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ŞTEFAN S. NICOLAU – THE FOUNDER OF ROMANIAN SCHOOL OF VIROLOGY

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Stefan S. Nicolau died on October 15, 1967, while still active in research and teaching.

He was one of the greatest Romanian scientists of the twentieth century, whose momentous discoveries in virus biology and virus-cancer relationship are still actively pursued by many laboratories worldwide.

Nicolau studied medicine at the University of Bucharest (1913–1919) and Cluj (1919–1920). His training in internal medicine had been interrupted in 1919, when he was mobilized and served as a commissioned officer in the Romanian Army during The National Reunification War.

After finishing clinical studies he started a prodigious didactic activity as assistant professor of General and Experimental Pathology in Cluj. Soon he joined The Microbiology Chair conducted by Constantin Levaditi, who became his most influential mentor, and whom he followed in Paris at the Pasteur Institute[1]. During 1926–1927 he pursued postdoctoral studies at National Medical Research Institute in London, UK. Nicolau joined these already famous laboratories, that were on the cusp of great discoveries in virology. He soon became a key member of these labs, having numerous important contributions in cell staining methods (such as introducing orcein staining for better preservation of elementary infectious bodies[2]) and serological studies (using murine models to investigate viral antigenic markers[3]). These technical advances facilitated many pivotal discoveries by Nicolau and his colleagues throughout the world.

Fascinated by every aspect of virology and involved in all, his work ranged from nucleic acids synthesis to epidemiology and production of vaccines[4,5]. He was eager to describe his latest findings, absorb those of others and implement all these in clinical domains. The collaboration between Levaditi and Nicolau was exceptionally

fruitful, producing new concepts in virology, a new Romanian scientific school, a research institute of the Romanian Academy- now called the Institute of Virology and a Virology Chair, established in 1942 at the "Carol Davila" School of Medicine in Bucharest.

Before 1930, the links between the study of filterable agents and bacteriology were so strong that viruses were considered inframicrobes[7]. The critical defining point came when scientists realized the differences in the process of multiplication: binary fission for bacteria vs the viral life cycle. Virology was a melting pot for diverse disciplines and experimental philosophies. The dichotomy between exogenous and endogenous interpretations of virus multiplication has split the virologists into two camps: those who believed that viruses were exogenous and autonomous agents versus those who claimed that viruses were cell products. Nicolau strongly adhered to the first group.

The experimental work of Nicolau was multilateral; he studied the biology of poliomyelitis[6], rabies[8], cancer and viruses[9], rickettsiosis[10], herpes viruses[11, 12], viral hepatitis[13], viral encephalitis[14], etc. He collaborated with numerous famous virologists of his era (Smorodintsev, Benyesh-Melnik, Giroud, Graffi, etc). Many new concepts evolved from his research:

– Tropism modification – the dermotropic herpesvirus became neurotropic after several intra cerebral passages in guinea pigs.

– Phenotypic segregation – it is possible to separate weak encephalitogenic strains (wild strains) from strong encephalitogenic (neuroadapted strains) of herpes viruses.

– Viral interference – despite the fact that both the vaccinia virus and the herpesvirus are neurotropic, as shown by the histopathology, they behave differently when injected concomitantly into the brain of the guinea pig, without causing encephalitis. This was an early indication on a phenomenon later called interference.

– The photodynamic effect of some dies – a property still used in protocols for viral mutagenesis.

– The virus-cancer relationships and the possibility of viral oncolysis[15]. By injecting strains of vaccinia virus in murine tumors, Nicolau observed a reduction in the size and dispersion of neoplastic tissues. A comprehensive discussion about this Romanian priority in the field of viral oncolysis was presented in 1995 by JC Sinkovics and J. Horwath[16].

The most challenging and, at the same time, the most rewarding period of Nicolau's career began after the founding of the Institute of Virology. He successfully managed to balance his new administrative tasks in the Institute and in the Board of the Romanian Academy with his research and teaching career. He preserved and cultivated his deep interest in music, the Japanese fine arts and history.

He had a generous and optimistic personality. One specific memory remained in my mind. It took place in the spring of 1967, when one of his young collaborators tried to escape from the communist regime in Romania, by swimming across the Danube to the neighboring Serbia. He was caught and arrested by the frontier police and later on he was "put on trial" in front of all members of the Institute, but there, the words of Nicolau granted his liberty.

Nicolau was an eloquent speaker, and his lectures are vivid illustrations his knowledge, lucidity and passion for his research area. He was a true mentor, who promoted young researchers, students and residents. His legacy is that research should be driven by passion and that collective work is compulsory in order to achieve a project's goals. He strongly believed that a collaborative environment is a key prerequisite for answering important biological questions and that all that is needed for success, including publication, teaching, and even performing community service must result from networking.

To his numerous postdoctoral fellows, students, fellow researchers and visitors from abroad, Nicolau will remain an inspiration for the pursuit of science.

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