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THE UNSUNG HERO OF SCIENCE: BARBARA MCCLINTOCK, WHO WON THE NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE IN 1983 FOR HER DISCOVERY OF MOBILE GENETIC ELEMENTS

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"They thought I was crazy, absolutely mad.
If you know you are on the right track, if you have this inner
knowledge, then nobody can turn you off, no matter what they say".
Barbara McClintock

"Back in the early 1940s, McClintock poked a stick into a sleeping genome's lair.
The chromosome breaks, jumping genes and reversible mutations, we now call
epigenetics, jumped out long before the world was ready to see them".
Nina Fedoroff

In 1983, American plant biologist and cytogeneticist McClintock, one of the great loners of modern science, received the first woman scientist's unshared Nobel Prize in Physiology or Medicine. Barbara McClintock's research, conducted in the 1930s, long before the structure of DNA was deciphered, included creating the first genetic map of ten chromosomes composing the haploid set of maize microspores and cytological determination of gene location within individual chromosomes. Two phenomena with which Barbara McClintock's name will forever be associated are crossing over and transposons. Her finding that chromosomes might exchange physical parts as part of gene exchange confirmed Morgan's theory of inheritance. Experiments in 1940-1950s with the phenotypes of hybrid maize kernels led her to the concept that genetic elements, which she referred to as Dissociation and Activator controling elements, could transpose and regulate the genes by inhibiting or modulating their action. Her revolutionary findings were ahead of their time, in conflict with the established concept of a stable genome and met with scepticism and opposition. Much later, the scientific world accepted her ideas on mobile genetic elements, and it was recognition she appreciated but never sought. McClintock considered the genome as a highly sensitive organ that responds to unexpected events, often by genome restructuring, which scientists today are trying to understand. In this review, the scientific path and achievements of Barbara McClintock are analyzed.

K e y w o r d s: Barbara McClintock, maize genetic map, crossing over, Ac/Ds controlling elements, transposons, Nobel Prize.

In the early 1900s, genetics was based on the laws of inheritance discovered by Gregor Mendel. During the first decade of the 20th century, the famous fly geneticist Thomas Morgan broke new ground in genetics. He proposed the chromosomal theory of inheritance and was the first to suggest a connection between genetic traits and the exchange of genetic material. But scientists had lacked the experimental techniques to prove it.

It was Barbara McClintock's research, conducted in the 1930s and 1940s, long before the structure of DNA was deciphered, that became a real breakthrough in the study of the chromosomal DNA behavior. She made discoveries that were so far beyond the understanding of the time and were ignored for more than a decade. But she persisted, trusting herself and was awarded by the Nobel Prize in 1983. What's amazing is that for these revolutionary genetic discoveries Barbara needed only an adequate object of study (hybrid corn), improved method of staining cellular DNA, a light microscope, and unwavering faith in what she saw through the lens.

Barbara McClintock was born Eleanor McClintock on 1902 in Connecticut, USA as the third of four children born to Thomas McClintock, a homeopathic physician and Sara McClintock, a piano teacher. McClintock was active, but solitary, self-contained child, a feature she later defined as her "ability to be alone". She showed early the independence of mind and action, so her parents determined that Eleanor, a "feminine" and "delicate" name, was not appropriate for her, and chose Barbara instead [1, 2].

During her high school years it became obvious that Barbara would not outgrow her childhood eccentricities and become an ordinary young woman. Barbara discovered science and set a goal to attend Cornell University to study biology. But the family had little money to support Barbara and beside she had problems in relationship with her mother, who preferred that her daughter marry rather than attend college because it could harm her chances of getting married, which was a common belief at the time [3].

McClintock in her laboratory, 1947 [1]

Barbara McClintock in cornfield, postcard. APS library [4]

Fortunately, McClintock's father returned from the Army Medical Corps in France in time to intervene. He respected his daughter's wish and allowed her to attend just before registration began, so Barbara enrolled at College of Agriculture at Cornell University in 1919.

