

Avery O T, MacLeod C M & McCarty M. Studies on the chemical nature of the substance inducing transformation of pneumococcal types: induction of transformation by a desoxyribonucleic acid fraction isolated from pneumococcus Type III. *J. Exp. Med.* 79:137-58, 1944.
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This paper presents detailed data indicating that the substance responsible for bringing about a predictable and heritable change in pneumococci is DNA. It represents the first experimental evidence that DNA molecules might be the carriers of genetic information. [The SCI® indicates that this paper has been cited in over 590 publications since 1955.]

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Having recently completed a book on the story of pneumococcal transformation and the discovery of the genetic role of DNA,¹ I find myself oversupplied with points to raise in this commentary. The years that I spent working on this project were full of excitement, which more than compensated for the frequent setbacks caused by the vagaries of the experimental system. Much of the excitement came from the growing recognition that the transformation phenomenon must have biological implications that went well beyond the single bacterial species involved in the research.

I arrived at Avery's laboratory in 1941, just after Colin MacLeod had left for New York University. Thus, MacLeod and I did not actually overlap in the laboratory, although he maintained close contact with the continuing work. He and Avery had spent the previous year in an intensive renewal of the attempts to identify the transforming substance after a hiatus of some three years when the problem had been temporarily set aside.

There was much accumulated information on the properties of the active substance together with some clues as to what it was *not* (e.g., protein, lipid, or RNA). As a result of a variety of experiments, we became convinced by the spring of 1942 that we were probably dealing with DNA. The following year was spent in an effort to bolster the evidence, since we were aware of the generally held view that nucleic acids were pretty much all alike and thus lacking in the diversity required for carrying genetic information. The analysis of a number of lots of highly purified material was fully confirmatory of our view. We agreed that it was time to write up the work, submitting it for publication on November 1, 1943.

It seems obvious that the paper became so highly cited because it revealed that DNA was likely to be the bearer of genetic information, a discovery that opened up broad new vistas in biological science. As a result of a combination of factors, however, there was a lag in the citation of the paper in the early years after its appearance. Furthermore, subsequent work designed to substantiate the finding was not widely cited, even though it added important new evidence. It described the preparation of a purified DNase² that proved highly active in destroying transforming DNA,³ thus rendering unlikely the notion that a contaminating protein was the active factor.

It now seems clear that research on pneumococcal transformation was the initial step in the current biological revolution, the extent of which could not even be imagined at that time. Although recognition of the work may have been delayed in many circles at the outset, its central importance is now acknowledged by most observers. Certainly, many honors have come to me as a result of my part in the discovery, including, in recent years, the first Waterford Biomedical Sciences Award (1977) and the first Who's Who in America Achievement Award in the Life Sciences (1984).

1. McCarty M. *Transforming principle: the discovery of the genetic role of DNA*. New York: Norton. 1985. 252 p.
2. Purification and properties of desoxyribonuclease isolated from beef pancreas. *J. Gen. Physiol.* 29:123-39. 1946. (Cited 90 times since 1955.)
3. McCarty M & Avery O T. Studies on the chemical nature of the substance inducing transformation of pneumococcal types. II. Effect of desoxyribonuclease on the biological activity of the transforming substance. *J. Exp. Med.* 83:89-96. 1946. (Cited 40 times since 1955.)