A Brief History of Genetics

A Brief History of Genetics

By

Chris Rider

Cambridge Scholars Publishing

A Brief History of Genetics

By Chris Rider

This book first published 2020

Cambridge Scholars Publishing

Lady Stephenson Library, Newcastle upon Tyne, NE6 2PA, UK

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

ISBN (10): 1-5275-5885-1
ISBN (13): 978-1-5275-5885-4

Cover
A cartoon of the double-stranded helix structure of DNA overlies the sequence of the gene encoding the A protein chain of human haemoglobin. Top left is a portrait of Gregor Mendel, the founding father of genetics, and bottom right is a portrait of Thomas Hunt Morgan, the first winner of a Nobel Prize for genetics.

To my wife
for her many years of love, support, patience and sound advice

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TEXT BOXES AND TABLES

FOREWORD

Genetics, the science of biological inheritance, has made extraordinary progress since its simple beginnings in the 1850s. It all started in a Czech monastery garden as the lone studies of a monk, Gregor Mendel. Mendel's pivotal work was at the time largely ignored, and was almost lost to science. Yet eventually his pioneering work led to scientific and technological developments at an ever-increasing pace. Today genetics is a powerful science, with its crowning glory being the total unravelling and decoding of the entire human genome. Never before has genetics had the capability to impact so broadly and incisively on our society and our way of life. It has provided a new means of establishing guilt and innocence in criminal prosecutions, it is central in building a better understanding of both infectious and inherited diseases, as well as cancer. Genetics has also enabled approaches for the medical treatment of a very wide range of diseases. Finally it offers prospects for new developments in food production. However all of these advances have their potential limitations and drawbacks.

Yet ordinary citizens, unless they have a background in biological science, can have little grasp of what genetics can and cannot achieve. How then can they engage with this remarkable progress? Also how can they contribute to any debate on the extent to which approaches such as the genetic modification of our food and genetic engineering in medicine should be allowed, if they lack any understanding of how this has been achieved and what the possible outcomes and drawbacks are? Although the words such as 'gene' and 'DNA' crop up increasingly in common parlance, they usually do so without any fundamental grasp of what they really mean.

This book is aimed at the lay reader and is an attempt to bridge the considerable and increasing gap between the knowledge and understanding of the general population, and the forefront of this fast-moving science. It is not a textbook and therefore does not need to cover a particular syllabus. Moreover, it does not attempt to provide a comprehensive coverage of the entire field of genetics. This has therefore left me free to choose those particular topics which I find interesting and I trust will prove informative.

My aim is to improve the understanding of the how the science of genetics has developed. This requires more than merely skating across the surface of the subject. But to those with a limited background, science can

sometimes be seen as being difficult. One reason for this is an abundance of scientific terminology, which to many is in effect a foreign language. An example of this, which emerges near the start of the book, is the term 'ovum' meaning the unfertilised female sex cell or egg. So why not just use the word 'egg'? The reason is that this word, whether referring to a human egg or a bird's egg, is used loosely to cover both the unfertilised female sex cell, and the fertilised first cell of the new individual. But genetically these two are very different from each other. The unfertilised female cell contains only half of the genes of the potential mother, whereas after fertilisation has taken place, the first cell of the new individual contains a full set of genes, half from the mother and half from the father. So the scientific term 'ovum' is used because it has a necessarily precise meaning, referring only to the unfertilised cell. Fortunately the word 'ovum' is at least a short one: much scientific terminology is more lengthy. Despite this, it is required and employed to cover precise meanings not readily conveyed in everyday language. I would encourage the reader not to be put off or discomforted by such terminology. I have provided an extensive glossary at the back of this book providing definitions of the scientific terms used here. It is also helpful to realise that in biology, as in the other sciences, there is always a certain logicality and rationality involved in the invention and adoption of the scientific terms now employed. But sometimes the original thinking behind the introduction of particular terminology may now have been obscured by the progress in scientific knowledge and understanding which has occurred since these terms came into usage.

My intention with this book is that it is not necessary for every reader to have a total and complete grasp of all the content I present here in order to make headway. I do hope however that it proves informative and fascinating, after all we are all made according to our genes.

Chris Rider
June 2020

ACKNOWLEDGEMENTS

I thank my immediate family for their encouragement, support and advice in writing this book. A number of friends have read early drafts, providing guidance and helping me to eliminate errors. Any of these which might remain are solely my responsibility. Finally, I am indebted to my teachers, colleagues and students over the years who have taught me so much.

