




L 8 ► Cellular Differentiation & Specialization


/ Molecular biology

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From the moment, the egg or zygote is fertilized, early development characterized by the rapid proliferation of embryonic cells, which then differentiate to produce many specialized types of cells that make up the tissues and organs of multicellular animals. As cells differentiate, their rate of proliferation usually decreases, and most cells in adult animals .are arrested in the G₀ stage

A few types of differentiated cells never divided again, but most cells are able to resume proliferation as required to replace cells that have been lost as a result of injury or cell death. In addition, some cells divide continuously throughout life to replace cells that .have a high rate of turnover in adult animals



A special characteristic of cell growth and cell division, is cell differentiation, which means: **changes in physical and functional properties of cells as they proliferate in the embryo to form the different bodily structures.** The earliest and simplest theory for explaining differentiation was that the genetic composition of the nucleus undergoes changes during successive generations of cells in such a way that one daughter cell inherits a different set of genes from that of the other .daughter cell



Therefore, the present idea is that instead of loss of genes during the process of differentiation, there occurs selective repression of different genetic operons. This presumably results from the buildup of different repressor substances in the cytoplasm, the repressor substances in .another cell acting on a different group of genetic characteristics

Cellular differentiation is regulated by many processes and substances including cell size, shape, polarity, density, metabolism, and extracellular matrix composition. The main types of molecular processes that control cellular differentiation involve cell signaling. Many of the signal molecules that convey information from one cell to another during the control of cell differentiation are known as growth .factors




:Cell Proliferation in Adults

The cells of adult animals can be grouped into three general categories with respect to cell proliferation

A few types of differentiated cells, including lens cells, - (1) nerve cells and cardiac muscle cells in humans, if they are lost .they **can never** be replaced

In contrast, most cells in adult animals enter G0 stage of the - (2) cell cycle but resume **proliferation as needed** to replace cells that have been injured or have died. Cells of this type include skin fibroblasts, smooth muscle cells, the endothelial cells that line blood vessels, and the epithelial cells of most internal organs, .such as liver, pancreas, kidney, lung, prostate and breast



Other types of differentiated cells, including blood cells, - (3) epithelial cells of the skin, and the epithelial cells lining the digestive tract, that have **short spans** and must be replaced by **continual cell proliferation** in adult animal cells. In these cases, the fully differentiated cells do not themselves proliferate. Instead, they are replaced via the proliferation of .cells that are less differentiated, called stem cells

Differentiation dramatically changes a cell's size, shape, membrane potential, metabolic activity, and responsiveness to signals. These changes are largely due to highly-controlled .modifications in gene expression



?What are Stem Cells

Stem cells are a class of undifferentiated cells that are able to differentiate into specialized cell types. Commonly, stem cells come from two main sources

Embryos formed during the blastocyst phase of embryological development (embryonic stem cells) □


Embryonic stem cells are derived from 4th or 5th day-old human embryo that is in the blastocyst phase of development □

