Major Concepts in Genetics

Concept 1 Children resemble their parents.

Since the beginning of human history, people have wondered how traits are inherited from one generation to the next. Although children often look more like one parent than the other, most offspring seem to be a blend of the characteristics of both parents. Centuries of breeding of domestic plants and animals had shown that useful traits — speed in horses, strength in oxen, and larger fruits in crops — can be accentuated by controlled mating. However, there was no scientific way to predict the outcome of a cross between two particular parents.

It wasn't until 1865 that an Augustinian Monk named Gregor Mendel found that individual traits are determined by discrete "factors," later known as genes, which are inherited from the parents. His rigorous approach transformed agricultural breeding from an art to a science. He started with parents of known genetic background — to provide a baseline against which to compare patterns of inheritance in the resulting offspring. Then he carefully counted the numbers of individuals showing the various traits in successive generations of offspring.

Concept 2 Genes come in pairs.

Rather than looking at the pea plant as a whole, Mendel focused on seven individual traits that he could readily distinguish. He found that each trait has two alternate forms. For example, seed color can be green or yellow. By analyzing the results of various crosses, Mendel concluded that each alternative form of a trait is specified by alternative forms of a gene.

To follow the inheritance of genes from parent to child, Mendel first needed to be sure which genes each parent carried. Since pea plants are naturally self-fertilizing, "pure-bred" strains were readily available. Each strain contained only one form of the gene that determined a trait. Pure-bred plants with yellow seeds only produced offspring with yellow seeds. Pure-bred plants with green seeds only produced offspring with green seeds. From the results of further experiments, Mendel reasoned that pure-bred plants must have two copies of the same gene for each trait.

Concept 3 Genes don't blend.

In general, offspring appear to be a mixture of parental characteristics. However, Mendel found that this is not true for the pea plant traits that he chose to study. Pure-bred pea plants when crossed did not produce offspring with blended traits.

For example, one might expect that a cross between pure-bred green-seeded and pure-bred yellow-seeded pea plants to produce offspring with seeds of an intermediate green-yellow color. After all, color blending happens when paint is mixed together. However, Mendel found that this cross produced offspring with only one color — yellow. No intermediate blends were seen, and the green color seemed to have disappeared.

Concept 4 Some genes are dominant.

Mendel believed that genes behave like atoms that compose a pure substance. Genes can combine in various ways, but always maintain their distinct identities. For example, in a cross between two pure-bred parents with different traits like seed color, the hybrid offspring would have both the gene alternates for green and yellow seed color.

Why then do offspring from such a cross have only yellow seeds? Mendel proposed that although both gene alternates are present, there is no blending of color because the gene alternate for yellow is "dominant" over the gene alternate for green. The dominant trait is seen whenever a single copy of its gene is inherited. When he crossed the hybrid offspring, green seeds reappeared in the next generation. Mendel reasoned that the "recessive" green trait is shown only when a copy of the recessive gene form is inherited from each parent.

Concept 5 Genetic inheritance follows rules.

When Mendel proposed that each trait is determined by a pair of genes, it presented a potential problem. If parents pass on both copies of a gene pair, then offspring would end up with four genes for each trait. Mendel deduced that sex cells — sperm and eggs — contain only one parental gene of each pair. The half-sets of genes contributed by sperm and egg restore a whole set of genes in the offspring.

Mendel found that different gene combinations from the parents resulted in specific ratios of dominant-to-recessive traits. The results of a cross between two hybrid parents — each carrying one dominant and one recessive gene — were key to his synthesis. For example, a cross between two yellow-seed hybrids produces three times as many yellow seeds as green seeds. This is Mendel's famous 3 to 1 ratio.

Concept 6 Genes are real things.

Mendel published his research, *Experiments in Plant Hybridization*, in 1865 and sent reprints to prominent scientists in several countries. However, his abstract notion of genes was not appreciated by naturalists of his time — who had been trained primarily to observe and categorize living things. Thus, Mendel's work lay fallow until 1900, when three European scientists independently confirmed his results.

By that time, there was strong evidence that cells are the basic units of life. Biological stains were developed that highlighted structures within cells — including thread-like chromosomes. Different organisms proved to have different numbers of chromosomes, suggesting that they might carry information specific for each life form. This study of the cell and chromosomal behavior was to give Mendel's abstract genetic work the physical context it needed.

Concept 7 Cells arise from cells.

For centuries people accepted the "spontaneous generation" of life from inanimate matter. If cells are the fundamental units of life, they too must have a reproductive mechanism that maintains the proper chromosome number in each cell.

