Using Mendel's Discoveries to Understand Simple Mendelian and Complex Genetic Disorders

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Abstract

This paper provides an overview of the concepts and application of Mendelian genetics relative to understanding and addressing contemporary genetics disorders. Mendel's studies are first introduced and then his major findings are applied to simple Mendelian disorders using the autosomal recessive disorder of sickle cell disease, including both the sickle-cell trait and sickle-cell anemia. This paper then relates simple Mendelian disorders to complex disorders, discussing their general relationships and how scientists are using these relationships to further understand complex disorders. For instance, scientists use tools such as genome-wide association studies to better understand the genetic basis of cancer, a complex disorder. This paper reveals how Mendel's findings have established a strong understanding of simple disorders that are now being used to investigate complex genetic disorders and develop treatments for them. These treatments are crucial to healthcare because complex disorders often affect many individuals and negatively affect their quality of life. By using established knowledge to create and improve treatments, researchers can help patients affected by complex disorders and improve the quality of life for these patients.

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Gregor Mendel's studies with pea plants in the 19th century discovered alleles, genotypes, phenotypes, Mendel's laws, and modes of inheritance [1, 2]. These concepts are the foundation of modern genetics.

Mendelian disorders are diseases related to specific defective genes. An example is sickle cell disease, a recessive disorder caused by the genetic makeup, or genotype, of aa (two recessive alleles). This disease creates sickled red blood cells' physical traits or phenotypes. Offspring can only get the disorder if both parents are affected (genotype aa) or are carriers (genotype Aa) [1]. The Law of Segregation states that a gene pair determining a trait separates and one allele (version of a gene) from each parent combines during reproduction [1, 2]. When two carrier parents are crossed in a Punnett square, a tool used to determine the probability of different offspring being produced during reproduction, the phenotype ratio is 3:1 (unaffected: diseased) and the genotype ratio is 1:2:1 (AA: Aa: aa) [1]. Both allele types possess an equal number, but there are higher chances that unaffected offspring or carriers of the disease will be produced. The Law of Dominance supports this by stating that a dominant allele (A) is expressed in homozygous and heterozygous states. The presence of one dominant allele is enough because it masks the effects of recessive alleles. The alleles in homozygous genotypes are the same (AA) and are different (Aa) in heterozygous genotypes [1, 2]. Because it is a recessive disorder, sickle cell anemia is thus not as commonly seen in pedigrees, tools used to map and track a particular disorder's frequencies in a family [3]. Sickle cell anemia can be treated by blood transfusions from unaffected donors with matching blood types, and may also be a target for gene therapy treatments soon.

Complex disorders such as cancer and heart disease are caused by a wider variety of factors than Mendelian disorders, but Mendelian disorder studies help develop tools to understand complex disorders [4]. 23% of genes related to a Mendelian disorder have at least one other connection with a complex disorder. In addition, Mendelian disorders often involve protein interactions and molecular mechanisms that are similar to complex disorders and can also mimic and foreshadow later-onset complex disorders [5]. The presence of one or more Mendelian disorder genotypes or phenotypes increases the risk of developing a complex disorder because of these relations. After being identified, Mendelian traits can reveal new pathways that cause disease, allowing scientists to visualize the genes potentially involved in complex disorders and how they interact [5]. By mapping complex disorder genes, scientists have found that each complex disorder is associated with a unique set of Mendelian conditions, allowing us to further understand the patterns of complex disorders [6]. Moreover, by using data collected from sequencing Mendelian disorders, scientists often find genes encoding proteins that are involved in complex disorders. Genome-wide sequencing of large samples can thus pinpoint genetic mutations and their effect on proteins that significantly impact disorder susceptibility in individuals [7]. Expanding on these connections, Mendelian animal models of rare disorders may allow for more understanding of complex disorder phenotypes. These models are thoroughly characterized, readily available, and often summarize the human disease phenotype. Because these animal models are simpler, they can better determine environmental factors causing complex disorders, compared to most complex disorder models. For example, a combined neurotoxin and genetic model for Parkinson's disease is being investigated as a promising animal model to provide insight into Parkinson's [5, 8]. Diseases such as cancer are currently treated with chemotherapy, radiation, or surgery. Heart disease is being treated surgically by unclogging blood vessels or diverting blood away from them. Enhanced treatments for diseases such as the ones mentioned above may be created from a better understanding of the basis of Mendelian and complex disorders, improving the quality of life for those affected by these disorders. This can be realized by applying animal models to complex disorders because the models can connect existing knowledge of disease genetics to environmental factors and toxicant susceptibility [8, 9].

Mendel's discoveries help scientists understand both Mendelian and complex disorders, allowing them to research and develop genetic treatments. His discoveries also help genetic counselors inform parents of the probability their children may receive a disease if the parents are affected or carriers for the disease. The study of disorders using Mendel's findings could allow scientists to determine the genes causing disorders, allowing them to provide gene therapy by using viral vectors to transmit normal copies of genes to patients. Nevertheless, scientists must exercise caution when applying Mendel's discoveries to genetic engineering, and adhere to regulations to prevent any possible negative side effects of genetic engineering.

Mendel's discoveries answered important questions related to inheritance and laid the groundwork for future advancements in genetics, making them one of the most important findings in biology to date.

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