CHAPTER 1

THE BEGINNINGS OF GENETICS: GREGOR MENDEL (1822-1884)

General Background

A major and essential property of all life is that key biological characteristics, or traits, are passed down successively through the generations, from parents to offspring. We can readily see this is the case for complex species, such as we humans and the animals, birds and plants, but it is also true in simpler organisms, such as bacteria and viruses. But how does this biological inheritance work? In higher organisms, each new individual animal, bird or plant contains millions or even trillions of different individual cells. Yet it starts its existence as a single egg or seed that has been fertilised by a single sperm or pollen grain. How can the biological traits of both the male and female adult parents be transferred into this first single cell? From there, how do these inherited characteristics emerge in the new individual as its complex body structure develops? How are inherited traits passed in this way unchanged across multiple generations?

Deep down we all believe in the power of biological inheritance. Innate in all of us is a belief that the biological characteristics of living things, whether plant or animal, are passed down from generation to generation. For instance, when visiting a zoo, we have every expectation that a baby elephant will have the trunk, grey skin colour, big floppy ears and other features of its mother and father. The same applies to other species and their traits, such as the long neck of the giraffe. Even within our own families it is second nature to scrutinise the faces of the young, or the photos of past generations, looking for features that have been passed down the family tree and which we can ascribe as coming from one ancestor or another, resulting in comments such as ‘Oh look, he’s got his mother’s nose’ or, ‘she has her grandfather’s eyes’. This is not restricted to humans and animals, but also applies just as well in plants. A gardener or farmer planting seeds fully expects that when the resulting plants have grown, they will closely resemble those of the seed stock variety.

This deeply embedded and ancient wisdom in the power of inheritance of biological characteristics has been exploited across the centuries. In many different human societies, selective breeding has been used to maintain and enhance desired inherited characteristics in many domesticated species. The ancient practice of breeding horses for speed is generally attributed as having starting in Arabia, but is now worldwide. This selective breeding not only continues today, but has grown and developed into the vast horse livestock trade for the breeding of racehorses. This industry now attracts huge financial resources from investors who fully anticipate a worthwhile return. In bygone eras other breeds of horse were developed by selective breeding throughout Europe and Asia to enhance their strength and stamina so they could be worked to haul carts and ploughs. Through careful evaluation of the available breeding stock, the animals with the desired traits were chosen for mating, and in turn their offspring were selectively mated. Through this careful but completely unscientific process, slowly over the generations, the desired traits in the various breeds of horse have been enhanced.

In a similar way, there are now a considerable number of dog breeds, which have been bred as working animals to carry out specific tasks, or as companion dogs to suit various fashions down the eras. The fundamental expectation underlying all of this selective animal breeding is that their characteristics will be maintained down the blood line.

Not only have animal breeds been developed in many livestock and companion species, but the equivalent breeding practices have been carried out in domesticated birds such as pigeons and poultry. Likewise in horticulture the yield of crops and their resistance to disease has also been improved by selective breeding down the centuries. Moreover, innumerable varieties of garden plants have been bred for their colour, shape and scent. Behind all these myriad breeding activities is a certainty in the power of inheritance across all living organisms.

Across the centuries many great minds have sought to explain biological inheritance. Philosophers from at least the time of ancient Greece had pondered such questions, but no real headway in understanding any of this was made until the late 19th century. Even then, the great thinkers of biology, including Charles Darwin, made no useful progress in this subject, key though it was to his theory of evolution. His understanding was of gradual change in the species over long periods of time as they adapt to environmental changes, but this is to be set against an overall background in which the biological characteristics are otherwise constant and unchanging.

It is an old cliché that a particular scientific discipline has a 'founding father'. Usually this is not a very appropriate statement, as most major scientific developments, even in their initial stages, result from the work of a number of scientists, whether working co-operatively or in competition with each other. But in the case of the science of inheritance, which is called genetics, there is indeed an indisputable founding father. This was a man who worked alone and single-handedly developed an original field of scientific research which went on to became the foundation of the science of genetics. He is a lone figure, not because he was reclusive: he corresponded with an eminent botanist of his day, and was active in his local scientific society. Rather his scientific isolation arose because he adopted such thorough and far-sighted planning in his experimental work. Most notably he also adopted a rigorous numerical approach in the interpretation of his results. Because of this, none of his contemporaries could properly appreciate what he was doing and what he achieved. Being so far ahead of his time, other scientists of his day were fundamentally unable to keep up with his thinking. Indeed his work at the time of its publication attracted no attention from the major scientific circles, and it was nearly lost to science until it was re-discovered over 30 years later, and after his death. This remarkable scientist was an Augustinian monk, Gregor Mendel, whose portrait photograph is shown below in Fig. 1-1).

