François Jacob

(1920–2013)

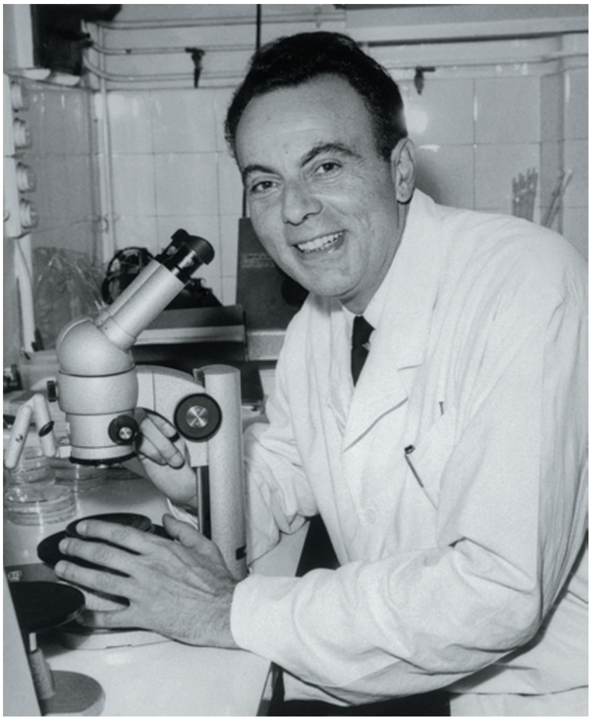
French freedom fighter who helped to uncover how genes are regulated.

François Jacob helped to answer a question that had been troubling geneticists for more than 30 years: how do the various tissues of multicellular organisms express different sets of genes when all cells contain the same genetic material? Along with two colleagues, Jacob devised the first conceptualization of gene regulation, opening the door to the study of development in animals and humans.

Jacob was born in 1920 in Nancy, northeastern France, to a middle-class Jewish family. He studied at the Lycée Carnot in Paris and went to medical school with the intention of becoming a surgeon. His studies were interrupted in June 1940 when, refusing to accept France's surrender to Germany, he escaped to London by boat to join the Free French Forces under General Charles de Gaulle. Jacob fought for four years as a medical auxiliary in Africa and France. When the war ended, he was named a Companion of the Liberation, the highest French military distinction of the Second World War. More than six decades later, he became Chancellor of the Order of the Liberation, the order's most important figure.

After the war, the injuries that Jacob had sustained to his arms and legs in 1944 prevented him from becoming a surgeon and he worked on producing antibiotics for the French army. He heard about a scientific revolution taking place as a result of physics coming together with genetics and microbiology. The war and its aftermath had led to a redistribution of scientists throughout Europe and the United States, which, combined with the availability of technologies such as X-ray diffraction, electrophoresis and electron microscopy, was spurring a wealth of new ideas and approaches in biology. Jacob was keen to contribute to these exciting new developments, and the microbiologist André Lwoff — one of the few French researchers involved in this new approach — invited Jacob to join his laboratory at the Pasteur Institute in Paris in 1950.

Fifteen years later, Jacob was awarded the Nobel Prize in Physiology or Medicine along with Lwoff and Jacques Monod for describing the 'operon model'. In this model, a repressor protein, encoded by a regulatory gene, binds to a cell's DNA upstream of a battery of structural genes that the trio named the operon. This binding prevents the structural genes from being transcribed into messenger RNA. The model emerged from elegant experiments investigating the factors that repress and trigger the multiplication of viruses in bacteria, and those that activate and suppress the synthesis of the bacterial β-galactosidase enzyme needed to break down lactose into its glucose and galactose components.



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During his early years at the Pasteur Institute, working with microbiologist Elie Wollman, Jacob also proposed a mechanism for bacterial conjugation, or mating. In this process, part of a bacterial chromosome is transferred from a donor bacterium to a recipient one. In all of these major research projects, Jacob's particular skill was being able to conceptualize the molecular mechanisms underlying complex observations.

In the late 1960s, Jacob switched to working with mice, to align his research with the Pasteur Institute's focus on human disease. It took time to build the genetic-engineering tools needed to analyse complex organisms and their embryonic development, but Jacob had made the right decision. Owing to their genetic similarities with humans, mice are now the models of choice for scientists studying human diseases. Jacob's choice of a type of germ-cell cancer to aid research into embryonic development in mice proved similarly prescient: the cells studied in his laboratory are the ancestors of the stem cells that are now grown in hundreds of labs across the world.

Jacob enjoyed interacting with people who were different from him, but not those who tried to imitate him, with whom he could be very harsh. When I joined his lab in 1981 as a postdoc, he gave me total freedom to pursue the questions that I deemed interesting, and this was the same for everyone who worked with him. If ever we hit on some potentially important result, he would jump up in excitement and ask to see the data. For him, only the science that was moving forward was important.

His immense scientific knowledge, combined with his wartime experiences, fuelled a lifelong commitment to combating racism and preventing the misuse of genetics. He presented his views on television, radio and in newspapers. He was also a member of the French national ethics committee for the life sciences.

Jacob was fascinated with the history of science and philosophy. In his 1973 book *The Logic of Life* (Pantheon), he explored the idea that biological knowledge has evolved in successive steps, from the study of morphology to that of the cell, and then to the study of genes and macromolecules. In several other works, such as his 1982 *The Possible and the Actual* (Pantheon), he sought to identify the features that characterize scientific knowledge as opposed to other types of knowledge. His death marks the end of a golden age of biology, in which members of a relatively small international community were free to pursue whatever question they wanted, with the possibility that they would make huge strides in discovery. ■

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