Barbara was awarded Cornell's "Graduate Scholarship in Botany", which provided support during the years of graduate studies, which went very successfully. Her B.S., MS and finally PhD degrees were devoted to plant breeding and botany [1]. During this time, she did not study corn plant, to which she would later devote her life's research.

At that time, genetics was still new trend not widely accepted as a scientific discipline because of the ideas that seemed too revolutionary. In the 1921 Cornell University offered only one introductory course in genetics taught by plant geneticist C. Hutchison. This course was opened only to graduate students, but Hutchison recognised Barbara's dedication for basic science and telephoned to invite her to participate. She took to it immediately. As she pointed later Hutchison's invitation served as a catalyst for her interest in genetics: "Obviously, this telephone call decided the fate of my future. I remained with genetics thereafter" [5].

In a different class Barbara learnt cytology taught by L. Sharp, whose main interest was the structure of chromosomes. Fascinated by the topic, she decided to combine genetics and cytology. In 1924 Barbara, a young graduate student in botany, joined an elite cytogenetics research group at Cornell's Plant Breeding Department [6]. She was appointed as paid research assistant to the cytologist L. Randolph, who had a position at Cornell sup-

ported by the U.S. Department of Agriculture to strengthen the maize plant breeding efforts.

In the summer of 1925, McClintock discovered a corn plant in the corn field at Cornell University that had three complete sets of chromosomes (a triploid).

This plant had been recognised by a keen eye because it had a thicker stock, broader leaves, larger anthers and microsporocytes. Applying Belling's technique of chromosomes staining with acetocarmine dye, which combines with nucleic acid to form a deep red conjugate, McClintock and Randolph studied the meiotic behavior of the chromosomes in the pollen of this unique plant and confirmed that it contained thirty chromosomes in each cell arranged in ten groups of three chrormosomes each during meiosis. The following 1926 they published their results and this jointly authored paper became the only evidence of their collaborative research [7]. Barbara was upset that her name appeared second on their article when she believed she had done most of the work.

McClintock was quick, imaginative, and perceptive while Randolph was more methodical and less gifted. The preparation of an idiogram of the maize chromosomes had been a primary concern to Randolph. But in the thin paraffine sections made from the maize root tip used by Randolph the chromosomes could not be reliably distinguished and existing techniques for chromosome staining were inadequate. McClintock solved both problems.

Firstly for her studies McClintock chose maize chromosomes during the first mitotic division of the microspore. In these germ cells only the haploid complement of chromosomes is present and it is easier to see them than in the root tip cells with a diploid complement. Barbara discovered that the condensed chromosomes during late mitotic prophase are longer and the relative length of their arms is more readily determined.

Secondly McClintock improved Belling's technique of chromosome staining without cells fixation by introducing the heating step in the acetocarmine staining protocol to increase the contrast between the chromosomes and the cytoplasm and to cause the microsporocytes to stick to the slide With this approach she was able to identify each visible chromosome through a light microscope [8]. This is how she shared her impressions: "I was so absorbed in looking at chromosomes. They were so beautiful. I simply couldn't tear myself away from them" [9].

This is how R. Wayne, an associate professor of plant biology at Cornell University assessed Barbara's methodical approachs: "Even today over 80 years after Barbara McClintock visualized individual chromosomes of maize it is still thrilling for my plant cell biology students to see the physical basis of heredity, the individual chromosomes in red against a relatively clear cytoplasm. They put unopened anthers of plants in a drop of acetocarmine on a slide, tease the anthers apart with iron needles, perhaps even ones that belonged to Barbara McC, to free the microspores, then gently heat the slide with an alcohol lamp. They press on the cover glass to flatten the cells and view the preparation with a bright field microscope. Unbelievable, it never fails, they literally see the invisible and the chromosomal theory of inheritance becomes materialized. They also get to see chromosomes in slides that had been prepared by McC herself" [10].

