MENDELIAN GENETICS (OR HOW THE MONK GOT TO PEA!)

Gregor Mendel (1822 – 1844) was the first man to examine the relationship between one generation and the next in a scientific manner. He published his work in 1865, but his work was ignored until the turn of the century, when microscopy became good enough to allow chromosomes to be viewed and Darwin's *Theory of Natural Selection* was widely accepted. For many years, people had known that it was possible to mate the best individuals in one generation together and so make the next generation better. In racehorses, for instance, winners bred winners, and the same principle holds true in cattle and, in an extreme form, in dogs. Mendel began by examining *which* characteristics were passed on from parents to offspring. He wanted to carry out experiments on animals, but as he was a monk, his Bishop (and later, the Pope), ruled that this was contrary to the vows of chastity that all monks take; he was, however, allowed to work on plants.

Mendel chose to work with peas. This was very fortunate, since the inheritance patterns of peas are simple compared to most other plants. In particular, they normally *self-pollinate*, so that, in the absence of Mendel's intervention, all his plants would **'breed true'**, i.e. would produce offspring identical to themselves. Mendel used 4 contrasting pairs of characters (or ***alleles***):

DOMINANT		**RECESSIVE**	
TALL	*v*	*DWARF*	*(height)*
PURPLE	*v*	*WHITE*	*(flowers)*
YELLOW	*v*	*GREEN*	*(seed colour)*
ROUND	*v*	*WRINKLED*	*(seed shape)*

These features were the **PHENOTYPES** of the plants with which he worked.

Whenever Mendel 'crossed', or pollinated, a plant with a character from the first column with one from the second, he found that all the plants in the next generation (= **F1**) were the same as the first named parent. Mendel called this character **DOMINANT**; the alternative allele he called **RECESSIVE**

Mendel's stroke of genius was to realise, 30 years before anyone could see inside a cell clearly enough to see the chromosomes, that there were **TWO** copies of the characters inside every normal cell. When a gamete is produced only **ONE** of these two characters is included in the gamete. Which one (of the two available) is found in any one gamete is **RANDOM**; given that there are 23 pairs of chromosomes in the human cell, there will be 2^{23} different ways that these 23 chromosomes can be chosen. Since the sperm and the egg are made in a similar way (by **MEIOSIS**) one couple could have 2^{46} *different* children!

Mendel gave the symbol of a **CAPITAL** letter to the **DOMINANT** character, and a **small** letter to the RECESSIVE character. Thus the first cross given above becomes:

Phenotype	*TALL*		*x*		*DWARF*		
Genotype	***TT***				***tt***		
Gametes	**T**	or	**T**		**t**	or	**t**
F1	all **Tt**						
Phenotype	all *TALL*						

When an **F1** plant self-pollinates:

Phenotype	*TALL*		*x*		*TALL*		
Genotype	***Tt***				***Tt***		
Gametes	**T**	or	**t**		**T**	or	**t**
F2	**TT**	**Tt**	**Tt**	**tt**			
Phenotype	3 *TALL* : 1 *DWARF*						

This type of inheritance is called **COMPLETE DOMINANCE**, because the F1 plants look **IDENTICAL** to the dominant parent. The 3:1 ratio that Mendel observed is found in all such simple inheritance; in Man, for example, the inheritance of 'tongue -rolling' follows this rule.

If a hybrid individual mates with one of the two pure 'Parental' types, then the offspring produced depend on which of the two parents was crossed with the F1. If the **DOMINANT** parent is crossed with an FI individual, then **ALL** their offspring will be of the **DOMINANT** type. If, however, the FI is crossed with a *recessive* parent, then their offspring will be in the ratio of 1:1 for **DOMINANT** *: recessive.* This type of cross can thus be used to tell if an individual that has the DOMINANT phenotype is pure. If so, all their offspring will be the same (**DOMINANT**). However, if the individual is actually a hybrid, **TWO** types of offspring will be produced. For this reason, this particular cross (FI x *recessive* parent) is known as a **BACK-CROSS** or **TEST-CROSS:**

Phenotype	*TALL*	*x*	*TALL*		***or***	*TALL*	*x*	*DWARF*			
Genotype	***Tt***		***TT***			***Tt***		***tt***			
Gametes	**T**	or **t**	**T**	or **T**		**T**	or **t**	**t**	or **t**		
Offspring	**TT**	or **Tt**	**Tt**	or **TT**		**Tt**	or **tt**	or	**Tt**	or **tt**	
Phenotype	*2 pure* ***TALL***		*: 2 hybrid* ***TALL***			*2 hybrid TALL : 2 pure DWARF*					

Until modern DNA testing became available, this was the only way of **guaranteeing** the pedigree of an individual.

