Gertrud Schüpbach

Gertrud (Trudi) Schüpbach, the Henry Fairfield Osborn Professor of Biology and professor of molecular biology, stands out as one of the most esteemed senior scientists in the fields of developmental biology and genetics worldwide. She has been honored by numerous awards that speak to her outstanding scientific contributions, including the Edwin F. Conklin Medal from the Society for Developmental Biology, and election to both the American Academy of Arts and Sciences and the National Academy of Sciences. In addition to her remarkable scientific accomplishments, she is well known for her generous spirit and leadership. Trudi's service to the scientific community has been exemplary, including serving as president of the *Drosophila* Board and of the Genetics Society of America. Most significantly, she has generously shared the wealth of mutants generated by her mutagenesis screens, promoting the advancement of our understanding of developmental pathways. Trudi's teaching and mentorship have also had a lasting impact by training new generations of scientists.

Trudi began her career as a Ph.D. student at the University of Zurich, studying the genetic pathways that control the development of the female reproductive system in the fruit fly *Drosophila melanogaster*. There, in the laboratory of Rolf Nöthiger, she established novel methods to produce mosaic animals composed of cells with different numbers of X chromosomes. Such mosaics allowed her to identify the origins of different cells that comprise the reproductive system and provided one of the first cell lineage descriptions of the "bursting" pattern of stem cell divisions in any organism. She then went on to show that sexual development of the female germ cells, which ultimately give rise to eggs, builds on genetic controls that are almost entirely distinct from those governing sexual development of the somatic cells that compose the rest of the animal. After completing her thesis in 1979, Trudi spent three years at the University of Zurich's Department of Zoology as an oberassistent and lecturer.

In 1981, Trudi moved to Princeton as a postdoctoral research associate with Eric Wieschaus, in what was then the Department of Biology. There, she turned to the more than century-old question

of how a single egg cell can give rise to a complex organism. Trudi's essential insight was her recognition that deciphering how the fundamental body pattern is generated as an embryo develops would require not only an understanding of the genes needed by the embryo after fertilization, but also an understanding of the genes that controlled the earlier construction of the egg in the ovary during the process of oogenesis. Tackling this problem head-on, Trudi initiated a large-scale mutagenesis screen to identify genes which when mutated caused sterility in females. Trudi's screen differed from previous and contemporary mutagenesis screens in its breadth, as she mapped the chromosomal locations and complementation behavior of all her mutants and characterized their phenotypes. Ultimately, she published the first completed saturation screen for oogenesis mutations in any animal, and this experiment remains the most complete genetic characterization of oogenesis. The screen has had a lasting legacy, providing a treasure trove of mutants for labs around the world. In addition to genes immediately involved in embryonic patterning, it yielded the very first alleles of *Drosophila* genes that play central roles in a wide range of cellular and developmental processes like cytoskeletal function, neurogenesis, and sex determination. Trudi's inspired naming of genes after royal families without heirs, vegetables, birds, and other everyday items that the mutant embryos or eggs resemble, has been a source of delight to the *Drosophila* community and beyond.

In 1985, Trudi was appointed to the position of research biologist and in her own laboratory began to reap the fruits of the mutagenesis screen. Mutants for two of the genes she identified, *gurken* and *torpedo*, provided the foothold to unlocking the mystery of how an embryo develops with both dorsal (back) and ventral (front) sides. Eggs laid by *gurken* and *torpedo* mutant flies were missing structures normally formed on the dorsal side, a so-called "ventralized" pattern. Strikingly, the embryos developing inside the mutant eggshell were also ventralized. In a landmark single-author paper published in the prestigious journal *Cell*, Trudi combined elegant cell transplantation and genetic mosaic experiments to show that *gurken* operated in the developing egg cell—the oocyte—whereas *torpedo* operated in the follicle cells that surround the oocyte and that the dorsal-ventral pattern of the embryo was generated by a sequence of communications between these two very different types of cells. The discovery of this cell-to-cell communication made the *Drosophila* ovary a

prime experimental model system for investigating the molecular mechanisms of cell communication in multicellular organisms. In 1990, Trudi was promoted directly to associate professor in molecular biology and in 1994 she was promoted to professor of molecular biology and appointed as an associated investigator of the Howard Hughes Medical Institute.

The importance of Trudi's characterization of communication pathways in the ovary was amplified by her lab's discovery that the *torpedo* gene encoded the *Drosophila* homologue of the vertebrate epidermal growth factor (EGF) receptor, and that the *gurken* gene encoded the homologue of its signaling ligand, Transforming growth factor α (TGFα). In humans, the EGF receptor signaling pathway plays a major role in growth control, and differentiation and mutations in these genes are associated with many forms of human cancer. The phenotypes Trudi identified in *Drosophila* provided an opportunity to dissect this crucial signaling pathway in a genetically tractable model organism. Through the 1990s, Trudi's lab used a combination of molecular and genetic approaches to characterize how the signal is produced in the oocyte, how it becomes locally deployed, how it is perceived and measured by the adjacent follicle cells, and how interactions between the two cell types generate a final pattern. There were many surprises in this analysis, for example, that the production of the signal was coupled to the repair of double-stranded breaks in DNA that occur naturally during the process of meiosis. Other studies showed that proteins involved in mRNA splicing played a central role in localizing the *gurken* mRNA, and thus the production of the signal to a very specific region within the oocyte. Each of these discoveries provided opportunities to investigate the molecular mechanism underlying these processes and thus extended the impact of Trudi's work beyond the strict analysis of cell signaling in the ovary.

Always a geneticist, Trudi turned again in recent years to mutagenesis screens to learn more about the cell communication pathway controlled by *gurken* and *torpedo*. This time, however, she used a sophisticated method to create patches of mutant follicle cells in order to identify essential genes missed by traditional genetic approaches because entirely mutant animals did not survive. These new screens yielded a plethora of genes whose roles were not readily predicted and whose analysis by new generations of graduate students and postdoctoral fellows have yet again highlighted the importance

of the *Drosophila* ovary as a rich model system for understanding fundamental cellular behaviors.

Trudi has also made many more intangible contributions during the course of her career that have earned her a place as a major leader in the fields of genetics and development. She has generously shared her expertise and her time organizing national and international conferences, including the quintessential Gordon Conference on Developmental Biology, and serving on editorial boards of prestigious journals (e.g., *Genetics, Developmental Cell*) as well as on numerous advisory boards both in the U.S. and Europe. For over 25 years, Princeton molecular biology majors have learned both the fundamentals and the intricacies of genetics in Trudi's core departmental course, MOL 342. Over 50 undergraduate and graduate students and postdoctoral fellows have been fortunate to have received Trudi's mentorship. Many of Trudi's former graduate students and postdocs—including many women—have been inspired to pursue careers in science, with nearly half holding faculty positions. Trudi's devotion to science and teaching has been paralleled by her devotion to her family, and she combines all these achievements with a modest and supportive personality that serves to enhance her stature.