Editorial Comments
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For the many readers of Clinical Chemistry, alkaline phosphatase represents but one of a dozen or more analytes for which the hospital's sophisticated analytical instruments print out results routinely. The physician is alert to any alkaline phosphatase value that exceeds the normal range. Even the second-year medical student knows that such increases correlate with liver or bone disease. So how can one explain the fact that every few years since 1968 an international symposium has been convened to review basic and clinical aspects of alkaline phosphatase research, and that this information is relevant to the clinical chemist?1

The fact is that this enzyme has held the combined interest of clinical chemists, enzymologists, physiologists, biologists, and clinicians since the 1930s. They share the view that a better understanding of the role of alkaline phosphatase and its isoenzymes would produce a more precise interpretation of an individual laboratory value. In addition, as the techniques of molecular biology have become available, their application has generated a wealth of new information about the genes that encode the alkaline phosphatase isoenzymes, including their chromosomal location. Finally, the discovery that the membrane insertion moiety of the enzyme is a phosphatidylinositol-glycan structure has generated new insights into the origin of macromolecular forms of alkaline phosphatase in the circulation.

That a malignant tumor can itself produce a particular isoenzyme has been most evident with the alkaline phosphatases. Thus, an osteogenic sarcoma enriches the circulation with bone alkaline phosphatase, whose concentration returns to normal after surgical resection of the tumor. More recent examples are the production of increased concentrations of the placental (PLAP), intestinal (IAP), and germ-cell (GCAP) isoenzymes of alkaline phosphatases by human tumors. These concentrations decrease with a reduction of tumor mass or activity. These findings have been reported most frequently for cancers of the ovary and testis. Accordingly, it is now appreciated that increases in serum ALP in cancer patients could be due to the tumor as well as to liver and bone alkaline phosphatases.

With the clearer knowledge of the structure and shape of molecules of alkaline phosphatase isoenzymes and with the generation of many specific monoclonal antibodies, it is now possible to attribute the major difference between PLAP and GCAP to glycine at position 429 in the GCAP molecule. This, in turn, has led to a plausible structural explanation of the L-leucine uncompetitive inhibition of GCAP. It is reasonable to expect that very specific monoclonal antibodies to individual isoenzymes will be generated, and that these will lead to superior immunoassays and, in turn, to more precise interpretations.

A historical introduction would not be complete without mentioning the names of major contributors over the years. These include H. D. Kaye, Oscar Bodansky, Earl J. King, A. B. Gutman, George Gomori, Solomon Posen, T. Nakayama, K. Higashino, Lars Beckmann, Harry Harris, and Florence Moog. We owe them our gratitude for building the body of knowledge on which the current symposium is founded. For my part, I thought that the field of the alkaline phosphatases was exhausted when I wrote my 1974 review on "Perspectives on Alkaline Phosphatase" in the American Journal of Medicine. How wrong I was!

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1 La Jolla Cancer Research Foundation, 10901 North Torrey Pines Road, La Jolla, CA 92037.

2 The proceedings published here are from the 1992 symposium held in Antwerp, March 13–14.