Introduction

A gene, the basic unit of heredity, is a segment of DNA containing all the information necessary to synthesize a polypeptide (protein). Protein synthesis determines much of the body's structure and function.

Structure

Humans have about 20,000 genes. Genes are contained in chromosomes in the cell nucleus and mitochondria. In humans, somatic (non-germ) cell nuclei, with certain exceptions (eg, RBCs), normally have 46 chromosomes in 23 pairs. Each pair consists of one chromosome from the mother and one from the father. Twenty-two of the pairs, the autosomes, are usually homologous (identical in size, shape, and position and number of genes). The 23rd pair, the sex chromosomes (X and Y), determines a person's sex. Women have two X chromosomes (which are homologous) in somatic cell nuclei; men have one X and one Y chromosome (which are heterologous). The X chromosome carries genes responsible for many hereditary traits; the small, differently shaped Y chromosome carries genes that initiate male sex differentiation, as well as a few other genes. Because the X chromosome has many more genes than the Y chromosome, many X chromosome genes in males are not paired. A karyotype is the full set of chromosomes in a person's cells.

Germ cells (egg and sperm) undergo meiosis, which reduces the number of chromosomes to 23—half the number in somatic cells. In meiosis, the genetic information inherited from a person's mother and father is recombined through crossing over (exchange between homologous chromosomes). When an egg is fertilized by a sperm at conception, the normal number of 46 chromosomes is reconstituted.

Genes are arranged linearly along the DNA of chromosomes. Each gene has a specific location (locus), which is typically the same on each of the two homologous chromosomes. The genes that occupy the same locus on each chromosome of a pair (one inherited from the mother and one from the father) are called alleles. Each gene consists of a specific DNA sequence; 2 alleles may have slightly different or the same DNA sequences. Having a pair of identical alleles for a particular gene is homozygosity, whereas having a pair of nonidentical alleles is heterozygosity.

Gene Function

Genes consist of DNA. The length of the gene depends on the length of the protein for which the gene codes. DNA is a double helix in which nucleotides (bases) are paired; adenine (A) is paired with thymine (T) and guanine (G) is paired with cytosine (C). DNA is transcribed during protein synthesis. When DNA replicates itself during cell division, one strand of DNA is used as a template against which messenger RNA (mRNA) is made. RNA has the same base pairs as DNA, except that uracil (U) replaces thymine (T). Parts of mRNA travel from the nucleus to the cytoplasm and then to the ribosome, where protein synthesis occurs. Transfer RNA (tRNA) brings each amino acid back to the ribosome where it is added to the growing polypeptide chain in a sequence determined by the mRNA. As a chain of amino acids is assembled, it folds upon itself to create a complex 3-dimensional structure under the influence of nearby chaperone molecules.

The code in DNA is written in triplets of the four possible nucleotides. Specific amino acids are coded by specific triplets. Because there are 4 nucleotides, the number of possible triplets is 4^3 (64). Because there are only 20 amino acids, there are extra triplet combinations. Some triplets code for the same amino acids as other triplets. Yet other triplets may code for things such as instructions to start or stop protein synthesis and in what order to combine and assemble amino acids.

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Genes consist of exons and introns. Exons code for amino acid components of the final protein. Introns contain other information that affects control and speed of protein production. Exons and introns together are transcribed onto mRNA, but the segments transcribed from introns are later spliced out. Transcription is also controlled by antisense RNA, which is synthesized from the DNA strand that is not transcribed into mRNA. The chromosomes also consist of histones and other proteins that affect gene expression (which proteins and how many proteins are synthesized from a given gene).

Genotype refers to genetic composition; it determines which proteins are coded for production. Phenotype refers to the entire physical, biochemical, and physiologic makeup of a person—ie, how the cell (and thus the body) functions. Phenotype is determined by the types and amounts of proteins actually synthesized, ie, how the genes are actually expressed. Gene expression depends on factors such as whether a trait is dominant or recessive, the penetrance and expressivity of the gene (see General Principles of Medical Genetics: Factors Affecting Gene Expression), the degree of tissue differentiation (determined by tissue type and age), environmental factors, unknown factors, and whether expression is sex-limited or subject to chromosomal inactivation or genomic imprinting. Factors that affect gene expression without changing the genome are epigenetic factors.

