

Barbara McClintock and the Discovery of Jumping Genes (Transposons)

By: Leslie Pray, Ph.D. & Kira Zhaurova (*Nature Education*) © 2008 Nature Education

Citation: Pray, L. & Zhaurova, K. (2008) Barbara McClintock and the discovery of jumping genes (transposons). *Nature Education* 1(1):169



McClintock's maize breeding experiments provided the first detailed descriptions of transposable elements. What exactly are these "jumping genes," and why are they so important?

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Some of the most profound genetic discoveries have been made with the help of various model organisms that are favored by scientists for their widespread availability and ease of maintenance and proliferation. One such model is *Zea mays* (maize), particularly those plants that produce variably colored kernels. Because each kernel is an embryo produced from an individual fertilization, hundreds of offspring can be scored on a single ear, making maize an ideal organism for genetic analysis. Indeed, maize proved to be the perfect organism for the study of transposable elements (TEs), also known as "jumping genes," which were discovered during the middle part of the twentieth century by American scientist Barbara McClintock. McClintock's work was revolutionary in that it suggested that an organism's genome is not a stationary entity, but rather is subject to alteration and rearrangement—a concept that was met with criticism from the scientific community at the time. However, the role of transposons eventually became widely appreciated, and McClintock was awarded the Nobel Prize in 1983 in recognition of this and her many other contributions to the field of genetics.

McClintock and the Origins of Cytogenetics

Barbara McClintock began her scientific career at Cornell University, where she pioneered the study of cytogenetics—a new field in the 1930s—using maize as a model organism. Indeed, the marriage of cytology and genetics became official in 1931, when McClintock and graduate student Harriet Creighton provided the first experimental proof that genes were physically positioned on chromosomes by describing the crossing-over phenomenon and genetic recombination. Although Thomas Hunt Morgan was the first person to suggest the link between genetic traits and the exchange of genetic material by chromosomes, 20 years elapsed before his ideas were scientifically proven, largely due to limitations in cytological and experimental techniques (Coe & Kass, 2005). McClintock's own innovative cytogenetic techniques allowed her to confirm Morgan's ideas, and these techniques are numbered among her greatest contributions to science.

Discovering TEs Through Experimentation with Maize

As previously mentioned, McClintock is best known for her discovery of transposable elements through experimentation with maize. However, in order to understand McClintock's observations and the logic that led to her discovery of TEs, it's first necessary to be aware that the phenotypic system McClintock studied—the variegated color pattern of maize kernels—involves three alleles rather than the usual two.

To better grasp this idea, consider every maize kernel as a single individual, originating as an ovule that has undergone double fertilization (Figure 1). During double fertilization, one sperm fuses with the egg cell's nucleus, producing a diploid zygote that will develop into the next generation. Meanwhile, the other sperm fuses with the two polar nuclei to form a triploid endosperm, which forms an outer protein layer known as the aleurone layer. As a result, the colored (or colorless, as the case may be) tissue that makes up the aleurone layer of the kernel is triploid, not diploid.

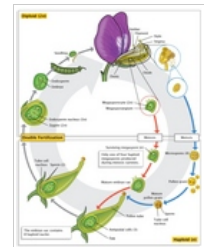


Figure 1

The Ac/Ds System of Transposable Elements

McClintock worked with what is known as the Ac/Ds system in maize, which she discovered by conducting standard genetic breeding experiments with an unusual phenotype. Through these experiments, McClintock recognized that breakage occurred at specific sites on maize chromosomes. Indeed, the first transposable element she discovered was a site of chromosome breakage, aptly named "dissociation" (Ds). Although McClintock eventually found that some TEs can "jump" autonomously, she initially noted that the movements of Ds are regulated by an autonomous element called "activator" (Ac), which can also promote its own transposition.

Of course, these discoveries were preceded by extensive breeding experimentation. It was known at the time from previous work by Rollins A. Emerson, another American maize geneticist and the "rediscoverer" of Mendel's laws of inheritance, that maize had genes encoding variegated, or multicolored, kernels; these kernels were described as colorless (although they were actually white or yellow), except for spots or streaks of purple or brown (Figure 2). Emerson had proposed that the variegated streaking was due to an "unstable mutation," or a mutation for the colorless phenotype that would sometimes revert back to its wild-type variant and result in an area of color. However, he couldn't explain why or how this occurred. As McClintock discovered, the unstable mutation Emerson puzzled over was actually a four-gene system, as outlined in Table 1.

Table 1: Maize Genes Studied by Barbara McClintock



Figure 2: Variation in kernel phenotypes is used to study transposon behavior.

Kernels on a maize ear show unstable phenotypes due to the interplay between a transposable element (TE) and a pigment gene.

