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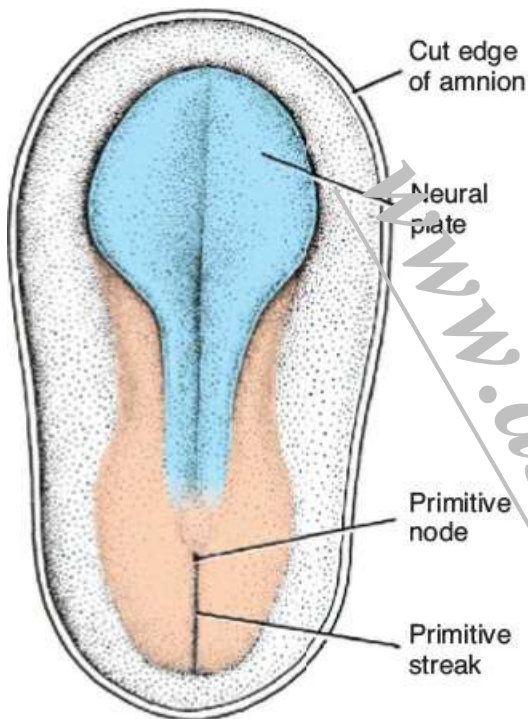
Figure Credits

Glossary of Key Terms

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Placode: A local thickening in the embryonic ectoderm layer that develops into a sensory organ or ganglion.



19 days

ODE TO A PLACODE

There once was a flat sheet of cells
That were stumpy and ugly as hell;
But one day they arose, stood tall on their toes,
and declared they were the best cells of all.

Presumptuously they cried that their lineage was high
and right proudly they bragged of their codes;
But soon it was clear, they weren't like the ear
and they were nixed in their dreams as placodes.

Semantics, they screamed, please maintain our dreams,
but their pleas were unheeded and late;
And now to this day in repast they must lay
as a misconstrued, flat neural plate!

T. W. Sadler
Sheepskin, MT

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Introduction to Molecular Regulation and Signaling

■ INTRODUCTION

Molecular biology has opened the doors to new ways to study embryology and to enhance our understanding of normal and abnormal development. Sequencing the human genome, together with creating techniques to investigate gene regulation at many levels of complexity, has taken embryology to the next level. Thus, from the anatomical to the biochemical to the molecular level, the story of embryology has progressed, and each chapter has enhanced our knowledge.

Embryonic development is directed by **genomes** that contain all of the information required to make an individual. The information is encoded in **DNA** in sequences called **genes** that code for proteins. In turn, proteins regulate the expression of other genes and act as signal molecules to orchestrate development.

There are approximately 23,000 genes in the human genome, which represents only one-fifth of the number (100,000) predicted prior to completion of the Human Genome Project. Because of various levels of regulation, however, the number of proteins derived from these genes is closer to the originally predicted number of genes. What has been disproven is the one gene—one protein hypothesis; through a variety of mechanisms, a single gene may give rise to many proteins.

Gene expression can be regulated at several levels: (1) Different genes may be transcribed, (2) DNA transcribed from a gene may be selectively processed to regulate which RNAs reach the cytoplasm to become messenger RNAs (mRNAs), (3) mRNAs may be selectively translated, and (4) proteins made from the mRNAs may be differentially modified.

■ GENE TRANSCRIPTION

Genes are contained in a complex of DNA and proteins (mostly histones) called **chromatin**, and the basic unit of structure of chromatin is the **nucleosome** (Fig. 1.1). Each nucleosome is composed of an octamer of **histone proteins** and approximately 140 base pairs of DNA. Nucleosomes themselves are joined into clusters by the binding of DNA existing between nucleosomes (**linker DNA**) with other histone proteins (H1 histones; Fig. 1.1). Nucleosomes keep the DNA tightly coiled, such that it cannot be transcribed. In this inactive state, chromatin appears as beads of nucleosomes on a string of DNA and is referred to as **heterochromatin**. For transcription to occur, this DNA must be uncoiled from the beads. In this uncoiled active state, chromatin is referred to as **euchromatin**.

