Innovators and Controversies

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The Gene: A Critical History. ELOF AXEL CARLSON. Saunders, Philadelphia, 1966. 313 pp., illus. $9.

There have appeared almost simultaneously several books dealing with the history of genetics. Why this upsurge? It is due partly, perhaps, to the circumstance of a succession of centennial celebrations, for Darwin and for Mendel, forcing a retrospective evaluation; partly also to the rise of molecular genetics, stimulating more probing analysis of the sources of the new learning; and perhaps most important, to the approaching twilight of a generation whose accomplishments are embodied in this history. Thus A. H. Sturtevant, one of the founders of classical genetics, has published *A History of Genetics*, frequently an autobiography; and the (longer) *Short History of Genetics* by L. C. Dunn also reflects the personal involvement of a participant.

"Classical" genetics has come to be identified with the work on *Drosophila*, which proved the chromosome theory of heredity and gave us the theory of the gene. T. H. Morgan began the work, and attracted to himself a constellation of first-magnitude luminaries. Sturtevant—the surviving member of the authors of *The Mechanism of Mendelian Heredity* (1915)—was one, C. B. Bridges another; and there was H. J. Muller, scintillating with ideas. Elof Carlson, the author of the book being reviewed, was a student of Muller's. Thus his book gives a second-generation view of the rise of genetics, full of tales of its ancestral heroes. Muller's powerful influence pervades the book; there are fervent tributes to him; but there is also an evident effort to establish an independent Carlsonian identity.

Carlson begins with the 20th century and follows the development of our present-day concepts of the gene, the central theme of genetics. He reconstructs the sequence of discoveries and clarifications by concentrating on controversies and their resolutions, and to this end uses direct quotations from the original papers of the protagonists. This is a good approach, combining the summary value of the historical essay with an exposure to the styles of the actors in the drama—a technique especially valuable in a book intended for graduate students. The other audience to which the book is addressed—students of the history of ideas—may find this treatment entertaining but the emphasis dubious.

The development of the gene concept lends itself easily to such a dramatic structure. It falls into three acts: In the first, a buried treasure, Mendel's paper, is rediscovered, a neglect is rectified, and victory is gained for the particulate concept in heredity. The second act—classical genetics—gives these particles their place in the cell, the chromosomal theory of heredity is proved, linear linkage of the particles is demonstrated, the gene as the basis of life is prophesied, and radiation "transmutates" the elementary particles. The third act brings us to a triumphant conclusion—the identification of the gene as a DNA molecule and the cracking of the genetic code. A well-made play, with a second-act climax in the style of the 19th century, with its inspired heroes, and their antagonists—not really villains those, but fuddled honest men. The heroes are the theorists who can bring about the survival of their ideas.

The initial chapter of the book shows Bateson on his way to give an address to the Royal Horticultural Society; he reads De Vries' account of his confirmation of Mendel's analysis, alters his manuscript to include the discovery. He then leads the supporters of Mendel to victory over the adherents of Pearson and Weldon. The latter believed inheritance to be continuous, dependent on the total ancestry of an individual, not on specific contributions from his parents. The change to the discontinuous inheritance of Mendelian segregation necessitated a radical transformation of outlook. Bateson's own experimental work and his insights into the physiological possibilities of the interactions among the new factors were fundamental to this movement.

It is difficult for us now to grasp the magnitude of this transformation. The Mendelian assumptions implied that the infinitely sensitive living substance was essentially a system of stable, independent units. Such assumptions were more understandable to a generation with the anti-Lamarckian essays of Weismann still in mind than they were in Mendel's day; but it was still not easy.

The next chapters deal with the controversy surrounding the effects of selection, involving W. E. Castle, W. Johannsen, and ultimately T. H. Morgan and his students. The words *genotype* and *phenotype* needed to be invented by Johannsen to clarify the distinction between the intrinsic character of the genetic unit—the gene itself—and its expression by the organism, as the character is classified in experiment. Castle did not appreciate this distinction, believing the units themselves were changed during selection. It is indeed valuable to be reminded of the horror with which the multiple factors that made possible an effective analysis of the effects of selection were viewed at the time. Each new factor was regarded as an arbitrary constant introduced into the equations to make them fit the data. Methods that made possible rigorous proof of multiple factors in quantitative inheritance were an automatic consequence of the next series of advances. These began with the discovery of associative inheritance, or linkage, by Bateson and Punnett.

