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1917—2008

A Biographical Memoir by

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ELIE WOLLMAN GREW UP in the early decades of the 20th century in the fertile ambiance that surrounded key discoveries in microbial genetics. His father, Eugène Wollman, emigrated from Minsk at a time when that city was part of Russia. The elder Wollman earned his medical degree in Liège, Belgium, and then moved to France where he began his career in Elie Metchnikoff's laboratory at the Institut Pasteur. He developed germfree husbandry techniques to be used for research on animal species that ranged from flies to guinea pigs. Eugène Wollman then made the first key discoveries on contagious and hereditary features of bacteriophages and the phenomenon of lysogeny: he found that the fusion between a phage and its host bacterium ultimately resulted in the transmission of the phage's newly acquired genetic material to the bacterium's progeny, without the viral phage killing its host. This pioneering work, carried out with his wife, Elizabeth, was confirmed and expanded by André Lwoff in the attic of the biochemistry building at the Institut Pasteur. It was there that his son, Elie Wollman, began his scientific career in 1945 after having escaped in 1940 from Paris to Lyon and then to Toulouse, a French free zone at that time during World War II. Working in the French resistance as a physician under a false name, he

moved to Albi in the Tarn region of France, where he met his future wife, Odile.

A milestone in Elie Wollman's career occurred during his meeting with Max Delbrück in 1947 in Paris. Delbrück was the leader of the phage group at Caltech. This was a very unusual research team because it brought together diverse scientists, including physicists, mathematicians, chemists, and biologists, with the specific goal of discovering the physicochemical laws that govern life rather than just matter. Delbrück, who at the time did not firmly believe in lysogeny, invited Elie Wollman to work in his lab for two years, thanks to a fellowship from the Rockefeller Foundation. In his book *Nazis, Women, and Molecular Biology* Gunther Stent narrated how as a newcomer to Delbrück's lab, he was asked to work with Elie Wollman. Stent was a young chemist who did not know anything about bacteriology. He was therefore poorly equipped to decipher the physicochemical laws that govern activation processes of the T4 phage, a phage strain that is unable to attach to bacteria unless it is cultivated in a tryptophan-containing medium. Delbrück told Stent: "Wollman and you are going to complement each other like liverwurst and rye bread. He's got the bacteriology, which you don't know from beans, and you've got the math and physics, of which he's largely innocent. Together you will make the perfect phageology sandwich." (Stent, 1998, p. 322). Stent wrote in his book how easy it was to recognize Elie and Odile Wollman among the crowd of tourists when he met them in the hotel lobby at Pasadena after their arrival by train from the East Coast. "Elie had on a natty double-breasted, pin-striped suit, while Odile wore a hat, and had a fox stole draped over her shoulders" (Stent, 1998, p. 322).

Elie Wollman's lifetime passion for microbial genetics was revealed on several occasions during his stay at Caltech. One instance occurred in the late 1940s, when Delbrück started

to lose interest in genetics because he was attracted to the ultimate scientific frontier, an understanding of brain functions. Delbrück asked his team to prepare a series of seminars based on papers of sensory neurophysiology that were written by eminent neuroscientists of the time. The only person to refuse to participate in this series was Wollman who bluntly responded, "I'm not interested in brain research. As a simple bacteriologist I certainly wouldn't understand the papers you picked out anyhow. Actually, as far as I'm concerned, phages and bacteria are good enough material for me, and I'll continue working on them, if you don't mind" (Stent, 1998, p. 364). Another incident occurred when Wollman personally transcribed all the discussions that took place in the summer of 1949 about what was known (and unknown) about phages. This work served as the working document for the conference "Viruses 1950," organized by Max Delbrück at Caltech in March 1950.

On his return to Institut Pasteur, Wollman played a pivotal role in discoveries on the organization of genetic material. This fundamental research laid the groundwork for the Nobel Prize that was awarded to François Jacob. By studying the structure and localization of the λ prophage in lysogenic bacteria, Wolman discovered the epigenetic switch from lysogeny to the lytic state that characterizes zygotic induction, or phage induction, following conjugation of lysogenic bacteria with nonlysogenic ones. He then showed that prophage induction is regulated by a lytic repressor, which was one of the first examples of a gene regulatory mechanism. His decisive contribution to the gene mapping of bacterial chromosomes took place in 1954-1955, thanks to the ingenious method of interrupted mating, or *coitus interruptus*.