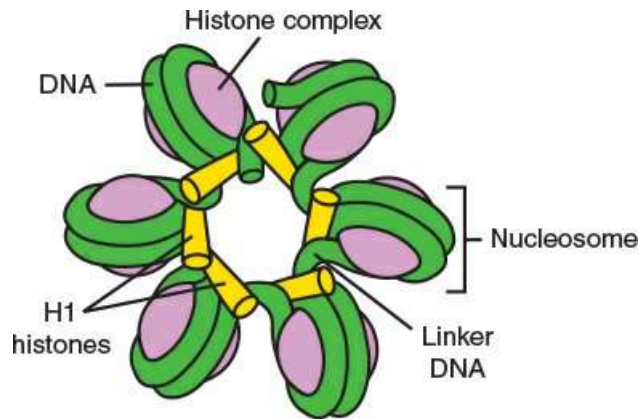


FIGURE 1.1 Drawing showing nucleosomes that form the basic unit of chromatin. Each nucleosome consists of an octamer of histone proteins and approximately 140 base pairs of DNA. Nucleosomes are joined into clusters by linker DNA and other histone proteins.

Genes reside within the DNA strand and contain regions called **exons**, which can be translated into proteins, and **introns**, which are interspersed between exons and are not transcribed into proteins (Fig. 1.2). In addition to exons and introns, a typical gene includes the following: a **promoter region** that binds **RNA polymerase** for the initiation of **transcription**; a **transcription initiation site**; a **translation initiation site** to designate the first amino acid in the protein; a **translation termination codon**; and a **3' untranslated region** that includes a sequence (the poly A addition site) that assists with stabilizing the mRNA, allows it to exit the nucleus, and permits it to be translated into protein (Fig. 1.2). By convention, the 5' and the 3' regions of a gene are specified in relation to the RNA transcribed from the gene. Thus, DNA is transcribed from the 5' to the 3' end, and the promoter region is upstream from the transcription initiation site (Fig. 1.2). The promoter region, where the RNA polymerase binds, usually contains the sequence TATA, and this site is called the **TATA box** (Fig. 1.2). In order to bind to this site, however, the polymerase requires additional proteins called **transcription factors** (Fig. 1.3). Transcription factors also have a specific **DNA-binding domain** plus a **transactivating domain** that activates or inhibits transcription of the gene whose promoter or enhancer it has bound. In combination with other proteins, transcription factors activate gene expression by causing the DNA nucleosome complex to unwind, by releasing the polymerase so that it can transcribe the DNA template, and by preventing new nucleosomes from forming.

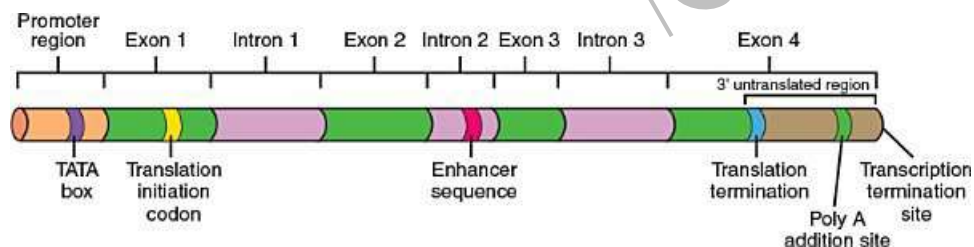


FIGURE 1.2 Drawing of a “typical” gene showing the promoter region containing the TATA box; exons that contain DNA sequences that are translated into proteins; introns; the transcription initiation site; the translation initiation site that designates the code for the first amino acid in a protein; and the 3' untranslated region that includes the poly A addition site that participates in stabilizing the mRNA, allows it to exit the nucleus, and permits its translation into a protein.