HARRY NOLLER, Ph. D.

Harry Noller was born in Oakland, California, and received his undergraduate training in biochemistry at UC, Berkeley. He did his graduate work on the mechanism of action of serine proteases under Sidney Bernhard in the Institute of Molecular Biology at the University of Oregon, where he received his Ph.D. in Chemistry in 1965. He was an NIH Postdoctoral Fellow at the MRC Laboratory of Molecular Biology in Cambridge, where he carried out proteinchemistry in the laboratory of Ieuan Harris in Fred Sanger's department. In 1966, he joined Alfred Tissières' laboratory for his second postdoc in the newly formed Dèpartement de Biochimie Genètique in the Institute de Biologie Molèculaire at the University of Geneva, where he began research on ribosomes. In 1968, he joined the faculty of the University of California, Santa Cruz, where he is currently Sinsheimer Professor of Molecular Biology, Professor of Molecular, Cell and Developmental Biology and Director of the Center for Molecular Biology of RNA.

Intending to study the functional roles of the ribosomal proteins by biochemical approaches, experiments in Noller's lab in the early 1970s pointed unexpectedly to a key functional role for ribosomal RNA. This unanticipated change in direction led to many studies over the following decades directed toward understanding the structure of ribosomal RNA and its functional roles in translation. Among these were the sequencing of the rrnB operon containing the first complete 16S and 23S ribosomal RNA sequences, and, in collaboration with Carl Woese, deducing their secondary structures by comparative sequence analysis. Genetic studies on rRNA in the Noller lab, using vectors based on the rrnB operon, showed that mutations in rRNA could confer severe functional phenotypes such as increased translational error frequencies and defects in tRNA binding.

Noller's group developed rapid chemical probing methods for mapping the sites of interaction of ligands with RNA, and used them to map the binding sites of the ribosomal proteins on rRNA, and to show that all of the main functional ligands, including tRNA, initiation factors, elongation factors and antibiotics, all interact with 16S and 23S rRNA. This same method was extended by Moazed and Noller in 1989 to identify intermediate states of translocation of tRNA on the ribosome, named 'hybrid states'. These findings showed that tRNA 'walks' through the ribosome by first moving its acceptor end on the 50S subunit, followed by movement of the anticodon end, together with mRNA, on the 30S subunit.

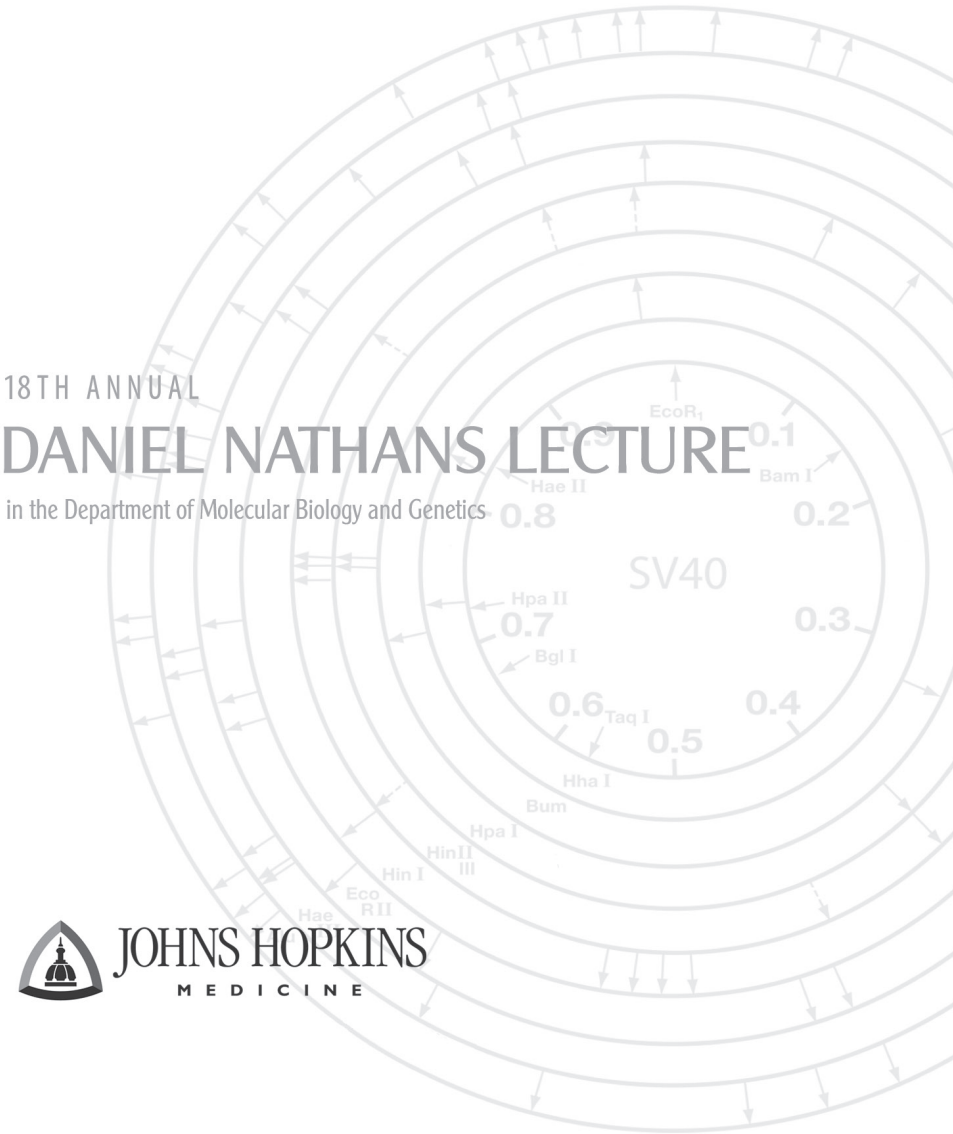
In 1992, the Noller lab showed that peptidyl transferase, the ribosomal activity responsible for catalysis of peptide bond formation, is unusually resistant to extraction with agents commonly used to extract and denature proteins, including vigorous treatment with SDS, proteinase K and phenol, but highly sensitive to treatment with ribonuclease, providing evidence that peptide bond formation is catalyzed by 23S rRNA. This was finally confirmed by crystallography in the Moore and Steitz laboratories in 2001.

