TAKING A CHANCE ON HEREDITY:
How Gregor Mendel Solved a Basic Mystery of Heredity

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Gregor Mendel (1822-1884) was an Austrian priest, botanist, and biologist. Classical genetics can be traced back to the work performed by Mendel in the 1860's. His work was largely ignored until about 1900. Darwin wrote his Origin of Species in 1869 (resulting from his Voyage of the Beagle from 1831-1836). Darwin was unaware of Mendel's work.

Mendel was interested in solving the puzzle of heredity. Little was known in his time about how certain inheritable characteristics were passed on from generation to generation by animals or plants.

Early Theories of Heredity

Before Mendel's time, several different theories of inheritance had been put forth.

Aristotle (384 - 322 BC) believed that the eggs and semen were formed from particles called pangenes which come together from all parts of the body. This theory, called pangenesis, was accepted as late as the 19th century, and was adopted by Jean Baptiste de Lamarck and Charles Darwin.

Darwin and Lamarck both believed that changes that occurred in various parts of the body during a person's life, so called acquired characteristics, could be passed on to the next generation.

Much of pangenesis has been disproved. The reproductive organs are not made up of contributions from body cells, and even great changes in body cells, which are acquired during a person's life, are not passed on to eggs and sperm.

However, certain particles from the parents are the basis of heredity and the particles are called ***genes***, after the word pangenes.

In the seventeenth century two contradictory theories of heredity prevailed. One, believed by the Dutch lensmaker Anton von Leeuewenhoek, was that all the inherited traits come from the father, and that the mother is only the incubator of the offspring. The other theory, believed by another Dutchman, Regnier de Graaf, was that the mother's egg contains all of the inherited characteristics, and the sperm is only the catalyst which stimulates the growth of the egg.

In the early nineteenth century the "blending theory" of heredity brought back the concept that both parents contributed to the inherited traits of the offspring. The blending theory held that the traits of the parents blended irreversibly, much as paints do, to form the traits of the offspring. More specifically the blending theory said that if a blue parakeet mated with a yellow parakeet the pair would produce a green parakeet. The theory said further that the pure blue and pure yellow colors would never again appear in future generations, and that if an isolated population of blue and yellow parakeets were left to mate among themselves, future generations would eventually all be a uniform green color.

All of the predictions of the blending theory in the parakeet example have been disproved.

Mendel's Experiments

In order to learn more about heredity, Mendel planted pure breeding strains of peas in his garden at the monastery. A ***pure breeding*** strain of peas is one for which all offspring obtained when the strain is crossed with itself (***self-pollinated***) continue to exhibit a certain trait. For example, a pure-breeding tall strain of pea will always breed true to produce pure tall plants, and a pure-breeding dwarf strain of pea will consistently produce dwarf plants when crossed with itself.

Starting with pure-breeding tall and dwarf strains, Mendel, in a controlled experiment, crossed the pure-breeding tall and the pure-breeding dwarf strains to produce a so-called **F1** generation pea plant. Mendel noted that ***all*** of the F1 generation plants were tall. The dwarf trait had completely vanished.

When Mendel crossed the F1 generation peas with pure-breeding dwarf peas, the dwarf trait reappeared: ***about*** 50% of the offspring were tall, and ***about*** 50% were dwarf plants.

When Mendel crossed the F1 generation peas with themselves, he found that the second generation had ***about*** 75% tall and ***about*** 25% dwarf plants.

On the basis of his experiments, Mendel hypothesized that traits, such as tallness, are affected by "factors" that come from both parents. We now call these factors genes.

Basic Concepts in Mendel's Theory of Gene Pairs

1. In most cells of an organism, genes occur in pairs. The gene pair of an offspring is determined by its parents. Each parent contributes one of the genes in its gene pair, chosen at random, to the gene pair of the offspring. This process is now called Mendel's Law of Inheritance.

2. Genes occur in alternative forms, called ***alleles***. For example, the gene affecting plant height occurs in one form causing tall plants, and another form causing dwarf plants.

3. The pure breeding tall plants carry two copies of the allele causing tallness. The pure-breeding dwarf plants carry two copies of the allele causing shortness. Such organisms which carry two matching alleles are called ***homozygotes***. Individuals which carry one copy of the allele causing tallness, and one copy of the allele causing shortness are called ***heterozygotes***.

4. In the heterozygote individuals, often one of these gene forms is ***dominant***. For example, in an individual pea plant with one allele for tallness and one dwarf-causing allele the allele causing tallness is dominant. This means that when two pure-bred plants, one a pure-breeding tall plant, the other a pure-breeding dwarf plant are crossed, giving rise to offspring which are heterozygotes, the tallness allele will dominate and the offspring will all be tall. When one allele dominates another, the allele which is dominated, the dwarf-causing allele in our example, is called ***recessive***.

