

Biotechnology essential to medical progress

By Jay A. Levy

This week's biotech gathering in San Francisco gives us an opportunity to highlight the advances in science and medicine that have resulted from biotechnological discoveries, and to encourage and anticipate future progress.

A major objective of this field is to find solutions to medical problems using approaches that include: genetics (manipulating DNA and its RNA counterparts); protein chemistry (producing cellular products for treatment); and cellular therapy (injecting cells directly into people to resolve a loss or combat a disease).

With the last approach, human cells can be modified to better recognize infectious agents or inhibit the over-response of some components of the immune system that leads to autoimmune diseases such as lupus and rheumatoid arthritis.

The field of genetics benefited from the development of the polymerase chain reaction that enables amplification of tiny quantities of DNA to permit detection of very low amounts of cellular genes or genes of infectious agents.

Microarray technology, a recent discovery, enables rapid evaluation of the expression of many genes of a cell. This approach involves putting on a microscope slide extremely small amounts of cellular DNA or DNA copies of RNA that gives rise to the proteins of the cell. This technology helped identify the SARS agent by demonstrating its relationship to the genes of the coronavirus family placed on a microarray slide.

AIDS research, in which I have been involved for many years, has certainly benefited from biotechnology. Molecular techniques led to the full identification of the sequence of HIV. Other procedures in biotechnology permitted the establishment of methods for detection of HIV and immune responses to the virus.

Moreover, through biotechnology, highly purified proteins of HIV were obtained, permitting the discovery of current drugs that specifically target these viral components. These medicines act against viral proteins with a specificity not possible without the knowledge gained from biotechnology research.

Essentially, biotech advances in this field have led to better diagnostic tests for defining HIV infection, for measuring the effect of the virus on the immune system and for the development of new drugs that help control the virus.

From my own standpoint, biotechnology conducted in research institutions and industry, promises to uncover novel approaches for improving immune function in HIV-infected individuals. For example, we have been working to identify an anti-HIV product of an immune cell called the CD8 lymphocyte that circulates in the blood and is present in lymphoid tissues of the body. This CD8+ cell antiviral factor (CAF) specifically inhibits

HIV replication in infected cells but does not kill those cells. The CD8+ cell antiviral response is present in HIV-infected individuals who are healthy, particularly those who have lived more than 10 years (some for over 25 years) without any signs of the infection. These long-term survivors control HIV through the activity of the CD8+ lymphocyte and CAF.

Obviously the identification of CAF would provide a major breakthrough for controlling HIV infection. But this novel protein is produced in such small amounts that standard procedures for identifying it have not been successful. CAF is most active when the CD8+ lymphocyte comes in contact with an infected cell; at this close interaction, the protein need not be there in high quantity. Biotechnology can help us to purify this potent anti-HIV factor by separating it from thousands of other products of the CD8+ cell.

The best promise, however, comes from the recent technological advances in mass spectrometry, which can identify components of proteins at the atomic level. This approach has been greatly improved so that several proteins present in a semi-purified sample of CD8+ cell secretions can now be identified; previously, only one could be found. In preliminary studies, mass spectrometry of CAF-containing fluid has narrowed the anti-HIV activity to about 50 proteins. We trust that further purification steps will reduce this number to a reasonable amount for final analysis.

Additionally, through the novel approach of microarrays, the cellular gene expressing CAF is being sought. By taking RNA from cells producing CAF, and those that do not, we can compare the relative representation of many cellular genes and identify specific ones that are found in CAF-producing cells. One of them could be the CAF gene. This microarray approach has permitted us to narrow down the 37,000 human genes to a handful (about 25), one of which may indeed be responsible for producing this elusive CD8+ cell antiviral factor.

Essentially, through advancements in biotechnology, problems we now face can be better approached thanks to improvements in protein identification procedures and in gene detection methods. Ten years ago, none of these directions could have been undertaken with the same efficacy as is possible today. We look forward to the announcements of new technologies, new approaches and new discoveries in biotechnology that will continue to advance our ability to control HIV, as well as cancer and other human diseases.

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