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Book Reviews

Avoiding Mistaken Identities

Gene Probes for Bacteria.
Edited by A. J. L. Macario and E. Conway de Macario.
San Diego: Academic Press. (1990). 515 pp. $89.00.

The ability to identify bacteria in specimens, particularly clinical samples from infected patients, has been the mainstay of diagnostic microbiology over the past century. Despite remarkable changes in the science and technology of microbiology during this time, the general approach is unchanged. The job of the clinical microbiology laboratory is to propagate, within reason, any pathogenic microorganism that exists in the specimen and then to identify the pathogen based on characteristic gene products (e.g., growth attributes, antigens, metabolic by-products). Secondary aims, which usually await pathogen identification, may include determining the antimicrobial susceptibility of the pathogen to optimize patient care and clonotyping the organism to track the course of a possible epidemic. For most, but not all, clinical situations this open-ended method works well because the variety of possible isolates is relatively large—large enough that the clinician is sometimes surprised by the result. Nevertheless, the growing armamentarium of pharmaceutical agents now available, with their idiosyncratic spectra of activities and toxicities, and the increased complexity and severity of medical illnesses, with their accelerated pace of progression, have intensified the demand for speedier identification and susceptibility characterization of the etiologic agents of disease.

Fortunately, for patient care, as the proficiency in treating infections has improved, so too has the means for more rapid diagnosis. Recently, the techniques have been exploited toward this realization. The last decade has brought the applied use of monoclonal antibodies, gene probes, and, most recently, various nucleic acid amplification methods, including the polymerase chain reaction. By shifting from gene product–based identification (e.g., serologic and biochemical techniques) to gene-based identification, pathogen growth and gene expression are no longer requirements, identification is considerably more rapid, and it becomes possible to detect hard-to-isolate or dangerous-to-grow pathogens. Yet a price is paid when these new techniques replace standard broad-based retrieval methods, since the high specificity of the direct genetic assays typically limits identification to a particular strain, species, or genus. As long as a yes or no answer will suffice for questions (such as Is it an HIV-based infection? Is the causative agent of gonorrhea present in the specimen?), there is reasonable success with this approach. On the other hand, if the question is open-ended (e.g., what is the cause of the pneumonia?), then the traditional, albeit slower, methods are preferable. The two approaches are clearly complementary and there are no plans to abandon the traditional clinical laboratory.

It is within this context that the recently published multiauthored book *Gene Probes for Bacteria* should be judged. The book is not meant to be a review of all diagnostic techniques in clinical microbiology, but rather a "comprehensive report on the current status of gene probes for bacteria useful in diagnostics." It consists of 17 chapters, each written by different authors and targeted on a different pathogen or group of pathogens. As a result, the overall perspective is not global but is instead rather unbalanced, having been defined by the limited number of special interest areas chosen for review. As a case in point there is no review of probes for the Legionella, pathogens for which a commercial diagnostic kit has been available for some time and a considerable amount of practical experience has accumulated.

Thematically, the book gains some consistency in that each chapter adheres to a strict organization: introduction, background, results/discussion, conclusions, gene probes versus antisera or monoclonal antibodies, future prospects, summary, experimental procedures, and references. Under the heading "Results/Discussion" the individual author either summarizes their own work or reviews the published literature on the subject; "Experimental Procedures" provides a laboratory manual for specific implementation. Unfortunately, this strict replication of chapter templates results in uneven success. In chapters in which the author summarizes the work of his own laboratory, the results/discussion sections make sense, although they have the effect of turning would-be review articles into contributions to scientific proceedings. In those cases in which the author summarizes a large body of work from multiple laboratories, the subheadings seem contrived.

The most serious criticism of this book is that it does not attempt to provide a general overview of the subject. Most readers will be interested in either specific methods, comparisons with existing methods, or some analysis of where the field is going. Thus, the editors had it right when they asked their contributors to discusss methodology, to contrast gene probes with experimental methods, and to speculate on future directions. Their mistake was in not doing this themselves in several introductory chapters. Much of the technology is redundant and could have been much better handled in one place where helpful illustrations could have been mustered without concern for cost. Likewise, the other topics deserved a broad reference point, rather than the limited perspective of a single pathogen. As an example, in no place can one find a table that lists all the commercially available probes, or one that lists all those in development, or one that shows an analysis of the relative advantages and disadvantages of various formats or compares the available formats with other methods of diagnosis (such as antigen-based systems).

