

# Gene Function

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The chromosomes within our cells contain an enormous amount of information. It is estimated that humans have somewhere around 30,000 genes. Each gene codes for an RNA molecule that is either used directly or used as a guide for the formation of a protein such as the insulin shown earlier. Information in our cells generally flows in a predictable order from the storage form of the information (DNA) through the working form (RNA) into the final product (protein). Further information on the topics on this page can also be found in most introductory Biology textbooks, we recommend Campbell Biology, 11th edition.<sup>1</sup> This pathway is used by all organisms and is diagrammed below.

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As shown, DNA is used as a guide or template for the production of more DNA. This process, known as replication, is addressed [here](#).

The process in which particular sections of DNA (genes) are used to produce RNA is known as transcription. We will cover transcription in some detail because alterations in the transcription of certain genes are very important in the development of cancer.

The set of genes that are 'on' at any given time is critical. The variable environment in which we live means that different genes need to be 'on' at different times. For example, if a meal contains large amounts of lactose, a sugar found in milk, then our bodies respond by turning on (transcribing) the genes that lead to the production of enzymes that break down lactose. If a different sugar or nutrient is present, the correct genes need to be turned on to process it.

## Transcription

The goal of transcription is to make an RNA copy of a gene. This RNA can direct the formation of a protein or be used directly in the cell. All cells with a nucleus contain the same exact genetic information. As discussed, only a small percentage of the genes are actually being used to make RNA at any given time in a particular cell. The transcription process is very tightly regulated in normal cells.

- Genes must be transcribed at the correct time.
- The RNA produced from a gene must be made in the correct amount.
- ONLY the required genes should be transcribed.
- Turning transcription off is just as important as turning it on.

You can picture this as a sophisticated production line, like you would find in a factory. You would want the assembly line working when you needed the product and shut down when you no longer needed the product.

Human chromosomes contain an enormous amount of information. Each chromosome is composed of a single extremely long piece of DNA comprised of millions of nucleotides. An individual gene occupies just a small stretch of a chromosome.

Shown in the animation below is the organization of the DNA in a chromosome. The DNA is tightly coiled and looped to take up less space, just like winding thread on a spool. The chromosome shown below has been copied or replicated and has a characteristic **X** shape. Chromosomes look like this prior to cell division.

## Steps of Transcription

In order for transcription to work, there must be some way of identifying where the process should start and stop. This is accomplished by special proteins, which bind to the start of genes that are to be transcribed. These proteins are called **transcription factors**.

The process of transcription is divided into several steps:

1. A transcription factor recognizes the start site (promoter) of a gene that is to be transcribed.
2. The enzyme that makes the RNA (RNA polymerase) binds to the transcription factor and recognizes the start region.
3. The enzyme proceeds down the DNA making a copy until the end of the gene is reached.
4. The enzyme falls off and the RNA is released. This copying process may be repeated numerous times.
5. If the RNA is one that codes for a protein, it will leave the nucleus and enter the cytosol.

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Remember that the gene depicted above is actually a stretch of nucleotides along a DNA molecule (the chromosome).

The inappropriate activity of transcription factors has been identified in almost all types of cancer known. Since these factors are essential to the orderly activities of a cell, a misbehaving component can have important effects for all of the other parts of the cell. Revisiting the production line analogy, a misbehaving transcription factor might lead to the assembly line being on when it is not supposed to, creating too much product. Alternatively, the line might not be on when it is needed, leading to a deficit of a particular product.

## Transcription Factors

Some examples of transcription factors that malfunction in human cancers are:

- *p53* (*TP53*) - The gene that codes for the p53 transcription factor (protein) is mutated in over half of all cancers of any type. The protein that the *p53* gene codes for is important because it controls the transcription of genes that are involved in causing cells to divide. More information on the *p53* gene can be found in the section on [tumor suppressors](#).
- *Rb* - The protein product of this gene is a transcription factor with an interesting function. It actually works by *blocking* other transcription factors. In this way, *Rb* prevents transcription of key genes required for cell division to progress. Initially described as a gene mutated in retinoblastoma, a cancer of the eye from which the gene derives its name, the *Rb* protein is now known to play a role in many different cancer types. More information on the *Rb* gene can be found in the section on [tumor suppressors](#).
- The estrogen receptor (ER) - This protein binds to estrogen that enters the cell. Estrogen is a steroid (lipid) hormone produced by the ovaries. The combination of protein and hormone then acts as a transcription factor to turn on genes that enable the target cells to divide. The receptor is active in the cells of the female reproductive organs, such as breasts and ovaries. Because of this, estrogen is recognized as a factor that enhances the growth of certain cancers arising in these tissues.

