Marcel Blanc

DARWIN, MENDEL, MORGAN: THE BEGINNINGS OF GENETICS

Traditionally genetics is said to be the science of heredity. At least this was how William Bateson defined it in 1906. Today this is no longer the case. Since about ten years ago, when biologists learned to extract genes from cells, to transfer them from cell to cell, to dissect them, to analyze them biochemically, in short to manipulate them, the term genetics has tended rather to designate the science of the action of genes in cells. (This is what was formerly called physiological genetics). In any case this is the form of genetics which today is in the forefront of biological research. (This is also called molecular genetics). This kind of genetics is also in the forefront in the media, because of its present or potential applications, in the realms of biotechnology, genetic therapy and so on.

Genetics as the science of heredity is today in particular the object of research in the area of population genetics. However, an important exception to this is the work of Barbara MacClintock on mobile genes. This research, which earned the Nobel Prize in

101

1983, has truly provided new insight into the mechanisms of heredity as such. But these studies remained unknown for almost forty years and were finally taken into account only when molecular genetics confirmed the existence of mobile genes.

The extraordinary present growth of molecular genetics obviously would not have been possible without the development of the science of heredity. This science was laid out in its basic form in the first quarter of the twentieth century. Its basic notions are genes and chromosomes, notions which are as fundamental for genetics as are atoms and molecules for atomic physics. Today every school child learns that hereditary makeup has a concrete existence in the form of rod-shaped corpuscles located in the nucleus of cells: chromosomes. And biologists today know that genes are definite portions of chromosomes, concrete physico-chemical entities made up of deoxyribonucleic acid (DNA), which they can manipulate almost at will.

How did biologists acquire their notions of genes and chromosomes? This is the subject of this paper which naturally does not pretend to exhaust the topic, for the history of the beginnings of genetics is extremely complex. Nevertheless, I will try to indicate the principal steps in the development of the science of heredity, and I will attempt to show by what means it was ultimately possible to arrive at notions of genes and chromosomes.

THE THREE ASPECTS OF GENETICS

The history of early genetics falls roughly between 1860 and 1920, and it is well known that two of its major figures were Mendel and Morgan. The theory of heredity based on the notions of genes and chromosomes was once called, in fact, the "Mendel-Morgan theory". It is also known that Darwin, more famous for his theory of evolution, played an important role in the birth of genetics. Two other names must be added to those of these three major figures: the German August Weismann and the Dutchman Hugo de Vries. (It would also be necessary to add the names of cytologists and experimenters such as Oskar Hertwig and Theodor Boveri).

There is something altogether strange in the history of the beginning of genetics: the people who figure in this history either

102

were unaware that they were playing a role in it or else were mistaken about the exact role which they had been assigned. It is highly probable that Mendel would have been very surprised to have been told that he was the founder of the laws of heredity. In the same way Hugo de Vries is known today as the rediscoverer of Mendel's laws and the "legitimate father" of the notion of gene. However, it would appear that his primary concern did not lie in this and that he thought of himself above all as a theoretician of the evolution of the species. Weismann is today famous for having refuted the notion of the heredity of acquired characteristics, while his theory of heredity (called the germinal line) has fallen into disfavor. What is curious in Morgan's case is that he represents somewhat the opposite of the preceding figures. He was fully conscious of creating the modern theory of heredity by making a synthesis of information on chromosomes and Mendelian genetics. But initially he was fiercely opposed to this Mendelian genetics!

To connect the major stages of early genetics with a *leit-motif,* I would first of all like to outline briefly the essential problems raised by genetics. Generally we tend to think that the purpose of genetics is to understand the laws which govern the fact that children to a greater or lesser degree bear a resemblance to their parents. But this is but one aspect of genetics, that of heredity as such. There are two other aspects, closely associated with this, and we will see that early research in genetics involved all three of these aspects, often simultaneously. The other two aspects are the genetics of development and the genetics of evolution. How are these three aspects related? To take an image to illustrate it, let us say that the aspect of heredity by which children resemble their parents is based on the fact that parents transmit to their children a sort of "building plan" (which today is called the genetic program). Following this plan and the instructions contained in this plan, the egg develops into an embryo, into a fetus, then into a baby and then an adult. And since this plan had already been used to "build" the parents, it is not surprising that their children resemble them. Thus it can be seen how heredity and growth are closely linked. But on the other hand, children never completely resemble their parents, nor are they exactly like their brothers and sisters. There are, therefore, variations in the building plan. And this is in fact characteristic of the species. It is because of this that all members

103

of a species resemble one another in general, from generation to generation. But can the individual variations in the building plan lead to a change in the form of the species? It is for this reason that genetics necessarily has a third aspect, one which involves the evolution of the species.

