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Barbara McClintock: A Paradigm of Dedication, Perseverance, and Love of Discovery

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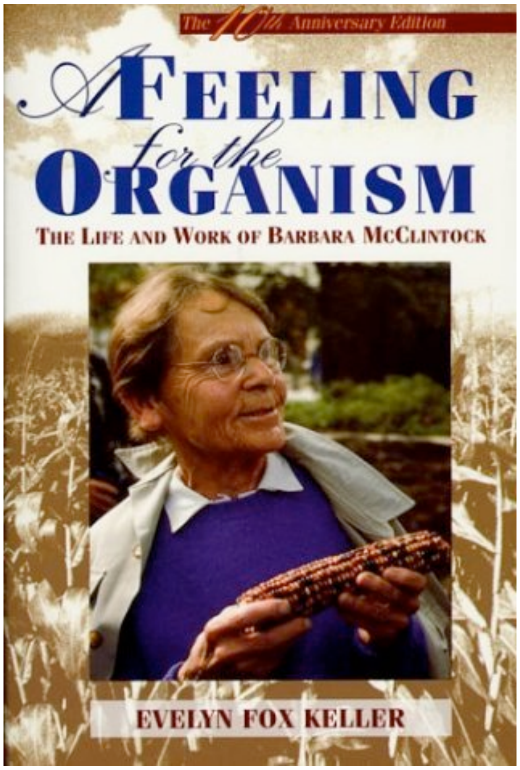

Photo courtesy of Times Books.

A timeless symbol of dedication and achievement, Barbara McClintock's story is encouraging to any type of researcher. Her career is filled with her many successes, awards, and honors. However, her struggle to gain recognition and self-trust provides confidence to young biology students in particular. Often faced with difficulty due to her personality and possibly gender, McClintock never allowed her thirst for knowledge to be quenched.

Over her long career, McClintock contributed a great deal to scientific knowledge. Her professional achievements are numerous. In 1927, she received a PhD in botany from the College of Agriculture at Cornell University (Keller 2). She was elected as Vice President of the Genetics Society of America in 1939, and in 1944, became a member of the National Academy of Sciences. McClintock was elected as President of the Genetics Society one year later (Keller 4). In 1971, she was awarded the National Medal of Science. She received the first MacArthur Laureate Award in 1981, as well as the Lasker Award for Basic Medical Research and a prize from the Wolf Foundation (Keller 13). Her greatest achievement occurred in 1983, when she became the first female scientist to win a solo Nobel Prize in Physiology or Medicine. She was awarded this prize for her discovery of genetic transposition.

Transposition, which is regarded by many as her most important contribution, was the most difficult achievement for her (Keller 4). Early on in her career, McClintock made several important scientific findings. In the 1920s, she discovered a way to identify maize chromosomes and distinguish distinctive parts of the set of chromosomes of each cell. In 1930, McClintock and Harriet Creighton worked together to prove the established theory of chromosomal crossover. Using two cytological markers on the same chromosome, McClintock and Creighton accomplished this task and confirmed chromosomal crossover during meiosis (Keller 40). McClintock also summarized how chromosomes change during reproduction in her "Chromosome Organization and Genic Expression" speech in 1951 (Keller 82).

Transposition is McClintock's most significant discovery because it plays a particularly important role in cell and molecular biology. The finding also answered several questions which had previously been unanswerable. Furthermore, her work in discovering transposition overruled a concept which had been generally accepted by biologists. McClintock worked for two years before realizing that the mutations she was observing were a type of controlled breakage in the maize's chromosome (Keller 125). McClintock was first clued in by observations that plants expressing genetic instability contained "regularly occurring and highly specific breaks in the chromosome" (Keller 127). This observation led McClintock to discover the first part of a two part transposition process. The regular pattern demonstrated a systematic removal of a part of the chromosome. After many crosses of maize offspring, McClintock was able to isolate the factor responsible for the dissociation observed (129). The Ds locus, she discovered, will only undergo dissociation mutations when the dominant factor, designated as Ac, is present (Keller 130). She further found that "the higher the Ac dosage, the later the occurrence of Ds" (Keller 132). All these clues led McClintock to the conclusion that as one sister chromatid gained a unit of Ac, the other sister chromatid lost a unit of Ac. Continuing research on Ac and Ds showed that both units "could sometimes be found in position[s] different from those originally identified" (Keller 133). When McClintock publicly announced transposition for the first time, the scientific community did not acknowledge the importance of her discovery because "transposition was absolutely nonsensical to biologists then" (Keller 136). For the first time, however, an explanation had been given to the insertions and deletions McClintock had noticed for quite some time.

