Health & Medicine

Edmund Beecher Wilson: America's First Cell Biologist

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Edmund Beecher Wilson ’29HON set the stage for a revolution in modern genetics with his pioneering research and inspired leadership of Columbia’s world-renowned department of zoology.

When Seth Low 1870C became president of Columbia College in 1890, it marked the beginning of some of the most dramatic changes in the institution’s history— from the move to Morningside Heights in 1897 to a major restructuring and expansion of the existing faculties and schools.

Low also placed a new emphasis on scientific research at Columbia and served as a guiding influence in establishing the zoology department in 1891 as well as the new School of Pure Science a year later. The new dean of the School was Henry Fairfield Osborn ’07HON, who had recently recruited to the zoology department a 35-year-old biologist from Bryn Mawr named Edmund Beecher Wilson.

Wilson would eventually lead the department and become one of the most influential cell biologists of all time. His own research and leadership paved the way for the groundbreaking work of future Nobel Prize winners Thomas Hunt Morgan and Hermann Muller ’10C ’16GSAS and elevated the department of zoology at Columbia to a position of international prominence.

Wilson was born in Geneva, Illinois, in 1856. He later wrote of his childhood: “It would not be easy to imagine a happier environment for a boy who somehow managed to combine a passion for natural history with an almost equal love for music.”

At the age of sixteen Wilson taught for a year at a country school. The following summer he reached a decision that would change the course of his life. Inspired by conversations with his cousin Sam Clarke, who was a student at Antioch College, Wilson decided to “try for a college education and a life devoted to biology.” He enrolled at Antioch but one year later followed in Clarke’s footsteps and transferred to Yale. He was offered a position there when he graduated, but his cousin was giving him glowing reports about graduate study at Johns Hopkins, so he applied there and obtained a fellowship to study biology. Wilson carried out most of his graduate work at Johns Hopkins under the tutelage of William Keith Brooks. About Brooks, he wrote: “From him I learned how closely biological problems are bound up with philosophical considerations. . . . He taught me to think about the phenomena of life instead of merely trying to record and classify them.” After Wilson obtained his Ph.D. in 1881, he decided to study in Europe for a year. With a loan from his brother, he sailed for England, where he met some of the most important British scientists at that time, such as Thomas Henry Huxley, Adam Sedgwick, W.H. Caldwell, and William Bateson.

While studying at Johns Hopkins, Wilson had heard of the Zoological Station in Naples. The station had been established by a group of European institutions to investigate critical problems in phylogeny and evolution. German biologists, the dominant force in research at the time, flocked to Naples, and its director, Anton Dohrn, was an important figure in the field. Wilson desperately wanted to do research at the Zoological Station but could not afford the dues of renting a table in the laboratory. Eventually Clarke, by now a professor at Williams College, came up with the solution: Williams College would rent a table, and Clarke and Wilson would split the time if Wilson would teach Clarke’s courses at Williams during his absence.

In Naples the sun and scenery of southern Italy had its customary effect on a “northern” scholar, driving him, as it did Goethe 100 years earlier, into lyrical flights. Wilson wrote, “That first year in Naples—it was not quite a year—was the most wonderful year of my life. I despair of conveying any notion of what it meant to me, and still means as I look back upon it through the haze of fifty years. It was a rich combination of serious effort, new friendships, incomparable beauty of scenery, a strange and piquant civilization, a new and charming language, new vistas of scientific work opening before me; in short a realization of my wildest, most unreal dreams.”

He completed his agreement with Williams College on his return, and after a year of teaching at MIT he was appointed in 1885 as the first chairman of the biology department at Bryn Mawr. He stayed there for six years before he received the offer from Columbia and eventually helped Bryn Mawr recruit his replacement, Thomas Hunt Morgan, a man ten years younger who also studied at Johns Hopkins. (Wilson would eventually recruit Morgan to Columbia.)