On the basis of chromosome total length, arm ratios and position of heterochromatic regions Barbara McClintock identified ten chromosomes composing the haploid set of maize microspore cell [11]. The longest was designated as chromosome 1 and the shortest as chromosome 10. She presented results in what she designated a "semi diagrammatic representation" of the chromosome set of Zea mays published in Science in 1929 (Fig. 1).

This article was only one page long, but its impact was monumental – in fact McClinock produced the first genetic map for maize before the structure of DNA had been identified or the notion of the genome discovered!

When Barbara finished her Ph.D. in 1927, she knew exactly what needed to be done next: the maize genetic linkage groups (genes that are inherited together because of their proximity on the same

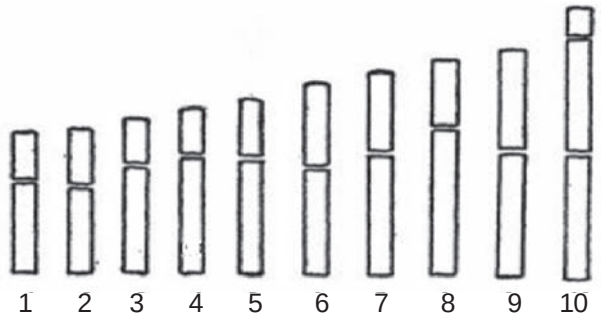

Fig. 1. Semi-diagrammatic representation of the 10 chromosomes in haploid set of Zea mays, as drawn by Barbara McClintock [11]

chromosome) had to be assigned to certain chromosomes.

For this purpose McC developed an original cytological and genetic analysis of hybrid corn. She crossed the triploid corn plant with normal diploid plant and got offsprings with one additional chromosome (2n + 1), known as primary trisomics. Primary trisomics for each of the ten maize chromosomes have been isolated.

McClintock observed that specific group of linked genes in the haploid microspores of a primary trisomic is inherited according not to Mendelian, but to trisomic inheritance ratio. The extra chromosome has been associated with a certain linkage group. It was now relatively simple for McClintock, using a technique of observing genetic ratios, to determine from cytological examination of the eleven-chromosome microspores, which chromosome of the haploid set is in duplicate and carries this group of genes. McClintock cooperated with and guided graduate students to determine the location of many genes grouped together on six of the ten chromosomes in corn. Thus, it was shown that *R-G* linkage group that coded for red endosperm layer (aleurone) color resided on the shortest chromosome10 [12], and chromosome 9 carries the genes for colored aleurone (*c*), shrunken endosperm (*sh*) and waxy endosperm (*wx*) and that the order of these genes is *c–sh–*running from the end of the short arm toward the middle of the long arm [13].

It was primarily due to McClintock that the quick progress in maize cytogenetics was achieved and in the early 1930s all ten linkage groups had been assigned to identifiable chromosomes.

Progress in McClintock's research continued. Studing the maize pollen grains during meiotic cell division she observed places where chromosomes were broken. These areas of damage McClintock linked to two phenomena with which her name will forever be associated – *crossing over* and *transposons*.

McClintock demonstrated that fragments of one chromosome can be attached to another chromosome in the process of interchange named as crossing over. She proved this phenomenon using the example of segmental interchange between chromosomes 9 and 8. Fortunately in certain strains of maize, chromosome 9 could be distinguished readily because its short arm possesses a very stainable terminal knob which passed on from one cell generation to another. McClintock was the first to describe and to use knobs as specific cytological.