McClintock performed a great deal of her work alone since she had no colleagues with whom she could collaborate. Although she corresponded daily with Witkin, and spoke on a regular basis with Rhoades and Stephens, "for the most part [communication was] one way" (Keller 145). The benefits of this kind of collaboration are demonstrated clearly in *The Double Helix: A Personal Account of the Discovery of the Structure of DNA* by James Watson. A central theme of Watson's account of the race to discover the structure of DNA is the power of competition and collaboration. McClintock lacked both of these, but she did not let it hinder her success. For these reasons, it is not surprising that McClintock was awarded the Nobel Prize in

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Medicine or Physiology, especially after her successes were ignored for so long.

The recognition deserved by McClintock was slow for a number of reasons. First, based on Keller's account, very few people had even the slightest idea of what McClintock was trying to explain the majority of the time. Most geneticists used organisms less complex than maize, and genetics was still a relatively unexplored field of science. Therefore, the people who actually had a chance of understanding, either had no interest or merely could not comprehend her ideas. The fact that McClintock was a female scientist may have played a role in her delayed recognition; however, there seems to be a certain amount of debate regarding this notion. In particular, a McClintock biography written by Nathaniel Comfort in 2001 seeks to debunk the "myth" that McClintock was a recurrent victim of sexism, as Keller makes an effort to convey. Based on Keller's account, it seems likely that McClintock may have been ignored for such a long time due to her quirky and remote personality.

Throughout McClintock's career, she struggled to gain acceptance for her work. To some extent, this was due to her identity as a woman in science. Evidence of this is provided by McClintock herself regarding her time at the University of Missouri. In *A Feeling for an Organism*, Keller writes, "[McClintock] believes a man would have gotten away with most of the things she did, but that being a woman and a maverick was simply too much" (84). Keller seems to agree by suggesting that "a man would probably have been penalized less harshly" (85). However, McClintock's gender only seemed to play a small role in her attempt at acknowledgment for her findings. To a larger extent, McClintock's difficulties seemed to be a result of her superior aptitude, impatience, and poor communication skills. Keller describes these difficulties by writing, "Most of McClintock's colleagues knew her to be very bright, but many found her somewhat difficult," and "at times, she was impatient with those who could not keep up with her" (50). A close friend of McClintock's, Marcus Rhoades, attests to the flaws in McClintock's ability to communicate: "Barbara couldn't tolerate fools—she was so smart" (50). McClintock's impatience, however, was somewhat unfair to her colleagues. Few biologists knew enough maize genetics to follow McClintock's data and complex analyses (9). Also, most geneticists worked with simpler organisms than maize. Additionally, her "writing was dense" (9). All these obstacles led to an increased sense of frustration for McClintock. This frustration led McClintock into an increased state of isolation, to the point where "she stopped talking and, except for the annual reports in the CIW Yearbook, stopped publishing" (142).

Although much of her work was done in the 1930s, 40s, and 50s, McClintock's visionary discoveries still have applications in 21st century biomedical research. In fact, a study by Zhang et al continued where McClintock left off. They recognized that she discovered that Ac/Ds transposable elements can produce major chromosomal rearrangements, but they wished to look into the mechanism behind this transposition. The researchers are also used maize as a model, and they concluded that the transposition mechanism may have led to chromosome evolution (2009). In another study by Wilson et al, a specific transposon called the PiggyBac transposon is used in preclinical gene therapy research. The transposon is used to integrate transgenes into the host cells' genome. The PiggyBac transposon has proven useful in delivering large transposable elements and has been successful in the mouse germline. However, the PiggyBac transposon has not been investigated extensively in human germlines. PiggyBac is particularly useful because it acts as a nonviral transposon, which can be utilized in gene therapy studies (Wilson et al. 2007). The PiggyBac transposon has also been utilized to reprogram somatic cells to pluripotent stem cells. These induced pluripotent stem cells maintain properties exhibited by embryonic stem cells, such as the ability to differentiate (Woltjen 2009). Transposons have also been used to promote mutagenesis, which provides information about specific gene functions. Using this technique and the PiggyBac transposon, Balu et al were able to analyze the Plasmodium falciparum genome (2009). This technique is incredibly useful in decoding unknown genomes.

The story of Barbara McClintock teaches a number of lessons to today's biology students. It is not only important that students learn from her positive qualities, but also from her flaws. First and foremost, McClintock demonstrates what can be achieved by hard work. Students should also recognize the importance of trusting their own judgment before succumbing to the masses. McClintock embodied brilliance as well as impatience. This impatience often left her isolated and likely delayed recognition of her work. Finally, McClintock's story demonstrates that mutual collaboration can be extremely beneficial to the formation of ideas. It is important to recognize the value of a few close friends, who will listen to you even when they have no idea what you are talking about.