Columbia allowed Wilson to travel in Europe for a year before he assumed his teaching duties, and that year was a *Wanderjahr* spent in Naples and in Munich, a year that changed his research program from investigations of phylogeny and evolutionary biology to cell biology and experimental embryology. This was in no small part due to the influence of Theodor Boveri in Munich, who became Wilson's closest friend. Boveri, an amateur musician and painter, was a brilliant experimentalist who later demonstrated that each individual chromosome conferred hereditary properties on daughter cells. Wilson said, "The best thing that he gave me was at the Café Heck, where we used to dine together, drinking wonderful Bavarian beer, playing billiards, and talking endlessly about all manner of things." On Wilson's return to New York, he began spending his summers at the newly established Marine Biological Laboratory in Woods Hole, where he met his future wife, Anne Kidder. He then settled into a life of research and teaching that lasted forty years.

Wilson left few notes describing his life and times. He was described as "a quiet gentleman" even in his obituary in the *Herald Tribune*. But the warm feelings expressed in the many memoirs by his colleagues and students attest to his gift for friendship.

Cell biology and development in the late 1800s

The last quarter of the nineteenth century saw the widespread acceptance of the cell theory, or the notion that all living things are composed of cells. Evolution provided the other major foundation for biology, and many researchers asked questions about how organisms and their parts become adapted to their environments and what causes homologies, or similarities in parts, across species. Since Darwin, researchers had often focused on vertebrates and asked about their evolutionary past and relationships to other species. This is especially interesting, obviously, because it is about the origins of humans. When the German popularizer of evolutionary theory Ernst Haeckel stated that individual organisms pass through the same stages in their development as species did in their evolutionary past (or the so-called biogenetic law according to which "ontogeny recapitulates phylogeny"), some saw this as a key research tool. Now they could learn about the evolutionary origin of vertebrates by studying individual development through embryology. Haeckel held that the first important stage of individual development is when the embryo forms three germ layers, namely the ectoderm, mesoderm, and endoderm. At this point, it is called a "gastrula," and Haeckel hypothesized that the earliest stage of evolution of vertebrates was a "gastrea" just like this embryonic stage.

While some biologists, especially in Germany, found this an enticing interpretation, Wilson launched one of the most effective challenges. His studies of cell lineage, in which he traced what happens to every cell as the egg divides into two, then four, eight, and more cells up to the gastrula stage, showed serious inconsistencies in what Wilson and many of his American contemporaries saw as Haeckel's speculative and unwarranted hypothesis. These cell lineage studies, carried out by Wilson and his colleagues largely at the Marine Biological Laboratory, established our basic understanding of cell division. Wilson saw these early divisions as products of both heredity and adaptation to surrounding conditions. As he put it, "The form of cell division is determined by two factors. The first factor is the inherited tendency of the cell to pursue a definite course, a tendency that we may assume exists by virtue of a corresponding molecular or protoplasmic structure. The second factor is the influence upon the cell of other cells in the colony. When the second factor is removed or modified, the first is correspondingly modified, and a complete readjustment takes place." This was written in 1892, but one could not ask for a more modern view of cellular development.

Two biologists from Columbia, Wilson and Thomas Hunt Morgan, and Wilson's friend Boveri, provided major contributions on which modern genetics and cell biology are based. Wilson pointed to "two fundamental questions which still remain in their essence without an adequate answer though metamorphosed. . . . The first of these is whether the embryo exists preformed or predelineated in the egg from the beginning or whether it is formed anew, step by step in each generation. The second question is that of mechanism versus vitalism—whether development is capable of a mechanical or physico-chemical explanation or whether it involves specific vital forces that are without analogy in the non-living world.” The second he felt had been decided in favor of mechanism and physico-chemical explanation. The first remained.

If preformation occurs, then the form must be there in the fertilized egg cell since that is the beginning of every organism. Where was it? Wilson carried out meticulous studies of the egg from its very beginning. By the 1890s, he used important technical refinements in optical microscopy, staining, and tissue sectioning, which put him in a position to perform incisive experiments to carry out careful observations of just what happens at each step of development. His beautiful drawings and clear, eloquent writing helped to convince others. His friend Boveri, to whom Wilson dedicated his most important book, also contributed to interpreting the role of the nucleus and chromosomes. Boveri demonstrated that when the nuclei of one species of sea urchin were transplanted into cell fragments of another, the resulting embryos followed the characteristics of the species from which the nucleus was taken. Morgan translated this paper into English but doubted that the experiments were correct. He himself failed to reproduce the results. Because he had found that removal of a part of the cytoplasm of a fertilized egg resulted in an imperfect embryo, he thought that the cytoplasm controlled development. However, Boveri came back with even more extensive results confirming his view of the primacy of the nucleus. He later extended these studies in a series of celebrated experiments in which sea urchin eggs were fertilized with two sperms: he found that after two cleavages, each of the separated blastomeres had different numbers of chromosomes, and each had different anomalies—leading him to conclude that the chromosomes, located in the nucleus, were the agent of heredity. Wilson agreed, concluding in a remarkably prescient comment that “chromatin is . . . nuclein, which analysis shows . . . to be composed of a nucleic acid, a complex organic acid rich in phosphorus. And thus we reach the remarkable conclusion that inheritance may perhaps be affected by the physical transmission of a particular chemical compound from parent to offspring.” This was written in 1895, five years before the rediscovery of Mendel’s laws.

