THE JOURNAL OF BIOLOGICAL CHEMISTRY

Vol. 286, No. 25, Issue of June 24, p. e4, 2011
*Printed in U.S.A.*

# Classics

A PAPER IN A SERIES REPRINTED TO CELEBRATE THE CENTENARY OF THE JBC IN 2005

## JBC Centennial
## 1905–2005
### 100 Years of Biochemistry and Molecular Biology

# The Molecular Genetics of Bacteriophage: The Work of Norton Zinder

**In 1966, Norton Zinder and Joshua Lederberg discovered that *Salmonella* could exchange genes via bacteriophages. They named this phenomenon "genetic transduction." This discovery set Zinder on a lifelong journey researching bacteriophage. In the two *Journal of Biological Chemistry* (JBC) Classic papers reprinted here, Zinder and Nina Fedoroff present their findings on the phage f2 replicase.**

**Properties of the Phage f2 Replicase. I. Optimal Conditions for Replicase Activity and Analysis of the Polynucleotide Product Synthesized *in Vitro***
**(Fedoroff, N. V., and Zinder, N. D. (1972) *J. Biol. Chem.* 247, 4577–4585)**

**Properties of the Phage f2 Replicase. II. Comparative Studies on the Ribonucleic Acid-dependent and Poly(C)-dependent Activities of the Replicase**
**(Fedoroff, N. V., and Zinder, N. D. (1972) *J. Biol. Chem.* 247, 4586–4592)**

Norton Zinder

Norton David Zinder was born in New York City in 1928. He attended the prestigious Bronx High School of Science and went on to Columbia University where he received his B.A. in biology in 1947. Zinder then joined the graduate program at the University of Wisconsin-Madison, studying under geneticist Joshua Lederberg.

Lederberg recently had found that *Escherichia coli* could mate and exchange genes (conjugation), a discovery for which he would be awarded the 1958 Nobel Prize in Physiology or Medicine. Zinder's assignment was to continue Lederberg's investigations using *Salmonella*. To do this, he needed to obtain large numbers of mutant bacteria. Rather than using the traditional method of exposing the *Salmonella* to mutagens and testing the survivors, Zinder decided to use a nutritionally deficient medium and penicillin (negative selection) to select for mutants (1). However, when he began investigating conjugation in *Salmonella*, most of his attempts at crossing the mutants failed. Fortunately, one mutant strain produced some prototrophs; but puzzlingly, Zinder's markers did not segregate. Further experiments showed that the mutants were exchanging genes via bacteriophages (2). Lederberg and Zinder named this new phenomenon "genetic transduction."

Zinder received his M.S. in genetics in 1949 and completed his Ph.D. in medical microbiology in 1952. He then accepted a position as assistant professor at Rockefeller University (then known as Rockefeller Institute for Medical Research). By 1964 Zinder had become a full professor of genetics, and approximately 10 years later he was named John D. Rockefeller, Jr. Professor of Molecular Genetics. In 1993 Zinder was appointed dean of graduate and post-graduate studies.

At Rockefeller, Zinder continued his studies of the molecular genetics of phages. He discovered the f2 phage, which was the first bacteriophage known to contain RNA as its genetic material, and demonstrated that RNA phage replication is not dependent on DNA (3).

Zinder's two *Journal of Biological Chemistry* (JBC) Classics reprinted here look at the phage f2 replicase. In the first paper, Zinder and his graduate student Nina V. Fedoroff show that the enzyme, purified on the basis of its poly(G) polymerase activity, could carry out the *in vivo* synthetic reactions involved in phage RNA replication. They also report that phage replicase activity is stimulated by salt and by a brief preliminary incubation at high ionic strength. The second paper, also by Zinder and Fedoroff and printed back-to-back with the first, compares the f2 poly(G) polymerase and replicase activities under a variety of conditions. They examined the effects of ionic strength, temperature, magnesium ion concentration, and template and substrate concentrations on the enzymes' activities. Based on their results, Zinder and Fedoroff suggest a distinction between initiation and polymerization sites on the enzyme complex.

Zinder remains at Rockefeller as John D. Rockefeller, Jr. Emeritus Professor and continues to research bacteriophage. Currently he is using genetics, biochemistry, and molecular biology to analyze the filamentous bacterial virus, f1, and its interactions with its host, *Escherichia coli*. His other studies relate to protein-DNA recognition, membrane anchoring, and questions of protein structure.

In recognition of his many contributions to science, Zinder has received numerous honors and awards. These include the 1962 Eli Lilly Award in Microbiology and Immunology from the American Society of Microbiology, the 1966 Award in Molecular Biology from the National Academy of Sciences, the 1969 Medal of Excellence from Columbia University, and the 1982 Award for Scientific Freedom and Responsibility from the American Association for the Advancement of Science. Zinder became a member of the American Academy of Arts and Sciences in 1968 and of the National Academy of Sciences in 1969.

Zinder's coauthor on the two JBC papers also has gone on to a distinguished career in science. Fedoroff received her Ph.D. in 1972 and was a staff scientist at the Carnegie Institution of Washington. She joined the faculty of the Pennsylvania State University in 1995 and became the Evan Pugh Professor, Penn State's highest academic honor, in 2002. She currently holds the Verne M. Willaman Chair of Life Sciences. In 2007, U. S. Secretary of State Condoleezza Rice named Fedoroff her science and technology adviser. She remains in this position today, serving U. S. Secretary of State Hillary Clinton. Fedoroff is a 2006 National Medal of Science laureate and a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the Phi Beta Kappa and Sigma Xi honor societies. Her current research focuses on the mechanisms that allow plants to withstand the environmental challenges of a changing climate.

**Nicole Kresge, Robert D. Simoni, and Robert L. Hill**

## REFERENCES


1. Lederberg, J., and Zinder, N. (1948) Concentration of biochemical mutants of bacteria with penicillin. *J. Am. Chem. Soc.* **70,** 4267–4268
2. Zinder, N. D., and Lederberg, J. (1952) Genetic exchange in *Salmonella. J. Bacteriol.* **64,** 679–699
3. Lodish, H. F., and Zinder, N. D. (1966) Replication of the RNA of bacteriophage f2. *Science* **152,** 372–377


DOI 10.1074/jbc.O111.000244