

STUDY OF MENDELIAN AND NON MENDELIAN INHERITANCE PATTERN

Chaudhari Sunil Shriram

Dept. Of Zoology, Cmj University, Shillong, Meghalaya

INTRODUCTION

Mendelian inheritance is a set of primary tenets relating to the transmission of hereditary characteristics from parent organisms to their children; it underlies much of genetics. They were initially derived from the work of Gregor Mendel published in 1865 and 1866 which was "re-discovered" in 1900 and were initially very controversial. When they were integrated with the chromosome theory of inheritance by Thomas Hunt Morgan in 1915, they became the core of classical genetics.

In breeding experiments between 1856 and 1865, Gregor Mendel first traced inheritance patterns of certain traits in pea plants and showed that they obeyed simple statistical rules. Although not all features show these patterns of Mendelian inheritance, his work acted as a proof that application of statistics to inheritance could be highly useful. Since that time many more complex forms of inheritance have been demonstrated.

From his statistical analysis Mendel defined a concept that he described as an allele, which was the fundamental unit of heredity. The term allele as Mendel used it [citation needed] is nearly synonymous with the term gene, and now means a specific variant of a particular gene.

MENDEL'S LAWS

The principles of heredity were written by the Augustinian monk Gregor Mendel in 1865. Mendel discovered that by crossing white flower and purple flower plants, the result was not a blend. Rather than being a mix of the two, the offspring was purple flowered. He then conceived the idea of heredity units, which he called "factors", one which is a recessive characteristic and the other dominant. Mendel said that factors, later called genes, normally occur in pairs in ordinary body cells, yet segregate during the formation of sex cells. Each member of the pair becomes part of the separate sex cell. The dominant gene, such as the purple flower in Mendel's plants, will hide the recessive gene, the white flower. After Mendel self-fertilized the F1 generation and obtained the 3:1 ratio, he correctly theorized that genes can be paired in three different ways for each trait; AA, aa, and Aa. The capital A represents the dominant factor and lowercase a represents the recessive. (The last combination listed above, Aa, will occur roughly twice as often as each of the other two, as it can be made in two different ways, Aa or aA.)

Mendel stated that each individual has two factors for each trait, one from each parent. The two factors may or may not contain the same information. If the two factors are identical, the individual is called homozygous for the trait. If the two factors have different information, the individual is called heterozygous. The alternative forms of a factor are called alleles. The genotype of an individual is made up of the many alleles it possesses. An individual's physical appearance, or phenotype, is determined by its alleles as well as by its environment. An individual possesses two alleles for each trait; one allele is given by the female parent and the other by the male parent. They are passed on when an individual matures and produces gametes: egg and sperm. When gametes form, the paired alleles separate randomly so that each gamete receives a copy of one of the two alleles. The presence of an allele doesn't promise that the trait will be expressed in the individual that possesses it. In heterozygous individuals the only allele that is expressed is the dominant. The recessive allele is present, but its expression is hidden.

Mendel summarized his findings in two laws: the **Law of Segregation** and the **Law of Independent Assortment**.

Law of Segregation (The "First Law")

The Law of Segregation states that when any individual produces gametes, the copies of a gene separate, so that each gamete receives only one copy. A gamete will receive one allele or the other. The direct proof of this was later found when the process of meiosis came to be known. In meiosis the paternal and maternal chromosomes get separated and the alleles with the characters are segregated into two different gametes.

Law of Independent Assortment (The "Second Law")

The Law of Independent Assortment, also known as "Inheritance Law", states that alleles of different genes assort independently of one another during gamete formation. While Mendel's experiments with mixing one trait always resulted in a 3:1 ratio between dominant and recessive phenotypes, his experiments with mixing two traits (dihybrid cross) showed 9:3:3:1 ratio. Mendel concluded that different traits are inherited independently of each other, so that there is no relation, for example, between a cat's color and tail length. This is actually only true for genes that are not linked to each other.