Mendel, Darwin, Weismann, De Vries and Morgan all approached genetics not by limiting themselves just to the question of heredity, but by considering all three of the above-mentioned aspects.

Mendel, in his famous 1866 work on "plant hybrids", made frequent reference to the theory of the evolution of the species (without ever mentioning Darwin's name, although he could have known the *Origin of the Species* by 1863 when his monastery acquired a German translation of this work in the beginning of that year). For example, in the introduction to his study, he announced that his work consisted in determining the laws governing the formation of hybrids and that it should allow solving the question "whose significance should not be under-estimated for the evolutionary history of organic forms". These laws of the formation of hybrids are what today are called Mendel's laws, and they are quite rightly seen as the basic laws of heredity. These laws, as is known, express the numeric relations of different types of descendents from parents of pure stock, differing at the level of one or several characteristics. Moreover, in his concluding remarks, Mendel examined how factors borne by sex cells and determining these characteristics combine their action in the course of development of an organism. The three aspects of genetics are thus all present in Mendel's work.

WAS MENDEL MENDELIAN?

Much controversy has arisen in recent years among scientific historians seeking to know to just what point "Mendel was Mendelian"; in other words, to what point can the fundamental notions of genetics today called Mendelian—i.e. the science of heredity—already be found in the work of Mendel. A certain number of biologists, and some very important ones at that, such as Theodosius Dobzansky, one of the founders of the modern theory of

104

evolution, have said that the science of heredity was the work of a single man. (In 1964 this author said, "It is rare to be able to attribute to a single researcher the merit of having given birth to an important branch of science. This is the case in genetics which resulted from the work of Gregor Mendel"). However, scientific historians, such as Albert Olby, Lindley Darden or L.A. Callender, and biologists such as J. Heimans, have noted that there is a tendency to read Mendel's work with twentieth century eyes; in other words to see more in it than Mendel actually put there. These scientific historians and biologists have affirmed that Mendel's writings must be read with the eyes of Mendel's contemporaries. And then it can be noted that Mendel was unaware of certain notions of Mendelian genetics of today. In the first place, although it would seem to be to Mendel's credit to have thought of living beings as a mosaic of basic characteristics with independent hereditary transmission (and in this, he was totally "Mendelian"), on the other hand, he did not have a clear notion of genes and alleles (i.e. variants of genes).

In most of his work Mendel only speaks of observable basic characteristics (which today would be called phenotypes), such as the smooth or wrinkled characteristic of pea seeds. It is only in the chapter on "Sex cells of hybrids" (and in the concluding remarks) that he speaks of the factors and elements, or the *Anlagen* (in German, a disposition, arrangement) which correspond to the different forms of a characteristic, or that he even speaks of the "internal makeup" of sex cells. It would seem that Mendel is here quite close to the modern concept of gene, that is an entity which underlies the characteristic and which determines it. Nevertheless, it is evident that, unlike us, he does not have the notion of a bi-univocal correspondence between the "element" and the "given form of the characteristic". When, in his concluding remarks, he says that during the formation of sex cells only dissimilar elements separate and are distributed in the distinct sex cells, this implies that a given sex cell could thus contain x identical elements of a given form of a characteristic. In other words, this suggests that similar elements do not segregate. This confirms the fact that Mendel did not use the same notation as we do to designate homozygotes. For example, today we designate a homozygote with the characteristics A as AA; Mendel designated it A. This is not a

105

simplification in means of writing; this betrays the fact that for Mendel identical elements which correspond to the form *A* of the characteristic are indistinguishable, inseparable, or, in other words, combined. This type remark leads to the admission that Mendel did not know the notion of "two genes per characteristic" (presuming of course that it is a simple Mendelian characteristic), in other words, two alleles per characteristic. This is evident in the explanation which he gives of the hereditary transmission of the color of flowers in the bean *Phaseolus*: Mendel supposes that three alleles A_1, A_2 and *a* can be present at the same time in the same plant. There is also, in the manuscript known by the name *Notizblatt*, the same type hypothesis, namely the simultaneous presence of three alleles for the color of pea seeds.

