empty lab left with nothing but broken glass and worn furniture. It was hard to readjust to the cool Belgian climate and the competitive atmosphere. Above all, he sorely missed the informal Californian work environment. To make things even worse, the military draft and life in the barracks was awaiting him.

Only De Somer’s contagious optimism and the companionship of a devoted technical aide could dispel his misery. His other consolation was his favorite magazine, the *Journal of the American Chemical Society*, and his correspondence with some of its authors.

One of these letters was addressed to Dr. Bernhard Witkop, the Director of the Chemistry Department at the NIH and one of the more authoritative members of the American National Academy of Sciences. Was it baffling naiveté or plain guts to ask a famous scientist for access to his compounds? Undaunted, Erik asked him to send his polynucleotide products to the Rega Institute so they could be tested for interferon. First he received a polite no, but then, several months later, out of the blue, Witkop sent him a request to test several compounds within the short time span of two weeks. It was the beginning of an intense collaboration.

In 1971, production of interferon had gained the upper hand and
induction with polynucleotides was moved to the backburner. Piet De Somer organized an international conference on interferon. Tom Merigan was one of the star participants. He had come to realize that inducers were, after all, not very promising. In the margins of the conference, he developed a plan to start clinical trials in Stanford for cancer patients with shingles. This viral disease, painful but innocuous for healthy people, was a calamity to immune-depressed patients. Merigan preferred the Finnish leukocyte interferon, which was the only source available in enough quantities to serve a few patients. The Rega Institute still had all of its hopes invested in the fibroblast production, which it claimed was much purer than the Finnish white blood cell interferon and did not carry the risks of all kinds of infections.

De Clercq did not play a significant role in the conference, he was distracted with teaching biochemistry in the medical faculty and his new research topics. He was fixated by a new enzyme discovered by two American scientists, David Baltimore and Howard Temin, who had been working independently from each other but had arrived at the same conclusion. Even more remarkable, their two papers were published in the very same issue of *Nature* in June 1970. They had found that certain RNA viruses, often acting as a silent passenger, but sometimes causing leukemia or solid tumors in animals, had the help of a unique enzyme, reverse transcriptase. It was an enzyme that only very specific RNA viruses carried.

Not until the beginning of the 1950s were scientists able to distinguish RNA viruses from DNA viruses. Now there had been an enzyme discovered in a certain kind of RNA viruses that made them behave in an unusual way. These viruses first transcribed their genetic material into DNA and only later back into RNA. An infection by this kind of RNA virus, later renamed retrovirus, had the same effect as an infection by a DNA virus, and thus could stay in the organism indefinitely. This activity was called reverse transcription. It totally upset the prevailing dogma. In those days, it was believed that DNA always transcribed into RNA in order to produce protein in the cell. The newly discovered enzyme reversed that order. It directed the information flow from RNA back to DNA, or from a gene’s message back to a gene. With reverse transcriptase, every RNA molecule in a cell could be used as a template to build a corresponding DNA.