Genetic engineering: A mammalian first

The molecular genetics techniques lumped under the term "recombinant DNA engineering" are starting to pay off. Four separate research groups using these new gene grafting methods have successfully spliced rabbit globin genes into bacterial genomes during the past few weeks. This represents the first incorporation of a mammalian gene into a bacterium. Genes from fruit flies, toads and other bacteria species have also been tranferred into bacterial hosts. Such stiff competition is likely to produce faster results—in this case, basic understanding of the mammalian hemoglobin system—but it's tough on the researchers in the meantime.

Recombinant genetic engineering is a new research tool that enables scientists to excise specific genes from an animal's DNA, splice it into a carrier molecule, send them both into a host organism, clone a batch of these hosts, then pick out the "recombinant" hosts with the new foreign genes (SN: 3/20/76, p. 188). Besides the potential for pharmaceutical, medical and agricultural applications, the tool carries the more immediate promise of being a highly useful probe for dissecting the structure of genes and the mechanism of gene control and action.

Two European groups and two American groups, using slightly different approaches, successfully inserted the rabbit globin gene into the intestinal bacterium *Escherichia coli*. This gene directs production of two proteins that form alpha and beta globin chains. Hemoglobin, the oxygen and carbon dioxide transporting molecule in red blood cells, is made up of these chains plus iron-containing heme proteins. Although other mammals have globin genes, rabbit reticulocytes (red blood cell precursors) are a convenient, accessible source of globin messenger RNA (mRNA), the starting material for this gene transfer.

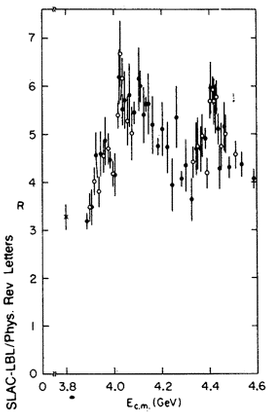
All four groups (Rougeon, Kourilsky and Mach from Geneva and Paris; Maniatis, Efstratiadis, Kafatos and Maxam from Harvard and Cold Spring Harbor; Higuchi, Paddock and Salser from the University of California at Los Angeles, and Rabbitts from Cambridge, England) started with globin mRNA prepared from rabbit reticulocytes. The mRNA was then purified to separate any unknown genetic sequences. Employing the so-called reverse transcriptase enzyme, they "created" double stranded copies of globin DNA from the purified mRNA. Using various techniques, each group spliced the new globin DNA into a carrier molecule—one type of plasmid or another. (Plasmids are circular, extrachromosomal genetic elements employed as carriers to taxi foreign DNA into new host cells.) *E. coli* cells (the bacterial hosts) were then "infected" with the plasmid-globin combination.

Logically, the next step would be to look for globin proteins in the bacterial cells. But Cold Spring Harbor geneticist Tom Maniatis explained to SCIENCE NEWS that no one has yet been able to find rabbit, toad or insect proteins (the end-products of foreign gene expression) in their bacterial hosts after recombination. Successful incorporation of the globin gene into the plasmids (and hence the host cells infected by the plasmids) was proven, instead, by making and tracing the uptake of radioactive globin DNA. Terry Rabbitts of Cambridge University presents a detailed account of this approach in the March 18 NATURE.

Each group has its own specific interest which is best served by inserting the globin gene, but, in general, this recombination should make it possible to study both the base-pair sequences of the globin gene itself, and the function and control of this and adjacent genes. His team, Maniatis explains, is interested in genetic control during development from egg to adult. After the team has perfected its technique for globin gene insertion, the researchers will use the system to probe the mRNA's produced during silk moth development. (A report of their technique will appear in the June CELL.) This, he says, will provide a system for studying the many genes, expressed coordinately (turned on and off) during growth and differentiation within silk moth developmental stages.

They will also study the mammalian globin gene itself, Maniatis says, and the sequences of the genes adjacent to it on the rabbit chromosome. During embryo development, fetal globin genes are turned off and adult alpha and beta globin turned on. The gene insertion techniques, he hopes, will also help the team probe this coordinate gene expression. □

New additions to the particles zoo



Evidence for new heavy particle: Ratio of hadron to muon production in e-p annihilation as energy changes. Peaks at 4.1 and 4.4 GeV are plainly visible.