Of course these remarks on the deficiencies and other weaknesses in Mendel's work are not at all intended to diminish it. The extraordinary creativity which Mendel manifested in conducting his experiments and in the conclusions which he deduced therefrom, which became his famous "laws", can only be lauded. Nevertheless, it is quite clear that Mendel did not think that he was establishing "the laws of heredity" by writing this essay on "the hybridization of plants". His primary concern was an agricultural one: what rules must be respected by farmers hoping to obtain new and stable varieties of plant hybrids. Mendel undertook his research in order to discover the laws for the formation of hybrids. And the Irish historian, L. Callender, even noted that Mendel was probably disappointed by his results with the peas. For the chief finding in his writing is that pea plant hybrids are unstable! (If one generation F_2 ($A+2$ $Aa+a$) is allowed to reproduce by self-fertilization, after ten generations there are 1023 A and 1023 *a* for only two A*a* hybrids!). If this conclusion is accepted, it would seem then that Mendel was not at all led into a trap by Nägeli when he undertook to establish hybridization in hawkweed, *Hieracium*. To the contrary, maintains Callender, he no doubt thought he would find in this species the laws for the formation of *constant* hybrids (which would be of great benefit to farmers).

All these reflections indicate why Mendel's work did not impress his contemporaries as being *the* solution to the problem of heredity. Mendel himself perhaps did not believe in the universality of Mendelian heredity. Just as he placed more emphasis on constant

106

hybrids (which he was unable to obtain with *Pisum*), he finally also had to stress heredity by *mixing*, which was the prevailing theory of heredity in the 19th century. (This theory held that the characteristics of the two parents had to be "mixed" in the descendents in such a way that they would have characteristics which were exactly intermediate to those of the parents).

We can understand, then, how Mendel's works were "forgotten"; now we must try to understand what led to their being rediscovered.

WHY DID DARWIN NEED A GENETIC THEORY?

The historian L. Darden has clearly shown that the beginning of this discovery took place with Darwin. The connection between Darwin and Mendel is far from being a direct one. We know that Mendel had read Darwin, but the opposite is not true, although it would seem that Darwin could have at least known Mendel's name from the work of the German botanist H. Hoffmann (1869) which he necessarily consulted to write *The effect of cross and self fertilization in the vegetable kingdom* (1876). However, Darwin's role at the beginning of this process of rediscovery of Mendel lies in the area of genetic theory. In 1869 Darwin published a "provisional hypothesis on pangenesis", within a work on *Variation in Plants and Domestic Animals*. His genetic theory was especially intended to explain the evolution and development of organisms (i.e. two of the three aspects of genetics referred to earlier) and was not much concerned with the laws of hereditary transmission as such.

In summary, Darwin's theory ran as follows. He imagined that the "building plan" transmitted by parents to their children was developed in the sex glands of the parents by an accumulation of messages coming from all parts of the body. More precisely, he hypothesized that each of the billions of cells in an organism sent to the sex organs kinds of messenger particles which he called "gemmules". The importance of this theory for Darwin was that it explained how the "building plan" of organisms could change under influence from the environment. Organs modified by use, such as a duck's foot or a giraffe's neck, sent gemmules which were

modified in number and in quality. In other words, Darwin's genetic theory furnished an explanation for the "heredity of acquired characteristics" and for the gradual transmutation of one species into another species, under the combined influence of the environment and natural selection.

Darwin's theory was refuted experimentally, first by his own cousin, Francis Galton, who challenged the hypothesis of the circulation of the gemmule in the blood. He transfused blood from black rabbits to white rabbits and then bred the latter. They produced only white rabbits, of course. When Galton reported his results to his cousin, Darwin still did not abandon his theory of pangenesis. He simply concluded that the gemmules must circulate in the body by some other means than blood!

The theory of pangenesis was refuted a second time by August Weismann, a German biologist who proposed his own genetic theory in 1883-1885. The special feature of this theory was that it held for a radical separation between cells in the germinal line—from which sex cells derive—and ordinary somatic cells. According to Weismann, only the former carried the complete "building plan" of the organism and are therefore capable of transmitting the characteristics of the species from one generation to another. As for development (= the building) of an organism, the "building plan" furnished by the germinal cells was cut up into pieces, with each cellular line responsible for the formation of one or another tissue receiving a particular piece. Using this theoretical basis as well as experimental results, Weissman refuted the theory of hereditarily acquired characteristics. Among the many experiments, for example, was that of amputating the tail of mice for generations. This did not prevent the new little mice from being born with tails. But if Darwin's theory had been correct, the tail which had been cut off could not have emitted gemmules, and the baby mice would have been without tails at birth.