Note: In concept 1 above, that each parent contributes one of the genes in its gene pair at random means that there is a 50% chance that the first gene will be donated to the offspring, and a 50% chance that the second gene will be contributed to the offspring.

Mendel found that he could explain the frequency of tall and dwarf plant offspring, which his experiments produced, using this theory of gene pairs.

In order to explain Mendel's theory in detail, let's develop some notation. Suppose we are interested in the height of pea plants, and the gene pair which governs plant height. Let's use ***A*** to represent the allele causing tallness, and ***a*** to represent the allele causing shortness. As we mentioned, in pea plants the tallness-causing allele is dominant over the dwarf-causing allele. It is common practice to use an upper case letter to represent the dominant allele, and a lower case letter to represent the recessive allele.

There are then three possibilities for the gene pair affecting plant height. An individual pea plant can have any one of the three possible makeups: ***AA***, ***aa, or "one of each."*** There is a real danger of confusion here. When one tries to symbolize "one of each" by a pair of letters, one can use either Aa or aA. Sometimes the order (Aa vs aA) carries meaning **--** for example when "Aa" is used to mean that the "first" parent contributed the "A" and the "second" parent contributed the "a." Other times, the order carries no meaning **--** for example, when one is simply trying characterize a heterozygote and one says type "Aa" when one could just have easily have said "aA."

If the individual has the makeup ***AA***, it will be a tall plant since both its alleles cause tallness. Such an individual is called a pure-breeding (or pure-bred) tall plant since it can only pass on an allele causing tallness to its offspring.

If the individual has the makeup ***Aa***, it will also be a tall plant because ***A***, the allele causing tallness dominates over ***a***, the dwarf-causing allele.

Finally, if the individual has the makeup ***aa***, it will be a dwarf plant since both its alleles are dwarf-causing. It is called a pure-breeding (or pure-bred) dwarf plant, since it can only pass on dwarf-causing alleles to its offspring.

With this notation, lets do some examples showing how the theory of gene pairs predicts the experimental results obtained in Mendel's experiments.

Example 1: What are the results of crossing a pure-bred tall pea plant with a pure-bred dwarf pea plant?

Solution: We will use ***A*** to represent the allele causing tallness, and ***a*** to represent the dwarf-causing allele. The table below is a visual reminder of this choice.

Allele	Causes
A	Tallness
a	dwarfness

Based on our notation, the representation of the genetic makeup of the parents will be ***AA*** or the pure-bred tall plant, and ***aa*** for the pure-bred dwarf plant.

According to Mendel's theory of gene pairs, all of the offspring will have the ***Aa*** makeup Mendel called these offspring the **F1** generation), and they will all be tall. This result is summarized below.

		Parent2 is ***aa*** (Pure Breeding Dwarf)	
		Parent2 contributes ***a*** (1st ***a*** in pair) with prob. = 0.5	**Parent2** contributes ***a*** (2nd ***a*** in pair) with prob. = 0.5
Parent1 is ***AA*** (Pure Breeding Tall)	**Parent1** contributes ***A*** (1st ***A*** in pair) with prob. = 0.5	***Aa*** prob. = 0.25	***Aa*** prob. = 0.25
	Parent1 contributes ***A*** (2nd ***A*** in pair) with prob. = 0.5	***Aa*** prob. = 0.25	***Aa*** prob. = 0.25

Table A.1: Result of Crossing Pure Tall with Pure Dwarf Pea Plants (Offspring are called F1 generation)

Let's make sure we understand how these results follow from Mendel's theory of gene pairs.

According to the theory, each of the parents contributes one allele (at random) to the offspring. Therefore the first parent (***AA***) contributes one of its alleles. It will certainly be an ***A*** allele since both of its alleles are ***A***'s. The second parent (***aa***) contributes one of its alleles, which must be an ***a*** since both of its alleles are ***a***'s. Therefore all of the offspring will have the genetic makeup ***Aa***.

The reason that all of the offspring are tall is that they are all of the form ***Aa*** and the tallness allele ***A*** dominates the dwarf allele, ***a***.

Example 2: What are the results of crossing an F1 generation plant with itself (or another 1 generation plant)? In other words, what are the probabilities that an offspring will be tall or dwarf, and what are the probabilities of the various allele makeups AA, aa, and "one of each." The information in the table below summarizes the answer that Mendel discovered through his experiments.

	Parent1: ***Aa*** (F1 Generation) **Parent2**: ***Aa*** (F1 Generation)
Genotype of Offspring	***about*** 25% ***AA*** (tall) ***about*** 50% ***Aa*** (tall) ***about*** 25% ***aa*** (dwarf)
Percent tallness/dwarfness in Offspring (from line above)	***about*** 75% tall ----------- ***about*** 25% dwarf

That is, he first discovered that ***about*** 75% of the offspring were tall, and ***about*** 25% were dwarf. Through further experimentation he determined the <u>genotype</u> makeup shown in the table above.

