

Cell Determination and Differentiation

Slide 2 If you were to closely inspect the tissues of a multicellular organism, you would find millions of cells of many different types. Think of your own arm as an example. Your arm contains on the order of several hundred million different cells, including skin cells, muscle cells, fat cells, neurons, bone marrow cells, cells of connective tissue, and several types of mature blood cells. Multicellular organisms begin life, however, as an apparently simple, single-celled zygote. How then do all of the cells and types of cells that make up an organism come to be from this single cell? One part of this puzzle should be clear to you from previous lessons. To go from a single-celled zygote to a many-celled mature organism, there must be many rounds of cell division, or mitosis. However, if zygotes only divided over and over to produce many cells, we would end up as big clumps of zygotes, rather than organisms with clearly defined parts, such as tissues and organs. There must be something that happens to cells that allows them to take on their mature form and role in an organism. In fact, there are two related processes – cell determination and cell differentiation – that allow cells to do just that. Both of these processes are fundamentally controlled by the cell signaling mechanisms discussed in the previous lesson, and are the focus of this lesson.

Slide 3 When you started out as a zygote it would be fair to say that you, as a single cell, had ‘great potential’ – well, at least great developmental potential. Think about it - that zygote really gave rise to every other cell that makes up your body. Because the zygote has the potential to form any other type of cell in your body, it is referred to as totipotent. During development, the zygote divides to produce other cells, which in turn divide to produce more cells. As this happens, the developmental potential of these cells is reduced, and cells become more and more restricted to particular developmental pathways. In other words, as development proceeds, cells become destined to particular fates – some cells will become skin cells, others will become muscle cells, and so on. This process of ‘sealing’ the developmental fate of a cell or cells is called cell determination. In fact, cell determination is a process that occurs in the development of most, if not all multicellular organisms, including other animals besides humans, and plants.

An excellent illustration of this process involves cell transplants in developing embryos. In the experiment illustrated here, cells from an early stage frog embryo are transplanted from one area of the embryo to another. Normally, cells in the area from which the transplants are taken develop into neural tissue. Cells in the area receiving the transplant normally develop into epidermal, or skin cells. If this transplantation is done early enough in development, the transplanted cells will form epidermal tissue, just like their new neighboring cells. In this case, the developmental fate of the transplanted cells had not yet been determined at the time of transplantation. However, if the transplantation is done slightly later in development, the transplanted cells will form neural tissue, just as they would in their normal location in the embryo. In this case, it is clear that the transplanted cells were determined at the time of transplantation.

In both of these cases, there were no clear physical differences in the cells when they were transplanted, yet there were differences in their developmental potential. This again is a clear illustration of what is meant by determination. The developmental fate of a cell is determined prior to the cell taking on its mature form, whether that is a muscle, skin, nerve, or other type of cell.

Slide 4 As we saw on the previous slide, most cells physically change after determination to take on their mature form and role for the organism. This process of change is called differentiation. Differentiation is an essential part of development for all multicellular organisms, and allows cells to perform highly specialized functions for the organism. Take for example the cells of a colorful flower petal. These cells originate as colorless, seemingly simple cells. However, during the development of the flower these cells develop to contain the pigment that gives the flower petals color, and ultimately attracts pollinators to the flower.

Another, more extreme example to consider are the special nerve cells called Purkinje fibers, which carry electrical impulses in the brains of animals. These cells, similar to the cells of the flower petal, start off as seemingly simple cells. However, during development they differentiate into extensively branched cells that may form up to 100,000 synapses, or associations, with other cells of the brain.

Slide 5 So, what exactly causes these changes in developing cells? What are the signals that lead to determination and differentiation of developing cells? It should not be too surprising that cell determination and differentiation are ultimately caused by changes in gene expression. One well-studied example of the molecular basis of cell determination and differentiation involves the development of mature muscle cells in vertebrates. Researchers have found that in muscle cells there are several genes in the DNA that act as 'master switches' for many other genes. In essence, the protein product that these genes code for acts as a transcription factor for other genes that produce proteins involved in the maturation of the cell. In the illustration on this slide, the 'master gene' under consideration is the myoD gene. When this gene is turned off, or is not being transcribed, other muscle-specific genes are also turned off. If myoD is active, on the other hand, it produces a transcription factor that binds to and activates another gene, which in turn activates yet other muscle-specific genes, such as genes that code for myosin and other muscle proteins. The activation of myoD results in the determination of the developmental fate of the 'immature' muscle cells, called myoblasts. When this gene is activated, the cell will become a muscle cell. The resulting activation of other muscle-specific genes allows the myoblast to physically differentiate into a mature muscle cell by producing the proteins characteristic of that cell type.

Slide 6 Investigations of cell determination and differentiation have led to many significant discoveries in biology and other areas. For instance, because many mature plant cells remain totipotent, it is possible to produce entirely new plants from individual cells or parts of plants. Plants produced in this way are genetically identical to the original plant, which can be of great use in genetic studies and studies of plant pathogens. Agriculture has also long relied on vegetative propagation, which fundamentally is a

matter of cell determination and differentiation, to produce crops such as potatoes, or to produce effective fruit trees by grafting.

In medical research, the processes of cell determination and differentiation are an essential component of stem cell research. 'Stem cells' refers to cells present in embryos and adult mammals that retain the ability to develop into many other cell types. In adult humans, stem cells have so far been found in bone marrow, in the brain, in blood, in some muscles, the skin, and in the liver. These types of stem cells so far appear to be able to differentiate into a limited number of cell types. Because of this, they are often referred to as multipotent, rather than totipotent. Normally, our bodies use stem cells to regenerate tissue, such as the skin, liver, or blood. Medical researchers hope to exploit the characteristics of stem cells to regenerate organs or parts of organs, in order to replace diseased or destroyed tissues and organs. In theory, stem cells could be used to re-grow damaged spinal columns, diseased heart tissue, or other parts of the body. Stem cell research also is an important tool in the search for cures for cancer. By better understanding what mechanisms control the determination and differentiation of cells, we are better able to understand the causes of different types of cancers, which typically result from abnormal cell division and differentiation patterns.