Mendel was born in 1822 in a village now named Hyncice which at that time was part of Austrian Silesia, but which as a result of multiple border changes during 20th century conflicts, now lies within the Czech Republic. His family were local ethnic Germans, his father being a small-scale peasant farmer. The boy Mendel was actually baptised as Johann. Through his father's work he would have become familiar with the importance of selective breeding in agriculture. Furthermore it is thought that the father introduced his son to plant grafting. This horticultural practice, widespread then as it remains today, is used to combine the favourable traits of two different strains or species of perennial agricultural crops, such as fruit trees and grape vines. In plant grafting, the root system from a robust and disease-resistant variety is attached to a stem and branches from a different variety with optimal fruit yield and quality. This is done by simply chopping through the stems of both plants and tightly binding the root stock of the one to the upper portion of the other. This technique is highly successful in many horticultural plants. Indeed it is a practice which was responsible for preserving European grape vines from a fungal disease which severely affected their roots and would otherwise have wiped out European vineyards. European wine production was saved by grafting its vines on to resistant American root stocks.

Fig. 1-1. Gregor Mendel, the founding father of genetics.

How fascinating it must have been for a boy with a sharp analytical mind to watch his father's grafted trees grow; the combined parts from two distinct individuals growing as one. It surely cannot have escaped his attention that the flowers and fruits on the grafted trees showed no dilution of the characteristics of the donor of the upper part of the graft, despite them growing on the roots of a different variety. Even such intimate contact with the different root stock did not result in any kind of change in the fruit and flower characteristics which had been inherited from the donor variety of the stem and branches.

The young Mendel showed exceptional progress in his education, initially in the local village school which had been established by his uncle, and later in senior schools in nearby towns. One of his senior school teachers was an Augustinian monk, who taught physics. Under his teacher's influence, and mostly likely with a desire to continue his education, Mendel entered the Augustinian monastery of St. Thomas, the Königskloster (King's cloister) in Brno, being ordained in 1847. Here he now took the religious name of Gregor, by which we know him today. He was released from much of his religious duties so that he could continue his education. In 1851 he was sent to the University of Vienna to study physics, mathematics and natural sciences. The country boy was now resident in a capital city and studying at a top university. Before the end of 1853 he was

back in Brno, now an inspiring teacher, mostly of physics. He was supported by the monastery in his considerable agricultural and scientific pursuits, keeping hives of different bee populations and growing varieties of plants in the walled garden. On top of this he kept meteorological observations and recorded sunspot activity, being one of many at that time who were attempting to forge a link between solar events and the weather. His research activities and his possible opportunities to promote his discoveries and enhance his scientific reputation, were cut short by his election to the position of abbot in 1868. He also held the presidency of the local scientific society and was appointed as chairman of a local bank. Clearly his meticulous and analytical mind had been recognised outside religious circles. As abbot he became heavily embroiled in a tussle with the government in 1872, over a new tax on religious houses, a fight which during his lifetime he appeared to be losing. He died from chronic kidney disease, a frustrated and embittered man in January 1884, not yet 62.

Out of all his various scientific activities, it is his studies of plant breeding and the inheritance of traits for which he is now so well known. His key experimental work was to grow and cross-breed varieties of pea plants, which he did within the monastery gardens. A major reason that he succeeded in unravelling the mysteries of genetics where others had failed was his very careful attention to detail in the design of his experiments. He had studied the plant breeding investigations of earlier scientists and had come to the conclusion that their progress could be improved upon by more thorough investigation, and that greater care of experimental details would lead to new revelations. A very basic, but fundamentally essential point about his research, is that he selected inherited traits or characteristics which appear with simple ‘either/or’ distributions in the population. He chose several pairs of such variant characteristics:-

Seed shape	round	*versus*	wrinkled
Seed colour	yellow	*versus*	green
Seed coat colour	white	*versus*	grey/brown
Seed pod shape	smooth arch	*versus*	deeply constricted
Seed pod colour	green	*versus*	yellow
Flower position on stem	along length of stem	*versus*	clustered at top
Stem length	long	*versus*	dwarf

The important point here is that an individual plant shows either one of the alternative traits or the other: there are no ‘halfway houses’ between the two alternatives. The alternative pea seed shape characteristics are illustrated below in Fig. 1-2.

Fig. 1-2 Alternative pea seed shapes. Top, wrinkled seeds; bottom, smooth seeds. Pea seed shape shows discontinuous variation, in that a seed is either wrinkled or smooth.

This type of variation within a population is known as ‘discontinuous variation’ and is found in all species. For instance, within the human A,B,O blood type system, there are four types: group A, group B, group AB or group O. Only these four types are possible, and there are no intermediates between them. By contrast, many perhaps more obvious biological characteristics, such as body height and skin colour, show instead continuous variation, in that between the extremes there is a continuous spectrum of the property across the population. Not only are intermediates or average values found, they are in fact usually much more abundant than the extreme values. Inheritance is still at work here, just in complex ways which even today are difficult to disentangle scientifically. Mendel was sufficiently astute to stick to the simple case of discontinuous variation.