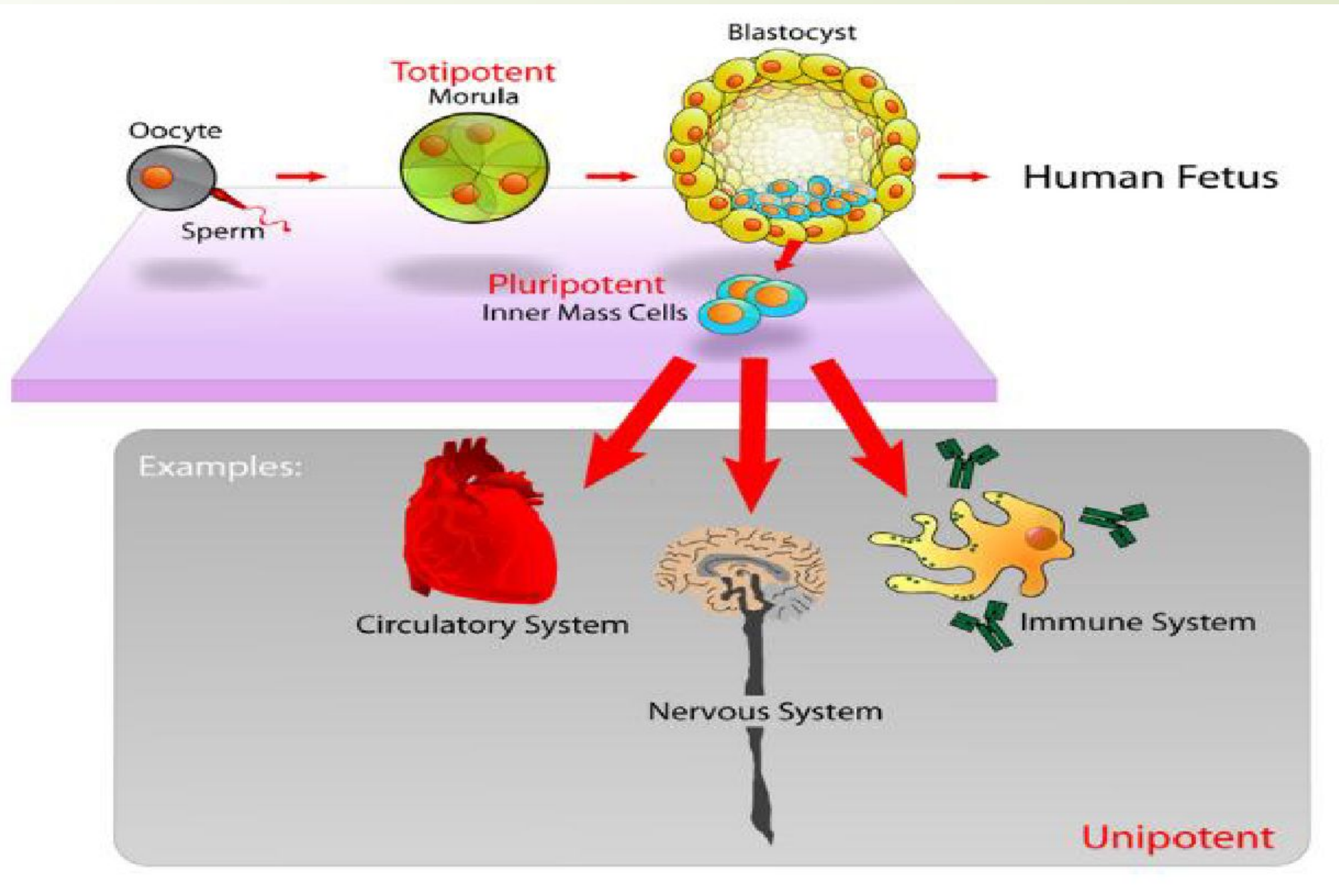
The blastocyst consists of an inner cell mass (embryoblast) and an outer cell mass (trophoblast). The outer cell mass becomes part of the placenta, and the inner cell mass is the group of cells that will differentiate to become all the structures of an adult organism. This latter mass is the source of embryonic stem cells - totipotent cells □