The mechanism of estrogen action is shown below.

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The small **green** ball represents estrogen. It is a small hydrophobic molecule and it enters cells by crossing through the lipid membrane. Once in the cell, the estrogen binds to its receptor (colored **orange**) and the complex binds to DNA in the nucleus causing genes to be transcribed.

Several drugs have been developed to try to block the gene-activating function of estrogen. A commonly prescribed example is tamoxifen, a drug that partially inhibits the activity of estrogen. Tamoxifen is colored **pink** in the animation below.

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These drugs should slow the growth of cancers that are growing in response to the presence of estrogen and its receptor. More information on estrogen receptors and cancer can be found in the section on [cancer treatments](#).

The importance of transcription factors to the division of cells has been stressed several times. Cancer results from uncontrolled cell division so the next process discussed is cell division. It is important to understand how this process normally functions so that we can appreciate what happens when things go wrong.

## Translation

After the messenger RNA (mRNA) is produced through the transcription process just described, the mRNA is processed in the nucleus and then released into the cytosol.

The mRNA is then recognized by the ribosomal subunits present in the cytosol and the message is 'read' by the ribosome to produce a protein. The information for the direction of protein formation is encoded in the sequence of nucleotides that make up the mRNA. Groups of three nucleotides (called codons) are 'read' by the ribosome and lead to the addition of a particular amino acid into the growing polypeptide (protein). The process is depicted schematically in the animation below.

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After the protein is formed it acquires its active folded state and is able to perform its functions in the cell. The proper folding, transportation, activity and eventual destruction of proteins are all highly regulated processes.

The genes that control these processes are often damaged and not functioning properly in cancer cells.

More information on this topic may be found in Chapter 1 of [The Biology of Cancer](#) by Robert A. Weinberg.

## Gene Function Summary

### The Central Dogma

- The DNA in our chromosomes contains genes that get transcribed into RNA.
- There are several different types of RNA (tRNA, mRNA, rRNA, etc.). They are composed of the same building blocks but have different functions, locations and structures.
- Messenger RNA (mRNA) may be translated into a protein. The standard information flow is:
  - DNA→RNA→Protein
- The set of genes that are 'on' at any given time is critical. Different genes need to be 'on' at different times depending on the needs and functions of any particular cell.

### Transcription

- The goal of transcription is to make an RNA copy of a gene.
- Transcription factors bind to the starting point of genes in order to identify the spot where transcription begins.
- *p53*, *Rb*, the estrogen receptor are all transcription factors that malfunction in cancers.
- The process of transcription is divided into several distinct steps:
  1. Transcription factor recognizes and binds to a gene's start site (promoter).
  2. An RNA-making enzyme (RNA polymerase) binds to the transcription factor.
  3. The enzyme makes an RNA copy of the gene.
  4. The enzyme falls off and the RNA is released.
  5. The RNA will either remain in the nucleus or it will exit into the cytosol.

### Translation

- The goal of translation is to make a protein using the information encoded in mRNA.
- The process of translation is divided into several steps:
  1. mRNA leaves the nucleus and is recognized and bound by ribosomal subunits in the cytosol.
  2. The ribosome 'reads' the RNA three nucleotides (one codon) at a time.
  3. The ribosome inserts the amino acid corresponding to the codon into the growing protein.

4. The ribosome encounters a stop codon and terminates protein synthesis.
5. The protein enters a highly regulated folding process and obtains a fully folded structure.

- Genes that control the proper folding, transportation, activity and eventual destruction of proteins are often damaged or malfunctioning in cancer.

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<sup>1</sup> Urry, L. A., Cain, M. L., Wasserman, S. A., Minorsky, P. V., & Reece, J. B. (2017). *Campbell Biology* (11th ed.). Pearson.