

The Study of Genetics: A Historical Perspective

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Abstract

The history of genetics began in the mid 19th century by a scientist named Gregor Mendel who determined the common ratios found in allelic frequencies of monohybrid crosses, and came up with several laws pertaining to inheritance, notably the law of segregation. His original 1866 publication 'Experiments on plant hybridization' did not receive much attention until the early 20th century when it was allegedly rediscovered by three scientists: Hugo de Vries, Carl Correns, and Erik Von Tschermak. From this re-discovery arose the birth of modern genetics, which was studied by pioneers like William Bateson (who expanded upon Mendel's law of segregation), R.C. Punnett (who famously created the template of the Punnett square), and Wilhelm Weinberg (who developed the Hardy-Weinberg equation). Unfortunately, the development of modern genetics introduced a number of controversies and political movements such as the anti-Mendel view on science that prevailed in the USSR known as 'Lysenkoism', and the widespread movement of eugenics during the mid 20th century. Despite the political complications involved with genetics, researchers such as Oswald Avery made new steps towards the mechanism and structure of DNA. In 1951 James Watson and Francis Crick came up with the double helix model of DNA with major contributions from Rosalind Franklin and Linus Pauling.

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Introduction

Genetics is the study of how life is carried through time. It investigates how the wide diversity of organisms can be simplified into long strands of four-letter code, and how this code is translated into twenty words. Gregor Mendel (1822-1884), a friar born into a poor Austrian family, is often considered the father of modern genetics, but his great research on conspecific hybridization was not truly appreciated at the time. Though his original publication, *Experiments on plant hybridization*, was published 1866 after tirelessly cross pollinating the common pea, it was not recognized as a ground breaking piece of evidence for genetics until the early 20th century (Mendel 1909). The branches of science that grew out of his rediscovery make up the fundamental pillars of modern genetics.

Mendel: The Father of Genetics

Born into an underprivileged Austrian family, Mendel had little prospects for becoming prosperous as he had little to no academic promise. Yet, through a series of lucky events

he managed to escape the life of his predecessors, eventually becoming an esteemed scientist. Though he failed many of his exams in college at first, Mendel became invested in religious studies and natural philosophy, until he eventually became an abbot at St. Thomas's Abbey in Brno of the Czech Republic (Mawer 2006). Later he both studied and taught physics at the University of Vienna under the supervision of the abbot C.F. Napp, who became a key role model for the rest of life (Willis 2014). Napp, along with a number of other friars and abbots at St. Thomas had a keen interest in heredity, which is where Mendel's obsession with inheritance began. It was in the Monastery at St. Thomas, under Napp's supervision, that the pea hybridization experiments took place within two hectares of land (Willis 2014).

Considering the scientific landscape of the mid-19th century that Mendel did his work, it is perhaps not surprising that his colleagues and friends could not make much of his paper *Experiments on plant hybridization* originally published in 1866; as it was too far ahead of their time. In his famous experiments, he categorized peas

into various traits based on appearance, for example, the colour of a pea plant could be either yellow or green (Mendel 1909). Given this example, Mendel found that by cross-pollinating a green pea plant with a yellow pea plant, a quarter of the offspring would be green and three quarters would yellow (on average). From this he deemed the yellow pea as a 'dominant' trait (A) and the green as a 'recessive' (a), which could be denoted algebraically to show what was occurring. He realized that each plant must have two traits, one inherited from each parent (Mawer 2006). By crossing Aa with Aa we would achieve three different variations: AA (25%), Aa (50%), and aa (25%). In addition to this, he found that by combining multiple trait pairs (i.e. AaBBCcDd.. etc) the number of possible variants would increase dramatically, such that for the seven trait pairs he worked with you could achieve 128 different combinations (Mendel 1909). Mendel also reasoned that in order for such crossing to occur, the pairs of traits (later called alleles) would need to separate from each other and be recombined during fertilization in order to make new combinations, a principle he called the law of segregation. What Mendel had discovered was the most basic mechanism of inheritance and genetic variation, though he had no way of knowing how it actually worked, since the concept of a gene or an allele would not be realized to exist until much later. For this reason, it is thought that people did not truly grasp what Mendel had explained, and his work soon became overshadowed by Darwin's theory concerning the origin of species (Mawer, 2006). Mendel spent a good portion of the rest of his life retrying his experiment with other species like hawkweed, as species similar to dandelions which are nearly impossible to control in terms of pollination, a project he later abandoned to focus on becoming an abbot until his death (Mawer 2006).