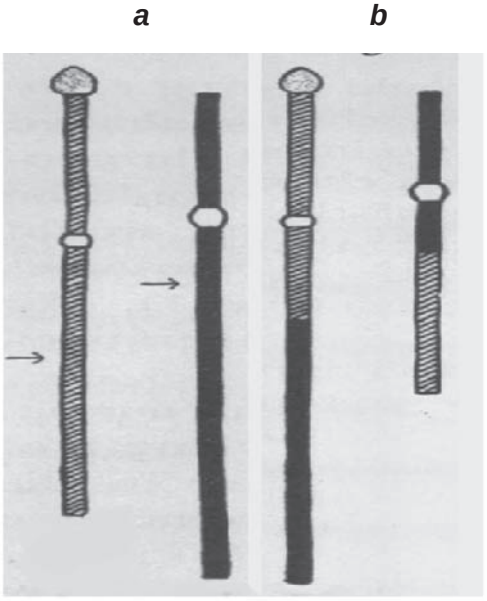

Fig. 2. Schematic drawing of the crossing-over between two chromosomes of Zea mays. ***a*** *– Diagram of the two normal chromosomes. The arrows indicate the places at which the interchange occurred.* ***b*** *– The two chromosomes produced as the result of the segmental interchange [15]*

To clarify what is termed "*crossing-over*" Barbara used a schematized representation of the interchange of chromosome parts (Fig. 2). A heterozygous plant was used with one chromosome knobbed and its homologue knobless. A morphological analysis of the knobbed chromosome 9 in progeny showed the length of the longer arm to be much greater, whereas the long arm of the knobless chromosome 8 was correspondingly shortened. This marked difference indicated that chromosomes actually physically exchanged their regions [14].

But until this the fundamental question remained unclear – does chromosomes crossing over seen under a microscope correlates with the exchange of genetic information, i.e. with genetic crossing over?

Barbara McClintock and her gradient student Harriet B. Creighton were first to prove reliable correlation between the two exchange processes. By an elegantly simple experiment in 1931 they showed that exchange of cytological, i.e., physical, parts of chromosomes during meiosis was accompanied by exchange between genes. They examined cytological crossing over between knobbed chromosome 9 with the knob–*c–sh–wx* order of genes previously defined by mapping, and interchanged chromosome

8. The most important was the result that followed: crossing over between the section below the knob on chromosome 9 and the attached piece of chromosome 8 was accompanied by genetic crossing over between loci *c* and *wx*. The new combination was visibly revealed as the appearance of certain new traits in the progeny – either colorless (*c*) or colored (*C*), either waxy (*wx*) or starchy (*Wx*) kernels [15].

The study done by Creighton and McClintock has been acclaimed as one of the great experiments in biology and was highly appreciated by Thomas Morgan who encouraged them to publish immediately [16]. The results of this 1931 paper gave further confirmation to Morgan's theory that chromosomes might exchange physical parts as part of genes exchange.

It may seem surprising that so many years passed between the Morgan's suggestion and the tests of his suggestion. The answer lies in the biological technology which had to be improved significantly. It was MacClintock who refined microscopic study for viewing individual haploid and paired maize chromosomes and for the first time used chromosom's knob as specific cytological marker.

During these productive years (1928-1931) McClintock remained at the position of instructor because guidelines of the Cornell University recommended promotion to associate or full professor only after 10-year probationary period.

McClintock's scientific contributions were both rewarded and recognized. She was sponsored by a National Research Council Fellowships to travel to research institutions across the U.S. and a prestigious Guggenheim Fellowship (resulting from excellent work and reputation) in 1933 to study in Germany for year. Her staying in Cermany lasted only for a few months due to the rise of the Nazi Party. Barbara returned to Cornell, her alma mater, and with some support from the Rockefeller Foundation managed to stay for almost three years as a research assistant at the Department of Plant Breeding. Although McClintock's fame was growing, she found that the university would not hire a female professor, the prospect of getting a professorship at Cornell was uncertain and she worried about finding a permanent job [17].

In 1936 a famous geneticist Lewis Stadler, the head of the genetics research group at the University of Missouri, Columbia and the expert in using X-irradiation to induce mutations in plants received the funds to establish a Ragional Laboratory of Plant Genetics. He identified McClintock as the best cytologist in the world for the appointment and offered her an Assistant Professorship in the Department of Botany at the University of Missouri. During her time at Missouri, McClintock expanded her research on the effect of X-rays on maize cytogenetics. She observed repeated cycles of chromosomes breakage and fusion and studied the behavior of broken chromosomes. This material later allowed McClintock to study the induction of chromosome transposable elements.