About a decade after the publication of Mendel's paper, scientists carefully documented the behavior of chromosomes during cell division (mitosis), using dyes to make them visible. First, each chromosome copies itself, and the duplicates line up at the "equator" of the cell. Then, duplicate copies of each chromosome are pulled toward opposite poles. Finally, the cell splits at the equator, producing two new cells with identical sets of chromosomes.

Concept 8 Sex cells have one set of chromosomes; body cells have two.

In sexual reproduction, offspring arise from the union of specialized sex cells — a female egg and a male sperm. Just before the rediscovery of Mendel's work, careful studies were made of chromosome behavior during the formation of sex cells (meiosis). First, homologous (like) chromosomes pair up at the cell equator where they actually exchange genetic information. Then, one chromosome from each pair is pulled toward each pole. At the end of this reduction division, each daughter cell receives only one homologous chromosome from each pair, ending up with one set.

Meiosis halves the set of chromosome and randomly assorts homologous chromosomes into sex cells. The full chromosome number is restored when sperm and egg unite. This exactly mirrored the behavior of genes as deduced by Mendel three decades earlier.

Concept 9 Specialized chromosomes determine gender.

People had long philosophized about the observed differences between males and females of a species. If one considers sex a trait, or set of traits, then it followed that sex is inherited. In 1905, closer study of meiosis revealed the chromosomal basis of gender.

Scientists noticed an oddball pair among the homologous chromosomes lined up at the cell equator during reduction division. One chromosome (X) was much bigger than the other (Y). In human beings, this mismatched pair of one X and one Y chromosome is seen exclusively in male cells. A matched pair of X chromosomes is found in female cells. Thus, XX chromosomes determine femaleness, and XY chromosomes determine maleness. Females produce only eggs with X chromosomes; males produce sperm with an X or a Y chromosome.

Concept 10 Chromosomes carry genes.

Thomas Hunt Morgan and his students at Columbia University ushered in the era of modern genetics when they showed the physical basis of heredity. Where Mendel had bred pea plants, the Columbia group studied inheritance in the common fruit fly. Unlike Mendel, who found readily identifiable traits, they spent months searching for a fly with any unique trait that could be studied.

Finally they discovered a single white-eyed male fly, which stood out from its normal, red-eyed peers. A cross between the mutant male and a red-eyed female produced only red-eyed offspring. White-eyed mutants reappeared in the following generation — the classic pattern of a recessive trait. However, the white-eyed trait was seen exclusively in males of the second generation. They concluded that white-eyed is a sex-linked recessive trait. The gene for eye color must be physically located on the X chromosome.

Concept 11 Genes get shuffled when chromosomes exchange pieces.

As Morgan and his coworkers identified more and more inherited traits in fruit flies, they noticed that flies often showed particular combinations of traits. This suggested that certain genes were "linked," and inherited together as a unit. They identified four such units or "linkage groups" — equal to the number of paired chromosomes observed under the microscope. This provided further evidence that genes are located on chromosomes.

Morgan's group used the phenomenon of linkage to construct maps of the fruit fly chromosomes. They found that linked genes are sometimes separated during meiosis, when the homologous chromosomes exchange pieces. How often a pair of genes are separated provides a measure of the relative distance between them on a chromosome. Distant genes recombine frequently. Nearby genes rarely recombine and are closely linked.

Concept 12 Evolution begins with the inheritance of gene variations.

Key to the theory of evolution by natural selection are new trait variations that arise spontaneously and make an organism more competitive in the struggle for survival. Following publication of Darwin's *On the Origin of Species*, in 1859, field stations were established where scientists could study the unique characteristics of organisms that had evolved to inhabit different environments. However, field observation could not explain the origin of variation or how new traits are inherited.

The new sub-discipline of experimental evolution emerged at the turn of the 20th century with the goal to recreate evolution in controlled experiments with agricultural plants and animals. It soon became clear that mutations in genes are the source of variation and that Mendelian genetics offered a statistical method for analyzing the inheritance of new mutations. By the early 1920's, experimental evolutionists had quietly become the first generation of geneticists.

Concept 13 Mendelian laws apply to human beings.

Although Mendel's laws were first tested in pea plants and fruit flies, evidence quickly mounted that they applied to all living things. Just as mutations had provided keys to understanding fruit fly genetics, pedigrees of families affected by diseases provided many of the first examples of Mendelian inheritance in humans.

Recessive inheritance was first described for the disorders alkaptonuria (1902) and albinism (1903). Among the first dominant disorders discovered were brachydactyly (short fingers, 1905), congenital cataracts (1906), and Huntington's chorea (1913). Duchenne muscular dystrophy (1913), red-green color blindness (1914), and hemophilia (1916) were the first sex-linked disorders. The simple concept of eye color inheritance — brown is dominant, blue is recessive — was published in 1907; however, scientists now believe that several genes are involved.