

Beadle and Ephrussi's Transplantation Technique for *Drosophila*

Boris Ephrussi and George Wells Beadle developed a transplantation technique on flies, *Drosophila melanogaster*, which they described in their 1936 article "A Technique of Transplantation for *Drosophila*." The technique of injecting a tissue from one fly larva into another fly larva, using a micropipette, to grow that tissue in the second larvae, was a means for investigating development of *Drosophila*. Through this technique, Beadle and Ephrussi studied the role of genes in embryological processes. Beadle and Ephrussi were the first to apply the transplantation method, which had previously been used in the study of larger insects, to the smaller sized *Drosophila*. Beadle and Ephrussi used this method of transplantation to determine if parts of the optic disc, the section of a larvae that later become the eye buds in the adult, could be extracted from one larva and transplanted into another. They later built upon this research to relate the production of molecules in cells to gene function.

Beadle and Ephrussi developed their technique of transplantation in *Drosophila* at the California Institute of Technology (Caltech) in Pasadena, California, where Beadle had arrived in 1931 after being awarded a US National Research Council Fellowship upon the completion of his PhD from Cornell University in Ithaca, New York. Ephrussi, who previously worked at the Institut de Biologie Physico-Chimique in Paris, France, joined Beadle at Caltech after receiving a Rockefeller Fellowship in 1934. Using Beadle's background in genetics as well as Ephrussi's experimental embryology background, the researchers analyzed genes that they hypothesized were relevant to the development of the eyes in *Drosophila*.

Beadle and Ephrussi studied gene expression, asking when, where, and through what mechanisms were genes active in the process of development in organisms. Prior to this experiment, researchers could little explain or describe the development of organisms in *Drosophila*, which had mostly been studied from a genetic viewpoint. They conducted their experiments and developed their transplantation technique at the Caltech in 1935.

Ephrussi and Beadle followed a protocol for transplantation. First, they designed an apparatus that had two binocular microscopes sitting on opposite sides of a narrow table. One microscope, microscope A, used by one person, had a stand and a mechanism for the change of objects. The other microscope, microscope B, which a different person used, examined a test tube mounted on an adjustable stand. Microscope B faced the first microscope, placed at an angle of forty-five degrees relative to the table. A hypodermic syringe attached to a pipette holder was tightened to the left of microscope A.

With the apparatus in hand, Beadle and Ephrussi constructed a micropipette. The micropipette enabled them to remove the tissue that accounted for the characteristic of the eye from the host larva, so they could then inject that tissue into another larva, so that the larva into which the eggs were injected could develop into a fly with a certain eye color. Beadle and Ephrussi created a glass capillary with an external diameter of about 0.7 millimeter (mm) and a thickness of 0.1 mm with a micro-burner. A capillary shaft ranging from a diameter of 0.1 to 0.16 mm was attached to the capillary. The bore of the shaft ranged from 0.06 to 0.12 mm in diameter, and the shaft was broken so that its length was between 2 and 3 mm. The researchers heated the bore to constrict it, and it at the base of the shaft. The diameter of the constricted portion of the shaft ranged from 0.01 to 0.03 mm. The final step in the process of making a suitable pipette required the shaft to be broken at such an angle that the tip was extremely sharp.

Beadle and Ephrussi washed the larvae for fifteen seconds in a solution consisting of ninety-five percent alcohol, and then they rinsed the larvae in a Ringer's solution, a mixture of salt and water used to extend the lifespan of excised tissue. They dissected the host larvae using sharp needles in a drop of the Ringer's solution. Beadle and Ephrussi varied the exact procedure depending on the stage of development of a larva, as well as the target tissue or organ. After preparation, which involved the act of etherizing the host larvae in alcohol, they extracted the tissue from the host under low magnification. The person doing the work held the pipette in his right hand, while using his left hand to manipulate the syringe to extract and inject materials. Beadle and Ephrussi then placed the donor larva on the stage and held it in position while they inserted the pipette on the ventral surface of the larva, close to the posterior end. Finally, they transplanted the tissue from one larva to another.

In their article detailing the technique, Beadle and Ephrussi noted that there was no best way of carrying out the procedure correctly. They suggested that the method yielded the best results after much practice, and that the techniques could be learned only through experience. In their articles, Beadle and Ephrussi note that this technique can be done with a number of tissues or organs, not just optic discs. The application of this technique allowed Beadle and Ephrussi to study the effects of genes in cell differentiation during the 1930's. Beadle and Ephrussi used this technique to investigate how genes affected embryonic development. They described the experimental results of their research in a 1936 paper titled "The Differentiation of Eye Pigments in *Drosophila* as Studied by Transplantation." From the results, Ephrussi hypothesized that genes operated through the action of hormones.

Additionally, the transplantation technique and the subsequent experimental results allowed the pair to establish the theory that genes controlled the order of chemical reactions in the cell, which led to the one gene-one enzyme hypothesis. The hypothesis, derived by the collaboration of Beadle, Ephrussi, and Edward Tatum, a scientist at Stanford University in Stanford, California, whom Beadle worked with while researching *Neurospora*, sought to explain the relationship between genotypes and phenotypes.

Beadle and Ephrussi's transplantation techniques yielded results that illuminated the mechanisms that affect the phenotype, or physical characteristics, of organisms. Later, Beadle and Ephrussi related the production of certain enzymes, as stated in their one gene-one enzyme hypothesis, to the function of genes. The action of genes provided the products that regulated enzymes in biochemical reactions. Many later molecular biologists used the technique of transplantation as a genetic tool.

Sources

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