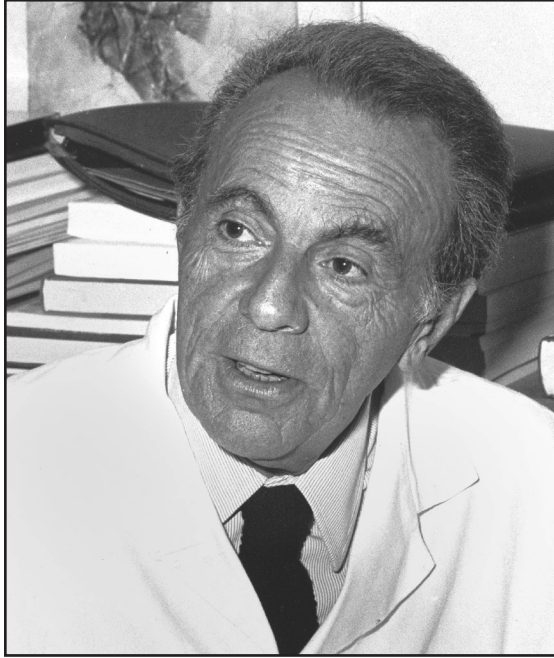

FRANÇOIS JACOB



17 JUNE 1920 · 19 APRIL 2013

WHO WAS FRANÇOIS JACOB? The man who, when 20 years old, left France in 1940 to join General de Gaulle in London, fought for 4 years in Africa as a medical auxiliary, and was severely wounded in August 1944 in Normandy? The molecular biologist who built the first molecular model of genetic regulation with Jacques Monod in 1961, and for this discovery received with André Lwoff and Monod the Nobel Prize in Physiology or Medicine in 1965, only 15 years after his first steps in research? Or the humanist who positioned recent transformations of biology in a broader historical perspective and scrutinized the developments of science, particularly of genetics, opposing any unethical use of scientific knowledge?

Jacob's scientific achievements are the easiest to describe. Five years after the end of World War II, in 1950, he went to work in André Lwoff's laboratory at the Pasteur Institute in Paris. He was one of a small international group of scientists who after the war built a new molecular vision of organisms. In 10 years, he provided a new description of lysogeny, a strange process by which a virus (a bacteriophage) remains silent within a host bacterium without lysing it; with Elie Wollman, he explained the mechanisms of genetic exchange between bacteria (i.e., conjugation); and with Monod, he built the famous model of genetic regulation, the "operon model." This model was the first to explain how the activity (i.e., expression) of genes was regulated within organisms. Since embryological development and differentiation are correlated with changes in gene expression, the operon model had a huge impact on the young community of molecular biologists, pushing many of them to abandon the study of bacteria and bacteriophages to initiate a molecular description of the mechanisms of embryogenesis.

François Jacob was a microbiologist, and microbiology contributed importantly to the development of molecular biology. So, his participation in the rise of molecular biology is not surprising. But he brought to this endeavor two major abilities. The first was his ability to design the experiments that were the best fitted to answer the question posed. The second was his extraordinary capacity to replace abstract genetic models with precise molecular mechanisms.

He himself abandoned bacteria and bacteriophages in 1970 to redirect his laboratory toward the study of mouse embryological development, a model for the study of mammalian (human) development. He used, as experimental material, cells called embryonal carcinoma cells, derived from teratocarcinomas (i.e., tumors of the gonads), which have properties similar to those of the early cells of the embryo. The first years were difficult because of the lack of appropriate (genetic engineering) tools, which were only developed in the 1970s and entered laboratories in the early 1980s. Retrospectively, however, the choice of

embryonal carcinoma cells foreshadowed the importance of extant studies on embryonic stem cells and their use in regenerative medicine.

Like Jacques Monod, but in a less visible way, François Jacob had a huge influence on the development of molecular biology at the Pasteur Institute, and more generally in France. During the last encounters I had with him after his retirement, he frequently expressed the feeling that biology had become highly different from what he had known, and that he would have been unable to contribute to its current developments. I countered that the opposite was true, not to cheer him, but because I was convinced of it: despite huge technological advances, biologists are still working within the paradigm that Jacob and the small group of molecular biologists elaborated in the 1950s.

