

MENDELIAN GENETICS AND ITS DEVELOPMENT

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Keywords: Mendelian genetics, molecular genetics, population genetics, genes, dominant, recessive, diploid, homozygotes, heterozygotes, chromosome theory of inheritance, recombination, genetic mapping, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), genetic code, restriction endonucleases, recombinant DNA, Hardy-Weinberg principle, molecular evolution, duplication and divergence

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Summary

The notion of inheritance can be traced back to ancient times. The laws of inheritance, however, were not established until relatively recently, by Mendel, and later extended by many others. Thus, the formal mechanism of gene transmission, Mendelism, has formed a cornerstone of modern biology. The deciphering of the language of biochemical communication within the cell and its relation to biological communication between generations was an important experimental breakthrough. From a biochemical point of view, a gene corresponds to a region along a molecule of DNA, and most genes code for the polypeptide chains that constitute proteins. Population genetics deals with the fundamentals of evolutionary change. But its scope actually is made much broader by the power of molecular methods.

1. The Classical Theory of Direct Inheritance

1.1. The Views of Hippocrates and Aristotle

Hippocrates (ca. 400 B.C.) believed that the reproductive material came from all parts of the body and hence that traits were directly handed down to the progeny. Aristotle (ca. 350 B.C.) pointed out difficulties, even impossibilities, with Hippocrates' view. Aristotle referred to the inheritance of such traits as the voice, hair, and way of moving, which could not contribute to the reproductive material, since they were intangible or concerned dead tissues, and he also referred to traits such as a beard or grey hair which may not be present at the time of reproduction.

Aristotle argued that the reproductive material should be regarded as being made up of nutrient substances which, while on their way to various parts, had been diverted to the reproductive path. Although the ideas of Hippocrates and Aristotle on heredity differ, they share the notion that inheritance is direct; namely, that substances derived from or intended for specific parts of the individual are handed down to the progeny. Hypotheses of this kind represent the simplest theory of heredity which one can postulate.

1.2. Darwin's Theory

Charles Darwin suggested in 1868 that all the cells and tissues of an organism threw off minute granules, both during development and at maturity. He further supposed that these granules circulated throughout the plant or animal, multiplied, and were passed to the reproductive cells. Thus, hereditary traits were considered to be transmitted to the progeny. In the offspring the granules were regarded as responsible for the development of cells or tissues corresponding to those from which they had been derived in the parent. As Darwin himself remarked, this theory of heredity resembles that of Hippocrates, differing mainly in specifying that granules were responsible for the hereditary transmission.

1.3. Experiments by Knight and by Goss

Rudolf Jacob Camerarius reported in 1694 on early pollination experiments and the existence of sexual reproduction in flowering plants. He showed that in the maize plant, seeds are not produced unless pollen is applied to the pistils. He concluded, therefore,

that the pollen is the “male” element and the pistils are the “female” element, and discussed his conclusion in relation to a number of theories on sexuality and fertilization.

During the eighteenth and nineteenth centuries, numerous experiments on the crossings of different species or varieties of plants and animals were performed. Joseph Gottlieb Kölreuter crossed different types of tobacco with one another from 1761 to 1766, and published the first information about hybrids between varieties that might resemble one parent or the other. Also, he provided clear evidence that in reciprocal crosses, the hereditary contribution of the two parents to their offspring was equal.

Although these studies failed to provide support for the classical theory, they also failed to lead to any alternative hypothesis. Of course, the notable exception is Gregor Mendel’s work. Some of the most promising earlier experimental studies were made by T. A. Knight and by J. Goss with garden pea, the species that Mendel subsequently used successfully.

Knight crossed two varieties which differed in color. One was unpigmented, with green stems, white flowers and a white seed coat. The other had purple stems and flowers and a grey seed coat. When an unpigmented plant was pollinated by a pigmented one, only pigmented progeny appeared the next year (the first filial generation). But, on self-pollination or on pollination by unpigmented plants, some pigmented and some unpigmented plants were produced in the succeeding year. These results were obtained even when the peas from within one pod were sown. However, he did not record the numbers of the two kinds, either for the progeny of individual plants, or in total, and thus failed to discover the underlying mechanism of inheritance.

In 1824, Goss obtained similar findings to those of Knight, but took the analysis a little further. He had removed the stamens from a normally green seeded pea, pollinated it from a yellow seeded variety, and had been surprised to find that the seeds which set (the first filial generation) were yellow like the male parent. When he sowed them the following year, he found that after self-pollination, some pods had all green, some all yellow, and many both green and yellow peas (the second filial generation). On sowing these the next year, he found on further selfing that whereas the green peas bred true, giving only green progeny, the yellow peas produced some pods with all yellow and some with both green and yellow peas intermixed (the third filial generation). The experimental work of the eighteenth and nineteenth centuries appears to have been designed either to obtain new and improved varieties of animals and plants for use in agriculture or horticulture, or to understand the nature of species by means of artificial hybridization, rather than to obtain information about the mechanism of inheritance.

2. Mendelian Genetics

2.1. Mendel’s Law of Inheritance

In 1866, Gregor Mendel performed crossing experiments similar to those of Knight, Goss and others, but recorded the numbers of progeny of each kind, and published his findings on the inheritance of seven different traits in the garden pea. One of the trait-

differences Mendel studied was that which Knight had used, namely, the presence or absence of pigmentation in the plant. Mendel found, like Knight, that the progeny from a cross between the two forms were pigmented (the first filial generation), and that on subsequent self-pollination, both pigmented and unpigmented plants were obtained (the second filial generation). But, Mendel further counted the numbers of each kind, and observed that the frequencies of pigmented and unpigmented plants closely approximated 3/4 and 1/4 of the total, respectively. The trait, presence of pigment, which is manifested in all the immediate progeny of the cross, and in 3/4 of the following generation, Mendel called the dominant trait, the other being the recessive trait. Mendel also confirmed Goss's third generation observations, namely, that the green peas bred true, whereas the yellow peas often did not. But Mendel went much further, and found that of 519 yellow seeds 166 bred true while 353 gave yellow and green seeds at a ratio of 3 to 1 like the previous generation. Mendel pursued his inheritance studies through five or six generations, and showed that the pure-breeding types in the filial generation remained pure-breeding, and the others gave a 1:2:1 ratio in each generation.

