

Obituary

Louis Selim Chedid, MD PhD

IEIIS honorary life member

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Louis Selim Chedid was born in Cairo (Egypt) in June 1922 and died in Paris in March 2021 at the age of 98. After obtaining his bachelor's degree in Cairo, he started his medical studies in Beirut and completed them in Paris, defending his medical thesis on artificial estrogen in 1947. After being trained in Egypt and the United States, he joined the laboratory of Robert Courrier at the College de France (1946). In 1952, he was recruited by the CNRS (National Center for Scientific Research, France). In 1955, he defended his PhD on hormones and infection and started working at the Institut Pasteur (Paris) in the laboratory of Therapeutic Chemistry under André Lamensans. He joined the Institut Pasteur in 1961 and was promoted to Professor in 1972. In 1973, he became the head of the Experimental Immunotherapy laboratory. In 1986, he moved to the H. Lee Moffit Cancer Center and Research Institute at the University of South Florida, Tampa where he founded a startup working on vaccine adjuvants (VacSyn). Louis Chedid was the co-author of 26 patents.

He investigated immune mechanisms with the goal of boosting the defense against infections. Among his main contributions is the identification with Edgar Lederer (1908–1988) of the muramyl dipeptide (MDP), the smallest active part of the peptidoglycan of mycobacteria present in complete Freund adjuvant.^{1,2} He then devoted part of his career to study homologs of MDP and their bioactivities, synthetic vaccines, and adjuvants.³ He also performed

numerous investigations on endotoxins including investigations on enhanced resistance to infection by endotoxins,^{4,5} LPS-induced abortion, production of interleukin-1 and tumor necrosis factor in response to endotoxins, the synergy between MDP and LPS, prevention of endotoxin-induced lethality, the influence of endotoxin on bone marrow cells, endotoxin tolerance, polyclonal activation, LPS-induced radioresistance, localization of injected ⁵¹Cr-labeled LPS, and studies on alkaly detoxified endotoxins. He offered the basis for an universal anti-endotoxin antibody: “*Thereafter, the presence of a few types of “R” (rough) antibodies or of serum factors reacting with rough antigens have the capability of coping, like master-keys, with a wide range of infection due to serologically unrelated organisms*”.⁶

He collaborated with eminent US scientists including JJ Oppenheim, HS Warren, CA Dinarello, SM Wolff, and JM Krueger. With the latter three, he investigated the links between slow wave sleep and IL-1,⁷ his most cited paper (462 citations), and addressed the links between sleep and MDP. A Romanian scientist, Constantin Bona (1934–2015) worked for a while in his laboratory on so-called nonspecific immunity before joining the Mount Sinai Hospital in New York, working on idiotypes and neonatal immunity. They are co-authors of 17 papers including reports on a Nocardia water soluble mitogen. Claude Leclerc started her bright career on vaccines and cancer at Institut Pasteur in his laboratory. Based on an idea of Agnès Ullman, she used the adenylate cyclase toxin from *Bordetella pertussis* to deliver antigen into the cytosol of the antigen presenting cell.⁸ Her work was a continuation of the work on synthetic vaccines pioneered by Louis Chedid and Michael Sela (Weizman Institute), using peptides corresponding to fragments of diphtheria toxin.⁹ In 1984, Claude Leclerc showed that intracellular delivery of MDP with the help of antibodies increased its adjuvanticity 10,000-fold.¹⁰ With Chedid, they hypothesized that the MDP receptor was intracellular: “*Specific receptors for MDP exist inside the macrophage [...]. To be active, MDP has to be present inside the cells in sufficient concentration*.”¹¹ before Dana Philpott's and Gabriel Nuñez' teams later identified the NOD1 & NOD2 cytoplasmic pattern recognition receptors in 2001/2002.

In 1964, he obtained French citizenship. He received the Bouchard Prize - Laureate of the Society of Biology (1954), and the Claude Bernard Prize of the City of



Paris (1978). He was a Knight of the National Order of Merit, a member of many learned societies (The New York Academy of Sciences; The Royal Society (London); Société Française d'Immunologie...) and an honorary life member of the International Endotoxin and Innate Immunity Society. He was a member of editorial boards of journals (Journal of the Reticulo-endothelial Society, now the Journal of Leukocyte Biology; Journal of Infectious Diseases) and of various national committees (CNRS, Inserm, Scientific Council and Board of Directors of the Institut Pasteur of Lille, and the General Assembly of the Institut Pasteur).

He was the husband of Andrée Chedid (1920–2011), a famous Egyptian-French poet and novelist, the father of Louis Chedid a famous French singer, and the grand-father of Mathieu Chedid, also a famous singer. He wrote a memoir in 2004 (*Mémoires vagabondes*), sharing his passion for scientific adventures and recounting a life at the interface of two cultures. He was an enthusiastic and warm scientist, happy to share his discoveries and his passion.

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