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.

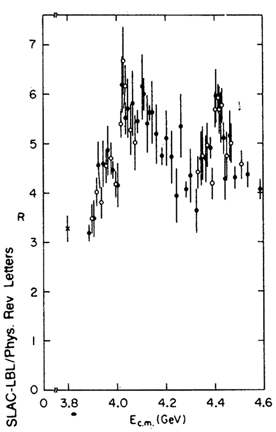
All four groups (Rougeon, Kourilsky and Mach from Geneva and Paris; Maniatis, Efstratiadis, Kafatos and Maxam from Harvard and Cold Spring Harbor; Higuchi, Paddock and Salser from the University of California at Los Angeles, and Rabbitts from Cambridge, England) started with globin mRNA prepared from 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