Though McClintock's reputation continued to grow and she was elected vice-president of the Genetics Society in 1939, her position at Missouri remained minor. Her independent and "unconventional" behavior did not correspond to the university's idea of a "female" scientist. She was also seen as "difficult" by many of her colleagues, in particular because of her quick mind and intolerance of second-rate work. She found herself excluded from regular academic activities, including faculty meetings. In 1940 Stadler decided to leave the University and the university administration was planning to eliminate his research group. McClintock considered herself betrayed. Besides she felt that a restrictive university atmosphere, teaching responsibilities, graduate student advising, deadlines for publications distructed her from her research work. She always wanted to be

Barbara McClintock in the lab at Cold Spring Harbor, April 1963 Photo: National Institutes of Health. Courtesy of the Barbara McClintock Papers, American Philosophical Society [20]

free to do exactly what she wanted to do. The value she placed on her freedom was one of the reasons she decided in 1941 to leave the University of Missouri and to seek employment elsewhere [18, 19].

Milislav Demerec, the Director of the Department of Genetics of the Carnegie Institution of Washington at Cold Spring Harbor, who knew and respected McClintock as a scientist, immediately offered her a permanent full-time investigator position with no interference and complete freedom to pursue research. In 1942 McClintock accepted the appointment.

The move to Cold Spring was a turning point in her career. Here McClintock's fate and the attitude towards her as a woman scientist began to improve. In 1944, at the young age of 42 she was elected to the National Academy of Sciences – only the third woman to be so elected. The following year she became the first female president of the Genetics Society of America. Freed to focus exclusively on her experiments, McClintock stayed at Cold Spring Harbor until her retirement in 1967 as a honorary scientist.

It was in Cold Spring Harbor that Barbara began her most important work and made her most significant discovery: mobile genetic elements known as *transposones.* Similar to her past studies, McClintock focused her attention on unique phenotypes, particularly on kernels colour. Maize kernels were very well suited to study the inheritance of the colour, because each kernel in a cob represents a new individual organism with its own combination of genes. Corn crops that contain hundreds of kernels allow Barbara to study a large number of individuals and perform statistical calculations in a short period of time [20].

Kernel color was previously described through simple Mendelian inheritance where purple is dominant over yellow, but McC drew attention to multicolored kernels that were described as colorless, but contained spots of purple or brown and this coloration disruption could later reverse in subsequent generations. The mechanisms of the mosaic color patterns of maize seed and the unstable inheritance of this mosaicism remained unclear.

Barbara linked the phenomenon of coloration disruption to mutations of certain genes that occur when chromosomes break. Among the progeny of plants that had received a broken chromosome she observed unstable mutations at an unexpectedly high frequency. What caught McClintock's eye was that it was always chromosome 9 that broke and it always broke at the same place with a regular loss of all markers distal to the *Wx*. Subsequent experiments indicated that in right to the *Wx* locus on chromosome 9 a particular site of breakage was located, which she called *dissociating locus*, or *Ds*. What exactly was *Ds* locus, and how these breakages were controlled? It was also apparent that for breakage to occur at the *Ds* locus a second locus was necessary, which she designated as *activator*, or *Ac* [21].

McClintock found that *Ds* locus functions as a controlling element that affected the behaviour of neighbouring genes. The clues that led McClintock from the chromosome breakage to transposition are illustrated in Fig. 3. Here are kernels having the genetic constitution *C Ds*/*c*, where *C* is the dominant allele required for synthesis of the purple pigment in the kernel surface and *c* is the recessive allele (colorless surface).

The kernel in Fig. 3,(A) is colorless, there is no *Ac* element present, and *Ds* inhibits the synthesis of colored pigment. Kernels in Fig. 3,(B) carry an *Ac* and against a purple background have colorless spots expressing the recessive *c* allele. The C → c variegation in these spots results from chromosome breakage at *Ds* just proximal to the *C* gene with subsequent loss of the dominant *C* allele and exposure of the recessive *c* allele.

