The one gene-one enzyme hypothesis, proposed by George Wells Beadle in the US in 1941, is the theory that each gene directly produces a single enzyme, which consequently affects an individual step in a metabolic pathway. In 1941, Beadle demonstrated that one gene in a fruit fly controlled a single, specific chemical reaction in the fruit fly, which one enzyme controlled. In the 1950s, the theory that genes produce enzymes that control a single metabolic step was dubbed the one gene-one enzyme hypothesis by Norman Horowitz, a professor at the California Institute of Technology (Caltech) and an associate of Beadle's. This concept helped researchers characterize genes as chemical molecules, and it helped them identify the functions of those molecules.

The three scientists involved in the development of the one gene-one enzyme theory were Boris Ephrussi, Edward Lawrie Tatum, and Beadle, but because Beadle participated in all of the experiments leading to the construction of the theory, the others granted that Beadle played the most significant role in its inception. Ephrussi worked at the Institut de Biologie Physico-chimique (Institute of Physico-chemical Biology) in Paris, France, and studied the genes of the fruit flies Drosophila melanogaster. He met Beadle, who worked at the Caltech in Pasadena, California after receiving a Rockefeller fellowship in 1930 that allowed him to research there from 1934 to 1935. At Caltech, Beadle and Ephrussi studied the genetic factors of eye pigmentation in Drosophila melanogaster.

At Caltech, Beadle and Ephrussi experimented with mutant fruit flies from 1934 to 1937. In an attempt to explain the eye color of flies through genetic components, Beadle and Ephrussi transferred larval tissues that would normally become adult eyes from one larval embryo to another embryo and recorded the results. Using twenty-six mutants that had different eye colors from each other, Beadle and Ephrussi transplanted eye tissue from a fly of each kind of mutant into the abdominal region of a wild-type, or normal, fruit fly. In all cases except two, the eyes transplanted into abdomens developed with the mutant eye color. Thus, the larvae had normal eyes and the transplanted, vestigial abdominal eye. This result suggested that it was the larval genes in the cells of the transplanted tissues, rather than the environment of the larval tissues, that led to mutant eye color.

The two exceptions involved fly larvae that would develop vermilion (v) and cinnabar (cn) eye color, colors that were mutations away from the normal eye color of brown. When the tissues of these mutants were transplanted into the wild-type, the transplanted eye tissue developed into the wild-type eye color, rather than the respective mutant color. Beadle and Ephrussi inferred from these results that some substance was diffusing into the mutant larval tissue from the surrounding host tissue that led to the development of the normal wild-type eye color. They hypothesized that the wild-type vermilion and cinnabar factors were genes that coded for enzymes necessary for the production of substances capable of causing wild-type eye development. Hence, although the one gene-one enzyme idea garnered popularity only after Beadle and Tatum's experiments on Neurospora, the theory originated from Beadle and
Ephrussi's previous trials with *Drosophila*.[7]

After Ephrussi left Caltech in 1935, Beadle worked with Edward Tatum at Stanford University.[9] in Palo Alto, California, in 1937. Beadle and Tatum worked to determine how exactly genes[4] regulated enzymes and controlled biochemical reactions. Prior to this time, few researchers in the US looked for the genetic causes of chemical reactions, and the field of biochemistry had developed largely within a medical context, while genetics had developed within the agricultural context. To elucidate the mechanism of how genes[4] worked and to further explore the questions arising from the *Drosophila*.[7] experiments, Beadle and Tatum focused on the red bread mold *Neurospora crassa*.[10]. Between 1937 and 1945, the two published a series of papers together.

Beadle and Tatum first created *Neurospora* mutants by irradiating *Neurospora* with x-rays. They subsequently germinated sexual spores in tubes of a complete medium, or physical environment, which contained amino acids, vitamins, and other organic substances. They then transferred *Neurospora* to tubes of a minimal medium, which lacked some of the nutrients that the *Neurospora* needed to survive. Beadle and Tatum reexamined any *Neurospora* mutants that failed to grow in the second, minimal medium to determine whether or not any new growth factor requirements had been induced. In almost all cases in which a mutant was unable to survive in the minimal medium, Beadle and Tatum remedied the failure to grow by adding a particular chemical?either a vitamin or a specific amino acid?to the medium. The results suggested that these chemicals, which were products of genes[4], were necessary for the genes[4] to encode a required enzyme in a biochemical pathway. In 1941 Beadle and Tatum published their results in "Genetic control of biochemical reactions in *Neurospora*," in which Beadle proposed the one gene?one enzyme hypothesis.

The information obtained from the experiments on *Neurospora* confirmed what Beadle had witnessed in *Drosophila*.[7] when he worked with Ephrussi. It confirmed that a gene specified the action of a single biochemical pathway, or one step in an overall set of reactions, and this was done through the production of a specific enzyme. Beadle and Tatum received the Nobel Prize in Physiology or Medicine[11] in 1958 for their work on the *Neurospora* and for demonstrating that genes[4] regulated chemical processes.

The hypothesis was modified after various studies, including that of Vernon Ingram who worked at the Massachusetts Institute of Technology[12] in Cambridge, Massachusetts. In 1957, Ingram showed that some genes[4] accounted for single polypeptide chains of a protein comprised of multiple chains. Subsequently, the idea was dubbed the one gene?one polypeptide hypothesis, after further investigation into the phenomena led scientists to conclude that genes[4] actually specify protein products.

### Sources

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