Another key preparative element in Mendel’s work was that he used pure breeding plant varieties, that is all their offspring were identical for the chosen trait. He may well have bought his seeds from local merchants as being pure-breeding but it seems unlikely that, as such a meticulous researcher, he did not check this for himself by generating his own seeds from them over at least one plant generation. Since pea plants seed only once each year, each generation adds a year to the length of the study.

However it was essential that the breeding lines he used were pure and uncontaminated with other traits.

Incisive scientific research requires thorough planning and meticulous foresight, so that experiments are designed to avoid potentially confounding influences. Mendel selected pea plants as his chosen plant for study because he knew that he could manually pollinate the plants with a high success rate, and that the shape of the flower minimises the chance of pollination from wind-blown pollen. He adopted the further measure of growing some plants in greenhouses to prevent this, and also to keep out pollinating insects. He also knew that he could prevent the plants from fertilising themselves. In general self-fertilisation is a common strategy in plants to avoid complete reproductive failure. Many plant species will pollinate themselves should they not be fertilised by pollen from a different individual, carried by the wind or visiting insects. Clearly any plants produced from self-pollination would be genetically identical to the parent plant, and would not be the cross-breeds which Mendel wished to produce and study.

A very big factor in Mendel's success was the application of numbers to analyse experimental results. This was no doubt due to his background in physics, but it was uncommon at the time within the biological sciences. He studied not just the qualities of the plants produced in his cross-breeding studies, but also the quantities in which they were produced. He cross-pollinated large numbers of plants to obtain sufficient progeny in order that his mathematical analysis of his results would be reliable.

In his first set of experiments, Mendel cross-bred his sets of pure-breeding variants. For instance he crossed plants with smooth seeds with those having wrinkled seeds. He also crossed plants with yellow seeds with those having green seed plants. He found in each case that the progeny had only one of the two characteristics of the two parents. Thus, in the cross-fertilisation of round with wrinkled seeded plants, all the progeny in this first generation of offspring plants had round seeds, and none had wrinkled seeds. In the cross-breeding of yellow and green seeded plants, all the resulting progeny had yellow seeds, and none had green seeds, and so on. He called the trait which had survived in the cross-breeding, rather obviously, the ***dominant*** one. The trait which had apparently disappeared he called the ***recessive*** one. Clearly at this stage all of the recessive inheritance appears to have been wiped out by the dominant inheritance.

Perhaps a lesser scientist might have been happy to call it a day, having reached this outcome. But Mendel must have wondered why, if a trait is recessive in this way, it had not been swamped out long ago by the dominant trait in the previous generations of the plants. How were recessive characteristics still surviving through the innumerable past generations?

Mendel's real progress was made when he took these apparently uniform first generation of progeny and cross-bred between them in turn, to generate a second generation of offspring.

In the second generation he saw that the recessive characteristic re-emerged, but only in a minority of the individual plants. The majority of this second generation showed the dominant trait. When Mendel examined the numbers, regardless of the particular pair of traits he studied, he found there was always almost exactly a ratio of 3:1 of dominant to recessive. (Actually Mendel's figures have been questioned as to whether they are in fact too good to be true).

So how can Mendel's observations over the two generations be explained? Mendel's simple but compelling explanation is arguably the greatest and most original element of his achievements. Mendel proposed that the inheritance of the traits he studied were due to discrete and undilutable elements, which we now call genes. Each gene governs a single trait and they exist in alternative forms. Some of these are dominant to others, which are therefore seen to be recessive. The dominant form of the gene can be represented by a capital ***A***, and the recessive one represented by a lower case ***a***. So for the characteristics he studied, as listed above, ***A*** will represent the element of inheritance giving rise to the round seeds, or yellow seeds, and so on. By contrast the recessive trait, that is wrinkled seeds, and green seeds, *etc.* will be represented by the lowercase ***a***.