MENDELIAN TRAIT

A **Mendelian trait** is one that is controlled by a single locus and shows a simple Mendelian inheritance pattern. In such cases, a mutation in a single gene can cause a disease that is inherited according to Mendel's laws. Examples include sickle-cell anemia, Tay-Sachs disease, cystic fibrosis and xeroderma pigmentosa. A disease controlled by a single gene contrast with a multi-factorial disease, like arthritis, which is affected by several loci (and the environment) as well as those diseases inherited in a non-Mendelian fashion. The Mendelian Inheritance in Man database is a catalog of, among other things, genes in which Mendelian traits causes disease.

NON-MENDELIAN INHERITANCE

Non-Mendelian inheritance is a general term that refers to any pattern of inheritance in which traits do not segregate in accordance with Mendel's laws. These laws describe the inheritance of traits linked to single genes on chromosomes in the nucleus. In Mendelian inheritance, each parent contributes one of two possible alleles for a trait. If the genotypes of both parents in a genetic cross are known, Mendel's laws can be used to determine the distribution of phenotypes expected for the population of offspring. There are several situations in which the proportions of phenotypes observed in the progeny do not match the predicted values.

Although inheritance of traits in fungi, viruses, and bacteria are all non-Mendelian, the phrase "non-Mendelian inheritance" is usually only used to describe the exceptions which occur in eukaryotic reproduction.

Non-Mendelian inheritance plays a role in several disease processes.

METHODOLOGY

In humans, many genetic traits or diseases are classified simply as "dominant" or "recessive." Especially with respect to so-called recessive diseases, this can oversimplify the underlying molecular basis and lead to misunderstanding of the nature of dominance. For example, the genetic disease phenylketonuria (PKU) results from any of a large number (>60) of alleles at the gene locus for the enzyme phenylalanine hydroxylase (**PAH**). Many of these alleles produce little or no **PAH**, as a result of which the substrate phenylalanine and its metabolic byproducts accumulate in the central nervous system and can cause severe mental retardation if untreated.

The genotypes and phenotypic consequences of three alleles are shown in the following table.

Genotype	PAH activity	[phe] conc	PKU?
AA	100%	60 uM	No
AB	30%	120 uM	No
CC	5%	200 ~ 300 uM	Hyperphenylalanemia
BB	0.3%	600 ~ 2400 uM	Yes

In unaffected persons homozygous for a standard functional allele (AA), **PAH** activity is standard (100%), and the concentration of phenylalanine in the blood [**phe**] is about 60 uM. In untreated persons homozygous for one of the PKU alleles (BB), **PAH** activity is close to zero, [**phe**] ten to forty times standard, and the individual manifests PKU.

In the AB heterozygote, **PAH** activity is only 30% (not 50%) of standard, blood [**phe**] is elevated two-fold, and the person does not manifest PKU. Thus, the A allele is dominant to the B allele with respect to PKU, but the B allele is incompletely dominant to the A allele with respect to its molecular effect, determination of **PAH** activity level ($0.3\% < 30\% \ll 100\%$). Finally, the A allele is an incomplete dominant to B with respect to [**phe**], as $60 \mu\text{M} < 120 \mu\text{M} \ll 600 \mu\text{M}$. Note once more that it is irrelevant to the question of dominance that the recessive allele produces a more extreme [**phe**] phenotype.

For a third allele C, a CC homozygote produces a very small amount of **PAH** enzyme, which results in a somewhat elevated level of [**phe**] in the blood, a condition called hyperphenylalanemia, which does not result in mental retardation.

That is, the dominance relationships of any two alleles may vary according to which aspect of phenotype is under discussion. It is typically more useful to talk about the phenotypic consequences of the alleles involved in any genotype, rather than to try to force them into dominant and recessive categories.

