Scientists Isolate Single Gene in Step to Heredity Co

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ever, the work has major implications for higher life because there is growing evidence that all living things, from the lowest single-celled bacterium to humans, receive their traits by fundamentally the same mechanism.

For this reason, the achievement probably brings much closer the day — less than 25 years off by some estimates — when it will be possible to cure human diseases or change inborn traits by injecting new genes. Because such methods could be misused, many scientists view this prospect with considerable ambivalence.

'Elegant' Experiment

The Harvard work, the experimental details of which are being published today in London in the journal Nature, was performed over two months last summer.

In an experiment that other scientists called "elegant," the term they apply to a sophisticated experiment that cuts to the heart of a complex conceptual problem with great simplicity, the Harvard team focused on the lactose gene, one of the largest and most thoroughly studied. It is one of 3,000 genes on the E. coli chromosome, the rod-shaped cell structure that bears the hereditary material.

They extracted the gene by using viruses as intermediary carriers. To do this they relied on the now classic techniques for which three American scientists—Max Delbruck, Alfred D. Hershey and Salvador E. Luria—were awarded a Nobel Prize last month.

These techniques are based on the fact that bacteria are infected by certain viruses, called phages. Phage particles enter the bacterial cells, pluck out small bits of the cell's genetic material (the DNA) and multiply.

The Harvard scientists used two such phages, known technically as lambda-plac5 and phi-80plac1, both of which contain the lactose gene picked up from E. coli cells, along with several other unwanted genes. The two phages differ mainly in that the sequence of chemical units that make up the lactose gene face in opposite directions, which was the key to the experiment.

The DNA in each of these phages is double stranded, shaped something like a twisted ladder, the rungs of which consist of chemically complementary pairs.

By treatment with special chemicals, these strands were unwound and separated. Then one strand from each phage was brought together in a test tube. Since only the lactose genes were opposite mirror images of each other, and therefor complementary, they immediately came together and formed a new double strand.

The remaining unwanted gene segments could not find complementary partners and hung on as loose single-stranded ends. These ends were then dissolved by treating with a special enzyme, or biological catalyst, that affects only single-stranded DNA.

The result was a purified segment of bacterial DNA that was responsible for only one genetic function, which is the ultimate definition of a gene. Large enough to be photographed with an electron microscope, it measured 1.4 microns, or .000055 inches, in length.

Many scientists have been working on the gene purification problem for some time, using a variety of approaches. Until now, they had succeeded only in isolating three or four genes together.

It was important to obtain a single pure gene so that its action and the action of other cell components on it could be studied without other genes present to complicate the situation.

The most immediate practical significance of the feat is its implications for understanding the mechanisms by which genes are controlled. The broad outlines of these mechanisms were sketched by two French scientists, Francois Jacob and Jacques Monod, whose efforts were rewarded by a Nobel Prize. The inner biochemical and biophysical workings of the process, however, remain to be elucidated.

The French scientists advanced the theory, now substantially verified, that genes were controlled by a negative mechanism. That is, they are kept turned off by a "repressor" until another substance, an "inducer," comes along and disengages the repressor, allowing the gene to express itself.

Thus a gene consists of three elements, together called an operon. The elements are a "promoter" that produces the repressor, an "operator" that starts the gene operating but is normally dampened by the repressor and a "structural" portion, which is placed into action by the operator and does the main work of the gene. It does this by directing the production of cell proteins which in turn govern cell reactions and the formation of protoplasm, the cellular material. The proteins, thus, specify genetic traits.

Operon Isolated

Therefore, what Dr. Beckwith and his team did was to isolate the lactose operon. The "lac operon," as it is called, controls the bacteria's ability to metabolize lactose by governing the production of an enzyme, called beta-galactosidase, which chews up the sugar. Enzymes are proteins.

The achievement clears the path for a detailed study of the workings of the Jacob-Monod mechanism in the test tube under controlled conditions. A variety of experiments are possible, not only with the lac operon but with other bacterial genes, now that the techniques have been perfected.

For example, it should be possible to zero in on the mystery of where on the gene the repressor binds to prevent its function, as well as where and how the gene directs protein formation. Such knowledge may permit scientists to turn genes on and off at will.

In addition, the purified gene could be used to study the chemical products of a gene in action uncontaminated by the products of other genes. Ultimately, it may also be possible to pin down the exact sequence of chemical units that make up individual genes.

It is generally believed that the operator is the crucial site for the regulation of protein production. Recently, other scientists at Harvard University isolated the repressor substance. Now that the gene has also been isolated, the effect of the repressor can more readily be studied.

Genes operate by first producing a substance called ribonucleic acid, or RNA that acts as a messenger, carrying the genetic information of the DNA to the site of protein manufacture in the cells.

Other Steps Possible

With a purified gene now available, it should be possible in the test tube to measure with great precision the nature of the RNA produced and follow the complex steps of

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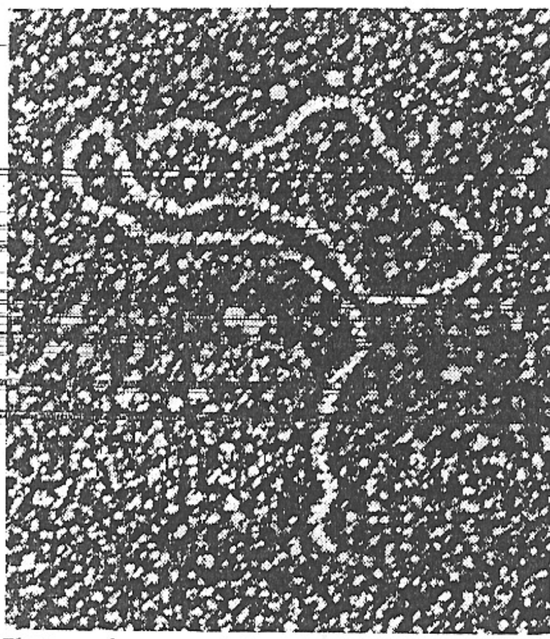
The team of scientists that isolated the gene are, from left, Dr. James Shapiro, Lawrence J. Eron and, their leader, Dr. Jonathan Beckwith, all of the Harvard Medical School.



Electron microscope photograph of single gene, twisted strand in center of the picture. It is .000055 inches long.