The Re-discovery

For many years, Mendel was forgotten. It wasn't until the early 20th century that his work was rather accidentally discovered by Hugo de Vries after observing the same 3:1 ratio in his own poppy breeding experiment without knowing it had already been realized almost 40 years before (Berkel et al. 1999). Though this was an unfortunate setback in his academic career, de Vries was able to confirm Mendel's notion that the law of segregation was analogous among many organisms, proving its existence in about 15 different species hybrid crossings (Magner 2002). A number of other botanists had similar experiences, slowly announcing the relevance of Mendel to the scientific world. Among them were Carl Correns (1864-1935) and Erik Von Tschermak (1872-1965) who discovered the 3:1 ratio of inheritance around the

same time that de Vries' experimental data was revealed to be seemingly copied from Mendel's original publication. Similar to de Vries, they claimed that they had come to their conclusions about inheritance ratio patterns and trait pair segregation prior to their knowledge of Mendel, though it is impossible to know how truthful this statement is. In a moderately competitive struggle, the three scientists vetoed any credit for Mendel's work, and claimed themselves to each be responsible for the re-discovery of Mendel's laws. Some critics believe, however, that Tschermak did not fully understand the principles of heredity to the same ability as de Vries and Correns, since his contributions to the alleged rediscovery were minute compared to his colleagues (Magner 2002).

Upon realizing the potential of Mendel's laws, a new field of science developed concerning the principles behind heredity and the transfer of allelic information. Great minds like William Bateson and R.C. Punnett, who developed the Punnett square, to visualize inheritance of traits, promoted Mendelism throughout their lives (Mawer 2008). Bateson came up with the idea of an allelomorph, or more simply written 'allele', which defined the expression of a gene pair (like Aa or AA) and looked significantly into Mendel's Law of Segregation: Gene pairs segregate during gamete production (Bateson and Bateson 1928). Confusingly, Bateson found this segregation to occur not only in germline cells but also occasionally in somatic cells, something Mendel would never have foreseen in his pea experiments (Bateson and Mendel 1915). In an attempt to perhaps find an all-encompassing view of evolutionary inheritance, Bateson also travelled the world in search of correlations between different environments and the variance of phenotypic traits, though he found nothing particularly groundbreaking and eventually abandoned his long journey (Magner 2002).

It was also around this time that Mendel's laws were being considered in the light of evolution. Wilhelm Weinberg (1862-1937), a German geneticist developed a simple formula to calculate the expected frequencies of dominant and recessive alleles in a population, which he deduced from studies he had conducted on twins (Province 2001). The famous equation was formulated again about six months later by another scientist named Godfrey Harold Hardy (1877-1947) who had not yet read Weinberg's publications. Note that prior to advances in global communication it was not uncommon for different individuals to come to the same scientific conclusion around the same time. Nevertheless, both scientists received credit for the derivation, which is now known as the Hardy-Weinberg equation:

$$p^2 + 2pq + q^2 = 1$$

where p and q are the allelic frequencies for two allele types in a population, assuming there is no evolution. The beauty of this equation is that it can be easily used to determine if (and how drastically) a population is undergoing evolution, by comparing the actual allelic frequencies to their expected Hardy-Weinberg (HW) equilibrium values. In reality, it is very rarely the case that HW equilibrium is actually occurring because it requires the control of certain environmental parameters like species interactions, which is generally impossible outside the lab (Province 2001).