The next controversy that is presented concerns the interpretation of linkage of characters in inheritance. The Bateson school conceived these associations as the consequence of differential multiplication of the different classes at a premeiotic stage—"gametic reduplication." This view was quickly challenged.

T. H. Morgan's search for an experimental animal—*Drosophila*—in which to study mutations, and his use of those mutations to study linkage, are the critical events. The story is an exciting one, and Carlson enjoys it. The mu-

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tants Morgan found in *Drosophila* soon gave opportunities for solving the problems: sex-linked mutants were discovered, and shortly the linkage between these was worked out on the basis of exchange of parts of chromosome at synapsis. The decision between the two models—crossing over and gametic reduplication—came as more mutants accumulated and the resulting data were found not to fit the gametic reduplication series in any plausible manner. The genes were arranged in a linear order, and maps of the chromosomes were made.

Here we are treated to one of the numerous set pieces that are interspersed throughout the book, some homiletic, some historicoanalytical. The "verdict of history" is passed on Bateson, Castle, and Morgan—defined as the relative survival of their views in textbooks—and an attempt is made to differentiate between this and their actual contributions. The victors in controversy are "sanctified," the vanquished forgotten. I shall return to this later.

Linear linkage once demonstrated, Carlson deals with the definitive establishment of the chromosome theory and the so-called "Classic Gene." The continuing quest for distinctive criteria for the understanding of the genotype by means of its developmental effects begins with the idea of Bateson and his followers that recessive mutants represented losses—absences—of genetic material. Whether one was dealing with a loss or a latency was an early question. But the evidence that destroyed the Presence and Absence Hypothesis was the discovery of a diversity of changes at the same locus. Multiple allelomorphs could not all be losses.

The Drosophila Group

The personalities emphasized by Carlson in these chapters are Morgan and the students gathered around him, the "*Drosophila* group." As always in any group effort, analysis of the contributing elements is inescapable. When three doctoral theses are—as were those of Sturtevant, Bridges, and Muller—foundation stones for a new science, the relationship of students and teacher becomes an intriguing subject, and it is this that Carlson examines in an "enigmatic" (sic) appraisal. Two previous chapters present the series of brilliant experimental analysis that provided the first genetic maps, proved that they were indeed maps of units residing in the chromosomes, and led to the "classical theory of the gene." I myself, belonging to a somewhat later generation (among the last of Morgan's students at Columbia), did not see those early years, but I know something of them.

The central question is the role of Morgan in the group, but as the discussion proceeds one is aware that Carlson is perhaps more concerned to establish Muller's place. We are given a picture of Morgan coming from experimental embryology, a geneticist *pro tem*, originally antagonistic to the Mendelian concepts, intrigued by the De Vries mutation theory into the search which led to *Drosophila* as an experimental animal, influenced by E. B. Wilson in the uses of cytology for explaining genetic results (this is a background for the critical crossing-over experiment), and, once the essentials were established, playing the role of publicist for the further advances which he assembled as the Theory of the Gene. Carlson has unburied an article of Muller's, written in defense of genetics for a Russian audience during the initial moves in the Lysenkoist attack, in which one of the main targets was the *Drosophila* work. This—like earlier, more specific discussions by Muller—has as its main point the role of the younger members of the group, to whose pressures Morgan yielded, in advancing a truly "materialist" genetics. Carlson contrasts this account with Sturtevant's recollection of the "fly room" as an Arcadian environment, where exchange of ideas was free, an example of cooperative research, in which Morgan set the tone. Why this difference? Carlson gives a tendentious interpretation of Muller's paper, based on the politics of the Stalinist era. I believe the roots are deeper and have some importance in the analysis of such group efforts.