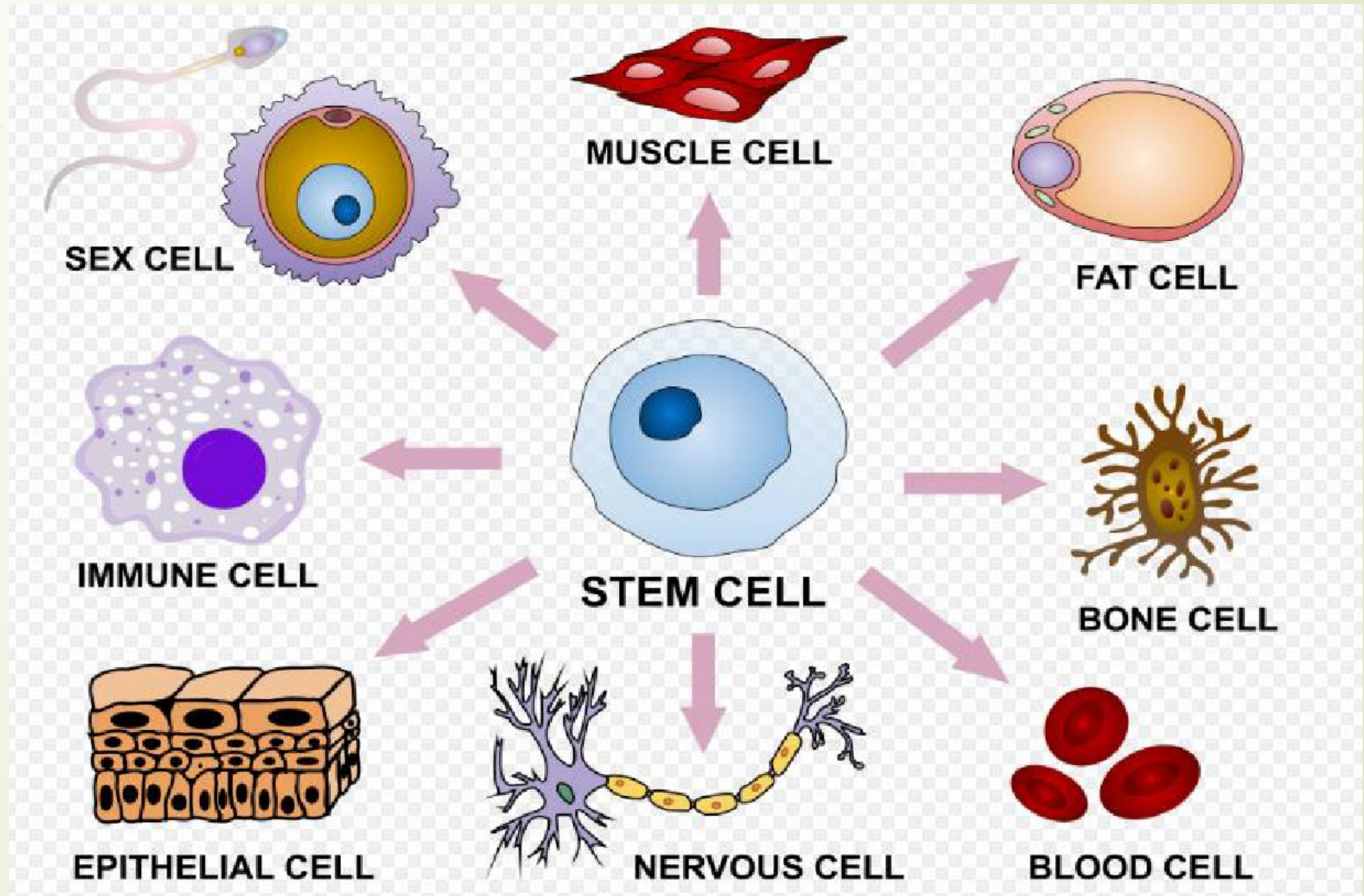
.Adult tissue (adult stem cells). Found throughout the body after development -2