Knowledge of the biochemical mechanisms that mediate gene expression is growing rapidly. One mechanism is variability in intron splicing, also called alternative splicing. Because introns are spliced out, the exons may also be spliced out, and then the exons can be assembled in many combinations, resulting in many different mRNAs capable of coding for similar, but different, proteins. The number of proteins that can be synthesized by humans is > 100,000 even though the human genome has only about 20,000 genes. Other mechanisms mediating gene expression include DNA methylation and histone reactions such as methylation and acetylation. DNA methylation tends to silence a gene. Histones resemble spools around which DNA winds. Histone modifications such as methylation can increase or decrease proteins synthesized from a particular gene. Histone acetylation is associated with decreased gene expression. The strand of DNA that is not transcribed to form mRNA may also be used as a template for synthesis of RNA that controls transcription of the opposite strand.

Traits and Inheritance Patterns

A trait may be as simple as the color of the eyes or as complex as susceptibility to diabetes. Expression of a trait may involve one gene or many genes. Some single-gene defects cause abnormalities in multiple tissues, an effect called pleiotropy. For example, osteogenesis imperfecta (a connective tissue disorder that often results from abnormalities in a single collagen gene) may cause fragile bones, deafness, blue-colored sclerae, dysplastic teeth, hypermobile joints, and heart valve abnormalities (see also Bone and Connective Tissue Disorders in Children: Osteogenesis Imperfecta).

Construction of a family pedigree: The family pedigree (family tree) can be used to diagram inheritance patterns. It is also commonly used in genetic counseling. The pedigree uses conventional symbols to represent family members and pertinent health information about them (see Fig. 1: General Principles of Medical Genetics: Symbols for constructing a family pedigree.). Some familial disorders with identical phenotypes have several patterns of inheritance.

Fig. 1

ols for constructing a family pedigree.

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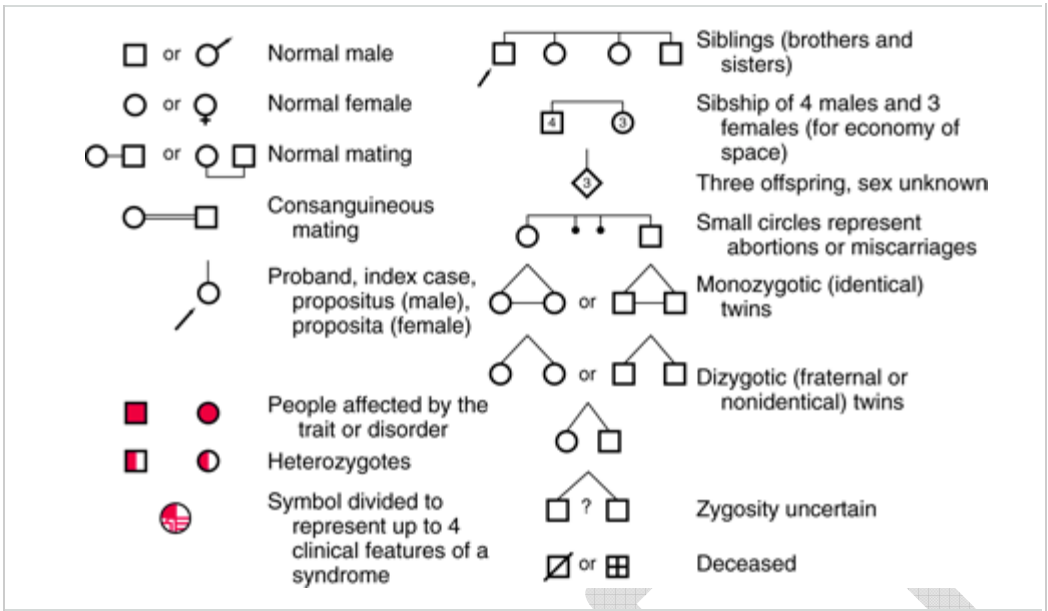

pedigree, symbols for each generation in the family are placed in a row and numbered with als, starting with the older generation at the top and ending with the most recent at the bott

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