

For the past 10 years a major portion of the efforts of this laboratory have been devoted to the study of the enzyme polynucleotide phosphorylase. The enzyme was discovered in 1956 by S. Ochoa and M. Grunberg-Manago, at New York University. Because it was the first known enzyme to catalyze the synthesis of polyribonucleotides, its discovery was of great interest. Subsequently, when it became clear that the enzyme could not be responsible for the synthesis of ribosenucleic acid in vivo, interest declined. The main argument against a biosynthetic role is that the enzyme does not copy a template RNA during synthesis: it polymerizes only those nucleotides supplied, either one nucleotide or some combination, and in random order.

It is, however, just this property which made the enzyme extremely useful. Polyribonucleotides of known composition, though not sequence, could easily be synthesized. For example, polycytidylic acid, a polymer of only cytidylic residues, was easily prepared.

We undertook as a long-range project, the detailed study of this enzyme, its mode of action, and the relation between its structure and function--a study which continues. One of the important prerequisites to such investigations is to develop a convenient procedure for the purification of the enzyme from the chosen source, in this case the bacteria Micrococcus lysodeikticus. After much effort a reproducible, useful procedure was developed. The availability of purified enzyme has had important applications to other investigations. One of these was the preparation of a variety of polyribonucleotides for use in work on the genetic code. As the demand for polynucleotides grew, several manufacturers of fine biochemicals adapted our purification procedures for the large-scale production of enzyme in order to prepare and market polynucleotides. For this purpose they made use of our publications as well as advice given personally.

Our efforts were undertaken because of interest in the question of enzymatic synthesis of polynucleotides. Currently, work in this laboratory is directed toward understanding the chemistry of the enzyme itself, in relation to its function. Recently, and quite unexpectedly, a new use for the polymers made with this enzyme has been developed. The polymers have proved of great utility in clinical investigations on interferon, and the induction of interferon activity in animal cells. Work at Merck, and at NIH, has shown that the polymers stimulate interferon production and thereby interfere with viral infection of animal and human cells. Most recently a combination of polyinosinic and polycytidylic acid were shown, by S. Baron and colleagues, of NIAID, to cure a viral infection of rabbit eyes. Dr. Baron and his co-workers are currently investigating the use of poly I and poly C as therapeutic agents against viral infection.

Thus, a research effort best characterized as "basic science" unexpectedly made available materials of great potential usefulness in clinical medicine.