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EDITORIAL

The Human Cornucopia

In the Middle Ages, therapies were picked from gardens or culled at random. If eating or drinking something was beneficial, then a "cure" was declared and another aid for health was added to the stash. This empirical testing and trying was carried into the chemistry lab where myriads of compounds have been subjected to a panoply of creative assays, in the hope of finding the few substances worth developing.

Increasingly, however, the ideas for new treatments are based on our ever growing knowledge of the human body, hence this special issue on Biologically Based Therapies. Cardiovascular biology, as described in a perspective by Kenneth Chien, is on the threshold of the molecular era, with new approaches and insights for treating hypertension, atherosclerosis, and heart disease.

Investigators delving into the minute machinations of the cell—from the receptors on the outer membrane, to the way information is transmitted within the cell, to the genetic programming of the cell itself—have contributed enormously to this growth in knowledge. Joan Brugge provides a perspective on the strategies by which elements of the signal transduction pathway can be foiled. Physical contact is important for proteins that are links in the message chain; small peptides are being designed that mimic the binding sites and could specifically interfere with a particular exchange.

Gene therapy has generated considerable excitement among researchers and in the lay press. Although the prospect of providing a normal gene to replace or complement a defective one seems tantalizingly close to realization, large technical problems still remain, as discussed in an article by Richard Mulligan.

Another level of intervention is our new found ability to manipulate a whole system of interacting cells, such as the immune system. The complex balance of multiple components must be delicately adjusted; too little of the right immune response will not defeat a virus or tumor, and too much of the wrong response will hurt, and could lead to allergies, chronic infection, or autoimmunity. The promise and pitfalls of various strategies based on the T cell are laid out in the article by Antonio Lanzavecchia.

Defects in tissues or organs result in the performance of approximately 8 million surgical procedures in the United States every year. Exciting progress in the field of tissue engineering, which comprises a range of approaches from the study of factors that can induce native tissue formation to the design of tissue or organ replacements from artificial substances, is described by Robert Langer and Joseph Vacanti.

Ongoing research is aimed at improving the art of human in vitro fertilization. Better understanding of the factors needed for growth and viability of the embryo as well as advances in preimplantation diagnosis should provide welcome increases in the rate of success. However, this is an area where there are many ethical as well as technological issues to be faced, as discussed by Robert Winston and Alan Handyside.

Underlying the potential and actual medical advances in this issue is a wealth of basic research. The original bacterial geneticists who discovered restriction endonucleases were not thinking of gene therapies for adenosine deaminase deficiency or cystic fibrosis. Yet the vectors currently being aimed toward clinical testing could not have been designed without the capability of specific DNA cutting. Arcane studies of how cells adhere to each other and how they migrate during fruit fly development have contributed to the characterization of molecules that may provide new keys to industrial development of antiinflammatory agents. These and other outgrowths of basic research that are being explored by biotechnology companies, as well as some of the financial problems encountered, are discussed in the accompanying Frontiers in Biotechnology special news section, edited by Jean Marx.

The authors in this issue were asked, rather than reviewing the past history, to provide a view of the state of the art and a realistic evaluation of the challenges that remain before these biologically based therapies can be found in the clinic. It is clear that however many problems remain, a better understanding of our bodies can give us the ability to better heal ourselves.

Barbara R. Jasny and Linda J. Miller