Laudatio for Prof. Dr. Charles M. Rice
by Prof. Dr. Peter Palese
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Charles Rice, “Charlie”, was born and raised in Sacramento, California. He grew up as a single child with many beloved dogs, which fueled an early interest in studying animals. He received a Bachelor of Science degree in Zoology from the University of California in Davis but, fortunately for us, a beginner’s biology class at the University of California Davis so fascinated him that he became interested in science. As many of us know, introductory classes can be quite boring, but Charlie soaked it all up and was on the road to becoming a scientist. He selected the California Institute of Technology (Caltech) in Pasadena in Southern California for his graduate studies in Biochemistry. A note to our Berlin audience – there are only three students for each professor at that university. Charlie excelled in his PhD as well as in his postdoctoral studies in the laboratory of Jim and Ellen Strauss. He determined the first genome sequences of Sindbis virus, an alpha virus. This RNA-containing, mosquito born virus was named after a town near Cairo in Egypt, and thanks to Charlie many of its Sphinxian secrets have been uncovered.

By 1987, Charlie succeeded in generating the first infectious DNA clone of Sindbis virus, which was a real game changer. Indeed, this accomplishment not only allowed molecular studies such as probing for the mechanisms regulating RNA synthesis and protein expression in the Sindbis virus life-cycle, but also made more applied endeavors possible such as the engineering of animal expression vectors. This was done almost three decades ago and it was just the beginning!

Charlie became interested in yellow fever virus, which - at the time - was believed to be related to Sindbis virus. Charlie’s work corrected this misconception and based (mostly) on his studies a new virus family, the *Flaviviridae,* was established. This family includes now not only yellow fever virus, Dengue virus and West Nile fever virus but also the hepatitis C viruses. In 1989, Charlie’s group successfully generated the first infectious molecular clones of yellow fever virus, a milestone which helped elucidate the mechanism of action of the highly successful yellow fever virus vaccine. Charlie’s early work on yellow fever virus and the use of chimeric yellow fever virus clones may very well lead to effective vaccines against dengue fever and even

malaria. The latter research was conducted at Washington University in St. Louis which attracted him with an independent faculty position. Moving from sunny Southern California to St. Louis must have been unfair punishment (anyone who knows about the weather there knows what I am talking about) and he endured it for fourteen years!

Despite these early successes, Charlie is best known for his work on hepatitis C virus. In 2001 he was recruited to lead a brand new multi-disciplinary Center for the study of hepatitis C, jointly run by the Rockefeller University, Weill Cornell Medical College, and New York-Presbyterian Hospital in New York City. Charlie set out to organize a strategic comprehensive study plan: first, map all the proteins of hepatitis C virus, then attack the RNA, and establish tissue culture systems, and finally develop suitable animal models. I remember one of Charlie's early hepatitis C papers showing that the 3' terminus of the virus's RNA (as published at the time) was wrong. Having the correct sequence, Charlie's group was the first to generate an infectious molecular clone which allowed the molecular studies on Hepatitis C virus replication in tissue culture, and in chimpanzees. These studies were essential for the rapid progress in the field.

I also want to mention the elegant work on the complex cellular receptors of hepatitis C virus. His group identified the tight junction proteins, claudin-1 and occludin, as essential hepatitis C virus entry factors, which together help explain why this virus preferentially infects human liver cells.

Another of his great scientific achievements is the body of work on the structure and function of the hepatitis C virus NS5A protein. This phosphoprotein is involved in viral RNA replication and has become an excellent target for several FDA-approved drugs which, combined with protease inhibitors, have revolutionized the treatment of Hepatitis C virus infection. In fact, Charlie's discoveries and, equally important, the many tools he developed, have been essential for identifying and characterizing these potent drugs against hepatitis C; undoubtedly one of the major medical breakthroughs of this decade. These combination treatments are curative in many patients which should not be forgotten in all the discussions about health policies.

Charlie is a charismatic leader and mentor. He has a large group which produced many scientists who are successful in their own right. He mentored well over 150 students and postdoctoral fellows throughout the years. He is a highly sought after reviewer of papers and programs and serves as a consultant for many non-profit as well as for-profit entities. On a personal level, he is a calm, well-liked, and friendly colleague. He and his dear wife, Peggy

MacDonald, exude friendliness! The welcoming atmosphere of the Rice laboratory cannot be matched - even their dog, who is a constant fixture in the lab, is exceptionally friendly.

Charlie is a Member of the National Academy of Sciences. He received many awards: let me just mention the Dautrebande Prize from the Belgian Royal Academy of Medicine and the Beijerinck Prize of the Royal Netherlands Academy of Arts and Sciences. His curriculum vitae is over 60 pages long.

Charles M. Rice has truly moved and advanced the field of Virology!