



# POSNA

## The Core Curriculum

### Genetics

#### Objectives

1. Define: genome, chromosome, gene, allele, intron, exon, codon, haploid, diploid, mutation, homeobox gene, transcription, translation, receptor, recombinant protein, karyotype, genotype, phenotype, penetrance, variable expressivity, anticipation, pleiotropy
2. Define the process by which genetic material is transferred from the nucleus to the synthesized protein

#### Discussion

A basic knowledge of the terminology of molecular biology and genetics is essential to the orthopaedist's ability to understand many of the conditions seen in children. As the genome project progresses toward its scheduled completion in 2003, an immense new body of knowledge is unfolding. It is not unreasonable to expect that this knowledge will dramatically change many longheld concepts of children's orthopaedic conditions. We already have a better understanding of many connective tissue disorders, and classification is becoming more logical based on genetic information (for example, Ehlers-Danlos syndrome has recently been reclassified in this manner). Thus, the orthopaedist must have the basic vocabulary to understand the ever-expanding knowledge base in this field.

- Genome - the total DNA in an organism. In humans, the 23 chromosome pairs contain 80,000-100,000 genes, and a total of 6 billion base pairs (bonding the double helix of DNA)
- Chromosome - single DNA molecule containing hereditary information
- Gene- a group of base pairs in the chromosome whose sequence provides the information necessary for cells to synthesize a particular structural protein or enzyme (one gene - one protein)
- Allele - alternate forms of a specific gene, may be maternal or paternal. If alleles are identical, organism is homozygous
- Intron - noncoding portion of DNA. Contains promoter regions, regulatory elements, and enhancers. Comprises the majority of DNA
- Exon - contain the code for the RNA of the transcribed template that will be used to produce the protein of the gene product
- Codon - a 3 nucleotide sequence on DNA determining the formation of a specific amino acid

- Diploid - cells with 2 sets of genetic material, one from each parent
- Haploid - genetic material from a single parent (gamete)
- Mutation - a permanent change, deletion, insertion, or rearrangement of base pairs bonding DNA helices.
- Homeobox gene - establishes a molecular coordinate system that determines body design and arrangement
- Transcription - transfer of genetic code from DNA to RNA. Exons are spliced together, introns are spliced out during this process which creates functional messenger RNA
- Translation - process by which messenger RNA transports the code for a protein amino acid sequence from the nucleus to the site of cytoplasmic synthesis
- Receptor - in the plasma membrane of cells, receptors bind with growth factor, hormones, or other proteins to induce a change in cellular behavior
- Recombinant protein - the product of manipulation of segments of DNA and/or RNA; the selected segments are recombined with other portions of genetic material and then introduced into the genome of an organism or cell to produce a recombinant protein
- Karyotype - the complement of chromosomes for an organism. For humans, this contains 22 pairs of autosomes, and one pair of sex chromosomes
- Genotype - genetic constitution at one or more loci
- Phenotype - the detectable expression of the genotype
- Penetrance - the probability that the phenotype will express the genotype
- Variable expressivity - different severities of phenotypic expression of the same genotype
- Anticipation - worsening of phenotype in successive generations
- Pleiotropy - diverse phenotypic manifestations of a single gene disorder

The process by which genetic material is utilized to produce synthesis of protein is initiated by a complex signaling process which activates certain genes and suppresses others. Control of protein synthesis is an obviously crucial first step in the composition of a cell or organism. A "preRNA" molecule is transcribed from the DNA in the nucleus passing along the genetic coding information contained the trinucleotide segments (codons), each of which contains the information for a specific amino acid. Introns from the RNA molecule are then spliced out, leaving the remaining exons which form a continuous coding sequence. This is messenger RNA, which carries the genetic information from the nucleus to the ribosomes of the cytoplasm. This process is translation. Another type of RNA, transfer RNA, interprets the code on the messenger RNA and delivers the appropriate amino acid from the cytoplasm to the ribosome to be incorporated into the protein being synthesized. Subsequent post-translational modifications usually include proteolytic cleavages to achieve the final form of the protein. The finished protein is transported by a specialized protein known as a chaperone.

It is by this process that mutations involving a single gene can have such a widespread effect. The best clinical example is evident in most forms of osteogenesis imperfecta. A variety of point mutations in the COL1A1 and COL1A2 genes result in transmission of genetic information producing faulty collagen with diminished mechanical strength.

## References

1. Cole W. Genes and orthopaedics. *J Bone Joint Surg(Br)* 1999;81-B:190-92.
2. Jaffurs D, Evans CH. The human genome project: Implications for the treatment of musculoskeletal disease. *J Am Acad Ortho Surg* 1998;6:1-14.
3. Rosier RN, Reynolds PR, O' Keefe RJ. Molecular and cell biology in orthopaedics. In: Buckwalter JA, Einhorn TA, Simon SR, editors. *Orthopaedic Basic Science. Biology and Biomechanics of the Musculoskeletal System*. 2 ed: American Academy of Orthopaedic Surgeons; 2000. p. 20-76.
4. Shore EM, Kaplan FS. Tutorial: Molecular biology for the clinician: Part I. General principles. *Clin Orthop* 1995;306:264-83.
5. Shore EM, Kaplan FS. Tutorial: Molecular biology for the clinician: Part II. Tools of molecular biology. *Clin Orthop* 1995;320:247-78.