Could we have predicted the results of Mendel's experiment, as given above, by using his theory of gene pairs?

Solution :
Using the statement in Mendel's Law of Inheritance, that "Each parent contributes one of the genes in its gene pair, chosen at random, to the gene pair of the offspring." we obtain table A.2.

Table A.2 tabulates the contribution of each parent to the offspring, as well as the various associated probabilities.

		Parent2 is ***Aa*** (F1 Generation)	
		Parent2 contributes ***A*** with prob. = 0.5	**Parent2** contributes ***a*** with prob. = 0.5
Parent1 is ***Aa*** (F1 Generation)	**Parent1** contributes ***A*** with prob. = 0.5	***AA*** prob. = 0.25	***Aa*** prob. = 0.25
	Parent1 contributes ***a*** with prob. = 0.5	***Aa*** prob. = 0.25	***aa*** prob. = 0.25

Table A.2: Distribution and Genetic Makeup of Offspring When Both Parents are F1 Generation

To understand Table A.2, let's look, for example, at the box that looks like

Aa
prob. = 0.25

This cell is at the intersection of

Parent1 contributes
A
with prob. = 0.5

and

Parent2 contributes
a
with prob. = 0.5

Therefore it represents an offspring plant to whom **Parent1** contributed the ***A*** allele, and to whom **Parent2** contributed the ***a*** allele. The probability of getting the ***A*** allele from **Parent1** was 0.5, and the probability of getting the ***a*** allele from **Parent2** was 0.5 as well.

While it is not explicitly stated in our statement of Mendel's Law, the contributions by the parents are independent of each other. That is, the contribution of **Parent1** is not influenced by the contribution of **Parent2**. Since the events are independent, the probability of both events occurring is the ***product*** of the probabilities. Therefore, the probability of Aa (where, here order DOES carry meaning: the A came from **Parent1** and the a came from **Parent2** it the product (0.5)(0.5) = 0.25.

The other three boxes in table A.2 which represent the various genetic makeups of the offspring of the F1 generation are formed similarly.

Examining the boxes that represent the various offspring, we see that

The probability is .25 of an offspring having the makeup **AA**
The probability is .25 of an offspring having the makeup **Aa**
The probability is .25 of an offspring having the makeup **aA**
The probability is .25 of an offspring having the makeup **aa**

Combining probabilities of like genetic makeups we get the following probabilities:
.25 for type ***AA***, .50 for **"one of each"** and .25 for type ***aa***.

Since the tallness allele, ***A***, is dominant, both the ***AA*** and ***Aa*** offspring will be tall, so the probability is .75 that an offspring will be tall.

So, the Mendel's Theory of Gene Pairs produces the above probabilities and these probabilities predict the results that Mendel observed, as described in the table at the start of Example 2.

Example 3: Cystic fibrosis (CF) is a lethal disease whose genetics can be studied much like tallness/dwarfness in pea plants. However, cystic fibrosis is a recessive disease, so if we label the disease causing allele a, a person must have genotype ***aa*** to actually get the disease. If a person is heterozygous for the cystic fibrosis allele, that is, if the person has genotype ***Aa***, he or she will not develop the disease, but will have the potential to pass on the disease to offspring. A person who can pass on a recessive disease, but does not suffer from the disease, is called a carrier of the disease.

The discussion of CF thus far is summarized in the tables below.

Allele	effect
a	causes cystic fibrosis but is recessive
A	normal allele, cannot cause cystic fibrosis

If a person has genotype	the person is:
AA	unaffected by CF, and cannot transmit CF
Aa	unaffected by CF, but a carrier
aa	affected by CF, and will transmit one CF allele

If two non-affected carriers mate, 1/4 of the offspring, on average, will get cystic fibrosis. This follows directly from Example 2, above.

genotype	***AA***	***Aa***	***aa***
percent of offspring with this genotype	25%	50%	25%

Thus 25% of the offspring of two carriers, on average, will get a double dosage of the recessive allele, and have genotype ***aa***.

About 1/21 of all Caucasians are non-affected carriers (genotype ***Aa***) of cystic fibrosis. Other races are rarely affected by cystic fibrosis.

Since couples usually form independently of whether or not they are carriers of cystic fibrosis, the probability of both members of a couple being carriers is the product of the probabilities that each partner is a carrier or (1/21)(1/21).

Since we showed above that 1/4 of the children of two carriers will get cystic fibrosis the probability of having both parents carries of CF AND also getting CF is the product (1/21)(1/21)(1/4) = 1/1764=

(1/21)(1/21)(1/4) = 1/1764.

Having two parents who are carriers is about the only way to get cystic fibrosis, because individuals who actually have cystic fibrosis, i.e. individuals who have genotype ***aa***, rarely live to childbearing age.

Therefore the frequency of cystic fibrosis in the Caucasian population is about 1/1764⊠