Inspired by Hugo de Vries, another important figure named Thomas Hunt Morgan (1866-1945) began working on breeding experiments with the species *Drosophila melanogaster*, otherwise known as common fruit fly (Magner 2002). As a species of fly that breeds rapidly, mates regularly, and expresses a number of visible phenotypic traits, it is the ideal animal for hybridization. In his experiment, Morgan discovered a novel trait (white eyes) that did not appear until the second generation of an initial cross between a mutant male (white eye) and a normal female (red eye). More importantly, the white eye trait was seen considerably more often in males than females. Through the application of Mendelian ratios and Punnett squares, he found that the ratios could only be explained if the traits were somehow linked to the sex chromosomes, in particular the X chromosome. Since males have one X chromosome and one Y chromosome, if the white eye trait was present in their mother's genetic code they would have a 50% chance of expressing the white eye trait (Figure 1). This was the first case of alleles being connected to the sex chromosomes, and for this discovery, Morgan received the Nobel Prize in 1933. In later years, the geneticist Hermann Joseph Muller (1890-

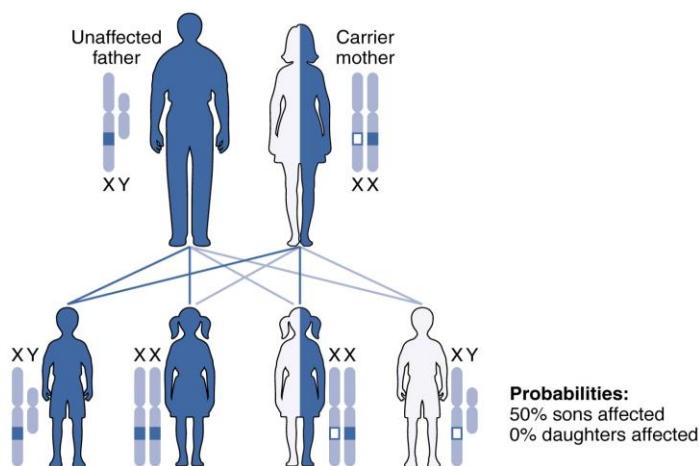


Figure 1: An X-linked recessive allele cross between an unaffected father and a carrier mother. This human cross is analogous to Morgan's original cross with *Drosophila melanogaster* (OpenStax College 2013).

1967) used ionizing radiation on *Drosophila* to induce hundreds upon hundreds of mutations in their genome, which persisted through many generations in the lab (Magner 2002).

The Rise of Political Empowerment

As genetics grew as a science, the general public became interested in its many prospects. Unfortunately, it is from this public interest that a number of negative perspectives emerged from the abuse of Mendel's concepts. Prior to turn of the century, a natural historian named Sir Francis Galton (1822-1911) created the concept of eugenics, which was unfortunately amplified by Mendel's rediscovery in 1900 (Kühl 2014). Galton distorted Mendel's idea of inheritance into the perception that traits like intelligence could be kept within a genetic lineage by sterilizing, segregating, or even executing individuals that were considered to have 'low quality' genes. He encouraged healthy families to reproduce more often and poor, unhealthy families to not reproduce at all (Kühl 2014). This concept was eventually associated into a number of political movements across the world including Canada, notably the Sexual Sterilization Act of Alberta in 1928 (Stahnisch 2014). This act gave permission to the Board of Eugenics to sterilize individuals they viewed as inadequate for the human population, generally targeting people who lived near the poverty line or those with mental illness. Up until the act was repealed 44 years later, around 4,700 Albertans were chosen to undergo sterilization by the Board (Stahnisch 2014). The politically dominated world during WWII also brought a significant increase in the prevalence of eugenics practice, particularly in Nazi Germany. After the war, the Genocide Convention was implemented globally to establish ethical law against certain means of eugenics (Quigley 2013). This was also an important worldwide movement for the implementation of equity between different races and cultures, which emerged in the 1970s, since that scientists with racist agendas were often compared with the Nazi eugenics movement (Kühl 2014). Many eugenics boards like the Sexual Sterilization Act of Alberta were removed for this reason (Stahnisch 2014).

In contrast to the eugenics movement, another view on Mendelism emerged that caused unrest in another way. In Soviet Russia in the late 1930's, a scientific movement known as Lysenkoism predominated as the norm for all scientific thought related to horticulture or heredity. Stemming from the out-dated ideas put forth by Lamarck in the 19th century, the movement rejected all statements related to Mendelian inheritance and Darwinian selection (Levins and Lewontin 1985). Lysenkoism was originally put

forward by Trofim Lysenko (1890-1976), an agriculturalist who believed that different types of grain could be transformed into one another (rye into wheat for example). This idea was only considered fact for 30 years, as societies views on genetics advanced. Notable supporters of the movement included Joseph Stalin who sentenced thousands of scientists to death, based on their apparent opposition towards Lysenko's ideas, and rejected important agricultural research that likely would have helped the widespread famine in the last few decades of the (Union of Soviet Socialist Republics) USSR. It was not until 1960 until the movement was reconsidered and the ban against Mendelism was removed (Levins and Lewontin 1985).