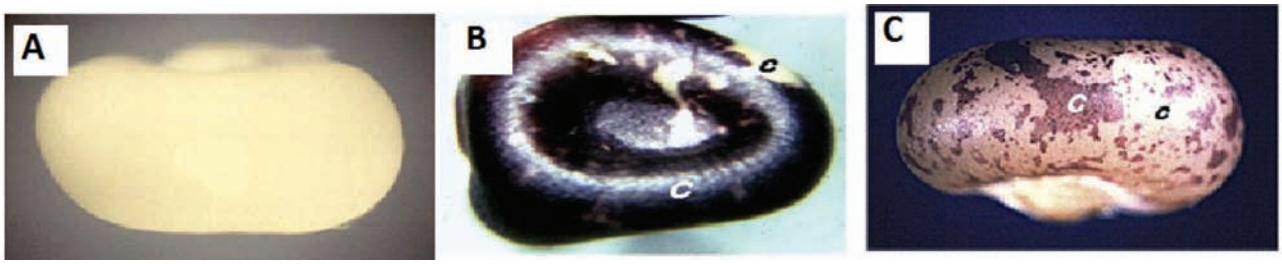

Fig. 3. Phenotypes of kernels that led McClintock from the chromosome breakage at dissociating locus to transposition. From [22]

McC noticed that the coloration disruption could later reverse in subsequent generations of plants which give kernels with a colorless *c* background with sectors of purple colored *C* spots, as illustrated in Fig. 1,(C). While studing this appearance an unexpected event was detected when *C* locus was not cut off, but rather changed its behaviour. It was this observation that marked the discovery of transposition.

It turned out that kernel colorless background was related to the fact that the location of *Ds* activity had moved: it was no longer to the right of *Wx*, as would be expected, but transposed to the *C* locus and inserted into the *C* gene itself, inactivating it and inducing expression of the colorless *c* allele. Barbara revealed that in a few kernels reversion of *c* to *C* took place early enough in development to have affected the gametes so that the revertant allele was passed on to the progeny. In this case the c → *C* variegation in a coloured spots (Fig. 1, C) was caused by transposition of *Ds* out of the gene. Now *C* locus functioned normally, *Ds* had gone!

Thus McClintock was the first to reveal the unprecedented property of *Ds* to transpose first into and then out of the *C* gene, first inactivating and then reactivating it. She reasoned that rather than a large, visible rearrangement, a submicroscopic chromatin segment carrying *Ds* was cut out and reinserted to the new position on the chromosome. Over time, she would come to realize that it was a DNA segment insertion into the area of genes that were involved in controlling kernel coloration. Scientists define these transposable genetic bits "*transposons*" in popular culture, they've been called "*jumping genes*"[23].

Between 1948 and 1950, McClintock developed a theory by which transposable elements regulated the genes by inhibiting or modulating their action. She referred to Dissociation and Activator as "controlling elements" to distinguish them from genes [24].

In fact, the results of Barbara's research were the forerunners of the discoveries that were awarded two Nobel Prizes in the mid-20th century. McClintock's discovery of transposition occurred at about the same time as Watson and Crick's studied the structure of DNA. Watson and Crick's epochal contribution, published in 1953 immediately clarified the mechanisms of gene inheritance and was recognized with the Nobel Prize within a decade in 1962 [25]. McClintock descriptions of the *Ac-Ds* transposable controlling elements family were the first example of an interaction between a regulatory factor and its DNA binding site These results were published in PNAS [24] well before Jacob and Monod's foundational work on the regulation of the *lac* operon in *E. coli* with which she later drew parallels [26] and for which they awarded the Nobel Prize in 1965 [27].