Although Weissmann's theory of the separation of the germinal line and the somatic line proved to be wrong, he was responsible for an important advance in genetic theory. Non only did he refute the concept of the heredity of acquired characteristics, but he was also one of the first biologists to maintain that the *material seat of heredity was to be found in the nucleus of cells*. To affirm this, he drew upon observations on fecundation made by cytologists such

108

as Oskar Herwig or Hermann Fol in the 1870's. These researchers had observed that fertilization consisted in the fusion of the nuclei of an ovule and a spermatozoid.

HOW DE VRIES REDISCOVERED MENDEL

In was Darwin's ideas with the corrections which Weismann had brought to them which put the botanist Hugo de Vries on the path toward the rediscovery of the work of Mendel. In 1889 Hugo de Vries published a book of theoretical reflections on genetics entitled *Intracellular Pangenesis*.

The term pangenesis alluded to Darwin's theory. De Vries in fact used this theory as his point of departure, but he also made major modifications in it. First he supposed that every organism could be considered from a genetic point of view as a mosaic of independent characteristics. Then he supposed that each characteristic is associated with an hereditary particle, which he called pangene. All cells of the organism contain the complete repertory of pangenes necessary to "build" an organism. The sex cells, then, are also provided with this complete repertory and can transmit it to descendents. De Vries' theory differed from Darwin's in that he believed that hereditary characteristics were not related to organs but to cells. Moreover, he did not believe in the heredity of acquired characteristics nor, consequently, in the emission of gemmules. On the other hand, like Weismann he thought that the complete repertory appeared in every cell and not only sex cells. To explain cellular differentiation, he hypothesized that only a certain number of pangenes could be expressed in a given tissue. This is essentially the idea accepted today with regard to the differential expression of genes in the course of development, except that De Vries imagined that the pangenes themselves left the nucleus and were implanted in the cytoplasm.

The genetic theory developed by De Vries, therefore, was in general the same as the theory accepted today. But what led De Vries to a rediscovery of Mendel was his reflection on genetic variation. According to his theory, an individual could manifest a new characteristic as soon as it acquired by chance a new pangene through mutation (= change) of an already existing pangene. This

109

organism thus would find itself in the possession of a pair of pangenes, each of which could determine a characteristic (or rather an alternative form of a characteristic). Which of the two would be expressed? De Vries devised the hypothesis that one would be active and the other latent. And in 1892 he observed pairs of characteristics in poppies and then in the large primrose *Oenothera*, whose hereditary transmission was in perfect agreement with the existence of a pair of pangenes, one dominant, the other recessive, and capable of segregating in the hybrid descendants in the ratio of three dominants to one recessive. Thus De Vries rediscovered Mendel's laws in his own work. He reached the Mendelian numeric relations by 1892 but waited until 1900 to publish them, after verifying that these laws were valid in thirty different species. Unlike Mendel, therefore, De Vries had a broad experimental sampling, and his results were not limited simply to the particular case of one species only. Also De Vries employed a theory of heredity which itself was based on information gleaned from cytology and theoretical genetic speculation.

Apparently De Vries learned of Mendel's writing through different channels. First, around 1895-96, in a book on "cross-breeding plants" by L.H. Bailey, who mentioned Mendel's essay in his bibliography. And then in 1900, at the same time that he was making final revisions in his announcement of the laws of the segregation of hybrids, he received a letter form his friend Professor Beijerink in Delft referring to an offprint of Mendel's paper.

It should be mentioned in passing that generally three names are cited with regard to the rediscovery of Mendel's laws: De Vries, Correns and Tschermack. But there is no doubt that De Vries was the most important person in this rediscovery. He performed experiments in segregation by 1892, which Correns and Tschermack were not doing before 1899. In addition, De Vries sent an offprint of his 1900 article in the *Comptes Rendus de l'Académie des Sciences de Paris* to the other two biologists, which led them to publish their own results.

