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Permalink

<https://escholarship.org/uc/item/2d7271bg>

Journal

Current Eye Research, 42(1)

ISSN

0271-3683

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Publication Date

2017-01-02

DOI

10.1080/02713683.2016.1252405

Peer reviewed



Published in final edited form as:

Curr Eye Res. 2017 January ; 42(1): 161–162. doi:10.1080/02713683.2016.1252405.

A tribute to Professor Steven L. Wechsler (1948–2016): the Man and the Scientist

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Abstract

Professor Steven L. Wechsler, a world-renowned eye researcher and virologist, passed away unexpectedly on June 12, 2016 at the age of 68. Many scientists came to know Professor Wechsler as a gifted researcher in the field of ocular Herpes Simplex Virus (HSV-1) latency, reactivation, and pathogenesis. Professor Wechsler published over 150 peer-reviewed scientific papers during his career, pushing forward the frontiers of his field eye research. His colleagues would say: “Steve literally wrote the book on herpes latency and reactivation”. He was the first to show that the HSV-1 latency associated transcript (LAT) is essential for the HSV-1 high spontaneous reactivation phenotype and that LAT has anti-apoptosis activity. This discovery of LAT’s anti-apoptosis activity, which is a key factor in how the LAT gene enhances reactivation, was published in *Science* in 2000 and created a new paradigm that greatly increased understanding of HSV-1 latency and reactivation. In collaboration with Professor Lbachir BenMohamed, an immunologist, they later demonstrated that LAT also acts as an immune evasion gene. He was a caring scientist who truly enjoyed working and sharing his experience and expertise with young researchers. He will be remembered as a significant pillar within scientific and ocular herpes research communities worldwide. Professor Wechsler’s dedication to science, his compassionate character, and wonderful sense of humor were exemplary. We, who were his friends and colleagues, will mourn his passing deeply.

The world of virology lost an outstanding leader in herpes latency, reactivation and pathogenesis, with the death of Professor Steven (“Steve”) Lewis Wechsler, Ph.D. Professor Wechsler passed away unexpectedly at the age of 68 in Irvine, California on Sunday, June 12, 2016. Many in the research community had come to know Professor Wechsler as a gifted scientist in the field of herpes latency and pathogenesis and a wonderful colleague with whom to work. His passing was met with great shock and sorrow. Many collaborators and colleagues from around the world reached out with memories of their interactions with Professor Wechsler over the years. Professor Wechsler was predeceased by his wife Elizabeth “Beth” Wechsler; who passed away in October 2015. He leaves behind a loving

and inspiring legacy and is survived by his children: Robert, Matthew, Michelle, and Adrianna Wechsler Zimring; son-in law Jason Zimring; and two granddaughters, Sedona Leah and Lorelai Sarah [1].

Professor Wechsler received his B.S. in Biology from City College of New York in New York, NY and his Ph.D. in Molecular Genetics from University of North Carolina in Chapel Hill, NC. He completed a postdoctoral fellowship in virology with Bernard Fields at Harvard Medical School in Boston, MA. From 1980 to 1986, he was an Assistant Member of the Department of Molecular Virology at the Gamble Institute of Medical Research in Cincinnati, OH, where he did important work on measles virus. In 1986, he was hired by Dr. Anthony B. Nesburn to serve as Director of Ocular Virology Laboratory and Director of Ophthalmology Research at Cedars-Sinai Medical Center in Los Angeles, CA. At Cedars-Sinai, Professor Wechsler began work on HSV-1 latency and reactivation, using the rabbit ocular model that mimics human recurrent HSV, which would become the main focus for the rest of his outstanding research career. In 2002, he was recruited to the University of California, Irvine Department of Ophthalmology as Professor and Director of Virology Research at the Gavin Herbert Eye Institute. He additionally held co-appointments as a Professor in the Department of Microbiology and Molecular Genetics and the Center for Virology Research at UC Irvine.

Professor Wechsler was an active and accomplished scientist who advanced the frontiers of scientific research throughout his career. He published over 150 scientific papers and with numerous well-planned and beautifully executed studies [2–4]. When Professor Wechsler first began working on HSV-1 latency in 1985, it was thought that all viral genes were turned off during latency. His laboratory showed the revolutionary result that one viral gene (originally called LR-RNA for latency related RNA, and now called LAT for latency associated transcript) was actually highly transcribed during latency. In collaboration with Dr. Nesburn and Dr. Oscar Perng, Professor Wechsler showed that LAT was the only viral gene abundantly expressed in the trigeminal ganglion (TG) latently infected with HSV-1. Professor Wechsler was then first to demonstrate that the HSV-1 LAT is essential for the HSV-1 high spontaneous reactivation phenotype and that LAT has anti-apoptosis activity. The discovery of LAT's anti-apoptosis activity, which is a key factor in how LAT gene enhances reactivation, was published in *Science* in 2000 [4] and created a new paradigm that greatly increased our understanding of HSV-1 latency and reactivation. Professor Steven Wechsler collaborated with Professor Lbachir BenMohamed, an immunologist, to later demonstrate how LAT also acts as an immune evasion gene by interacting with the phenotype and function of anti-viral CD8⁺ T cells [5–7]. In their most recent work, Professors Wechsler and BenMohamed were investigating the role of 6 microRNAs important for LAT function. They found that microR-H2 acts to help maintain latency and confirmed the hypothesis that at least one of the LAT microRNAs plays a role in HSV-1 latency. Professors Wechsler and BenMohamed also recently developed an improved mouse model of UV-B induced ocular reactivation of HSV-1 (strain Mckrae) [8; 9]. This new UV-B mouse model will allow for detailed investigations of the underlying mechanisms of immune evasion during the latency/reactivation cycle.

Professor Wechsler, known for his innovative thinking and creativity, was a meticulous scientist and superlative grant writer who contributed to the field of herpes simplex research in many ways. He continuously received grant funding from the National Eye Institute of the National Health Institute. Professor Wechsler worked with an outstanding group of collaborators, Rafi Ahmed, Nigel Fraser, Homayon Ghiasi, Clinton Jones and Oscar Perng, outside of UC Irvine as well. Above all, Professor Wechsler loved discovering new biological phenomena, teaching science and playing a winning game of poker on the side. He was a pioneer in HSV-1 latency, reactivation and pathogenesis and his work has added a breadth of knowledge to science. His colleagues would say: “Steve literally wrote the book on HSV-1 latency.”

Professor Wechsler was also an Ad Hoc reviewer for the *Journal of Virology*, *Journal of General Virology*, *Virology*, *Infection and Immunity*, and *Investigative Ophthalmology and Visual Sciences*. In 2007, he was honored with the Athalie Clarke Research Association Achievement Award (Senior Faculty Award) at University of California, Irvine.

Through the years, Professor Wechsler mentored numerous postdoctoral fellows, and graduate and undergraduate students pursuing careers in academia and various other industries. He was an excellent mentor; supportive and simultaneously firm yet kind. With his wonderful sense of both responsibility and humor, Professor Wechsler helped many students, post-doctors, and young scientists alike, encouraging hard work and self-dependency for their scientific career development. He used to say “*Everything I needed to know I learned from StarTrek*”. He truly enjoyed working with young researchers and sharing his experience and expertise. As a strong team player, Professor Wechsler served a crucial role in helping many younger investigators write important and fundable NIH grants.

Professor Wechsler was tirelessly devoted to his research and continued to work from home despite severe illness, reflecting his passion until the very end. His dedication to science, his personality, and his strong character were exemplary. Professor Wechsler will be remembered as a significant pillar within the scientific and herpes research communities worldwide and we mourn his passing deeply.

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Figure 1.