Muller himself did write a graceful obituary of Morgan (not mentioned in the book), paying tribute to Morgan's generosity towards his students—"opening the doors of his laboratory and, indeed, of his mind" to a group of young co-workers. Along with this tribute ("Morgan's evidence for crossing over and his suggestion that genes further apart cross over more frequently was a thunderclap, hardly second to the discovery of Mendelism") there are references to Morgan's abhorrence of "speculation" and to his skepticism. I believe that this difference in temperament between Muller, who seems to have valued himself most as prophet, and Morgan, who held prophets in no great honor, was a crucial one. The satiric thrusts against speculation must have been enormously deflating, however valuable as training to the young student. Another factor, evident in Muller's early papers, is his pride of parenthood in each insight—to the extent that collaborative ideas are given special mention in Muller's papers, and usually receive only general acknowledgement in the writings of the rest of the group. Sturtevant discusses the exchange of ideas in his chapter on the fly room, giving instances of several important ideas never previously attributed to their originators—and concludes with the thought that, on balance, all in the group came out even. This may perhaps represent justice, but it hardly contributes to the actual history of ideas. And with Muller's very early vision of the gene as the basis of life, history was always important to him; he saw himself on a large stage.

A revealing criterion of this difference of attitude is found in Muller's and Morgan's evaluation of Bridges. Both wrote admiring obituaries of him; I remember Morgan's once saying to me that he thought perhaps Bridges had made the solidest contribution of them all. It was the substantial experimentation, the ingenuity of method, the fantastic observational power that Morgan esteemed, considering the ideas common coin of the laboratory. But for Muller, all these experiments were performed in service of the ideas. Bridges himself did value Muller's ideas and used to remark on the importance of Muller's contributions in the early period.

It was in fact a fortunate combination, Morgan's skepticism and Muller's system-building. When to this is added Sturtevant's extraordinary analytical power, and the brilliance of Bridges' experimental talents, the achievements fall into place. There is no enigma, as Carlson seems to imply. There emerges the *raison d'être* of any group effort—complementary gifts enhancing one another.

Not So Classical Genes

Some of the controversies that flurried around the major developments also appear in these chapters: Goldschmidt's alternative to crossing over (migratory genes, finding their places on the chromosome according to variable forces of attraction), Castle's "rat trap" (a three-dimensional map of the chromosome obtained by mixing data from different *Drosophila* experiments)

—curiosities now, but hotly debated at the time. Most important for Carlson, the beginnings of Muller's mutation experiments, and his expositions of the properties of the gene, are set out.

The treatment of the classical gene concludes with the presentation of Muller's paper in 1921, contrasting it with Morgan's Croonian Lecture before the Royal Society in London. Morgan presented a factual summary, Muller a "prophetic vision" (this before his experiments with x-rays), in which the concluding question was whether geneticists would not be forced, in pursuit of the gene, to become bacteriologists, physiological chemists, and physicists, in addition to being zoologists and botanists—this apropos of the possibility that filterable viruses might be "naked genes," susceptible to biochemical analysis. The process of mutation was defined as a change in the individual gene conceived as a material particle.

The next stage in the development, as Carlson presents it, comes from the analysis of mutable genes, particularly in plants, an analysis which gave rise to the notion that there might be subunits which segregated out to give the variegated individuals or, as a later hypothesis had it, subgenes arranged in a linear series. The splitting of the genetic atom was not yet to be, and the hypothesis was discarded. Subunits of the gene reappear in a later chapter in a test of the continuity of genetic material in the chromosome.

The problem of continuity and integration became a serious one, as presented in a series of chapters on position effect, a discovery of Sturtevant's which showed functional interaction between neighboring elements of the chromosome. This effect, originally discovered in a case analyzed as an example of frequent mutation, became generalized with the production in Muller and Altenberg's experiments of numerous rearrangements by x-rays, and became more precisely defined when specific studies of definite regions were undertaken by different people.