Beside his scientific accomplishments, François Jacob helped to interpret the recent transformations of biology in various books published in parallel with his scientific work. In *The Logic of Life: A History of Heredity*, he described the whole history of the life sciences as a succession of steps corresponding to the progressive deciphering of the most central and fundamental levels of organization within organisms, the last being the molecular revolution in which he had participated. This new history of biology was highly original and well informed of the most recent developments in the history, philosophy, and sociology of science, borrowing from Michel Foucault and Thomas Kuhn. His most original contribution in this field was probably his second book, *The Possible and the Actual*, first published in 1981. In it, he popularized the now-familiar idea that evolution acts like a tinkerer (i.e., bricoleur) not as an engineer, an idea that has been used as an argument against the proponents of Intelligent Design. But, in a less obvious way, this book was also a description of the activity of scientists as tinkerers: they tinker with ideas and models. His last historical and philosophical book, *Of Flies, Mice, and Men*, adds interesting information on the recent history of biology, as well as on the work of scientists, and compares science with other human activities, such as the construction of art and myth. What is remarkable in the contributions of François Jacob is that he was able to establish a new vision of scientific activity, freed from myths and naiveties, in agreement with recent science studies, without renouncing the specificity and value of scientific knowledge. Whereas most historians and sociologists of science have more or less been inclined to a certain form of relativism, François Jacob always defended the unique value of scientific knowledge. This defense does not stem from the specific qualities of members of the scientific community, or from the processes by which new knowledge is elaborated, but from the sieves that scientists have constructed to discriminate between valid and invalid forms of knowledge. The first

is the free discussion between scientists that precedes the adoption (or rejection) of a new theory or model. The second is the experimental testing to which a new model is immediately submitted: a single hit can sink the most beautiful model! For François Jacob, his reflective work on science and its history was no different from his scientific pursuits—it was not a hobby. Doing and defending science were a single task.

His involvement in ethical issues was first and foremost linked to his determination to defend science. It was the reason for his rejection of Lysenkoism, and for his fight within the French Academy of Sciences in favor of scientists who had been imprisoned in the USSR. But his ethical commitments had other roots, which he described in his autobiography *The Statue Within* (1987). Unique in its style and literary qualities, this autobiography opened the doors of the French Academy to him.

François Jacob always said that the most important years of his life were those spent in Africa, in the 2nd armored division headed by General Leclerc. The title of which he was most proud was “Companion of the Liberation,” an order created by General de Gaulle and of which François Jacob was the Chancellor at the end of his life. And the most significant decision of his life had been to join de Gaulle in London in 1940. These statements seem strange to people who, like me, knew François Jacob far later as a renowned scientist and a Nobel Prize winner. But they explain how he saw the relations between science and ethics. Unlike Monod, François Jacob did not think that there was a privileged relation between science and ethics. But this does not mean that scientists should not argue for the ethical use of science—they must act as individuals in accordance with their own ethics. Let us recall that François Jacob made the most significant and demanding ethical choice of his life in 1940, long before he became a scientist.

Although born into a Jewish family, and faced with anti-Semitism early in his life, François Jacob was not religious. What was most important for him was not ideas and beliefs, but the ability of the individual to say “no,” to oppose what was ethically unacceptable. This explains his attachment to General de Gaulle and his Prime Minister, Pierre Mesmer, with whom he had shared identical commitments, despite differences in political and philosophical convictions.

In his autobiography, François Jacob described General de Gaulle, after the first encounter in London, as a “gothic cathedral.” This impression was exactly the one that François Jacob himself gave to the young students entering his laboratory. He was not fully able to make the people around him feel at ease. He was probably, in part, responsible for this state of things, as he was sometimes awkward in his relations with other individuals. But it is not easy when the people

before you have in mind your extraordinary scientific accomplishments, your Nobel Prize, and the heroic choices of your life!

Behind the gothic cathedral was a man of deep fidelity in friendship. It is one of my deepest regrets not to have been able to go beyond the “statue without,” and not to have shared more with him, in particular during the last years when, despite his age, his mind was as brilliant as ever.

Elected 1969

MICHEL MORANGE

Professor

République des Savoires

Ecole normale supérieure, Paris