

Eric Wieschaus (1947-)

Eric Wieschaus studied how genes cause fruit fly larvae to develop in the US and Europe during the twentieth and twenty-first centuries. Using the fruit fly *Drosophila melanogaster*, Wieschaus and colleague Christiane Nüsslein-Volhard described genes and gene products that help form the fruit fly body plan and establish the larval segments during embryogenesis. This work earned Wieschaus and Nüsslein-Volhard the 1995 Nobel Prize in Physiology or Medicine. Into the early decades of the twenty-first century, Wieschaus continued his thirty year tenure as a professor at Princeton University in Princeton, New Jersey.

Wieschaus was born in South Bend, Indiana, on 8 June 1947. When he was six his family moved to Birmingham, Alabama, where he attended Catholic school. Wieschaus and his four siblings explored nearby woods, creeks, and lakes, collecting specimens from the local fauna. While Wieschaus later said that he enjoyed exploring nature throughout his youth, he primarily pursued drawing and painting, not science, and he planned to become a professional artist. Between his junior and senior years of high school, Wieschaus participated in a summer program at the University of Kansas in Lawrence, Kansas, funded by the US National Science Foundation, headquartered in Washington D.C. The program exposed Wieschaus to university laboratories, in which he dissected vertebrates of different species. In the summer following his senior year, a neurobiology lab at the University of Kansas invited Wieschaus to investigate the neural signals of the vagus nerve in tortoises, to dissect organisms, and to collect data. Wieschaus stated that this experience shaped his decision to pursue biology instead of art.

In 1965 Wieschaus enrolled at the University of Notre Dame, in South Bend, Indiana, for his undergraduate studies. Wieschaus first studied *Drosophila* in his sophomore year in Harvey Bender's lab where, as a student worker, he prepared food for the flies and learned basic genetics. During this time, Wieschaus took embryology courses from Kenyon Tweedel, and he studied the processes of cleavage and gastrulation in living embryos. Wieschaus, who originally had pursued art, later said that his predilection for visual aesthetics steered him towards developmental biology. In 1969 Wieschaus graduated from the University of Notre Dame with a degree in biology.

In 1969 Wieschaus moved to New Haven, Connecticut, to pursue graduate studies at Yale University. Wieschaus began his graduate career in Donald Poulson's laboratory. Poulson characterized the early stages of embryogenesis of *Drosophila*, and he described embryonic abnormalities in flies with mutations to their Notch genes. Poulson's work causally associated a phenotype and a specific gene during embryogenesis. Wieschaus later said that he learned from Poulson how the shape of an embryo can influence the shape of the later adult organism.

In his second year at Yale, Wieschaus joined Walter Gehring's lab as Gehring's only graduate student. Gehring taught him techniques for culturing embryos and for investigating the cell fates of embryos at the blastoderm stage. Many scientists argued that the cells in an early embryo were fated for specific body parts in adults, and they worked to find out which cells would develop into adult body parts. In 1972 Gehring moved his lab to the Biozentrum at the University of Basel in Basel, Switzerland, where Wieschaus continued his graduate work. Wieschaus studied the fate of individual cells removed from the embryo, but he failed to culture those cells in items like Petri dishes (culture media). This failure led him to investigate the development of cells in embryos instead of in culture media. From those investigations, Wieschaus determined that blastoderm cells in the early embryo were fated for specific segment identities in the larvae rather than for specific body parts in the adult.

Wieschaus worked with Elisha Van Deusen and Larry Marsh later in his graduate career. They

studied genes called maternal effect genes, which make products used to generate egg cells, a process called oogenesis. The researchers described egg cells that developed abnormal features during oogenesis. Their results indicated that genetic signals from the egg cells could direct early embryogenesis and control how early embryos developed patterns. In 1974 Wieschaus completed his PhD from Yale, and his dissertation earned him Yale's John Spangler Nicholas Prize.

After graduating from Yale, Wieschaus moved to Zürich, Switzerland, to conduct post-doctoral work with Rolf Nöthiger at the University of Zürich. In collaboration with Janos Szabad and Trudi Schüpbach, Wieschaus investigated the segmentation of *Drosophila* embryos, hypothesizing that cells in the embryos may be determined for specific segments in larvae as early as the blastula stage. During this time Wieschaus developed a romantic relationship with Schüpbach.

While in Zürich, Wieschaus also discussed his work with Christiane Nüsslein-Volhard, whom he had met in Basel. The two discussed experiments they wanted to develop together. Like Wieschaus, Nüsslein-Volhard also studied fruit fly embryogenesis, and she drew similar conclusions about the genetic control of segmentation. Wieschaus later reported that Nüsslein-Volhard was one of the most important influences on his work. In 1978, officials at the newly created European Molecular Biology Laboratory in Heidelberg, Germany, asked Wieschaus and Nüsslein-Volhard to co-lead a project to study how mutations occurred in *Drosophila* embryos. This opportunity allowed the two researchers to work together for the first time and to pursue the experiments they had previously discussed.

Nüsslein-Volhard and Wieschaus investigated the genetic mechanisms of how a fertilized *Drosophila* egg becomes a segmented embryo. In *Drosophila* embryos, shortly after fertilization, the cells organize into fourteen distinct body segments. To investigate this process of segmentation, Nüsslein-Volhard and Wieschaus exposed flies to mutagens. The researchers described how those flies produced embryos that developed features (phenotypes) in the segments that differed from segments of normal embryos. To determine which genes contributed to the mutant phenotypes, the researchers bred, in systematic patterns, adult flies that had the mutated genes, a procedure called genetic screening, which enabled the researchers to correlate mutated genes with mutated phenotypes. Prior to their work, scientists had identified roughly a handful of genes in *Drosophila* that, when mutated, changed the phenotypes of the embryo. By attempting to characterize every gene that impacted embryogenesis by randomly mutating large numbers of flies, Wieschaus and Nüsslein-Volhard discovered novel mutant phenotypes almost daily. Wieschaus later recalled that the rate of discovery in these experiments made them the most stimulating and exciting of his career.

In 1980 Nüsslein-Volhard and Wieschaus published "Mutations Affecting Segment Number and Polarity in *Drosophila*". They reported fifteen genes that, when mutated, caused defects to the segments of fly embryos. They further classified the genes into groups based on how, and in what order, they affected segmentation. First, they identified three gap genes, which help to determine the identity of each segment of the embryo. Second, they identified six pair-ruled genes, which affect segment identity in an alternating pattern. Third, the team identified six segment-polarity genes, which establish the anterior-posterior axis of each segment. Later research showed that the segmentation genes have homologs in many species, including humans, indicating that this mechanism of developmental control has been conserved for greater than six-hundred million years of evolution.

In 1981 Wieschaus and Schüpbach accepted positions at Princeton University in Princeton, New Jersey, and they married in 1983. Wieschaus continued to study segmentation genes, gastrulation, and zygotically active genes, and he collaborated with Schüpbach to characterize oocyte patterning. In 1995, Nüsslein-Volhard and Wieschaus shared the Nobel Prize in Physiology or Medicine for their work on segmentation in *Drosophila*, with Edward B. Lewis, who had helped identify the Hox genes of the bithorax complex in *Drosophila*, and who had demonstrated the phenotypes of flies with homeotic mutations. In 1995 Wieschaus received the Genetics Society of America Medal.

Into the early decades of the twenty-first century, Wieschaus remained a Squibb Professor of Molecular Biology at Princeton, a Howard Hughes Medical Institute investigator, and a member of the National Academy of Science. Since receiving the Nobel Prize, Wieschaus continued to research the embryonic development of *Drosophila melanogaster* and how genes influence that development.

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