The late Werner Heisenberg was described as bored with the spate of new particles being discovered by physicists. If he could read the March 29 PHYSICAL REVIEW LETTERS, he would have reason for increased ennui. In the pages of that issue a few more particles are added to the growing menagerie (now well over 100).

The first is a new entrant in the heaviest-particle-ever-discovered sweepstakes, another of the series of psi particles that appear after collisions of energetic electrons and positrons in the SPEAR storage ring at the Stanford Linear Accelerator Center. The experiment is operated by a consortium of physicists from SLAC and the Lawrence Berkeley Laboratory. New particles, technically designated resonances, have appeared from time to time as the energy of the electron and positron beams is increased. The new one appears at an energy of 4.4 billion electron-volts and is denominated psi (4414). Thirty-eight physicists signed the paper reporting this discovery.

Resonances are particles with extremely fleeting lifetimes. Their main purpose in life seems to be to serve as intermediate states between something and something else. In this case the something is the annihilation of electron and positron into a burst of energy; the something else is the appearance of longer-lived daughter particles. The term comes from a mathematical analogy with a mechanical resonance: The presence of a particle resonance is signaled by a sudden increase in the production of daughter particles (in this case particularly, an increase in the ratio of the production of hadrons to the production of muon pairs, which can come from electron-positron annihilation without the intermediation of a resonance).

Sometimes this kind of phenomenon strains the definition of a particle. A data enhancement at 4.1 billion electron-volts has been repeatedly seen and was reexamined in this run, but because of some of its characteristics the physicists still hesitate to call it a particle.

Theorists are interested in the psi particles because they appear to be evidence for the existence of a new particle characteristic (quantum number) called charm. Charm was introduced to explain some anomalies in the behavior of previously known particles. In doing so, it has opened a whole new game. (Heisenberg would have been bored about five quantum numbers ago. He believed in the unity of physics, and particle physics is far from unified. It's more like the woman in the hair lotion commercial: "My split ends are developing split ends.")

Meanwhile, back in the domain of the original precharm quark theory, a couple of empty slots seem to have been filled by another SLAC experiment, this one done with the linear accelerator itself (G. W. Brandenburg and 10 others).

The quark theory arranges the particles

in multiplets (say groups of 8 or 10). In a multiplet certain characteristics will be constant throughout while others vary according to the principles of the branch of mathematics called Lie groups. The mathematical characteristics of the elements of the different Lie groups can be translated into physical terms and used to predict the existence and properties (quantum numbers) of members of the particle multiplets that have not yet been discovered by experimental physicists.

The theory predicts two octets of the class of particles called axial-vector mesons, but up to now only one, the B meson, has been found. The present experiment reports two more, designated Q_1 and Q_2 with masses of 1.3 billion electron-volts and 1.4 billion electron-volts respectively. Their existence is "in accord with the multiplet structure implied by the quark model." □

Scrutinizing community mental health

For $5 billion a year, we get a community mental health system that may or may not be doing its job. Mentally and emotionally troubled people are no longer burned as witches, nor are they (always) locked away under shameful conditions in state hospitals. But does the community mental health center (CMHC) system provide the best possible services to the people who need them? Does it provide a necessary service to the community? Is there a better alternative?

These questions can't be answered conclusively, and because the system is so complex, some researchers feel that the community approach can't even be evaluated at present. But after more than a decade of operation, it is certainly time to begin asking questions. And that is just what went on last week in New York at the annual meeting of the Kittay Scientific Foundation.

The rationale for and history of community mental health was recalled by Frank M. Ochberg and Lucy D. Ozarin of the National Institute of Mental Health. In 1955, a commission was set up to study mental health needs and resources. Six years later the commission reported to President Kennedy, Congress and the public. One of its major recommendations was: "Make reasonable efforts to operate open mental hospitals as mental health centers, i.e., as part of an integrated community service with emphasis on outpatient and aftercare facilities as well as inpatient services."