During recent years, the Noller lab has solved the crystal structures of functional complexes of the complete ribosome, showing how the tRNAs, mRNA and protein synthesis factors interact with the ribosome and revealing functionally important conformational changes in ribosome structure. These structures provide a structural basis for detailed descriptions of the molecular mechanisms underlying protein synthesis. In collaboration with the Tinoco, Bustamante and Ha laboratories, biophysical approaches have revealed internal movements in single ribosomes in real time. The results of all of these studies, together with those from many other laboratories, have finally shown that the ribosome is a complex macromolecular machine whose functions are based on RNA, rather than protein.

18TH ANNUAL

DANIEL NATHANS LECTURE

in the Department of Molecular Biology and Genetics



JOHNS HOPKINS
MEDICINE

DANIEL NATHANS, M.D.

The Daniel Nathans, M.D., Lecture in Molecular Genetics was established in 2000 to honor his extraordinary contributions to science and to Johns Hopkins University. The lecture provides a forum in which eminent scientists have the opportunity to share their most recent discoveries with the Johns Hopkins community.

Dr. Nathans obtained his bachelors degree from the University of Delaware and his medical degree from Washington University in St. Louis. Following completion of a residency in internal medicine at Columbia-Presbyterian Medical Center and two years as a clinical associate at the National Cancer Institute, he went to Rockefeller University where he began his studies on protein synthesis in the laboratory of Dr. Fritz Lipmann. In 1962, he was recruited to the microbiology department of the Johns Hopkins University School of Medicine by Dr. Barry Wood. Dr. Nathans remained on the faculty at Johns Hopkins until his untimely death in 1999. From 1995 to 1996, he served as interim president of Johns Hopkins University. He was also a Howard Hughes Medical Institute senior investigator.

In the late 1960's, Dr. Nathans switched his research focus to the study of viral tumorigenesis. Using simian virus 40 as a model, he pioneered the use of restriction enzymes to construct physical maps of genes and genetic elements. His work laid the cornerstone for the ensuing revolution in molecular biology. In 1978, he shared the Nobel Prize in physiology or medicine with his colleague Hamilton O. Smith and with Swiss scientist Werner M. Arber. In 1993, Dr. Nathans was awarded the U.S. Nation Medal of Science.

The Daniel Nathans Papers are now available on the National Library of Medicine's Profiles in Science site at http://profiles.nlm.hih.gov

You are cordially invited to attend

The Eighteenth Annual

Daniel Nathans, M.D., Lecture in the Department of Molecular Biology and Genetics

RNA Mechanics in the Ribosome

Harry Noller, Ph.D.

Robert Louis Sinsheimer Professor of Molecular Biology
and Director of the Center for Molecular Biology of RNA
University of California, Santa Cruz
Santa Cruz, California

Thursday, April 26, 2018

4:00 p.m.

Wood Basic Science Auditorium JHU School of Medicine

Reception to Follow Lecture