In spite of the overall lack of perspective in the book,

many of the individual contributions are excellent and can be recommended as authoritative reviews of their respective subject matter. The most notable among these are the chapters on extra-intestinal Escherichia coli (P. H. Williams), mycobacteria (P. W. Andrew and G. J. Boulnois), corynebacteria (R. Rappuoli and R. Gross), campylobacters (B. L. Wetherall and A. M. Johnson), Salmonella (F. Rubin), and mycoplasmas (R. Dular). In summary, this is an interesting work with some useful information for the specialist who is interested in a particular contribution relating to a particular pathogen; otherwise, readers should look elsewhere.

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The Mourning News: Basic Protein Purification Methods

Protein Purification Methods—A Practical Approach. Edited by E. L. V. Harris and S. Angal.
New York: Oxford University Press. (1990). 336 pp. $40.00.

With the rapid advance in our understanding of biological mechanisms, it has become clear that the biologist in the 90s will need to apply a variety of techniques in answering complex cellular and molecular questions. However, a common lament in labs, besides the diminishing amount of funding, is the lack of students and postdocs who have a solid training in protein biochemistry. The impressive and exciting advances in molecular and cellular biology have channeled a large proportion of students into the skills of manipulating DNA. However, it is surprising and disappointing that many are not learning the basic skills of manipulating proteins. One is commonly confronted with the biologist who can recite the sequences that are cut by various restriction enzymes but not the residues at which proteases cleave peptide bonds. The problem is confounded by the practitioners of protein chemistry who often promote the impression that diddling with proteins requires much patience and experience, implying that neither quality is required in other fields of study. We mourn the possibility that in our lifetime protein biochemistry might regress into a black art like its medieval progenitor, alchemy. This description is, of course, a tongue-in-cheek exaggeration but only just that. Protein biochemistry is a highly technical field of study. Its tools are immensely useful in probing the secrets of the protein or the cell. We are witnessing the complementary use of both protein biochemical and recombinant DNA methods in answering problems in all fields of biology. This trend emphasizes the recognition that total reliance on DNA technologies is insufficient to answer many questions rapidly or directly.

One does not need to be a protein virtuoso, juggling blots, beakers, and columns with blazing speed and unerring accuracy, to be admitted into the protein club. Most of us started at the beginning. All roads lead back to fundamental methods in protein purification and characterization. Because proteins comprise a heterologous group of biopolymers that differ greatly in their size, charge, and solubility, no single method can be applied in their purification. Purification schemes must be tailored to take advantage of the biochemical properties of the protein, as well as the cellular properties of the tissues that provide the most abundant source of material. The choices one makes concerning each step in a purification protocol are based on common sense and a good quantitative assay. As a result, it is relatively easy to purify a protein although the overall yields are dependent on attention to detail and utilization of the most appropriate techniques. Not every protein needs to be purified using the latest techniques such as high pressure liquid chromatography or capillary zone electrophoresis.

Fortunately, our research leads us to study many different proteins, perhaps interacting factors in our system of interest, but where do we go if we want to get started? Usually one walks down the corridor to an accomodating lab for advice, or better yet for help. Others pick up the phone and set up collaborations with a protein biochemistry lab. In any case it is necessary to gather some background information at the library. Unlike the several excellent compendiums of cloning techniques (Maniatis and sons of Maniatis), there is no comparable source of practical methods in protein biochemistry. *Methods in Enzymology* remains a good source of information for specialized applications, but where does one start, and how far back into history does one pursue a good method?

A good place to start is with *Protein Purification Methods—A Practical Approach*, edited by Harris and Angal. What sets this book apart is that, as the title emphasizes, this book compiles a comprehensive, but not imposing, set of protocols on various aspects of protein purification. This point is important because other books describe the latest, but maybe unproven, methods. Harris and Angal are careful to include only those methods that one would try first in designing a purification scheme. It begins with the basics—how to measure protein concentrations, how to prevent proteolysis, and how to concentrate a sample—and ends with chromatography separations based on protein structure (charge, hydrophobicity, cofactor binding), size, or enzyme activity.

The book is fairly comprehensive. Electrophoresis and chromatography are well covered, but more importantly the most useful methods within these areas are presented. Each section is a logical extension from the previous one and the advice and protocols are presented in a very matter-of-fact and commonsense fashion. For example, those who liberally dose their preps with cocktails of expensive protease inhibitors will recognize that the section on preventing proteolysis during purification should save much time and money. In contrast to other similar books, each topic describes, in a refreshing manner, the basic theory underlying each method and weighs the ad-