The issue that was then at stake was to answer how the genetic material of bacteria is transferred at the time of

conjugation. The answer to this question was facilitated by the use of highly recombinant strains of *Escherichia coli* that had been discovered by William Hayes and had the unique advantage of having mutant strains with defective genes for particular traits. But it was the simple kitchen blender that was the key tool for demonstrating that the transfer of genetic material at the time of conjugation was sequential and occurred in a linear manner. Because of their stay in California, Odile and Elie Wollman knew about this kitchen item that was still relatively rare in Europe. According to this legend, Elie Wollman borrowed her kitchen blender from Odile in order to carry out the experiment, since he had no money in his laboratory to buy a new one.

The design of the experiment was as simple as it could be: the donor and recipient bacteria were mixed and conjugation was allowed to proceed. After a fixed time of incubation, the culture was put in the blender and the blender adjusted to a speed that disrupted the cell pairs but did not disrupt the individual cells. The genetically deficient recipient cells were then plated and screened for recombinant markers transferred by wild-type donor cells. Depending upon the time of incubation and the donor strains, different genes were transferred from the donor to recipient cells. This approach allowed Wollman to reconstruct the position of genes on the chromosome and to develop, decipher, and posit the first model of gene mapping in a living organism. Although the initial model was linear, Wollman and François Jacob quickly used their intuition to propose and test the idea that it was in reality circular. Although he fully recognized Wollman's contribution to this key experiment, it is Jacob who made it known to the international scientific community.

As a microbial geneticist and probably in line with his father's earlier experiments on Enterobacteriaceae, Wollman moved on to characterize another important factor in the

transmission of genetic material in bacteria. He showed that the fertility factor that is present in the genetic material of some strains of Enterobacteriaceae but absent in other ones can exist either in an integrated or autonomous state. In the first case the fertility factor replicates as part of the bacterial genome whereas in the autonomous state it behaves as if it were independent from the bacterial genome. Together with Jacob he called this genetic element an "episome." Episomes have since been renamed plasmids and found to play a crucial role in transmission of antibiotic resistance.

Wollman left this fertile field of research in 1966 to rescue the Pasteur Institute from a major financial and management crisis. He became vice director in charge of research and devoted himself full-time to this task. He laid the groundwork for a profound reorganization of research and teaching in this venerable institution, which enabled the institute to smoothly enter the new age of molecular biology. Wollman continued to play a major role in the organization of biological research in France for the next 20 years.

Wollman received many prestigious scientific honors during his career, including the Rapkine Foundation (1953) and Lecomte du Nouy Foundation (1956) prizes, the Essec Award in 1958, and the Leopold Charles Meyer prize of the French National Academy of Sciences in 1976. His scientific and administrative achievements were recognized on several occasions. He was bestowed the honor of Chevalier of the French Legion of Honor. He was also awarded Commander and Officer of the National Order of Merit, and Commander of the Order of Academic Palms.

In addition to all these French distinctions, Wollman was greatly respected throughout the rest of the world. He was a founding member of the European Molecular Biology Organization and an honorary member of the Royal Academy of Medicine of Belgium. He was elected to the National

Academy of Sciences as a foreign associate in 1991. Wollman was interested in Latin America for both personal and scientific reasons. As a child he traveled with his parents to Chile where his father was the director of the Institute Sanitas in Santiago from 1929 to 1932. It was here that Wollman became fluent in Spanish. Consistent with his political philosophy, he helped several Latin American scientists develop strong research programs despite the limited funding possibilities in their home country. When they were at risk because of political turmoil and dissent, he helped them find a position in France.

Wollman's multinational contribution was a gift of his family, as he walked in the steps of his father. As one illustration, his father was instrumental in establishing a collaborative relationship between the Malbrán National Institute of Microbiology at Buenos Aires and the Pasteur Institute at Paris. Wollman visited the Malbrán Institute with his father in 1929. He returned to Buenos Aires in August 1958 to found the Pasteur Pavilion at the Malbrán Institute. Wollman carried with him some bacteriological materials. Thanks to these materials, coupled with his mentoring, several young Argentinean scientists earned their doctorates one year later in the Faculties of Science and Agronomy of Buenos Aires (Kreimer and Lugones, 2003).

To recapitulate, Elie Wollman was an active part of the international intellectual wave in the development of modern molecular biology. His determination to remain in his very field of scientific expertise is remarkable and illustrates very well what a true scientist should be: a humble character who knows very well the limits of his knowledge and does not spend his life in self-promotion. Wollman displayed this quality very early in his life and remained true to it throughout his career, despite having many opportunities to put himself on the stage. This is why, as scientists, we will

forever be attached to the accomplishments and memory of Elie Wollman.

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