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Coffin JM, Hughes SH, Varmus HE, editors. Retroviruses. Cold Spring Harbor (NY): Cold Spring Harbor Laboratory Press; 1997.

Homage to Howard Temin



It is deeply sad that one voice is missing from this book, that of Howard Temin. He died in early 1994 at age 59. He was a pioneer. I want to take a few pages to point out that the modern history of retrovirology depended on two critical contributions by Howard. These discoveries are described in more detail in the first chapter by Peter Vogt.

Along with Harry Rubin, Howard devised the first cell culture focus-forming assay for a retrovirus, the Rous sarcoma virus. This work opened up the study of retroviruses in cell culture, providing the first truly quantitative assay of viral transformation and the first quantitative assay for a retrovirus (although in 1958, the concept of a retrovirus was still to be developed).

Howard's second major contribution was to realize that the ability of Rous sarcoma virus to stably transform cells implied that this RNA virus must transfer its genetic information to DNA—otherwise, he reasoned, how could transformation be so stable? This latter insight was first presented in his Caltech thesis in 1960 and became his personal research challenge over the next 10 years. In 1964, it was enshrined as the provirus hypothesis, an explicit proposal that an integrated copy of viral DNA maintained the genetic stability of a retroviral infection. Only when Howard and I were able to demonstrate in 1970 that the virions of retroviruses have a reverse transcriptase was the notion widely accepted in the scientific community.

Ten years in the scientific wilderness is a long time; few have had to bear the silence of their colleagues for so long. I can remember meetings in the 1960s when Howard would present his latest data supporting the provirus notion only to be greeted by either skeptical questions or quiet, polite disbelief. Howard's conviction that there had to be a provirus never seemed to waver over the whole decade. He knew he was right—and he was—but what fortitude it took to keep looking for the experiment that would show it! My first reaction when I realized that I had seen the reverse transcriptase was to call Howard, because I so much wanted him to know that he was vindicated in his commitment to the idea of a provirus. But he had already found out for himself.

It is worth considering how deep was the insight that led Howard to the provirus. Although the pregnant analogy to known lysogenic bacteriophage might have guided Howard, people who were at Caltech at that time assure me that Howard was unlikely to have arrived at the notion of a DNA intermediate through this route. Apparently, the influence of Max Delbrück—who was totally committed to the study of lytic phages and did not really believe in the importance of phage lysogeny—was so great that there was little discussion of lysogeny at Caltech then. Furthermore, Howard has minimized the importance of lysogeny as a precursor to his concepts. Therefore, he must have arrived at the concept of

a DNA intermediate simply from the persuasive power of such a concept to explain the properties of the transformed state. He was particularly influenced by the morphological difference between cells transformed by particular Rous sarcoma virus variants, which he felt had to mean that the viral genome continued forever to affect the transformed cell.

Howard was a towering presence in modern biology. Those who knew him recognized and cherished the penetration of his razor-sharp intellect. Many molecular biologists range widely in their interests, but Howard displayed an unwavering commitment to the study of retroviral genetics and transformation of cells in culture during almost 40 years of research.

David Baltimore.

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