The Discovery of DNA

Despite the atrocities that occurred when combining scientific notions with politics, scientists continued to objectively determine the material inside the cells that passed hereditary information. Earlier in the 20th century, prior to the predominance of Lysenkoism, Russian biochemist Phoebus Levene (1863-1940), an esteemed scientist that produced over 700 publications made the initial steps towards discovering the components of genetic material. He is credited for discovering the carbohydrate component of both DNA and RNA and how their components are connected, as well as the structure of nucleotides in 1919 (Ray 2008). Later on, Oswald Avery (1877-1955) devised an ingenious experiment to find out that it was DNA that carried the vital information needed for protein expression in the next generation of cells (O'Connor 2008). Using strains of *Streptococcus pneumoniae*, the most common cause for pneumonia at the time, Avery heated the bacteria with a virulent strain of DNA until all that was left was their genetic material. He then applied a number of enzymes including proteases (protein digesting enzymes), RNases (RNA digesting enzymes) and finally DNases to the mixture, and then added a colony of non-virulent bacteria. The results suggested that only in the test where the DNase was added did the colony *not* express any virulent cells. This is because normally, bacterial cells such as *S. pneumoniae* will take up DNA drifting around their cell and incorporate it into their genome, but with an enzyme that degraded all of the virulent DNA this did not occur (O'Connor 2008). After reading the original 1944 publication of Avery's experiment, another scientist named Erwin Chargaff (1905-2002) was inspired to create an institute dedicated to nucleotide chemistry. Through tireless research, he eventually came to the conclusion that nucleotides matched up predictably along a chain of DNA: adenine always bonded to thymine and cytosine always bonded to

guanine. He also was one of the first geneticists to realize that the order of such nucleotides varies depending on the species of organism (Ray 2008).

With these discoveries, the stage was set for the final observation that would lead to an understanding of DNA structure. In 1951, Francis Crick and his colleague James Watson came up with a model for the structure of DNA (Deoxyribonucleic acid) based off of X-ray diffraction images. This revealed the now well-known structure: the double helix (Ray 2008) (Figure 2). It is important to note, however, that it was Rosalind Franklin and Maurice Wilkins who worked with X-ray crystallography, and that Watson and Crick merely used their photos for the construction of their famous model. Additionally, an American biochemist Linus Pauling made crucial measurements in the study of molecular bond angles that

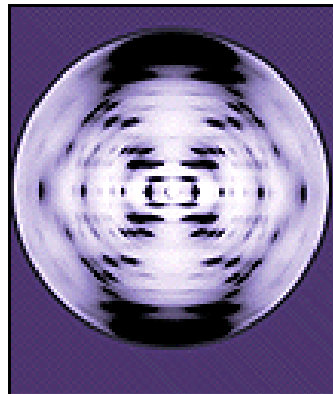


Figure 2: The x-ray diffraction pattern of DNA observed by Rosalind Franklin, indicating the double helix structure (National Institute of Health 2008).

were used by Watson and Crick (Ray 2008). Unfortunately for Pauling, his calculations led him to come up with another model for DNA structure that turned out to be false, but even so, many people believe that Pauling, Franklin, Wilkins and even Chargaff should be credited for the discovery of DNA in addition to Watson and Crick (Ray 2008). Aside from credentials, this would become one of the most important models in the

history of science, providing a physical structure to the material that transcends through generations.

Conclusion

It is thought that all modern genetics is in one way or another, an extension of Mendel's famous observations. The advancements made in the past century on the science of heredity is truly staggering, going from a general idea of how traits are inherited to the discovery and understanding of both the structure and function of DNA. Perhaps one day, when coding the genome of an organism becomes as easy as using fingerprint scanner, scientists will still look back with admiration at the friar who started it all, tending his peas in the monastery garden.

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Picture Credits

Figure 1: *[X-linked Recessive Inheritance]* [Wikimedia Commons] [OpenStax College] [2013]

Figure 2: *[Xray DNA]* [Wikimedia Commons] [National Institute of Health] [2008]