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Frontiers in Biotechnology

The line between pure research and practical application has always been difficult to draw. Some like to claim they are doing pure research with no practical purpose in mind. There is an implication that "pure" is not only nobler but also more difficult intellectually than "applied" research. Equally vociferous are those on the applied side who suggest that they labor for the good of mankind, whereas the ivory tower types are simply enjoying themselves. Those demarcations are gone forever, or should be. It is a wise person who can state with certainty what basic research result will never be practical, or what applied research will not lead to new basic insights, or which is intellectually more demanding.

This issue of *Science*, assembled under the fine editorial supervision of Kelly LaMarco, is devoted to frontiers in biotechnology, and anyone reading through the issue will be fascinated both by the practical ramifications of theoretical studies and the theoretical ramifications of practical studies.

The article by Adams *et al.* contributes a short cut of immediate practicality and great interest to the understanding of the human genome. By providing expressed sequence tags of complementary DNA, a large number of new genes are being uncovered (particularly in the brain). At the same time, lighthouses are being provided along the chromosomes to guide the way for weary sequencers struggling with foggy restriction maps. In the DNA area, Erlich *et al.* discuss the polymerase chain reaction, a tool that has become so powerful that focus is being directed at making it more accurate (10^{-5} nucleotide mistakes per cycle). This, together with methods to warn on the multiplication of contaminating sequences, has increased the power of the PCR for forensic analyses and research applications.

Intermediary metabolism was declared a dead subject by the conventional wise men some years ago, but modern metabolic engineering has brought it back to life. The metabolic pathways of bacterial factories now operating around the globe can be improved by enhancing copies of a gene at a rate controlling point, adding a gene to remove a poisonous product, or adding several genes to introduce a new pathway into an organism that stops short of the desired product. Bailey points out that this metabolic engineering has already had many practical results and is developing new theory. Stephanopoulos and Fellino are applying recombinant DNA technology to metabolic pathways, concentrating on the problem of branch point control. Among the clever ideas is to insert into the derived organism a similar enzyme, but from a different species, so that it has a different control architecture. This introduces new flexibility and better metabolic characteristics into the old organism.

If Edward Jenner were alive today, he would undoubtedly be delighted at the incredible development of the vaccinia virus. Moss traces its history down to its modern reconstructions, in which it serves as a magnificent molecular tour bus designed to carry foreign genes into unsuspecting organisms. These passenger genes can in some cases be important tools for scientific research, and in other cases the proteins they generate will provide immunity against infection. As a vehicle for research, the recombinant vaccinia vector has already established itself, and as a vehicle for producing live vaccine, it needs improvement, but is rapidly approaching practicality for such dread diseases as rabies, rinderpest in cattle, and AIDS. Immunity can be approached as Waldmann does in discussing the use of monoclonal antibodies in diagnosis and therapy. At one extreme is the monoclonal antibody OKT3, which has been approved by the Food and Drug Administration for treatment of acute renal allograph rejection. It is far from a perfect application, but is the only example so far of a monoclonal antibody licensed for clinical use. Monoclonal antibodies can also be used to kill bad tissue, such as cancer tissue. The antibody power is enhanced by attachment of a biological poison such as ricin or a physical agent such as an alpha emitter, which can be used to damage tissue adjacent to that with which the antibody interacts.

This selection of a few examples illustrates the enormous power of a combination of basic research and practical application. The increasing power and benefit of these tools makes one wonder how anyone could possibly suggest that all biotechnology be stopped in its tracks, but the power of the methods does raise the legitimate question that caution should be exercised in its application. The authors in this issue are illustrative of the workers in this area who are excited by the power of the methods and alert to minimize their side effects.—DANIEL E. KOSHLAND, JR.