As laid out graphically in the top part of Fig. 1-3, each plant receives two doses of each gene, one from each parent. Thus pure breeding plants of the dominant trait will be ***AA***. When their flowers produce female ova, the unfertilised seed, or male pollen, these will carry only a single dose, but this can only be a single dose, ***A***. On the other hand, plants breeding pure for the recessive trait must be ***aa***, because even a single dose of ***A***, the dominant form would give rise to the appearance of the dominant characteristic. Therefore the ova and pollen of this recessive strain can only be ***a***. This means that in Mendel's first cross-bred generation, where ***A*** pollen from the dominant strain fertilised ***a*** ova from the recessive strain, or when ***A*** ova were fertilised by ***a*** pollen, the result could only be the hybrid condition, ***Aa***, that is plants with one copy of each of the inherited forms. Since the single copy of the recessive ***a*** form has no effect in the presence of the dominant ***A*** trait, the plants can only show the dominant characteristic. However although its effect is not apparent, in these hybrid plants the ***a*** trait still exists. It has neither been lost nor diluted, just masked by the dominant ***A***. So when these ***Aa*** plants in turn mature and produce their ova, these will have either a single ***A*** or ***a***, in a 50:50, equal ratio. Likewise the pollen they produce must be either ***A*** or ***a*** in equal proportions. As illustrated in the lower part of Fig. 1-3, there are four possible outcomes of fertilisation here,

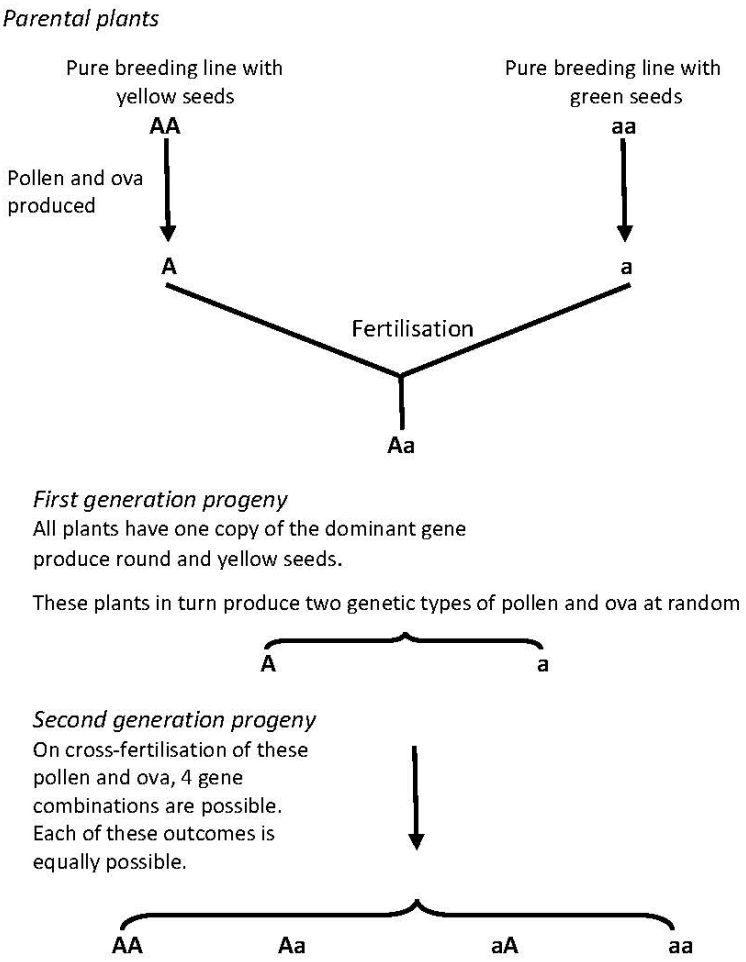


Fig. 1-3. Cross-breeding for a single characteristic – seed colour.

Each plant carries two copies of the gene, which has two variants. Gene **A** is for round seeds and is dominant to gene **a** which gives wrinkled seeds
The parental plants are pure breeding. This means they have two identical copies of the gene, a state referred to as being homozygous. One parent is for the dominant gene, and the other is homozygous for the recessive gene.
The first generation progeny obtained from the cross-breeding are all heterozygous, they have one copy of each gene variant, but the dominant characteristic is expressed.

In the second generation of progeny obtained by breeding the first generation, there are 4 possible combinations of the gene. The one on the left is homozygous for the dominant gene, **A**, and will therefore have yellow seeds. The next two combinations in the middle are both heterozygous but, having one copy of the dominant gene, will also produce yellow seeds. Only one combination, on the right, has two copies of the recessive gene, **a**, and therefore produces green seeds. Overall this gives a 3:1 ratio of plants producing yellow seeds to those producing green seeds.