The three chapters on the various aspects of the position-effect phenomenon record the efforts that were made during the '30's to clarify and extend the uses of genetic techniques in the analysis of the gene. Carlson's protagonists here are Muller, Goldschmidt, and L. J. Stadler (who independently of Muller discovered the mutagenic effects of x-rays in plants). The form in which the controversy presents itself is that of a question: how to recognize a true intragenic mutation? It was partially forced on geneticists by the difference in the response of maize and *Drosophila* to x-rays—in maize, a spectrum of losses, different from the spontaneous mutants; in *Drosophila*, a spectrum of position effects superposed on quite ordinary mimics of spontaneous mutants. Stadler, with a judicial temperament, found no recourse other than continued refinement of the criteria by which genetic effects could be discriminated from each other; the emphasis was on operations according to Bridgman's *Logic of Modern Physics*. Goldschmidt, pushing the implications of position effects and rearrangements, and with a flair for the extreme statement, denied the existence of genes as particulate units: function in the chromosome was completely integrated. Muller attempted to resolve these questions in various ways, all of them indirect, finally settling for a detailed investigation of a specific region, the "scute" locus, in which many breaks had been detected and for which the phenotypes were described in enormous detail. Early on, Serebrovsky and Dubinin had used this locus to elaborate their hypothesis of linear subgenes, defined by their behavior in compounds: different subgenes in homologous chromosomes would produce the dominant phenotype; alterations (losses) of the same subgene would produce a mutant effect. This simplistic view of genes and development was quickly exploded; but the problem of complementation reappears in modern dress in a later, molecular biological chapter. The emphasis here is on Muller's use of these rearrangements toward the definition of discontinuous genetic units, the "left-right" test. Chromosome-carrying breaks immediately to the left and to the right of a locus, brought together, give recombinants which allow the localization of the effect in that specific region.

The important discoveries associated with the giant chromosomes, in such an account, are oddly cast in supporting roles to the analyses of the nature of mutational events. The localization of specific genes to special bands on the salivary gland chromosomes, the counting of bands in relation to the number of genes as estimated by various techniques (a major interest of Muller's), all these are given importance so far as they have a relation to Muller's "left-right" test, and to his concept of the gene.

Carlson elevates the "left-right" test in Muller's hands to a position of unique importance. One can only ascribe this emphasis to some lapse of memory: such analyses were a routine element in any genic localization. In any case, the "discontinuity" of the genetic material inferred from the correlation of breakpoint in the chromosome with phenotypic effect (if one depended on these experiments alone) is ambiguous: the mutants are all survivors of a population of irradiated chromosomes; what is needed here, and has not been provided, is a survey of the characteristic phenotypes produced by a group of chromosomes selected only for rearrangements in the region. Thus the argument has a flavor of special pleading, an unfortunate failing but understandable in an enthusiast.

A similar weakness appears in the chapter on target theory, the attempt to determine the size of the gene by calculations of the volume sensitive to x-rays. Muller rejected such calculations, on the grounds that they involved too many unverified assumptions, which Carlson details. Here, apparently, the calculation came out wrong: the size of the gene was too small as estimated by these methods if Muller's other values, based on the giant chromosomes, were to be accepted. Yet target theory has given values in radiation experiments which are in agreement with independently ascertained dimensions of viruses and DNA molecules. One gains the impression from Carlson's account that the fulfillment of prophecy took precedence over the difficult fact. The chief virtue of the target-theory attempt, he finds, is its attraction of physicists to genetics.

Toward Molecular Genetics

With the next chapter, The One Gene–One Enzyme Hypothesis—A Prophecy Fulfilled, we move into biochemical genetics, the unsung and rediscovered hero being Garrod, who found and correctly interpreted the first biochemical genetic character. The question is raised, as it has often been, why Garrod's work did not "generate a close cooperation between biochemists, pathologists and geneticists." I believe there are some fairly simple answers. Garrod had found the cases best suited for the biochemistry of his time. Work in this direction did continue. For example, J. B. S. Haldane, who is here relegated to a footnote, was indeed interested in the relation between genes and enzymes; he found it necessary to know more about enzymes and proceeded to write one of the frequently consulted texts of that time in order to prepare the ground for such an effort. Geneticists, on the other hand, were concerned with the role of genes in development and were not really convinced that the function of genes in cell metabolism (in the steady state) needed understanding as a necessary first step. Beadle and Ephrussi's transplantation work in *Drosophila* is justly emphasized: it started as an explanation of the role of genes in development and led, in the *Neurospora* work of Beadle and Tatum, to a general technique for the study of pathways of biochemical synthesis in organisms. Here an essential factor was the biochemical background. As it turns out, "one-gene-one-enzyme" was valuable perhaps more as slogan than as definitive statement—a fact apparent in later chapters leading to the operon concept; and the emphasis is now on one-gene-one-polypeptide.

