Rhoades '82

BARBARA McCLINTOCK: STATEMENT OF ACHIEVEMENTS

Resume. Barbara McClintock's major achievements can be summarized as follows: She was the first to show in a eucaryotic organism (and before similar work in procaryotic organisms) that:

1. Controlling elements are organized as two element systems involving a distant controller and a responding element adjacent to or in the affected structural gene.
2. Not only do the controlling elements regulate the expression of a structural gene but they are also capable of specifically inducing mutation in that structural gene.
3. The system of controlling elements acts in a spatially and temporally specific manner in the modulation of gene activity and the induction of mutations.
4. Sensitive genes can be pre-set by a controlling element leading to a change in function at a predetermined time in a later generation.
5. Controlling elements undergo changes in "state" which are revealed by modified regulatory and developmental properties.

Background. When Barbara McClintock began her graduate work at Cornell in the middle 1920's the foundations of maize genetics had been firmly laid but comparatively little cytological work had been done. The carmine smear technique, which greatly facilitated cytological studies, had just been developed by Belling. McClintock quickly found that carmine smears of maize sporocytes at midprophase of meiosis yielded preparations of extraordinary beauty and clarity. Maize could now be used for detailed cytogenetic analyses of a kind heretofore impossible with any organism and McClintock in the succeeding years published a series of remarkable papers which clearly established her as the foremost investigator in cytogenetics. Her first major contribution was the demonstration that the chromosomes were individually recognizable by their relative lengths and arm ratios, distinctive chromomere patterns, and deep-staining knobs in characteristic positions. This was followed by such significant studies as the analysis of translocation heterozygotes, the correlation of cytological and genetical crossing over, the assignment of linkage groups to specific chromosomes, the physical location of gene loci by deficiencies, the formation of dicentric bridges and acentric fragments as a result of crossing over in inversion heterozygotes, the somatic and meiotic behavior of unstable ring chromosomes, the occurrence of nonhomologous pairing, the structure and function of the nucleolar organizing region, the production of viable homozygous deficiencies that simulated gene mutation and formed a pseudoallelic series, and the genetic and cytological consequences of the breakage-fusion-bridge cycle. Her recent studies on the evolutionary history of races of maize as disclosed by the number and location of specific chromosome knobs have been conducted with typical precision and elegance.

Her consummate skill and versatility as a cytologist are perhaps best evidenced by the fact that in the few weeks she devoted to Neurospora there resulted what remains more than thirty years later as the definitive paper on the meiotic chromosomes of this fungus. So difficult cytologically is Neurospora that not even the correct chromosome number was known prior to her studies but McClintock showed that each of the seven chromosomes was cytologically distinguishable at meiotic prophase and she was able to demonstrate induced structural changes in the chromosomes.

Major Contribution

McClintock's outstanding contribution is her analysis of the control of gene action in maize and the discovery of the two-unit interacting system. This concept was the precursor of the regulator-operon theory of gene regulation that won for its promulgators, Jacob and Monod, the Nobel Prize in 1965. Her finding that the transposition of controlling elements from one chromosomal location to another was accompanied by a change in gene action afforded a new and revolutionary insight into chromosome structure and genic expression. It was during her studies of the breakage-fusion-bridge cycle that she detected an unexpected burst of unstable genes in her stocks. Genic instability had been observed repeatedly by others and it had been established that it was under genetic control but she discovered a new kind of genic element, regulatory or controlling, which had profound implications for our understanding of gene function and regulation in development. Her finding that controlling elements can move from place to place in the genome, that they can modify expression of a gene by insertion in or near that gene, and that gene expression can be restored when the controlling element is excised afforded a new and revoluitionary insight into chromosome structure and gene expression. She pioneered a new era in genetic research. So unusual and novel were her findings that for a decade her conclusions were not accepted by many workers and it was not until comparable mobile genetic elements or transposons were found in a wide range of diverse organisms that the significance of her work was appreciated. She was ahead of her time and only in recent years has she been given credit for having opened up a new field of genetic enquiry which has had a profound impact on genetic theory.

Some major conclusions about controlling elements reached by McClintock are as follows:

1. Controlling elements are organized as two element systems involving a distant controller and a responding element adjacent to or in the affected structural gene.
2. Not only do the controlling elements regulate the expression of a structural gene but they are also capable of specifically inducing mutation in that structural gene.
3. The system of controlling elements acts in a spatially and temporally specific manner in the modulation of gene activity and the induction of mutations.
4. Sensitive genes can be pre-set by a controlling element leading to a change in function at a predetermined time in a later generation.
5. Controlling elements undergo changes in "state" which are revealed by modified regulatory and developmental properties.

All of her conclusions were based on convincing supporting data.

As a result of McClintock's studies it is evident that programmatic information can be encoded by DNA, that this information can be expressed in unexpected ways, including abrupt changes in levels of gene expression and that these effects are due to controlling elements capable of modifying the action of virtually any structural gene irrespective of that gene's specific biochemical function.

One of the remarkable things about Barbara McClintock's surpassingly beautiful investigations is that they came solely from her own labors. Without technical help of any kind she has by virtue of her boundless energy, her complete devotion to science, her originality and ingenuity, and her quick and high intelligence made a series of significant discoveries unparalleled in the history of cytogenetics. A skilled experimentalist, a master at interpreting cytological detail, a brilliant theoretician, she has had an illuminating and pervasive role in the development of cytology and genetics. It is no exaggeration to say that hers has been one of the most influential minds in biology in the 20th century. Her work has been characterized by a sustained intellectual brilliance which made it possible for her to grasp the conceptual order underlying the origin of her unstable genes. These investigations led her to the concept of genetic regulation. In her discoveries and in her interpretation of their meaning, she was many years ahead of her time. Genetics would not occupy its present high estate were it not for her magnificent and pioneering contributions.