MORGAN, FOUNDER OF MODERN GENETICS

The modern notion of genes derives directly from the concept of De Vries. The word gene was itself coined by the Dane Johansenn

110

in 1909, from the word "pangene" proposed by De Vries in his "intracellular pangenesis". But Johansenn also emphasized that by the word gene he meant a unit of heredity, and with the sense also of a unit for calculating the numerical proportions of the various types of descendants in cross-breeding. Genes were thus conceived as being only "logical beings", and an entire school of biologists, including Thomas H. Morgan, in the early 20th century rejected the idea of a material nature for genes. In fact, *they even ridiculed* those who followed Sutton and Boveri in thinking that genes could be particles located on chromosomes. Sutton and Boveri in 1902 had noted that pairs of chromosomes segregated during the formation of sex cells, just as cytological observation had shown.

This segregation was exactly the same as that of the Mendelian elements. And because, since Weismann, it had been accepted that the genetic patrimony was situated in the nucleus of the cells, it was very tempting to equate genetic patrimony with chromosomes and to place the Mendelian elements, that is the genes, on these chromosomes.

Morgan was an embryologist by training, and the study of genetics was of interest to him primarily in order to understand how organisms developed. When he had become acquainted with the work of De Vries in the realm of evolution, he was also interested in learning how genetics, through the use of mutations, controlled evolution. De Vries had observed mutations in plants. Morgan, therefore, selected an animal, the fruit fly, in an attempt to determine these mutations.

At first Morgan was opposed to the chromosome theory of heredity, that is to the notion of genes located on the chromosomes, for two reasons. First because genes, in the Mendelian system, were only conceivable as abstract objects (units for calculation). And secondly, for an embryologist the idea of genes as concrete objects located on chromosomes conjured up the *homonculus*, the theory of preformation. However, this theory, which holds that the adult organism in simply an enlarged version of the reduced model which exists in the egg (and even in the sex cells), had been refuted by embryology. But at that time genes, as concrete objects determining characteristics, could be thought of as "reduced models" of the characteristic. And Morgan, as an embryologist, rejected this idea. He opposed the chromosome theory of heredity until 1910.

111

And then he discovered that the "white eye" mutation was always transmitted together with an X chromosome which determined the sex. Next his team found more and more mutations which were transmitted along with sex chromosomes. It became clear that genes could be carried by chromosomes. This was confirmed by observing the simultaneous transmission of Mendelian elements (that is their non-segregation, in violation of Mendel's law). This is the *linkage* phenomenon. Finally the observation of the phenomena of breaking and connecting of chromosomes (crossing over) led Morgan and his team to draw up a chart designating genes on chromosomes. In 1915 this team was able to publish a book, *"The Mechanism of Mendelian Heredity"*, which was the synthesis of chromosome data and Mendelian genetics. The modern theory of heredity was thus established. The subsequent major steps, as we know, were those involving elucidation of the physical and chemical nature of genes in 1944 and 1953, and those clarifying the mechanisms which lead from the gene to the characteristic, or more exactly to protein. In 1985 this type genetics, called molecular genetics, began to be able to explain certain aspects in the development of multi-cellular organisms (such as segmentation in the fruit fly), while its contributions to the theory of the evolution of the species continue to call into question the Darwinian foundations of this theory.

Marcel Blanc
(Paris)

BIBLIOGRAPHY

ALLEN G.E., "Thomas H. Morgan et la naissance de la génétique moderne", *La Recherche*, 166, 592-599, 1985.
BLANC M., "Gregor Mendel: la légende du génie méconnu", *La Recherche*, 151, 46-59, 1984.
BOWLER P.J., "Hugo De Vries and Thomas Hunt Morgan: the mutation theory and the spirit of Darwinism", *Annals of Science*, 35, 55-73, 1978.

112

DARDEN L., "Reasoning in scientific change: Charles Darwin, Hugo De Vries and the discovery of segregation", *Stud. Hist. Phil. Sci*, 7, 127-169, 1976.

MAYR E., *The Growth of Biological Thought*, The Belknap Press of Harvard University Press, 1982.

OLBY R.C., *Origins of Mendelism*, Schocken Books, 1966.

OLBY R.C., "Mendel no Mendelian?", *Hist. Sci.*, 17, 53-72, 1979.

OREL V., and ARNOGATHE J.R., *Mendel, un inconnu célèbre*, Belin, 1985.

SERRE J.L., "La genèse de l'œuvre de Mendel", *La Recherche*, 158, 1072-1081, 1984.

Proceedings of the symposium on *"Past, present and future of genetics"*, Brno, 26 August-1 September 1982.

The Origin of Genetics: A Mendel Source Book, (C. Stern, E.R. Sherwood eds), W.H. Freeman, 1966.

113