Several investigators attempted to determine the role of chromosomes in sex determination. The initial findings were somewhat confusing, largely due to the use of different organisms and staining procedures. Thomas Montgomery was the first to propose that chromosomes play the most important role in determining what sex an individual organism will be. In 1902, Clarence Erwin McClung, a professor at the

University of Kansas and a former student of Wilson’s, identified a body in grasshopper nuclei that he called an “accessory chromosome” because he found it in only half of the sperm cells. He concluded that it had to do with sex determination, since male grasshoppers had one more chromosome than the females. In 1902, a student of McClung’s named W.S. Sutton ’07P&S enrolled as a graduate student at Columbia and worked with Wilson, studying chromosomes and their role in heredity.

Wilson performed his own important studies on the role of chromosomes in sex determination between 1905 and 1912. He counted and identified the chromosomes of sperm cells before and after the reduction division. Wilson and a former student of Morgan’s named Nettie Stevens (then at Bryn Mawr) simultaneously but independently performed the definitive studies that demonstrated the role of chromosomes in sex determination. Wilson found that in two insects, the female has one more chromosome than the male, while Stevens found that the male has a smaller Y chromosome to one half of the sperms while a larger chromosome went to the other half. The type found by Stevens (XX for females and XY for males) was much more frequent than the type found by Wilson (XX for females and XO for males). These findings form the basis for our modern view of sex determination and formed the beginning of our general chromosomal understanding of heredity. Wilson’s paper was submitted ten days before Stevens’s and was published two months before in *The Journal of Experimental Zoology*. But Wilson added a footnote stating that he was aware of Stevens’s studies (“now in the course of publication . . . by whose kind permission I am able to refer to her results”) and described them briefly. He also concluded that “McClung’s hypothesis may, in the end, prove to be well founded.”

Morgan, in contrast, did not accept this conclusion; he argued that a French scientist Cuenot had demonstrated that a mouse mutant in hair color (now called agouti) failed to give pure yellow-colored mice on repeated cross-breeding with black mice, “demonstrating” the lack of Mendelian inheritance. (Studies in the past decade have shown, however, that the reason is that mice homozygous at the lethal yellow agouti locus die in utero at the preimplantation stage, which explains the absence of purebred yellow mice). By 1911, however, Morgan discovered that eye color, body color, wing shape, and sex in the fruit fly all segregated together with the X chromosome, and hence he was forced to agree with the Mendelian nature of chromosomal inheritance against which he had fought for over a decade.

Wilson and Morgan also rapidly extended their findings to human genetic diseases when each separately concluded that color blindness in the published pedigrees follows Mendelian inheritance. Morgan stated that color blindness “follows the same scheme as does white eyes in my flies,” and Wilson referred to the same conclusion in an equally brief note. This apparently was the first definite specification of the linkage of a characteristic in man with the sex chromosome.

Despite their differences of biological interpretations at times, these two Columbia professors were neither competitive nor antagonistic in their personal interactions. Nothing could be further from the truth; they were intimate friends at every level. According to developmental biologist Ross Granville Harrison, “Wilhelm Ostwald in his interesting book on great men of science classified them according to their talents as romantics and classic. . . . To the romantic, ideas come thick and fast; they must find quick expression. His first care is to get a problem off his hands to make room for the next. The classic is more concerned with the perfection of his product, with setting his ideas in proper relation to each other and to the main body of science. His impulse is to work over his subject so exhaustively and perfectly that no contemporary is able to improve upon it. . . . It is the romantic that revolutionizes, while the classic builds from the ground up. Wilson is a striking example of the classic, and it is interesting to note that for many years his nearest colleague and closest friend (Morgan) was an equally distinguished romantic.”