each equally likely and therefore occurring equally often. ***A*** ova may be fertilised with either ***A*** pollen or ***a*** pollen, giving progeny which are respectively ***AA*** or ***Aa***, and ***a*** ova may be fertilised again by the two types of pollen, giving ***aA*** or ***aa*** plants. The ***Aa*** and ***aA*** plants are exactly the same, as Mendel found that it did not matter which whether ***A*** or ***a*** is contributed by the female ova or the male pollen. So adding this up we get ***AA***, ***Aa*** and ***aa*** plants in a ratio of 1:2:1. Now the ***aa*** plants will have the recessive trait (eg. wrinkled seeds) whereas the ***AA*** plants must have the dominant characteristic (eg. round seeds). However as we saw in the first generation cross, the hybrid ***Aa*** plants will also have the dominant trait, because ***A*** dominates over the recessive gene, ***a***. Thus in appearance, ***AA*** and ***Aa*** plants have the same dominant characteristic. So appearance wise, the second generation plants are dominant to recessive in a 3:1 ratio. This is exactly what Mendel found, so his theoretical explanation perfectly fits his experimental data.

As a result of his various experiments Mendel proposed three laws of inheritance:-

1) That individual inherited characteristics are controlled by indivisible unit factors which are inherited as pairs, one from each parent.

With this postulate, the concept of ‘the gene’, as an indivisible unit of inheritance, is born. Mendel did not use the word ‘gene’ himself; it came into use later on. Mendel’s first law also proposes that both parents contribute equally to the inherited genes of their progeny.

2) That genes exist as different forms carrying instructions for variants of a particular characteristic. When an individual inherits two different variants, one will be dominant and the other recessive.

These alternative forms of the gene are called alleles. Their existence within the general population of an organism accounts for the observation that individual plants or animals within a particular species show inherited variations in their characteristics. To introduce more unavoidable

terminology, individuals who have inherited two different alleles, *Aa*, are referred to as being heterozygous. In these heterozygous individuals it is the characteristic of the dominant allele which is expressed. However, as we have seen, the recessive allele is not diluted out, but exists silently to be passed on intact to future generations.

Just to complete the nomenclature here, individuals with two copies of the same allele, *ie.* ***AA*** or ***aa***, are called homozygous. To assist with these and other necessary but unfamiliar scientific terms, please refer to the Glossary at the back of this book.

3) When the gametes, the unfertilised ova of the female, and the sperm of male animals or pollen of male plants are formed, the pair of alleles are separated and each gamete receives one copy of each gene on a random basis.

This means that each member of the next generation receives a unique set of both its parents' genes. Its siblings too receive their own unique sets of the parents' genes. Overall this is like shuffling a pack of playing cards before dealing them out to the players at the start of a card game. The major difference however is that rather than 52 cards in the pack, there are hundreds of thousands of genes to be dealt.

One thing which emerges from Mendel's work is that the resulting appearance of an individual does not always reveal the genes that it has inherited. As we saw in Fig.1-3, an individual showing the recessive characteristic, such as smooth seeds or green seeds, must be ***aa***, that is having a double dose of the recessive genes, as even one copy of the dominant gene would over-ride it. In other words, the homozygous recessive individual will always be readily identifiable. However, those individuals displaying the dominant characteristic, must have at least one copy of the dominant gene, but may be either heterozygous, ***Aa***, or homozygous dominant, ***AA***. So this brings us to the term genotype, defining which genes an individual has, as distinct from the appearance of the individual, the phenotype. As we can see here, two different genotypes, ***Aa*** and ***AA*** both have the same phenotype.

Genotype versus phenotype

Whilst considering this issue of genotype and phenotype, there is another non-Mendelian way in which phenotype departs from genotype, and this is due to environmental factors that the individual experiences. The

genes which we inherit are the instructions by which our bodies are constructed. However such construction requires the necessary raw materials. If there is any shortfall in the supply of these materials then the instructions in the genotype will not be fully carried out, and so the expected phenotype cannot be achieved by the individual. We are surrounded by examples of the influence of such environmental factors on phenotype, but let me start with a personal one.

Some years ago when my children were still young, we made a family outing to a beautiful, semi-fortified manor house in rural Oxfordshire. Amongst the historical treasures which had been collected there was a 17th century helmet of an infantryman in the English Civil War. One of the volunteer custodians encouraged us to try it for size. It was far too small for me, but fitted my children, then around 10 years of age and far from full grown, perfectly. It so happens that my family tree is entirely English in origin as far back as it can be traced. So this increase in head size cannot be explained by the effect of genetic changes. Instead the considerable increase in height and body size which has occurred in the population since the Civil War is due to the much better nutrition available to recent generations. People can now grow fully to the size instructed by their genes, unlike the rank and file of foot soldiers in the Civil War who could not. To put it another way, the growth of Civil War infantrymen had been stunted by their poor diet, so the potential of their genotypes could not be realised.

The downside of increased food availability for the current generations in many countries over more recent years has been the dramatic rise in the incidence of obesity. Again the widespread and common obese phenotype which has emerged recently within the populations of a number of countries does not arise from genetic changes, but from the environmental change of the ready availability of excess dietary calories alongside reduced physical activity.