Gene	Description
C'	Dominant allele on the short arm of chromosome 9 that prevents color from being expressed in the aleurone layer of the maize kernel, causing a so-called "colorless" phenotype (which is actually white or yellow in color). This is also known as the inhibitor allele.
C	Recessive allele on the short arm of chromosome 9 that leads to color development.
Bz	Dominant allele on the short arm of chromosome 9 that leads to a purple phenotype.
bz	Recessive allele on the short arm of chromosome 9 that leads to a dark brown phenotype.
Ds	Genetic location on the short arm of chromosome 9 at which chromosomal breakage occurs.
As	A factor of unknown location (at least when McClintock was conducting her research) that impacts the expression of Ds.

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Adapted from [McClean, 1997](#)

In her experiments, McClintock bred females that were [homozygous](#) for *C* and *bz* and that lacked *Ds* (denoted *CCbzbz--*, where the dashes indicate the absence of *Ds* alleles) with males that were homozygous for *C'*, *Bz*, and *Ds* (denoted *C'C'BzBzDsDs*) to yield [heterozygotes](#) with an aleurone layer that had the [genotype](#) *C'CCBzbzbz--Ds*. (Remember, in double fertilization, the sperm provides one set of alleles, and the egg provides two.) Because of the presence of the dominant inhibitor allele *C'*, the offspring kernels were expected to be colorless, no matter what their genetic makeup at the *Bz/bz* locus. In fact, upon crossbreeding, many of these kernels were indeed colorless. However, McClintock also observed many kernels with colorless backgrounds and varying amounts of dark brown spots or streaks, and she concluded that individual cells in those kernels had lost their *C'* and *Bz* alleles because of a chromosomal break at the *Ds* locus. Without either the *C'* allele (to prevent color expression) or the *Bz* (purple) allele, the cells that had experienced a breakage at the *Ds* locus ended up with some brown coloring.

Within the affected seeds, the amount of colored streaking or spotting depended upon when during seed development the [somatic cell](#) mutation at *Ds* occurred. If this mutation occurred early in development, then, as the one [mutant](#) cell continued to divide, more cells in the mature kernel would have the brownish phenotype, and the spot or streak of color on the kernel would be larger. On the other hand, if the mutation occurred later in [development](#), the spotting would be smaller, because the kernel would undergo less [cell division](#) prior to maturity.

Expression of Ds in Maize

McClintock also performed additional experiments to demonstrate that the phenotypic effect of *Ds* depended upon the presence of another element, which she called *Ac*. McClintock had trouble [mapping](#) both the *Ac* and *Ds* elements, however, noting that they changed their positions on the chromosome in different maize plants. In fact, further experiments showed that *Ds* didn't just break chromosomes, but it could actually move from one chromosomal location to another. When *Ds* inserts itself into the *Bz* allele, for example, it causes a mutation in the *Bz* gene (but only when *Ac* is present), thereby destroying the ability of the *Bz* gene to produce any pigment at all. *Ds* can also excise from the *Bz* allele (again, only in the presence of *Ac*), causing *Bz* to revert back to its purple or brown phenotype. Again, the amount of purple or brown depends upon when during development *Ds* is inserted or excised. If excision happens prior to fertilization, then the affected kernel will be entirely purple or brown, depending upon the *Bz/bz* genotype.

Years after McClintock discovered the *Ac/Ds* system, scientists were finally able to study both TEs in much more molecular detail. Today, we know that *Ac* elements are about 4,500 base pairs long and are similar in structure to other [DNA transposons](#).

McClintock and the Theory of Epigenetics

Beyond her discovery of TEs and her revolutionary cytogenetic research techniques, Barbara McClintock was also the first scientist to correctly speculate on the basic concept of epigenetics-or [heritable changes in gene expression that are not caused by changes to DNA](#) sequences. Mainly, she recognized that genes can be expressed and silenced during [mitosis](#) in genetically identical cells. McClintock proposed this theory before [the molecular structure of DNA](#) and more than 40 years before the concept of epigenetics was formally studied, thereby further cementing her reputation as an innovator in her field.

Summary

Barbara McClintock's discovery of transposable elements in *Zea mays* changed the way scientists think about genetic patterns of inheritance. Although not widely accepted at the time of its discovery, McClintock's observation of the behavior of kernel color alleles was revolutionary in its proposition that genomic [replication](#) does not always follow a consistent pattern. Indeed, as a result of both autonomous and activator-controlled transposition at different stages of seed development, the genes of maize kernels are capable of producing a variety of coloration patterns. Over time, McClintock's work with TEs became widely accepted, and McClintock eventually earned a Nobel Prize for her discoveries in this area. Today, McClintock is also recognized for her groundbreaking cytogenetic techniques, as well as her early speculations on the concept of epigenetics. Thanks to these and other valuable contributions to the field, Barbara McClintock is rightly viewed as one of the pioneering figures in modern genetics.

References and Recommended Reading

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