Wilson wrote *The Cell in Inheritance and Development* as a set of lecture notes for his first course in cell biology when he came to Columbia. It went through three editions, the last published in 1927. The field was undergoing such rapid change that much of the information was outdated by publication time, but the textbook was enormously influential nonetheless. In each section, he surveyed the field and identified the major questions in clear and muscular prose; he was also admirably fair in setting the historical context. But most significantly, his arguments for or against a hypothesis were clear and commanding. When the evidence itself was unclear, Wilson suggested his own interpretations, most of which turned out to be correct when later studies provided more decisive results. He left no doubt where he stood on unresolved questions, an approach that gave the text the wonderful flavor of a conversation with an agile mind. By concentrating a large part of the book on the role of the cell as an agent of heredity, he provided a focus for a field that was full of disparate information and random descriptions. Its reception as a signal contribution helped shift the balance of power away from the German investigators.

The last edition received a highly unusual honor—the Elliott Medal from the U.S. National Academy of Sciences—the first and only time a textbook was so honored.

Wilson the teacher

Some scientists may say that they want only to uncover the secrets of nature, but the added glory of influence on the thoughts and works of their peers must be an added bonus. (Skeptics might call it the driving force behind their commitment to work.) Yet such influence is difficult to measure. In their own publications, scientists generally refer only to the most recent work of others, and papers published just five years ago often seem to disappear into a realm of quiet obscurity. But the influence that teachers have on their young (or not so young) students has a far longer “time constant” than most publications. One hears it at celebrations and Festschrifts of retiring scientists. Wilson makes a superb case study of this influence. He took his teaching responsibilities seriously, and the comments published by his students stress his personal involvement and the care he took in preparing his lectures. He supervised the teaching throughout his department and had a tremendous influence in shaping the thinking of a generation of influential biologists.

Hermann Muller, who went on to win the Nobel Prize for discovering the role of X rays in causing mutations, reflected this influence in a memoir of his days as a student:

“The excitement of the advances in chromosomal theory made by Wilson from 1905 to 1910 communicated itself through the Department of Zoology at Columbia. This helps to explain why it was that most of the first batch of youngsters who became Drosophila workers with Morgan had been undergraduates in Columbia College in the latter part of this period and others came through by the same route afterwards. Lured on by their first course in biology, where they were molded by William Sedgwick and Wilson’s text and by the teaching of Gary Calkins and James McGregor, both former students of Wilson’s, some of them had the privilege of taking in their sophomore year Wilson’s thrilling one-semester course on heredity and the chromosomes, variation and evolution. They usually took Wilson’s superb course on cytology, with its unequalled laboratory training and demonstrations, in their third or fourth year after entering as freshmen. After this stimulating and thoroughly systematic preparation, their embarking upon the adventure of the fascinating new work on chromosomal heredity in Drosophila that had just been opened up by Morgan (1910 and 1911) was the logical continuation, now grown more specific in its direction, of the quest to which they had already become dedicated, calling for the ways of thinking, the knowledge and to some extent even the technique acquired during their previous years of training. And the striking similarity in the attitude of all of them toward the new problems was in no small measure a reflection of the degree to which this common training has been driven home. Thus it is likely that only these *Drosophila* workers, of the earlier years, fully realize to what an extent modern genetics traces its descent through Wilson."Alfred Henry Sturtevant '12C '14GSAS similarly noted that "no small part of the success of the undertaking (Morgan's *Drosophila* work) was due also to Wilson's unfailing support and appreciation of the work—a matter of importance partly because he was the head of the department."

At Woods Hole, "Wilson played the role of elder brother," wrote Frank R. Lillie, the embryologist who would go on to become president of the Marine Biological Laboratory. Lillie was thrilled by Wilson's remark to him in 1891: "I believe I am going to destroy the germ layer theory of development." To an eager student of 21 engaged in his first investigation, there was something sacrosanct about this theory, in which he had been indoctrinated as an undergraduate student; this remark taught him the difference between scientific theory and dogma.