A further and quite distinct illustration of the difference between genotype and phenotype arises in the petal colour of hydrangea bushes. In general petal colour in plants is a genetically determined characteristic. It is a prime example of the traits worked on by plant breeders over the centuries in their efforts to develop new flower varieties. This is again the application of genetic selection in what has often been a highly lucrative trade. But in the case of hydrangeas, the typical pink or blue flower colours depend not so much on genes, but on the nature of the soils they are grown in. Acidic soils facilitate the uptake of aluminium salts by the root system, and this allows for the synthesis of the blue pigments in the flowers. Soils which are not acidic do not support this, and the flowers remain pink. So in this instance pink versus blue is not a genetic difference but an environmental one. That

is, it is not a genotypic difference but a phenotypic one. Gardeners whose soil is not acidic and whose hydrangeas normally grow pink, can change them to blue by feeding them with proprietary solutions rich in aluminium salts.

Mendel's Law of Independent Assortment

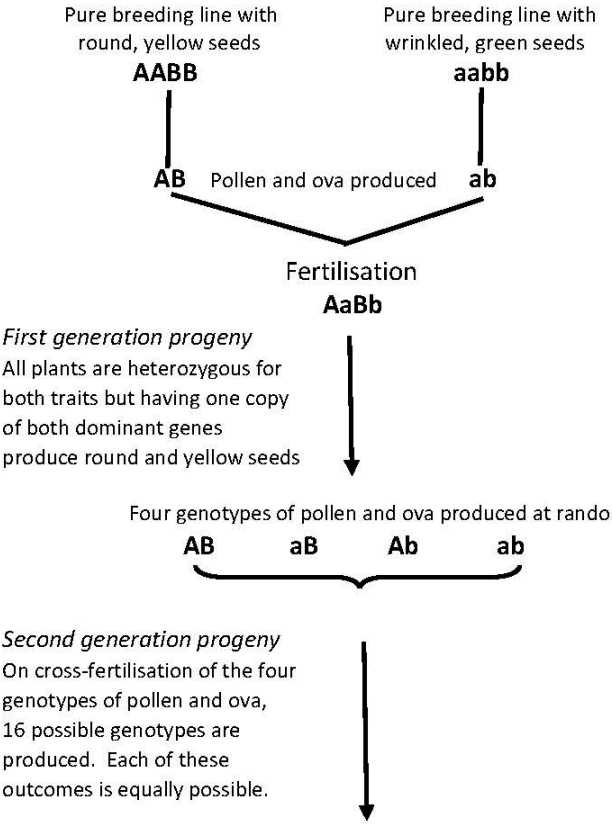
Not content with his advances thus far, Mendel carried out further breeding experiments in order to substantiate his findings and extend his theories. He conducted similar work on a number of other single traits, which produced the same results. This confirmed that his theory of the gene as an immutable unit of inheritance applied to other characteristics, not just seed colour and shape. However he also performed experiments in which he investigated two different traits at the same time, and we need to explore these more complex experiments in order to understand some of the studies described in the next Chapter. One of Mendel's two trait experiments involved seed shape, wrinkled *versus* round, combined with seed colour, green *versus* yellow. He had already established that the gene for round seeds, ***A***, was dominant to the gene for wrinkled seeds, ***a***, and that the gene for yellow seeds, ***B***, was dominant to the gene for green seeds, ***b***. Therefore pure-breeding plants with round, yellow seeds must be ***AABB***, and likewise pure-breeding plants with wrinkled and green seeds must be ***aabb***. What happens when ***AABB*** is crossed with ***aabb***? The results are illustrated diagrammatically in Fig. 1-4.

As may be seen in Fig. 1-4, all the progeny of such a cross must inherit one domain gene and one recessive gene for each trait. They are therefore ***AaBb***, i.e. they are homozygous for both traits and therefore have the dominant phenotypes, that is they have round and yellow seeds. So far this is essentially the same as the cross-breeding experiments of a single trait. Yet when these first generation plants are cross bred with each other to produce the second generation, the outcome is somewhat different. Mendel found that there was a majority of plants showing both dominant characteristics, in the case of the experiment illustrated that is round and yellow seeds. There were also some plants with one dominant and one recessive characteristic, that is round and green seeds, or wrinkled and yellow seeds. These were less common than the doubly dominant plants, and the two singly dominant types were equal to each other. Finally only a tiny proportion of the second generation progeny exhibit both recessive characteristics, i.e. wrinkled and green seeds. In fact the ratio of plants in each of these four phenotypes was 9:3:3:1.

