duced by the host.

Also, one might introduce a gene for the immunizing portion of a disease-causing agent or vaccine into the chromosomes of the host in such a way that it is expressed at the time that vaccination would ordinarily take place. Such a gene would then become an inherited vaccine—each animal, in a sense, would have its own built-in vaccination shot—eliminating the need to vaccinate every animal.

**Prospects for Application**

These are exciting prospects. But the animal breeder must consider how to integrate these new methods into a breeding program aimed at improving the whole animal and not just a specific trait controlled by a single-cloned gene.

Probably the first applications will be to introduce genes that will control specific diseases that cause severe economic loss. Theoretically, this can be done without altering the other important genes carried by a highly productive strain of animals. The breeder, however, must test carefully the altered strain of animals to determine if some undesirable side effect has been introduced, as was done by introducing sex-linked slow feathering into egg-production crosses of chickens by conventional breeding methods.

Animal breeders in collaboration with molecular geneticists will conduct basic studies on gene identification and cloning, on gene regulation after transfer, and on the effect of transferred genes on productivity. These studies will provide the basis for using these new methods to augment conventional breeding programs aimed at providing healthier and more productive animals.

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**A Revolution in Immunology—Monoclonal Antibodies**

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The construction of antibody-secreting cell lines—hybridomas—by fusing antibody-secreting lymphocytes with appropriate tumor cell lines—myelomas—has forever changed immunology. Indeed, the monoclonal revolution has spread far beyond the shores of its mother discipline and now laps the coasts of biochemistry, neurobiology, developmental biology, agriculture, medicine and toxicology.

This article will describe the technology of hybridoma production. A companion piece by David Snyder tells how monoclonal antibodies are used to solve many problems.

Hybridoma technology, like recombinant DNA technology, is rooted in basic biology and is the capstone of years of basic research in cell fusion. It is a procedure in which two different kinds of cells are artificially caused to fuse to form a single hybrid cell. Such hybrids are particularly interesting because they incorporate the genetic potential of both parent cells. This technique has made it possible to construct and study the properties of cell hybrids made from such combinations as normal cells with cancer cells, mouse cells with human cells, and even human cells with those of mosquitoes.

**Early Research**

In 1973, Jerold Schwaber and Ed Cohen, working at the University of...
Plant virologist checks the temperature of liquid nitrogen storage tanks in which hybridomas are preserved.

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Chicago's LaRibida Institute, were the first to produce antibody-secreting hybridomas by fusing normal antibody-producing human cells (B lymphocytes or B cells) to antibody-producing mouse tumor (myeloma) cells. Their hybridomas displayed the capacity for unlimited growth in culture characteristic of the myeloma parent while retaining the antibody-producing characteristics of the normal B cell.

But it was George Kohler and Cesar Milstein who devised and demonstrated a deliberate and rational strategy for the construction of continuous cell lines which secrete monoclonal antibodies of a desired specificity. In 1975 they fused a mouse myeloma cell line with lymphocytes from mice that had been previously immunized with a particular antigen. They then screened the resulting hybridoma clones to identify those that were secreting monoclonal antibodies specific for the immunizing antigen. Their success, which has been widely reproduced, revolutionized immunology and created an industry.

**Monoclonal Antibodies**

A different state of affairs results by harvesting lymphocytes from recently immunized animals, constructing hybridomas by cell fusion, and isolating those that secrete monoclonal antibodies to the immunizing antigen. Each of the selected hybridomas produces an antibody that recognizes only a particular determinant of the assortment presented by a complex antigenic mixture. Using the mouse system, it has been possible to produce hybridomas secreting antibodies to antigens as diverse as viruses, bacteria, and bacterial toxins, cancer-associated antigens, and to a long list of hormones, enzymes, and drugs. This method also has been applied to the production of human, bovine, porcine, and sheep monoclonal antibodies. This pinpoint technology offers several advantages over conventional polyclonal antisera.

**Advantages of Monoclonal Antibodies**

- Once stabilized, hybridomas can be frozen and stored for weeks, months or years, until they are...

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**Polyclonal Antiserum**

The power of hybridoma technology can be appreciated by examining the contrasts between monoclonal antibodies and antibodies produced the traditional way. Most antigens of practical interest display many distinct antigenic determinants. Indeed, a bacterium, virus, or foreign-tissue graft presents the immune system with an extraordinarily complex "forest" of highly immunogenic antigens. Typically, many determinants in the complex antigen mixture trigger the activation of one or more of the animal's B cell clones to divide and differentiate into antibody-secreting populations of cells. In the body, the monoclonal antibodies characteristic of each activated B cell clone pool, and, consequently, the serum harvested from the animal is an intimate polyclonal mixture of many different antibody molecules. Furthermore, the composition of this polyclonal mixture will change from day to day and from animal to animal. Thus, polyclonal antisera, even when prepared by well-standardized procedures, tend to differ from batch to batch. While sometimes purification procedures can be devised that specifically isolate those members of the serum's antibody population which bind to the immunizing antigen, such procedures succeed only in producing a mixture of structurally distinct antibodies which share a capacity to bind to some of the determinants presented by the antigen.
needed. Thus, they provide a perpetual source of well-defined, homogeneous monoclonal antibodies.
- Large amounts (grams, even kilograms) of a particular monoclonal antibody can be obtained with a relatively modest investment of resources and personnel.
- Monoclonal antibodies specific for a particular target antigen can be obtained even when the antigen is grossly impure or present only in trace amounts.
- Monoclonal antibodies react with determinants in an all or none fashion, so there is no need to resort to absorption to improve specificity.

For these reasons, monoclonal antibodies have had an enormous impact on experimental biology and biotechnology. More and more, monoclonal reagents are replacing useful, but undefined, polyclonal antisera. Increasingly, hybridoma technology will provide the standard analytical and reference reagents for the fields of food technology, veterinary medicine, and agriculture.