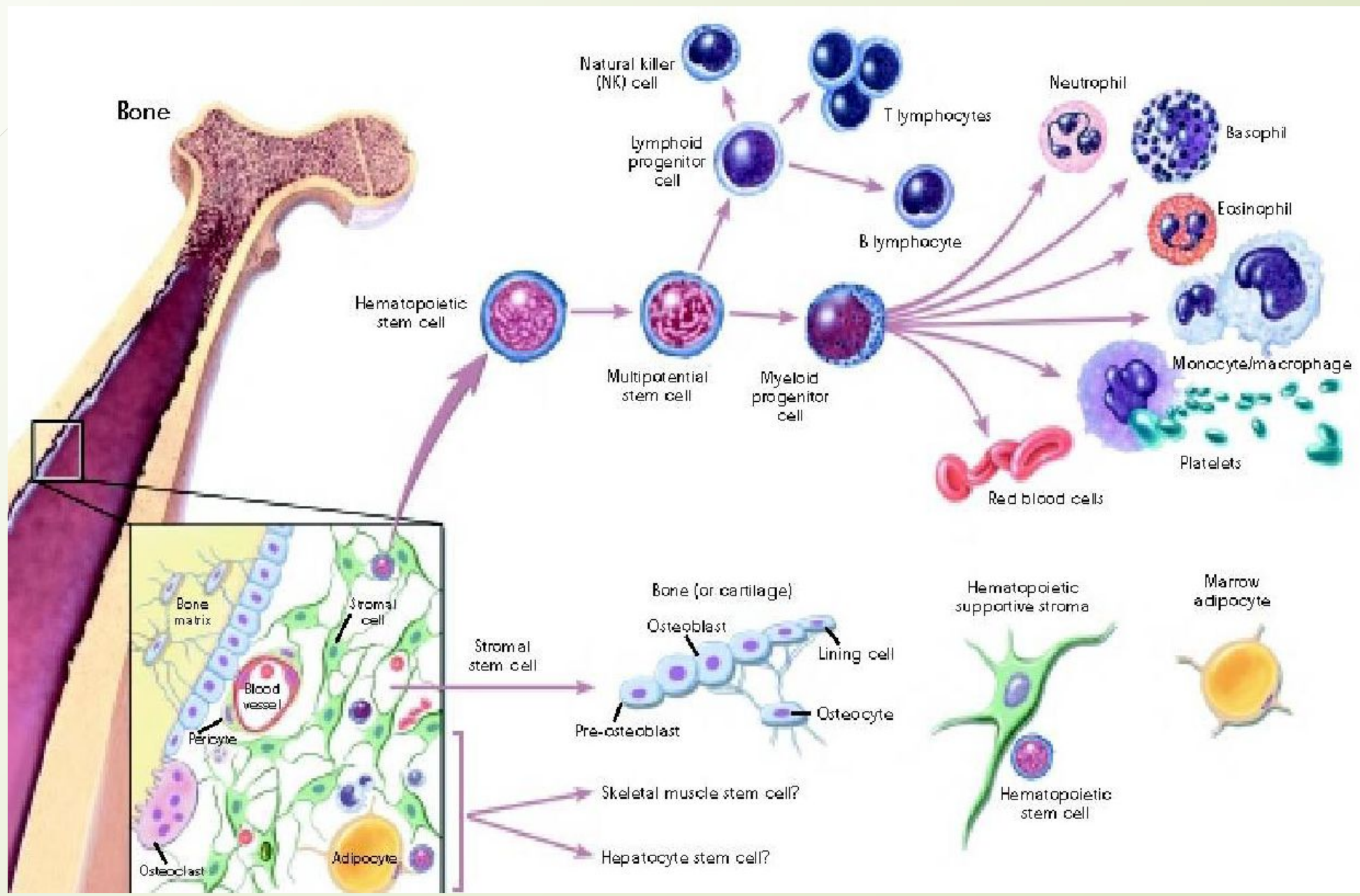
Potency: Stem cells are categorized by their potential to differentiate into other types of cells. Embryonic stem cells are the most potent since they must become :every type of cell in the body. The full classification includes


- ❑ **Totipotent** - the ability to differentiate into all possible cell types. Examples are the zygote formed at egg fertilization and the first few cells that result from the .division of the zygote
- ❑ **Pluripotent** - the ability to differentiate into almost all cell types. Examples include embryonic stem cells and cells that are derived from the mesoderm, endoderm, and ectoderm germ layers that are formed in the beginning stages of .embryonic stem cell differentiation

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- **Multipotent** - the ability to differentiate into a closely related family of cells. Examples include hematopoietic (adult) stem cells that can become red and white blood cells or platelets
 - **Oligopotent** - the ability to differentiate into few cell types. Examples include (adult) lymphoid or myeloid stem cells
 - **Unipotent** - the ability to only produce cells of their own type, but have the property of self-renewal required to be labeled a stem cell. Examples include (adult) muscle stem cells









The central problem in the study of development is the question of how a single cell, the fertilized egg give rise to the many cell types of the mature .organism

Fertilized egg → 2-cell stage → 4-cell stage (blastomere) → 8-cell stage

.four are pigmented smaller, located at the animal pole (micromeres)

.four are unpigmented larger, located at the vegetal pole (macromeres)

8-cell stage → blastula stage → gastrula stage (morula stage)