There follows a chapter on plasmagenes—one of the weakest in the book, apparently farthest from Carlson's interest. It begins with an egregious historical error, crediting Boveri with the recognition of the function of the nucleus in heredity (it was Haeckel), and noting the inheritance of coiling in snail shells as an example of cytoplasmic inheritance. (Sturtevant showed this inheritance to be Mendelian but dependent on genes determining the character of oogeneisis in a female, their effects being recognized in the development of the eggs she formed—that is, maternal inheritance.) It seems clear now that there are in the cytoplasm replicating units additional to those in the chromosomes, the DNA of the mitochondria, for example. Carlson, however, is concerned with Rhoades's and Sonneborn's analyses of cytoplasmic inheritance and with the question whether chromosomal genes act by releasing into the cytoplasm replicas which there become autonomous. The episode—plasmagenes were in vogue for a few years, then became discredited with the discovery that the initial case (kappa in *Paramecium*) was an intracellular virus-like body—is intrinsically interesting as an example of an analysis pursued to its appropriate conclusion. Carlson believes its importance to have been in stimulating the idea of nuclear transplantation. This is incorrect. Since I was responsible for the initial suggestion [see R. Briggs and T. J. King, *Proc. Nat. Acad. Sci. U.S.* **38**, 455 (1952)] for the amphibian work, I can say that those experiments were designed to determine whether changes occur in nuclei during embryonic differentiation, as judged by their capacity to carry out developmental functions in the egg cytoplasm—a problem conceptually independent of the plasmagene idea, although having obvious uses in exploring it.

The road to molecular genetics is taken in the next chapters, by way of Pseudoallelism versus Intragenic Recombination, whose heroes are Lewis and Pontecorvo (they supply experiments but, more important for our author, have models which can be pitted against each other as stages in the analysis of fine structure of the gene). Next the familiar story is put together—we progress from Griffith to Avery, from Delbrück to Benzer and the use of genetic recombination at low frequencies in the large populations of the bacterial viruses to correlate frequency of recombination with distance along the DNA molecule. The Watson-Crick discovery provides the basis for a genetic code of nucleotides, and recombination becomes a matter of internucleotide bonds. The sites of mutation are nucleotide bases, the unit of function the minimal sequence of bases. And so to the next chapter, detailing the functional approach by way of "complementation: maps, patterns and units," in which the units of function in microbial and nonmicrobial systems are explored, by Lewis in *Drosophila*, by Giles and Catcheside in *Neurospora*, and later by Carlson and his students in *Drosophila*. The complementation maps eventually are subjected to an attempt at molecular explanation, in terms of the folding of proteins read off an RNA template, by Crick and Orgel, and are left for the present as premature.

Having got so far, we are ready for a chapter—The Operon—presenting a summary of the regulatory systems controlling gene action. A few statements inadequately cover the work of Brink and McClintock in maize, and there is a fuller development of the scheme eventually worked out by Jacob and Monod for the galactosidase system of *Escherichia coli*. Carlson presents the operation as serving to dissolve the "impasse between nuclear and cytoplasmic controls," the latter having been proposed for regulation in protozoa.

Finally The Coding Problem is presented, by way of Gamow, Crick, and Brenner, with its apotheosis in the biochemical demonstration, by Yanofsky and his co-workers, of colinearity of gene and protein. The thrill of these discoveries is still felt, even though they have lost the initial bloom of novelty.

One of the impressive characteristics of the recent history of molecular genetics is the emergence, in molecular format, of the same sequence of ideas that were elaborated in "classical genetics." Linear linkage is proved, and distance is correlated with recombination frequency on the assumption that the chance of recombination is equal everywhere along the genetic map. In both cases the assumption is not borne out, and localizations are carried out by tests with overlapping fragments of the genetic material. The point is that the hypothesis of a linear order imposes its particular logic and sequence of experiments, even though the details of the two systems differ greatly.