In nature, many characters follow another pattern; that of **INCOMPLETE DOMINANCE** In this pattern, the two parents produce an F I generation which is half - way between the two parental types but *identical* to neither. In roses, for example, a cross between a red rose and a white rose gives a pink flower. This can be shown thus:

Phenotype	*RED*	*x*	*WHITE*	
Genotype	***RR***		***WW***	
Gametes	**R** or **R**		**W** or **W**	
F1		**RW**		
Phenotype		*PINK*		

When two F1 interbreed:

Phenotype	*PINK*	*x*	*PINK*	
Genotype	***RW***		***RW***	
Gametes	**R** or **W**		**R** or **W**	
F2	**RR** or **RW**	or	**RW** or **WW**	
Phenotypes		*1 RED : 2 PINK : 1 WHITE*		

The inheritance of sex in animals follows this pattern too:

Phenotype	*MALE*	*x*	*FEMALE*	
Genotype	**XY**		**XX**	
Gametes	**X** or **Y**		**X** or **X**	
Genotype	**XY** **XY**	or	**XX** **XX**	
Phenotype	*50% MALE*	*:*	*50% FEMALE*	

Because males have only one copy of the 'X' chromosome, it follows that **EVERY** gene on this chromosome will behave as if it were dominant; they have no alternative gene to 'correct' a mistake. Females, however, can **carry** the defective gene but **not** show any symptoms. 'These are known as **'CARRIERS'**, since they can pass on the gene to their children. Certain diseases are inherited in this way, and because the sex of the offspring is very important in deciding if they will inherit the disease, these are known as **'SEX-LINKED'** conditions. Examples include **colour-blindness** and **haemophilia.**

Let **X*** = the defective chromosome (for whatever allele) and let **X** = the normal form.

Then:

Phenotype	*MALE*	*x*	*CARRIER FEMALE*
Genotype	**XY**		**X*X**
Gametes	**X** or **Y**		**X*** or **X**
F1 Genotype	**X*Y** **XY**	or	**X*X** **XX**
F1 Phenotype	*1 AFFECTED MALE*	*:*	*1 NORMAL MALE*
	1 CARRIER FEMALE	*:*	*1 NORMAL FEMALE*

It is rare, but **NOT** impossible, for a female to have these conditions. For this to happen, a **carrier female** must mate with an **affected male**. When this happens, 50% of their female offspring *could* be affected. In Man, colour-blindness affects 1 in 20 males, but only 1 in 400 females. This is not life-threatening, but means that the affected person cannot do certain jobs, e.g. BT engineer, pilot, soldier. The commonest form of the disease is **'red / green' colour-blindness,** in which these two colours look the same. Total colour-blindness, in which the world looks back and white, is very rare indeed, though common in many animals.

Haemophilia is **very** much rarer, affecting about 1 in 50, 000 males. These people cannot make **FACTOR VIII,** which is essential for the clotting of the blood. Even a small cut bleeds for a long time, and serious wounds can be fatal. It is also a painful condition, since bruising occurs easily. Queen Victoria was a mutant, (and a carrier), who passed the gene for haemophilia on to 3 of her children. Her daughter Alice had a daughter who married the Czar (or Tzar) of Russia and they had a son (Alexis, the heir to the throne) who was a haemophiliac. The pain and distress that this caused the Royal family meant that the Czarina invited a faith-healer and monk called **RASPUTIN** into the palace. He had some distinctly unmonk-like habits, but could ease the pain of their son. This distracted the Czar from many of the problems of the Russian people and was certainly one of the factors leading to the October Revolution in 1917.

Queen Victoria had 9 children and they married into 5 of the royal families of Europe, sadly still affecting some of them. The British Royal Family are entirely descended from Queen Victoria's son, Edward VII, who was **not** affected, and so our 'line' is free of this disease, unlike that of Spain.

Haemophiliacs can now inject themselves with Factor VIII, which was prepared from donated blood. Sadly, some of this blood, prepared in the early 1980's, proved to be contaminated with the HIV virus, so many haemophiliacs became innocent AIDS victims. They have now won some compensation from the Government (it was almost John Major's first act as Prime Minister) but this cannot compensate for an early death. Nowadays, the blood is heat-treated to kill any HIV before it is released for **any** use.

An adult female haemophiliac was, until recently, an impossibility, since the bleeding associated

with her periods would have proved fatal. Now, however, more haemophiliacs can be expected to live and to have affected children, which will increase the risk of a carrier marrying an affected male. With modern Factor VII injections, presumably their female children could live and have children of their own, thus further increasing the gene in the population. This is unlikely to improve the genetics of the human race and shows the unintentional long-term effects that modern medicine may have.

The recommended medical solution to this dilemma (help the individual, but harm the species) is to screen the young embryos in such pregnancies so the parents are given the choice of aborting affected foetuses who may be carriers.

Note that, nowadays, modern genetic engineering has enabled **baby hamster kidney cells** (really!)* to be engineered to produce Factor VII, which, therefore, having never been in contact with human blood, **cannot** contain HIV. The use of one's own blood to replace blood lost in elective surgery is known as *'auto-transfusion'* and is one way of ensuring that 'transfusion shock' is minimized. This technique can also be used as a way of (temporarily) boosting the RBC count in your blood. This is very useful for endurance athletes and, since it is their own blood they are getting back, virtually undetectable. Lassi (?) Virren was a Finnish Olympic athlete - *'The Flying Finn'* who, uniquely, won **all** the endurance races in the 1956 Helsinki games. He later admitted that he had used 'blood doping' to allow him to cheat to win.

* see these web-sites for more on haemophilia:

- http://www.efbweb.org/topics/genetic/menu3_5.htm
- http://news.bbc.co.uk/1/hi/health/2752353.stm
- http://www.haemophilia.org.uk/news/pr021217.htm
- http://www.health.qld.gov.au/haemophilia/haema.asp
- There are around 5000 haemophiliacs in England, around 2200 with severe haemophilia requiring regular treatment with clotting factors. Around 700 of these are aged up to 21.

For more on Gregor Mendel, see:

- http://www.mendelweb.org/
- http://www.accessexcellence.org/AB/BC/Gregor_Mendel.html
- http://www.sonic.net/~nbs/projects/anthro201/

The last site is a student's own web-site!