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Nobel Prize in Medicines 1946

Hermann Joseph Muller

The Nobel Prize in Physiology or Medicine 1946 was awarded to Hermann J. Muller "for the discovery of the production of mutations by means of X-ray irradiation"

That children resemble their parents, that striking features in both domestic animals and cultivated plants are transmitted from one generation to another, or in short, the circumstance that characteristics descend from generation to generation, has attracted interest during all periods in human history and has stimulated the inquiring spirit which is the origin of all organized knowledge. Innumerable attempts to explain such transmission have been made during the course of time. The manner of attacking the problem in our own time by empirical and experimental methods has led to the development of the modern theory of heredity. This is a relatively young science. The year 1946 marks an anniversary, for it is now exactly 80 years since Gregor Mendel published his first experimental studies, in the course of which he found that characteristics were passed down independently from parent individuals, and combined themselves freely in daughter individuals. These observations may be said to constitute the initiation of modern heredity research. In 1866, however, the time was hardly ripe for further development, and it was not before the turn of the century that the importance of Mendel's work was realized.

During the intervening period much has happened within the sphere of the biological sciences. The conception that all living beings are built up of similar bricks, the cells, had been fortified, and the main features of the general structure of the cells of both plants and animals were known. Above all, the intricate processes which are reflected in the cell division had been analysed and been shown to imply that, at every cell fission, certain parts of the cell nucleus, the so-called chromosomes, were divided up with great exactitude and distributed exactly equally over the daughter cells. Further, the mechanism of fertilization had been elucidated - how two cells, one from each parent organism, fused together into the fertilized egg cell. From the latter is subsequently developed the definitive organism in which different properties, characteristic of the parent organisms, recur.

If characteristics of different kinds are to pass from generation to generation, they must all, of course, be found represented in some way in this fertilized egg cell or - as it can also be expressed - this cell must contain certain factors which condition the development of different properties when the daughter organism is formed. These so-called hereditary factors, or to use a more convenient name, genes, had, and perhaps still have, something of a mystic shimmer over them. They not only affect, but they guide and determine the development of the whole organism, even that of man. As the total number of all the characteristics which distinguish, for example, one species of animal from another is extremely large, the number of genes must also be very large. In spite of this, they must all find a place within the microscopically small individual cell.

As early as during the first years of this century, the opinion was advanced that the chromosomes were the bearers of the genes, and that the care with which Nature arranges that at cell division the chromosome substance is distributed exactly equally over the daughter cells in reality aims at guaranteeing that the supply of genes in the daughter cells shall be like that of the mother cells, and the daughter organisms like the parent organisms.

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At that time, however, ideas were vague and hypothetical, and the gene was a philosophical idea rather than a tangible reality for empirical research.

In about 1910, however, a group of research workers, with Morgan, Muller, Bridges, and Sturtevant as the central force and Morgan as the leader, started a series of operations which created a fresh foundation for heredity research. Morgan's contribution was rewarded with theNobel Prize in 1933.

The works of this group of men gradually led, among other things, to the «materialization» of the gene - if I may be permitted to employ the expression - the conception lost most of its mystic shimmer, and the gene was now apprehended as a little cell organella which was accessible thanks to different experimental methods, perhaps a giant molecule of protein character, and, as Muller had first suggested, probably resembling the simpler types of virus which have been dealt with earlier this evening.

The gene conception is of importance, from the point of view of principle, for fundamental biological problems of the most varied kinds. Different plants and different species of animals differ in their different characteristics, the sum total of which

characterizes the individual species. Behind them lie the conditioning and cooperating genes, and it is more than a paradox to say that that which constitutes the essentials in the individual species of plant or animal is less the developed organism than the set-up of genes met with in the different parts of the cells. In all increase of the living substance the primary process is an increase in the substance of the genes which is to be carried on to the daughter individuals, to shape them into counterparts of the parent individuals. The development from lower to higher organism, which is the basis of the modern theory of development, involves - apart from the reproduction of the genes in the propagation of the species - also a progressive series of changes in the stock of genes.

