Biology

Julie Ann Miller reports from Philadelphia at the Third International Congress for Recombinant DNA and the Second Annual Congress for Hybridoma Research

Alternative in antibody production

A radically new method has succeeded in producing monoclonal antibodies — the specifically binding biological substances now widely used in research and regarded as promising diagnostic and therapeutic tools in medicine. Monoclonal antibodies are currently made by a procedure developed in 1978 (SN: 12/23 & 30/78, p. 444). In the standard procedure, spleen cells that make antibodies are fused with cancer cells to provide lines of antibody-producing cells that can reproduce themselves indefinitely under laboratory conditions. But so far this procedure has not worked as well for human cells as for mouse cells, it is not as efficient as scientists would like and it results in genetically abnormal cells of little value for the study of cancer.

Investigators from the University of Pennsylvania School of Medicine now announce success with an alternative technique, called lymphocyte transfection. Zdenka L. Jonak, Virginia Braman and Roger H. Kennett mix normal mouse spleen cells (lymphocytes) and DNA taken from human leukemia cells (called Reh), instead of fusing the spleen cells with intact cancer cells. Human DNA taken up by the lymphocytes directs the mouse cells to grow and divide, acting like cancer cells in this regard. In control experiments mouse spleen cells mixed with normal human placental DNA do not show these characteristics.

The mouse spleen cells that were transformed with human leukemic DNA still produce antibodies. All the descendants (the clone) of a single cell make antibody of the same specificity — monoclonal antibody. In these experiments a mouse was immunized with human cells before its spleen cells were used in the procedure, so some of the transformed cells produce mouse antibodies binding to components on the surface of human cells.

"The technique of lymphocyte transfection has a great potential in the production of human monoclonal antibodies," Jonak says. As a step in that direction she and colleagues are now purifying DNA from mouse cancer cells to use in transforming human antibody-producing cells.

The scientists suggest that their method provides a means of producing lines of cells that will grow in laboratory culture making other specific biological products for research and commercial use. It also provides a system in which scientists can study the acquisition of cancer characteristics in a normal cell under carefully controlled conditions.

Rare cell-growth factor via gene-splice

A key protein for studying the immune system has been produced by recombinant DNA techniques. In a last-minute addition to the meeting program, Tada Taniguchi of the Tokyo Cancer Institute described his recent accomplishment—isolation of the gene for human T cell growth factor, also called interleukin-2. In the body, interleukin-2 is produced by activated T cells, cells from the thymus gland that participate in a variety of immune reactions. Interleukin-2 is thought to have several actions, including inducing production of one form of interferon and triggering the killing of foreign cells by T cells and other cells of the immune system. Interleukin-2 also stimulates long-term growth of T cells under laboratory conditions, thus allowing study of their development. But very little of the material has been available and nothing known about its protein structure, Taniguchi says.

In the recent work, carried out in collaboration with the Ajimoto Co. of Japan's food industry, the source of genetic material was human leukemia cells. Taniguchi reports only a single copy of interleukin-2 among the complement of human genes. The gene isolated by Taniguchi produces interleukin-2 when placed in animal cells growing in culture or in bacteria, where the protein is now being made in amounts much greater than are available from other sources. Taniguchi says he plans to investigate how the activity of the gene is controlled.

Biomedicine

Eating away your pain

A promising new treatment for chronic pain appears to have been found by Samuel Seltzer and colleagues at Temple University Health Sciences Center in Philadelphia. It consists of eating a low-protein diet combined with supplements of the amino acid tryptophan. Tryptophan is known to increase brain levels of the nerve-transmitting chemical serotonin. Serotonin in turn appears to reduce pain perception.

Seltzer and his team conducted a four-week, double-blind study on 30 patients suffering from chronic jaw pain, ongoing pain radiating along one or more nerves or from other forms of chronic pain. All the patients were placed on a diet that was low in protein. The reason was that all amino acids in protein, not just tryptophan, compete for space in the bloodstream. Thus if other amino acids were kept to a minimum in the bloodstream, tryptophan supplied through a special supplement would be in a better position to get through the bloodstream into the brain and to influence pain perception. Then half of the patients were given a daily supplement of 30 grams of tryptophan, while the other half were not given the supplement.

As Seltzer and his colleagues will soon report in the JOURNAL OF PSYCHIATRIC RESEARCH, not only was there a greater reduction in reported pain among the tryptophan-supplement group than among the placebo group, but there was also a greater reported tolerance to pain applied experimentally to an upper tooth. These results "lend credence to the hypothesis that tryptophan reduced pain sensitivity," Selzter says.

Unmasking a gout enzyme

A severe lack of a particular enzyme underlies the Lesch-Nyhan syndrome, which is characterized by mental retardation, self-mutilation and early death. The enzyme is hypoxanthine (guanine) phosphoribosyltransferase, or HPRT. A partial deficiency in HPRT is responsible for about one out of every 200 cases of gout. These discoveries were made 15 years ago by William N. Kelley of the University of Michigan Medical School in Ann Arbor and co-workers. Yet only now has the molecular structure of an HPRT underpinning either of these diseases been identified—and once again courtesy of Kelley and his team.

As they report in the February PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (No. 3), an HPRT variant from a gout patient was found to contain the same 217 amino acids as a normal HPRT except for one. The amino acid serine in position 109 had been substituted by the amino acid leucine.

Kelley and his co-workers are now trying to identify the amino acid quirk or quirks present in HPRT in Lesch-Nyhan victims.

Expediting new drugs

During 1981 and 1982, the Food and Drug Administration set a 20-year record in the number of new drugs it approved for marketing (SN: 11/21/81, p. 327; 12/5/81, p. 359; 4/10/82, p. 247). Now further proposals to streamline the testing and ultimately FDA approval of new medicines has been announced. For instance, investigators would be able to screen new drugs in humans more quickly than at present to determine which are the most promising. They would also be able to meet with FDA earlier to discuss new drug testing in humans and thus save perhaps months of misdirected research.

The proposed improvements between FDA and drug researchers would also help implement the new Orphan Drug Act (SN: 1/8/83, p.22). It is aimed at making more available new drugs that would benefit only a few patients with rare diseases.

After the proposals are reviewed by the Office of Management and Budget and are published in the FEDERAL REGISTER, there will be a 60-day comment period. FDA will then decide whether to implement the proposals or not.