Essentially similar results to these were obtained by Mendel for a total of seven trait differences in garden pea. Prior to this time, the classical theory of inheritance supposed that traits are transmitted directly from parent to the offspring, but Mendel concluded that there exist discrete particles responsible for the appearance of particular traits. Namely, each parent contributes particles, or genetic units, to the offspring. Now, these particles are called genes. Mendel saw that a gene can exist in different forms called alleles. Each individual receives one gene from each of its two parents regarding a particular trait-difference; and these genes do not influence one another in any way but separate uncontaminated at the time of formation of the reproductive cells. By counting carefully the number of progeny having a given phenotype, Mendel was able to make some important generalizations. With this hypothesis, one allele of the gene for seed color gives rise to yellow seeds, the other to green seeds. Moreover, one allele can be dominant over the other, recessive allele. In this case, yellow is dominant. Mendel showed this when he crossed a green seeded pea with a yellow seeded pea. All of the progeny in the first filial generation had yellow seeds. However, when these yellow peas were allowed to self-fertilize, some green seeded peas reappeared. The ratio of yellow to green seeds in the second filial generation was very close to 3:1. Mendel concluded that the green allele must have been preserved in the first filial generation, even though it did not affect the seed color of those peas. He explained that each parent plant carried two copies of the genes; namely, the parents were diploid, at least for the traits he was studying. According to this concept, homozygotes have two copies of the same allele, either two yellow alleles or two green alleles. Heterozygotes have one copy of each allele. The two parents in the first crossing above were homozygotes; the resulting hybrid peas were all heterozygotes. Further, Mendel reasoned that sex cells only contain one copy of the gene; namely, they are haploid. Homozygotes can therefore produce sex cells, or gametes, that have only one allele, but heterozygotes can produce gametes having either allele. This explains what happened in the crossings of yellow with green peas. The yellow parent contributed a yellow gamete; the green parent, a green gamete. Therefore, all the first filial peas obtained one yellow and one green allele. They had not lost the green allele at all, but since yellow is dominant, all the peas were yellow.

However, when these heterozygous peas were self-fertilized, they produced yellow and green gametes in equal numbers, and this allowed the green phenotype to reappear.

Mendel also revealed the principle which became known as Mendel's law of independent assortment: namely, each of the genes segregates from the other and pairs again in an independent fashion, thus giving rise to new combinations of traits. This law deals with two or more pairs of genes and discusses the behavior of genes or non-alleles at separate loci.

2.2. The Diversity of Mendelian Traits

After Mendel's work was rediscovered, it became clear that the simple Mendelian model did not adequately predict experimental observations in all situations. Mendel suggested that dominance was a general characteristic of traits, similar to the principles of segregation and independent assortment. However, shortly after 1900, several different patterns of dominance were documented. In 1905, William Bateson and others reported the occurrence of incomplete dominance, namely where the heterozygote is intermediate between the two homozygotes. They found experimentally that the so-called blue Andalusian variety of *Gallus domesticus* (really grey) is the heterozygote from a cross between a black and a white variety. Many instances of incomplete dominance were established soon afterwards, both in animals and in plants.

Genes may have more than two alleles. In diploid organisms, many different genotypes can exist when there are multiple alleles. In 1904, Lucien Cuenot obtained individuals with a black coat and others with a yellow coat from the breeding of different strains of albino mice (*Mus musculus*). On crossing each of these with the normal grey, he found that the black coat color was inherited as a Mendelian recessive and the yellow as a Mendelian dominant trait. Furthermore, from crosses involving both the genes for black and for yellow fur, he found that these genes behaved as alleles towards one another, with yellow dominant over black. Namely, the genes for yellow, grey and black fur formed a series of alleles. There are six possible genotypes with respect to three alleles, the three homozygotes and the alleles. One of the best-known examples of multiple alleles concerns the four human blood-groups, O, A, B and AB. These correspond to the presence or absence of two antigens, A and B, in the erythrocytes. There is a reciprocal relationship between the presence of antigens in the red cells, and of antibodies in the serum. Four blood-groups are inherited as Mendelian traits determined by three alleles A, B and O. Of the six genotypes, AA and AO are indistinguishable in phenotype and constitute blood group A, and similarly BB and BO are indistinguishable as group B. The hypothesis of more than one gene affecting a single trait, each with additive effects, has been found to explain data on the inheritance of many quantitative traits. There is no reason to suppose that the inheritance of quantitative traits showing a continuous range of variation differs in any fundamental way from that of qualitative traits which show Mendelian inheritance. Quantitative traits can be understood by partitioning the genetic, environmental, and genotype-environment effects. Some genes may be lethal. Pleiotropy occurs when one gene affects several traits. Some genotypes may not always have the same phenotype, a phenomenon resulting from incomplete penetrance or variable expressivity of genotype.

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Biographical Sketch

Hikoyuki. Yamaguchi graduated from the Faculty of Agriculture, University of Tokyo in 1953. In 1970 he became Professor of the Faculty of Agriculture, University of Tokyo. He was Visiting Professor of Radiation Genetics Studies, Sao Paulo State University in 1968 and 1980. He was Director of the Research Center of Nuclear Sciences and Technology, University of Tokyo from 1976 to 1978.