It is manifest that the study of the structure of the gene and of the possibilities which may conceivably exist of effecting its reproduction artificially, the fundamental vital process, or even artificially modifying it and thereby changing the organism, must present itself as a fascinating sphere of work. After some years Muller left the Morgan group and devoted his labours entirely to this sphere; in the first place to the tempting, but difficult, task of finding methods of changing the heredity factors artificially.

It was known, already at the turn of the century, that apparently sudden changes may appear spontaneously in the hereditary mass, which result in changes in the characteristics of the organism. We now know that these changes may be of different types, and among them occur also disturbances in individual genes. These are very rare, however. Even in such a convenient experimental object as the banana fly, introduced by Morgan, where the generations succeed each other rapidly, and thousands of flies can be examined, it is only seldom that mutations are observed. Muller grappled with the task of trying to change the frequency of mutations. He first created procedures, technically extremely elegant, by which the mutation frequency could be measured exactly. When this task - which took several years - had been completed, the effect of different agents on the frequency of mutations was investigated, and the discovery for which the Nobel Prize is now awarded was made, viz. that irradiation with X-rays evokes large numbers of mutations. Experiments could be arranged, for instance, so that nearly 100 per cent of the offspring of irradiated flies showed mutations. Thus a possibility had been created for the first time of influencing the hereditary mass itself artificially.

This discovery aroused a great sensation already when it was first published in 1927 and rapidly led to a great deal of work of different kinds and in the most varied directions. The mechanism of the effect of rays was studied by many research workers, with Muller at their head. Greatly simplified X-ray irradiation, as also ionizing irradiation, could be likened in general to a shower of infinitely small (even compared with the individual cell) but highly explosive grenades, which explode at different spots within the irradiated organism. The explosion itself (or the fragments it throws up) tears the structure of the cell to pieces or disturbs its arrangement. If such an explosion happens to take place in or close to a gene, its structure, and therewith also its effect on the organism, may be changed.

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Muller's discovery of the induction of mutations by means of rays has been of tremendous importance for genetics and biology in general.

The foremost instrument of experimental genetics is just the mutations of genes. Thus the whole teaching structure of the Morgan school is based on the utilization of certain spontaneous mutations. Now, when Muller has created a means of simply producing in every laboratory an unlimited number of these otherwise so rare phenomena, it is obvious that genetic research in general must be greatly stimulated thereby. The effect of irradiation is absolutely universal, mutations appear after irradiation within all organisms, from simple viruses and bacteria up to the most highly organized plants and mammals. One of the principal causes of the amazingly rapid development which genetics has undergone during the last two decades is the realization of these technical possibilities.

For the fundamental question, the problem of the mechanism of the reproduction of genes and the basis of the mutation processes, Muller's discovery has created new lines of research which impinge on different branches of science. Muller himself has been indefatigable within this field and has, himself and through his pupils, led the development.

The extended knowledge of the mechanism of the mutation processes has influenced and stimulated the work in numerous fields outside theoretical genetics, and both theoretically and practically important results have been reached. Merely to exemplify the diversity and the varied nature of the spheres touched upon, I beg to adduce a few examples: applied genetics, especially plant improvement, which is of such practical importance, the theory of evolution, metabolic research, a number of spheres within the realm of medicine, especially perhaps eugenics and the theory of disease in general.

Just this multiplicity of spheres which are affected by Muller's discovery indicates its fundamental character. It is already one of the most important foundation-stones of the complex structure of modern biology, and Mendel, Morgan, and Muller together will always stand out as the creators of the modern science of heredity.

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Muller's contribution to its development extends far beyond the discovery for which the prize is now awarded. For more than three decades he has been in the front rank as regards both the scientific work and the eager but inspiring discussions of the results within the field, and these are the most important incitement to future development. He is now more active than ever, and, as the donator wished, the Nobel Prize can now be awarded to a man at the height of his scientific creative power.

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http://www.nobelprize.org/nobel_prizes/medicine/laureates/1946/press.html