

Hershey and his heaven

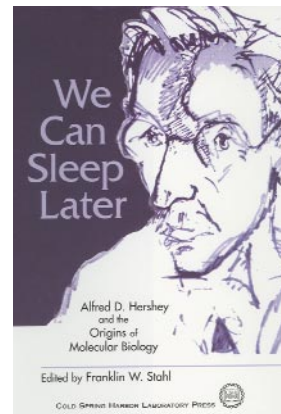
We Can Sleep Later: Alfred D. Hershey and the Origins of Molecular Biology

edited by Franklin W. Stahl

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Alfred Hershey, together with Max Delbrück and Salvador Luria, was one of the three founders of what was sometimes known as the Phage Church. This was the group of brilliant investigators who in the middle of the last century realized the unique experimental advantages of bacteriophages such as the T phages and lambda, and used them to discover an extraordinary amount of the basics of molecular genetics. The trio (described by Hershey as “two enemy aliens and a misfit”) ended up sharing a Nobel Prize in 1969. Each was seen to have a distinct role in the church — Delbrück was the Pope, Luria was the priest/confessor, and Hershey was the saint. Saints are interesting characters, even to the non-religious, and this book constitutes a worthy memorial to Hershey. It contains many essays and reminiscences from his associates, which provide a good portrait of an elusive man — taciturn, rigorous, dedicated, almost ascetic, and hence saintly in more than a few respects.

The book also includes reprints of some of Hershey’s more important writings, in particular the paper reporting the celebrated Hershey–Chase experiment (1952), which provided a wonderfully direct and pleasing demonstration that genes are made of DNA. The experiment’s appeal lies partly in its elegant use of radioisotopes to label protein and DNA separately, but also in its reliance on simple equipment, including a kitchen gadget, the Waring blender. Characteristically, Hershey included his meticulous assistant Martha Chase in the authorship of this and other papers; he said that the experiment would not have been possible without her abilities.

It is often remarked that the Hershey–Chase experiment did no more than confirm what had already been established by the beautiful work of Avery, published eight years earlier, which convincingly showed that the principal and perhaps only component of the ‘transforming principle’ capable of transferring heritable genetic information from one bacterial

strain to another was DNA. However, Avery and his colleagues were working with an odd and difficult system, examining capsular antigens in *Pneumococcus*, and their work was not easily extended, generalized or repeated in other laboratories. Avery died in 1956, too soon to receive full credit for his work. There remained doubts as to whether DNA could really be the complete answer, doubts which Hershey himself shared, and he wondered whether there might be a further, or alternative, protein-based mode of inheritance. The results of his experiment left few in doubt about the importance of DNA.

This story has significant resonance today, in the analysis of mammalian prion disease, but now the boot is on the other foot — most of the evidence points towards an exclusively proteinaceous infectious agent for prion disease, yet it remains hard to exclude some crucial further component, perhaps a nucleic acid. In 1953, Hershey made the barbed and prescient remark: “My own guess is that DNA will not prove to be a unique determiner of genetic specificity, but that contributions to the question will be made in the near future only by persons willing to entertain the contrary view”. Towards the end of his life (he died in 1997), he became interested in DNA-independent forms of heredity such as cortical inheritance in protozoa.

Hershey was responsible for many other important, rigorously executed and tightly argued pieces of research on bacteriophage, which are well discussed in this book. He is also remembered for the concept of ‘Hershey Heaven’. When asked what his idea of happiness would be, he replied “to have an experiment that works, and do it over and over again”. This is an idea that has become proverbial in molecular biology and it strikes a chord with any experimental scientist. Many of us spend our working lives searching for that happy state.

The title of the book seems scarcely appropriate for a man who famously

napped twice a day (in a cycle that was convenient for phage genetics, but less so for human interaction), but reflects a final important role for Hershey, as a stringent and constructive editor of scientific papers. He was one of the begetters of the marvellous 1971 Cold Spring Harbor monograph *The Bacteriophage Lambda*, and “we can sleep later” was his exhortation to lagging writers to get their manuscripts for this book in on time. That volume, and the first in the series, *The Lactose Operon*, set the tone for the long and important series of Cold Spring Harbor monographs, which have had profound influence in the world of molecular biology. It is particularly fitting that Cold Spring Harbor should honour the memory of Hershey in this way. □

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