Two genes

A for round seeds is domain to **a** which gives wrinkled seeds
B for yellow seeds is dominant to **b** which gives green seeds

Parental plants



(Fig. 1-4 continues on next page)

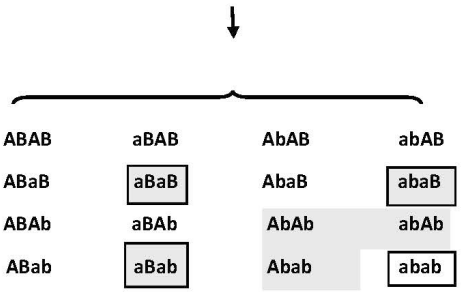


Fig. 1-4. Cross-breeding with two genes.
In the second generation of progeny there are 16 possible gene combinations. Of these, 9 have at least one dominant gene for both traits and therefore the resultant plants produce round, yellow seeds. 3 combinations (boxed with grey shading) have two copies of the recessive gene for seed shape, **a,** and therefore produce wrinkled yellow seeds. Another three (highlighted in grey shading without a box) have two copies of the recessive gene, **b**, for seeds colour and therefore will have round but green seeds. Finally, one combination is doubly recessive and therefore will produce wrinkled, green seeds (bottom right on the grid, boxed without shading). Overall a 9:3:3:1 ration of the 4 possible phenotypes.

Those who are mathematically astute, such as Mendel himself, will immediately realise that 9:3:3:1 is the outcome of multiplying two 3:1 ratios together. The rest of us need to use a diagram such as the one at the bottom of Fig. 1-4 to appreciate that in the second cross-bred generation there are 16 possible outcomes, which taken together give rise to the observed ratio of the four phenotypes. The important point here is that the observed outcome of the experiments concurs precisely with mathematic predictions based on the random association of the gene variants. The two characteristics have been inherited entirely separately from each other in a free distribution. The alternative possibility might have been that since the dominant combination of the two genes, ***AB***, and the recessive combination, ***ab***, were present in the parental plants, they might have stayed together during the cross-breeding. This would have skewed the outcome in favour of the original pairings of the genes showing a tendency to stay coupled or linked together. Very significantly, this is definitely not the case.

These findings demonstrate further that the gene is an independent unit of inheritance, because it is unaffected by the circumstances and combinations in which it exists. This outcome is referred to as ‘Mendel’s Law of Independent Assortment’. It codifies the random inheritance of different genes. That is the combinations of them which occur in the parents

do not stay linked together but are freely broken up to create new, random combinations. It has been verified in many different cross-breeding experiments in numerous species of plant, animal and insect. However it is also the case that it is not universally true. Some gene combinations do in fact demonstrate linkage, by showing a tendency to remain in parental combinations. Such exceptions are in fact very informative, as we shall see in the following Chapter.

The Re-discovery of Mendel's work

Mendel had provided dramatical new and highly original insights into heredity, especially in the context of plant breeding, an area of great scientific and indeed commercial interest at that time. It is therefore rather surprising that his work fell into obscurity. He published his findings in two papers in the local scientific journal, '*The Proceedings of the Brunn Society for the Study of Natural Science'.* Although this might appear to be a relatively obscure journal, it was apparently circulated around the learned societies of Europe. Mendel also attempted to promote his work by writing in detail about it to one of the leading botanists of the day, Carl Wilhelm von Nägeli, in Zurich. However von Nägeli showed no interest in Mendel's work. The most likely explanation for such a lack of interest is that Mendel was simply too far ahead of everyone else. His extensive use of mathematics to analyse his work and explain his findings probably rendered his papers too obscure for most botanists. It is also the case that his concept of the undilutable, individual genes ran counter to the prevailing concept of a mixing and diluting of inheritable traits down the generations.

Either way, it was in 1900, some 35 years after his death, that Mendel's work was rediscovered independently by four plant breeding scientists, working quite apart from each other. One of the key figures in this rediscovery was the Dutch botanist, Hugo de Vries. He conducted plant breeding experiments similar to Mendel's and arrived at the same conclusions. He had read Mendel's papers but omitted to refer to them in his own paper. In this respect he was soon put right by the German botanist, Carl Correns. Correns had been a student of von Nägeli, with whom Mendel had corresponded fruitlessly. Correns however, unlike his former teacher, did not overlook the significance of Mendel's work, and had replicated it in his own plant breeding experiments. A third European to rediscover Mendel's papers was the Austrian agronomist, Erick von Tschermak. His maternal grandfather had been a botany professor who, remarkably, had taught the young Mendel when he was a student in Vienna. Von Tschermak was involved in the breeding of new varieties of agriculturally important