The 1950 PNAS article [24] was one of the several efforts Barbara made to communicate her findings on transposition in the wider scientific literature. She received only few reprint requests for her article and concluded that there was little interest in her work. Barbara reported in person her data on gene transposition in 1951 at the influential Cold Spring Harbor Symposium on Quantitative Biology [28]. At its conclusion the geneticist Evelyn Witkin recalls, that "there was baffled silence after her talk and little or no discussion of her densely documented evidence and argument for transposable elements and their effects on gene expression. Here, her conclusions were too radically in conflict with the established genetic concept of a stable genome, and her data too complex, to allow for rapid or easy acceptance, although a small number of geneticists who had come to know her work well believed it to be profoundly important" [29].

Indeed, when shortly after the 1951 Cold Spring Harbor Symposium, Alfred Sturtevant, one of the century's leading expert in mapping the genes on a chromosome, was asked about what McClintock had said, he answered: "I didn't understand one word she said, but if she says it is so, it must be so!" Such was the intellectual respect for McClintock and such was the strangeness of concept and complexity of her experimentation [30].

By her own admission, McClintock had neither a gift for written exposition nor a talent for explaining complex phenomena in simple terms. She filled her long talks with terminology that she invented to describe what she saw and evoid the use of illustrations to help the audience along. But there are more important factors: McClintock's work was ahead of its time, the concept that genetic elements can move would undoubtedly have met with resistance regardless of author and presentation. Barbara was upset about other people's lack of understanding and acceptance of an idea that was so clear and reasonable to her [30].

In fact, because opposition to her revolutionary findings and icy reception to her transposon reports she stopped publishing her results in professional journals and ceased giving lectures since 1953. She

only shared her research with a small circle of loyal colleagues. publishing little more than summaries of her results in the annual Yearbooks of her employer, the Carnegie Institution of Washington at Cold Spring Harbor and occasional overviews for symposia [31].

Though McClintock continued doing research. She officially retired from her position in 1967, and was made a Distinguished Service Member of the Carnegie Institution. This honor allowed her to continue working with graduate students and colleagues in the Cold Spring Harbor Laboratory. She was dedicated to her work, and was happiest in the cornfield or in her laboratory. "I was just so interested in what I was doing I could hardly wait to get up in the morning and get at it" – she said [32].

Not until the late 1960s and early 1980s, after biologists had determined that the genetic material was DNA, the manner in which information was encoded in the genes had been deciphered and methods had been devised to study, isolate and. reintroduced individual genes into living organisms, did members of the scientific community begin to verify early MacClintock's findings and her concept of mobile genetic elements. Transposable elements (TE) were seen in many organisms-bacteriophages, prokaryotic (*E. coli*) and eukaryotic organisms (yeast, Drosophila, humans, etc.). Genome sequencing projects have shown that TEs make up ~50%, while coding DNA only ~2% of the primate genomes [33].

During this period scientists were able to show the molecular basis for transposition. In the 1970s *Ac* and *Ds* controlling elements were cloned and *Ac* was shown to encode transposase, which is required for the element to move within the genome. This enzyme is able to cleave both the ends of the transposon and target sites where the element is to be inserted. *Ds* has a mutation in its transposase gene, which means that it cannot move without another source of transposase. Thus, as McClintock observed, *Ds* cannot move in the absence of *Ac* [30, 34].

Since McClintock's discovery two general categories of Transposible elements have been identified based on their manner of mobilization – DNA transposons and retrotransposons. DNA transposons move using a cut-and-paste mechanism, while retrotransposons move in a copy-and-paste fashion, when the transposable DNA is copied into RNA which is convertied back into DNA through reverse transcriptase to be inserted into the genome. Retrotransposons amplify themselves faster than DNA transposons to become abundant in eukaryotic genomes [35].

Subsequent research has shown that transposons can insert themselves into genes, causing mutations. Transposons can land near genes and influence their expression levels, acting as regulatory elements. In humans, transposon insertions can disrupt genes involved in development or disease pathways. Because transposon movement can be destructive most transposon sequences in the human genome are silent and kept inactive by epigenetic defense mechanisms such as DNA methylation, chromatin remodeling, and miRNAs [36].