Wilson also played a large role in recommending younger scientists for positions in other institutions. The most famous, Morgan, took Wilson's place at Bryn Mawr and then was recruited by Wilson to Columbia. Marcella O'Grady, who graduated from MIT in biology under Wilson's tutelage, was then recruited by him to Bryn Mawr. She later chaired the biology department at Vassar College. On Wilson's recommendation, she went on a European tour, where she worked with Boveri. They rapidly established a solid working relationship that evolved into a romantic attachment. They were married within the year and had a fruitful working collaboration that lasted many years. On his untimely death she returned to the United States, where she became the chair of biology at Albertus Magnus College in New Haven. There she translated her husband's book on the chromosome theory of cancer, which focused attention on the origin of cancer as a problem of cellular proliferation, a precursor of the view that we still hold today.

Wilson’s love for music

It seems that everybody in Wilson’s family played an instrument. His father played the violin and cello, his mother and sister played the piano (as did both of his aunts), and his brother Charles was a violinist. Wilson began by taking singing lessons, and although he did not have a good singing voice, he says that these lessons left him “with an inveterate habit of reading all of music in *do re mi* language.” He learned to play the flute, but when he went to Johns Hopkins, he developed a lifelong passion for playing the cello. He wrote, “I was too old to take up so difficult an instrument with any hope of mastering it.” But he eventually became an accomplished cellist and reveled in playing quartets in Bryn Mawr, Philadelphia, and New York. His friend Anton Dohrn, the director of the Zoological Station, was also “music mad”; he introduced him to the musical society of Berlin, where he came to know Joseph Joachim and the brothers Robert and Felix Mendelssohn, who “between them owned a whole quartet of fine Stradivari fiddles.” He wrote, “Music has always seemed to me to be the most mysterious of fine arts, a language sui generis and one that cannot really be translated into words.” He also said, “I have always loved music, and to it I owe some of the greatest pleasures of my life.” Another of his greatest pleasures was watching his daughter, Nancy, develop into a fine professional cellist.

Cell biology and developmental biology, then and now

Wilson’s books are peppered with terms such as “cellular biology,” and he may have been the first to use it. The title of his magnum opus, however, was *The Cell in Development and Inheritance*. The two fields of cell and developmental biology started as one, led by Wilson and Boveri with the aim of providing a cellular basis for the mechanisms of inheritance.

Wilson is credited with being the first American cell biologist; indeed, the American Society for Cell Biology awards an E.B. Wilson medal every year to a distinguished cell biologist. But his contributions are best described in Gilbert’s *Developmental Biology*, the standard textbook in the field. He remains an ancestor to both fields. Cell biology diverged from the study of development when the new methods of cell culture—the electron microscope, radioisotopes, and the ultracentrifuge—were developed. These new technologies allowed its practitioners to concentrate more on the biochemical basis of the components of the cell and the function of the proteins in complex cellular events such as the biogenesis of organelles, cell division, and cell-to-cell interaction. Developmental biology and embryology concentrated on the original problems of morphogenesis, induction, and patterning, helped by the ease of manipulation of some large embryos and fueled by the remarkable advances in genetics of model organisms such as fruit flies, worms, zebrafish, and now the mouse. But it is remarkable how much overlap there has always been between the two fields, and it continues to increase, as a brief perusal of the major journals of each field would show. Yeast genetics, which played an important role in cell biology and developmental biology, is becoming increasingly focused on the function of individual proteins in the context of a multicomponent signal transduction pathway. Thus the future of the two fields harkens back to their origins. The revolution produced by the discovery of DNA and the development of methods of its manipulation has affected every field of biology.

Now that we are in the "post-genome" era, it is pretty clear that the problems of cell and developmental biology need to be addressed with a new perspective. DNA encouraged biologists to think reductively, but cell and developmental biology have shown that the problems of real cells and organisms are produced by complex systems of interaction. These new views of complexity bring us back to the Wilsonian ideal, where the unit of heredity is the cell. Perhaps this is the reason why science historian Jane Maienschein, in discussing the future of biological research in its second century in an essay entitled "Old Wine in New Bottles," found that Wilson's agenda of research is the same as that of today's biologists, whose study of evolution, inheritance, and development is solidly based on understanding the structure and function of cells.

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