

Gene Transfer

Gene therapy is the process whereby the information encoded within a gene is used to treat a disease by correcting a genetic deficiency, or by altering a cell's genome to restore the normal physiological function of an organism. (Or more simply put: using genes to treat diseases). To understand how gene therapy works, one needs to have a basic understanding of the human body and how a human cell functions. In this section, we give a very brief introduction to human cellular biology, providing enough background so that the layman can understand how gene therapy works. The aim of the section is to attempt to dispel any possible misconceptions the public has about gene therapy, and to introduce the topic to those interested in pursuing further education in this area.

Basic Human Anatomy

The human body is made up of many different organs that each have a specific role in maintaining the good health of an individual. The brain is involved in thought, reasoning and, in general, controlling our actions; the heart pumps blood around our body supplying all the organs with essential nourishment; the lungs load our blood with oxygen that helps supply the energy we need to function; the

stomach, kidneys, liver, intestine and bladder all function in unison to extract nutrients from our food and dispose of unwanted toxins. Each organ plays an essential and unique part keeping us alive, see figure 1.

In order to carry out its appointed role, an organ comprises of billions of cells of different types, each arranged in tightly controlled structures that form the overall architecture of the organ. It is the cells that are actually responsible for the proper functioning of the organ. If something goes wrong with an organ, then in order to treat it, we must restore the proper functioning of these cells.

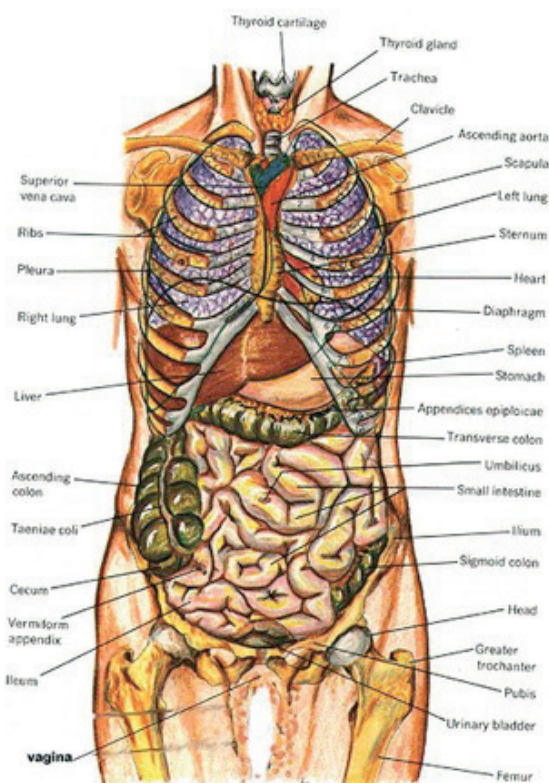


figure 1 diagram of human body

Basic Cell Biology

Most cells are made up of similar components: a nucleus, the part of the cell containing genetic information; a variety of organelles, sub-cellular structures that carry out specific functions required by the cell, analagous to the way that different organs carry out specific functions of the body (e.g. lysosome, mitochondrion, golgi etc); the cytoplasm, the liquid in which the nucleus and organelles are suspended, and the plasma membrane, the structure that surrounds the cell and maintains its shape. A typical cell is shown in figure 2.

In many ways, it is the nucleus that is the

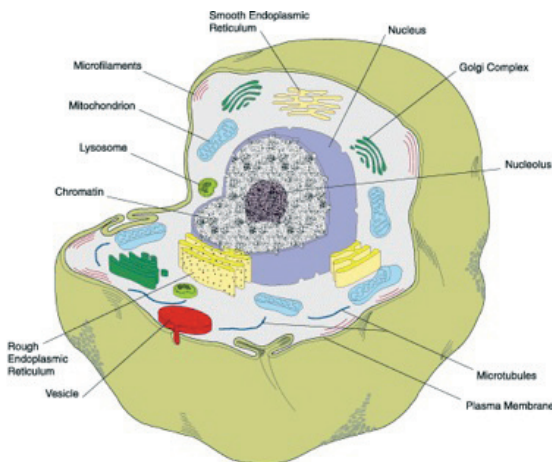


figure 2 diagram of human cell

most important organelle of a cell, in that it contains all the information necessary to produce each constituent of the cell. Each organelle and cellular structure is made up of protein, sugars and lipids (fatty compounds), and the nucleus not only contains the blueprint for the production of each of these components, but also the information necessary for their correct assembly and final location. This information is contained within the cell's DNA, which is the major constituent of the nucleus and is tightly condensed in a highly organised manner within the nuclear membrane.

Human Chromosomes

Inside the nucleus our DNA is arranged into 23 pairs of chromosomes (or 22 pairs, and one X chromosome and Y chromosome if you are male). These 46 chromosomes are collectively known as the human genome, as they contain all of the genes that act as the blueprint of the human body. We can think of our DNA as a long linear molecule that is split into 46 separate pieces (i.e. the chromosomes). Within each chromosome there are thousands of genes lined up sequentially one after another, and separated by intergenic regions. Each gene is a unit of DNA that encodes for a specific protein, with a unique function. It is the combination of many different proteins, and their actions on other molecules like sugars and lipids, that make up the basis of the organelle, and by consequence, of the cell itself, see diagram below: So one can imagine that in a disease, where an organ is not working properly because its constituent cells are malfunctioning, we can often trace the malfunction to a faulty protein that is not performing its allocated task.

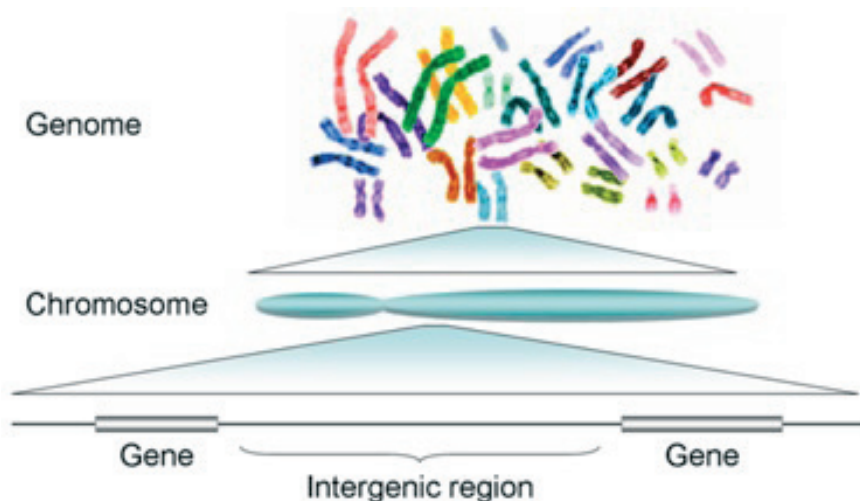


figure 3 diagram of human genome

These protein malfunctions can either be genetic, or acquired during (1) an infection, (2) a faulty immune response to one's own cells, (3) pre-mature tissue degeneration, or (4) the formation of cancer. So, in any circumstance where a disease, of any type, can be traced to a malfunction of a protein, or where a protein of known activity can restore the proper functioning of a cell, gene therapy can be applied. This is simply because we can now use the correct gene to deliver the correct version of the protein to the cell we want to repair. It is important to note that by delivering genes specifically into diseased cells, there is very little chance of passing this new genetic information in the future to our children. In order to do so, the cells that comprise our genitalia would have to be the target for gene transfer, a process that is illegal, and extremely technically demanding.