MicroNobelHero: André Lwoff (1902-1994)

(Harald Brüssow)

Source: Wikipedia

Claim to fame: Discovered lysogeny in bacteriophages (Nobel Prize in Physiology or Medicine, 1965, together with François Jacob and Jacques Monod)

Writing on lysogeny in 1953, André Lwoff, Nobel Prize Laurate (1965) and first president of the Federation of European Microbiology Societies (FEMS), noted: "For many young scientists the future is more important than the past, and the history of science begins tomorrow". He stressed, however, that "it is interesting to know how phenomena were discovered, how the problems were born, attacked and solved, and how and why our ideas have evolved". His personal biography vividly illustrated how microbiology developed in the 20th century and can serve as a guide for young scientists to develop their own creative scientific curiosity.

From Ciliates to nutritional genetics

Born in 1902 in France to a painter and psychiatrist Russian couple fleeing tsarist oppression, André Lwoff studied biology and medicine in Paris and became assistant of E. Chatton, a leading protozoologist of his time. Lwoff's first study objects were ciliates. When studying kinetosomes of ciliates, he noted genetic continuity for subcellular structures. In 1921, he joined the Pasteur Institute in Paris, led by Mesnil and then Roux, where he established pure cultures of ciliates and studied the nutritional requirements of microbes. The loss of biochemical functions in parasitic flagellates and *Haemophilus influenzae* bacteria led him to the concept of growth factors (haematin, factor V) which laid the foundations of biochemical genetics. In 1938 he became head of microbial physiology at Pasteur.

Phages and Lysogeny

Interrupted by WWII, scientific travelling resumed in 1946 when he attended the Cold Spring Harbor Symposium. He was impressed by the work of the US Phage Group around M. Delbrück, S. Luria, and A. Hershey. Delbrück had vigorously advocated working with the virulent coliphages T1 to T7 (earning him the nickname *Snow White and the Seven Dwarfs*). In the words

of Lwoff, Delbrück "the founder of the phage church did not believe in the existence of lysogeny". For Lwoff science was not a matter of belief, but of experimental results. He developed a single cell drop technique and demonstrated that infectious phage is released by lysis from a single lysogenic cell. From this and other experiments in his lab, he concluded that "(a) in lysogenic bacteria the phage is perpetuated in a noninfectious form which was called the prophage. (b) Bacteriophage is not secreted but is liberated by the lysis of a lysogenic bacterium. (c) The production of bacteriophage is the result of an induction by irradiation with ultraviolet light".

Poliovirus

Lwoff attended another Cold Spring Harbor Conference in 1953, which draw his attention to animal viruses. At the conference he was intrigued by a proposal that malignant cancer cells might owe their potential to genetic material from oncogenic viruses induced by carcinogenic agents, drawing obvious parallels to lysogeny. In addition, Lwoff got a generous grant from the US National Foundation for Infantile Paralysis, including visits to the labs of prominent US animal virologists (Melnick, Enders, Salk, Dulbecco) to learn cell culture work with animal viruses. Subsequently, Lwoff started working with poliovirus at the Pasteur, later reflecting that it was "foolish to abandon the still quiet field of lysogeny in order to intrude into the jungle of animal virology. To enter a new field at the age of fifty-two is unwise anyhow; but unwise decisions debouch on the unexpected which is the salt of research". Lwoff developed one-step growth cycle analyses for different strains of poliovirus at different temperatures. He discovered that virulent strains had retained the capacity to replicate at elevated temperatures; a capacity lost in avirulent poliovirus. This discovery rationalized the use of poliovirus vaccine strains propagated continuously at 23°C. Lwoff hypothesized that fever, combined with tissue acidification during inflammation, restricted viral replication in vivo. In a period dominated by molecular biologists, he thus took early steps into innate immunity research.

What is a virus?

In the 1950s, Lwoff struggled with the question: What is a virus? He defined viruses as "infectious particles possessing only one type of nucleic acid, inability to grow and to divide, absence of metabolism, absence of the information for the enzymes of energy metabolism and the absence of transfer RNA and of ribosomes". He proposed with others the terms virion, capsid, and capsomere, which are still in use today. He was less successful with viral taxonomy which he considered necessary for international understanding but which described as an "equivalent of a religious war" between different schools of thought.

Afterthoughts

Shortly before retirement he became director of the Cancer Research Institute in Villejuif near Paris, working with Simian Virus 40. After retirement, he spent his time with painting, a passion inherited from his mother. Some of his personal experiences are still important to scientists from today. Lwoff remembered that "a director told me once that my work was devoid of any interest for the Pasteur Institute". He decided for himself that "the scientists transcended the director and the board of trustees, and that everything good for science was good for the Pasteur Institute". Stressed scientists working in a highly organized scientific endeavor should not forget Lwoff's word "research pertains to ludic activity on a playground". He was a cultivated individualist who preferred work with his own hands together with his wife in a small research group.