McCintock's radical idea on transposon movement has since formed the basis of modern genetic engineering. Now transposons can be used as tools to introduce foreign DNA into cells and organisms, enabling genetic studies and the development of new therapies.

Neverthelesss, McClintock viewed her primary contribution to science not so much as the discovery of mobile elements, but as elucidation of genetic control systems. In the 1960s and 1970s, she developed a vision, unique in its time, of the genome as dynamic system highly responsive to external stimuli [37].

She drew attention to the fact that transposons typically do not move unless the cell is placed under stress, such as by irradiation or the breakage-fusion-bridge cycle, and thus their activation during stress can serve as a source of genetic variation for evolution [38].

In 1983, Barbara McClintock, at the age of 81 received the Nobel Prize which she so richly deserved and which she appreciated but never sought. It was the first woman scientist's unshared prize in Physiology and Medicine. McClintock learned of her success over the radio, she did not own a telephone.

But during the ceremony McClintock delivered a Nobel lecture titled "The Significance of Responses of the Genome to Challenge" and mobility was not her keyword [39]. She raised important questions about how cells control their genomes, stating: "I am very much interested in the nature of changes that occur in the genome, when the genome meets something very unexpected." The genes do not change – only the pattern of their activity changes. She understood that both internal and external forces could shape that pattern and appreciated the genom's

significance as a highly sensitive organ of the cell, correcting common errors, sensing the unexpected events, and responding to them, often by restructuring the genome which scientists today are trying to understand.

McClintock spent her years post Nobel Prize as a key leader and researcher in the field at Cold Spring Harbor Laboratory on Long Island, New York. She never married or had children. McClintock died of natural causes in Huntington, New York, on September 2, 1992, at the age of 90.

НЕОСПІВАНА ГЕРОЇНЯ НАУКИ: БАРБАРА МАККЛІНТОК, ЯКА В 1983 РОЦІ ОТРИМАЛА НОБЕЛІВСЬКУ ПРЕМІЮ З ФІЗІОЛОГІЇ ТА МЕДИЦИНИ ЗА ВІДКРИТТЯ МОБІЛЬНИХ ГЕНЕТИЧНИХ ЕЛЕМЕНТІВ

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У 1983 році американська ботанік і цитогенетик Барбара МакКлінток, одна з найбільш самобутніх постатей сучасної науки, стала першою жінкою-науковицею, яка отримала Нобелівську премію з фізіології та медицини одноосібно. Її дослідження, виконані ще у 1930-х роках, задовго до розшифрування структури ДНК, включали створення першої генетичної карти десяти хромосом, що складають гаплоїдний набір мікроспор кукурудзи, а також цитологічне визначення розташування генів в окремих хромосомах. Два явища, з якими назавжди пов'язане ім'я Барбари МакКлінток – це кросинговер і транспозони. Її відкриття про те, що хромосоми можуть обмінюватися ділянками під час обміну генами, підтвердило теорію спадковості Моргана. Досліди 1940–1950-х років із фенотипами гібридних зерен кукурудзи привели її до концепції, що генетичні елементи, які вона назвала «Дисоціація» і «Активатор» можуть переміщувати та регулювати роботу генів, інгібуючи або модулюючи їхню дію. Її революційні відкриття випереджали свій час, суперечили усталеній концепції стабільного геному та зустріли скептицизм і протидію. Лише значно пізніше наукова спільнота прийняла її ідеї щодо мобільних генетичних елементів, і це було визнанням, яке вона цінувала, але ніколи не прагнула здобути. МакКлінток вважала геном високочутливим органом, який реагує на несподівані події, часто шляхом реструктуризації геному, що вчені досі намагаються зрозуміти. У цьому огляді проаналізовано науковий шлях і здобутки Барбари МакКлінток.

Ключові слова: Барбара МакКлінток, генетична карта кукурудзи, кросинговер, елементи Ac/Ds, транспозони, Нобелівська премія.

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