The results of this recommendation were summed up by Congress in the CMHC Amendments of 1975. The amendments called community mental health care "the most effective and humane form of care for a majority of mentally ill individuals" and said the federally funded community mental health centers "have had a major impact on the improvement of mental health care." It gave three reasons: They foster coordination and cooperation between various agencies responsible for mental health care, which in turn has resulted in a decrease in overlapping services and more efficient utilization of available resources. They bring comprehensive care to all in need within a specific geographic area regardless of ability to pay. And they result in a system of care that ensures continuity of care for all patients, "and thus are a national resource to which all Americans should enjoy access."

But this sort of glowing optimism is not universal, not even within NIMH. Ochberg and Ozarin pointed out some of the achievements of "The Golden Age of Mental Health" (c. 1963 to 1975), but acknowledged several shortcomings: gaps in follow-up care, an inability to even evaluate the quality of care and trouble getting research findings implemented. And they mentioned a new problem: "How do we reconcile the strength and values of the community mental health concept with the current reality of political, economic and bureaucratic catastrophy?"

Others at the Kittay symposium were less gentle with the CMHC concept. George Serban of the New York University Medical Center is medical director of the Kittay foundation. He sees the history of community psychiatry in a different light. "Supported by scanty social evidence produced by fragmented social research, community psychiatry," he charges, was "used by social activists, self-styled guardians for the rights of the mentally ill, as a springboard for personal political objectives. The correlation between mental illness and social class," he explains, "became the justification for attempts to replace the medical model with the social-political one, which allegedly would have cured not only the social imperfection of society but also our mental illness."

But it didn't, says Serban. The move away from the medical model and what he calls "massive indiscriminate discharge from the hospital" of mental patients produced a "revolving-door policy." Voluntary treatment in the community leads to multiple rehospitalizations, says Serban, due to patients' lack of interest in treatment.

Charges and countercharges were only half of the symposium. The other half was devoted to research. Data presented from a number of studies could possibly plug some of the gaps in the CMHC system.

Serban's own research with schizophrenic patients discharged to voluntary community aftercare clinics shows that 70 percent of them do not attend psychiatric facilities or take their required medication. Most end up back in the hospital, 42 percent for antisocial acts. Serban proposes that community treatment in structured programs must be made legally mandatory for such patients. (During discussion at the meeting, legal and ethical problems were raised in regard to this proposal.)

Leo Srole of Columbia University described a foster care program for chronic mental patients that has been in operation in Geel, Belgium, since the 15th century. A similar model may be workable with some patients in the United States.

Thomas S. Langner of Columbia University discussed his 10-year study of Manhattan children. His data have implications for the prevention of mental health problems. Langner's work documents child abuse as the single most important, but correctable, family determinant of juvenile delinquency, aggressivity and other forms of youthful antisocial behavior.

While this and much other research may be important to the future of community mental health, NIMH representatives admitted to bureaucratic and administrative problems in getting research data out of the laboratory and into the streets. □

Diabetic blindness successfully treated

Loss of sight is one of the more serious side effects of diabetes. About 48,000 people in the United States are blind because of diabetic retinopathy. An additional 300,000 have the condition and are in danger of losing their sight. The National Eye Institute has now issued results of a study suggesting that such blindness can be prevented in a significant number of cases.

The underlying causes of diabetic retinopathy are still unknown, but researchers do know that the resulting blindness is due to a proliferation of blood vessels in the eye. These vessels bleed and do permanent damage to the eye. For about 15 years, eye surgeons have attempted to treat the condition with light. Photocoagulation, produced by a green argon laser light or a white xenon arc light, can seal off some of the damage-causing blood vessels. The eye institute's study now shows conclusively that this treatment is effective.

In 16 different medical centers around the country, 1,720 patients were given the light treatment—in one eye only. After two years, blindness has showed up in 129 untreated eyes but only in 56 treated eyes. With blindness occurring in such a small proportion of the treated eyes, the photocoagulation technique is considered successful enough to be applied to the untreated eyes (except where blindness has already occurred) and can now be considered an accepted form of therapy. Results will be published in the April AMERICAN JOURNAL OF OPHTHALMOLOGY. □