Winners and Losers

The two concluding chapters contain Carlson's historical reflections and his view of the current status of the gene concept. In the latter chapter, after decisions as to which concepts of the gene have survived (mostly Muller's) and which have not (he relegates plasmagenes to the graveyard, in the same year that mitochondrial DNA has seen them firmly established), he concludes very much in Muller's style, but at a different level, with a discussion of open problems. Most of his discussion of cistrons as functional units is already outmoded; clearly the problem is the elaboration of techniques for direct measurement of message in appropriate materials.

Carlson lays great stress on the "comparative approach," the use of a variety of experimental material, to permit generalizations concerning genes. It is hard to imagine anyone's disagreeing with the *apologia pro Drosophila sua*; the problem is to obtain relevant data—these are beginning to appear possible to obtain in the studies of molecular hybridization. Carlson ends up with a comparison of gene sizes in different organisms, in which the fallacies of Muller's different approaches are maintained: the assumption of equal distribution of genetic effect per unit length, the assumption that the giant chromosomes represent extended DNA fibers (in fact, the bands are highly compacted), and so on. Molecular data have superseded such ruminations: measurements of DNA content of bands have been made, and the size of specific genes (hemoglobin, tryptophan synthetase, to name two examples) is already known.

The historical reflections are gathered under a series of headings and are presumably addressed to the audience of graduate students. From a discussion of "Mendel's patient wait for recognition" and Discontinuity in Discovery Carlson turns to Research Eclipse and Research Impasse, the Fallacy of Occam's Razor, and the Ambiguous Role of Philosophy in Genetics. Under Scientific Progress: Human Limitations, we are told, apropos of Muller's failure to undertake the study of bacteriophage genetics in 1922, that "The tragedy of genius is that it is associated with its possessor," and that Muller chose to remain with *Drosophila*. The Necessity for Straw-Man Models is a useful exposure of the "bead on a string" model of the gene as legend, invented for controversial purposes. These are discussions appropriate for graduate student bull-sessions, but are hardly commendable as analytical essays. "Mendel was the wrong person to have discovered Mendelism" because he lacked the requisite talents as publicist to gain acceptance for his work. "Research eclipse" and "research impasse" turn out to be elegant terms for the obvious: that interests change and people do what is most exciting, which is often what is most feasible. The "role of philosophy" is ambiguous for Carlson because scientists of diverse philosophies contributed to the gene concept. His discussion hardly provides the required searching examination of the relation between the point of view behind a professed philosophy and the springs of creative effort in science.

Entertaining reading as the book makes, particularly if one is acquainted with the material, it carries more than its share of annoyances. This is rather a romantic than a critical history of the gene concept. The heroes of each chapter play their roles in the controversies, doing battle for their theories. But science is not founded on hero-worship. It represents an effort, painful on occasion, to transcend the individual limitations of the human beings who contribute to it, to create a body of objective knowledge. And it has little to do with prophecy, except in so far as a prophecy facilitates a discovery. I believe Muller's preoccupation with his prophecies was a distraction from his fascinating experimental ingenuity and his bold and imaginative perceptions.

The cornerstone of the structure of the book is the importance given to controversy in science. Is it simply human aggression appearing as a driving force, or does it serve some other role? Ordinarily, as Carlson points out, scientists are not prone to make public retractions of their exploded hypotheses. If the controversy were central, an etiquette would have developed which would require such action. Evidently, if the chief interest is to discover the facts, the discarded theories diminish in importance.

If one examines the "losing" sides of the controversies detailed by Carlson, the concepts which he "consigns to the graveyard," one finds it difficult to avoid feeling that the mistake of the losers (in this sense a mistake is an unrewarding line of inquiry) arose from taking a minor feature and exalting it. Eventually, however, both the objections and the alternatives find a bearable place in the framework of theory. When T. H. Morgan first propounded crossing over between chromosomes as an explanation for genetic linkage, R. A. Emerson drew up a list of objections, improbable consequences of the theory. They are such phenomena as deficiency, unequal crossing over, and other, rare occurrences which, when found, constituted important items in the proof of the chromosome theory. Apparently the intuition that guides successful experiment lies in a sort of pattern recognition, the ability to distinguish the main lines from the decorative turns.