SOCIETY AND CULTURE ETHICS

Huntington's disease, particularly the application of the genetic test for the disease, has raised several ethical issues. The issues for genetic testing include defining how mature an individual should be before being considered eligible for testing, ensuring the confidentiality of results, and whether companies should be allowed to use test results for decisions on employment, life insurance or other financial matters. There was controversy when Charles Davenport proposed in 1910 that compulsory sterilization and immigration control be used for people with certain diseases, including HD, as part of the eugenics movement. In vitro fertilization has some issues regarding its use of embryos. Some HD research has ethical issues due to its use of animal testing and embryonic stem cells.

The development of an accurate diagnostic test for Huntington's disease has caused social, legal, and ethical concerns over access to and use of a person's results. Many guidelines and testing procedures have strict procedures for disclosure and confidentiality to allow individuals to decide when and how to receive their results and also to whom the results are made available. Financial institutions and businesses are faced with the question of whether to use genetic test results when assessing an individual, such as for life insurance or employment. Some countries' organizations, such as the United Kingdom's insurance companies, have agreed not to use this information. As with other untreatable genetic conditions with a later onset, it is ethically questionable to perform pre-symptomatic testing on a child or adolescent as there would be no medical benefit for that individual.

There is consensus for only testing individuals who are considered cognitively mature, although there is a counterargument that parents have a right to make the decision on their child's behalf. With the lack of an effective treatment, testing a person under legal age who is not judged to be competent is considered unethical in most cases.

Prenatal genetic testing or preimplantation genetic diagnosis to ensure a child is not born with a given disease has some ethical concerns. For example, prenatal testing raises the issue of selective abortion, a choice considered unacceptable by some. Using preimplantation testing for HD requires twice as many embryos to be used for in vitro fertilisation, as half of them will be positive for HD. For a dominant disease there are also difficulties in situations in which a parent does not want to know his or her own diagnosis, as this would require parts of the process to be kept secret from the parent.

REFERENCES

1. Walker FO (2007). "Huntington's disease". *Lancet* **369** (9557): 218. doi:10.1016/S0140-6736(07)60111-1. PMID 17240289.
2. Brown (2002), Section 2, Chapter 6: 6.2. Assembly of a Contiguous DNA Sequence
3. Lodish et al. (2000), Chapter 7: 7.1. DNA Cloning with Plasmid Vectors
4. Davey Smith, G; Ebrahim (2003). "'Mendelian randomization': can genetic epidemiology contribute to understanding environmental determinants of disease?". *International journal of epidemiology* **32** (1): 1–22. doi:10.1093/ije/dyg070. PMID 12689998.
5. Wolf, YI; Rogozin; Grishin; Koonin (2002). "Genome trees and the tree of life.". *Trends in genetics: TIG* **18** (9): 472–9. doi:10.1016/S0168-9525(02)02744-0. PMID 12175808.
6. Gavrillets, S (2003). "Perspective: models of speciation: what have we learned in 40 years?". *Evolution; international journal of organic evolution* **57** (10): 2197– 215. doi:10.1554/02-727. PMID 14628909.
7. Myers RH (2004). "Huntington's disease genetics". *NeuroRx* **1** (2): 255–62. doi:10.1602/neurorx.1.2.255. PMID 15717026.
8. Subramaniam S, Sixt KM, Barrow R, Snyder SH (2009). "Rhes, a striatal specific protein, mediates mutant-huntingtin cytotoxicity". *Science* **324** (5932): 1327–30. doi:10.1126/science.1172871. PMID 19498170.
9. Cattaneo E, Zuccato C, Tartari M (2005). "Normal huntingtin function: an alternative approach to Huntington's disease". *Nat. Rev. Neurosci.* **6** (12): 919–30. doi:10.1038/nrn1806. PMID 16288298.
10. Wexler NS, Young AB, Tanzi RE, et al. (1987). "Homozygotes for Huntington's disease". *Nature* **326** (6109): 194–197. doi:10.1038/326194a0. PMID 2881213.