What then is the value of controversy? For the scientific community, the repetition of arguments, the multiplication of communications, presumably has the value of redundancy in information theory—the message comes through.

This role of controversy in creating a climate of acceptance is valuable. So there are two social aspects of a discovery: that it be made, and that it be absorbed into the fund of general knowledge. Carlson's ideal scientist is presumably a practical theorist: he will have had his prophetic vision, have stimulated enough collaborators to see its fulfillment, and have had the skill to maneuver all of the advantages that accrue from recognition.

But personalities such as we assume Mendel to have been, and as we know Darwin was, that are not interested in gaining proselytes are refractory to these demands. For recognition, they required a Huxley, or, after a generation, a Bateson. Carlson makes a point of Mendel's presumed discouragement after his letters to Naegeli. Mendel, in my view, wrote to Naegeli because Naegeli knew about hybrids; the only species hybrid Mendel tested gave results inconsistent with the crosses of garden pea varieties; generalization was impossible—it would have been an act of faith, for which Mendel had other outlets.

What was needed to create a climate in which such an exception was not fatal was the growth of biology, the comprehension of the role of the nucleus in heredity, the appreciation of the experimental method. Mendel is credited, in a textbook of statistics, with the first attempt in biology to test quantitatively the expectations from a mathematical theory. In the mid-19th century, Helmholtz and other physiologists were pioneering in applications of physical methods. Mendel may perhaps be viewed better as part of this movement, in view of Sturtevant's emphasis on Mendel's training in, and teaching of, physics. But the climate required for acceptance of a theory is one that makes it easy to put to one side apparent exceptions to it, with confidence that further investigation will justify their neglect. Until the Weismannian discussions, there was no such justification: Mendel, says Correns, could not have known about nuclei.

A similar argument applies to Garrod, as has already been noted. The *Neurospora* work, which generalized Garrod's perception, could not have been carried through without the armamentarium of modern biochemistry and the techniques for the production and selection of mutations.

The Hero as Scientist

In effect, we deal here, as Dunn has noted, with the problems posed by such sociologists of science as R. K. Merton, who have analyzed the frequencies with which discoveries in science are made singly or in multiple, finding a preponderance of multiple discoveries. Delayed general acceptances are important in such a context. Being before one's time means supplying only part of the evidence required for the visualization of the total structure. In Mendel's case the lack was the evidence of cellular structures that could carry such units. Garrod was dealing with a multicellular organism, in which the problems of embryonic differentiation and gene function had not yet been clarified, and the biochemistry of enzymes was itself embryonic. So they remained special cases. But once the needed ingredients were available, they could be combined to form a viable structure. One is reminded of the self-assembly of the components of the bacterial virus coat: provide the necessary protein components and the proper conditions, and the assemblage forms the structure. It is not unlikely that some such process is at the root of the tendency for multiple discovery: the appropriate information must be available before the new idea can appear; and if this is so, then the chance of its appearance will be a function of the number of people who are interested in the problem.

Where does this leave the hero? Merton is concerned to point out that geniuses differ from other folk not so much in having unique ideas, but in having more of them. One then has an insight into scientific history closer to Tolstoy's view of secular history as due to the mass movements of people, rather than to the specific dynamism of their leaders. These are important, sometimes critically so, but in response to the pressures of the age. So also in the history of science: as information accumulates, new combinations of facts yield new insights, the individual hero serving almost as a vehicle for transmission of the collective intelligence of the culture of which he is part.

This interdependence of advances in different fields points to a regrettable shortcoming in Carlson's range of view: it is parochial. He seems unaware, for example, of the interrelations between cell biology and genetics, omitting any reference to the work beginning in the late '30's which revived the interest in nucleic acids, provided methods for their study in chromosomes, pointed up their consequence for protein synthesis, and in general laid the groundwork for the microbial experiments in which the definitive answers were obtained. There has come into existence a canonical text, in which bacterial transformation begins the story and all the other work is forgotten. It provides a rich chapter of history, important in displaying the contingencies governing advances in science.

Finally, a word about the style of the book, which ranges from lively to grandiloquent. A good editor could have spared us such sequences as the following: "Like Pandora's box the gene through the mind of genius unleashes a horde of implications which are both awesome and prophetic."

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