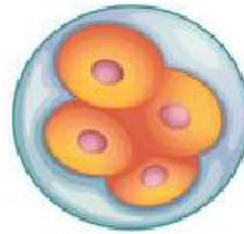
Human Embryonic and Foetal Development



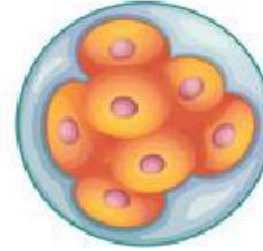
Fertilized egg



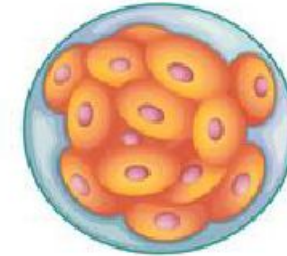
2-cell stage



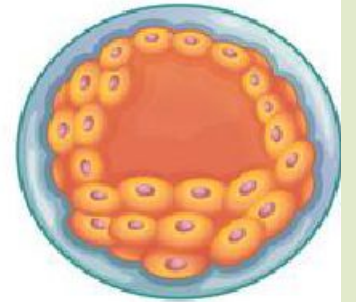
4-cell stage



8-cell stage



16-cell stage



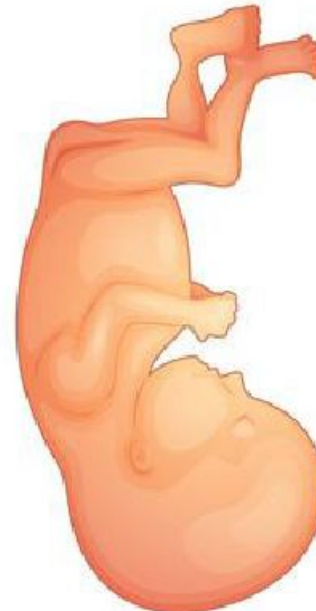
Blastocyst



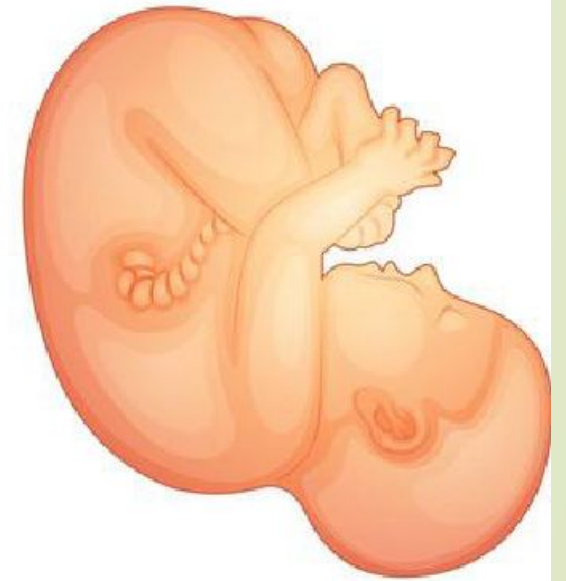
Foetus - 4 weeks





Foetus - 10 weeks




Foetus - 16 weeks



Foetus - 20 weeks




The development begins when a **sperm** fertilizes an **egg** and creates a single cell that has the potential to form an entire organism. In the first hours after fertilization, this cell divides into identical cells. In humans, approximately four days after fertilization and after several cycles of cell division, these cells begin to specialize, forming a hollow sphere of cells, called a **blastocyst**. The blastocyst has an outer layer of cells, and inside this hollow sphere, there is a cluster of cells called **the inner cell mass**. The cells of the inner cell mass go on to form virtually all of the tissues .of the human body



The cells then rearranged to form three germ layers, which give rise to different tissues

The outer germ layer (ectoderm) from which arise the nervous-1 system and epidermal layer of skin

The inner germ layer (endoderm) form the epithelial lining of the -2 digestive tract and respiratory passage and contributes the essential tissue of associated organs., such as liver and pancreas □



The middle germ layer (mesoderm) gives rise to the most of the -3 cells of organism, such as those found in the muscles, skeleton, connective tissues, blood, kidneys, gonads, and certain other organs. The process of functional and structural specialization of these cells is called differentiation. For example muscle cell precursors elongate into spindle- shaped cells that synthesize and accumulate myofibrillar proteins. The resulting cell efficiently converts chemical .energy into contractile force

Morphological modification during differentiation are accompanied by chemical changes. In the example given, formation of the muscle cell results from the synthesis of several specific proteins such as **actin & myosin**

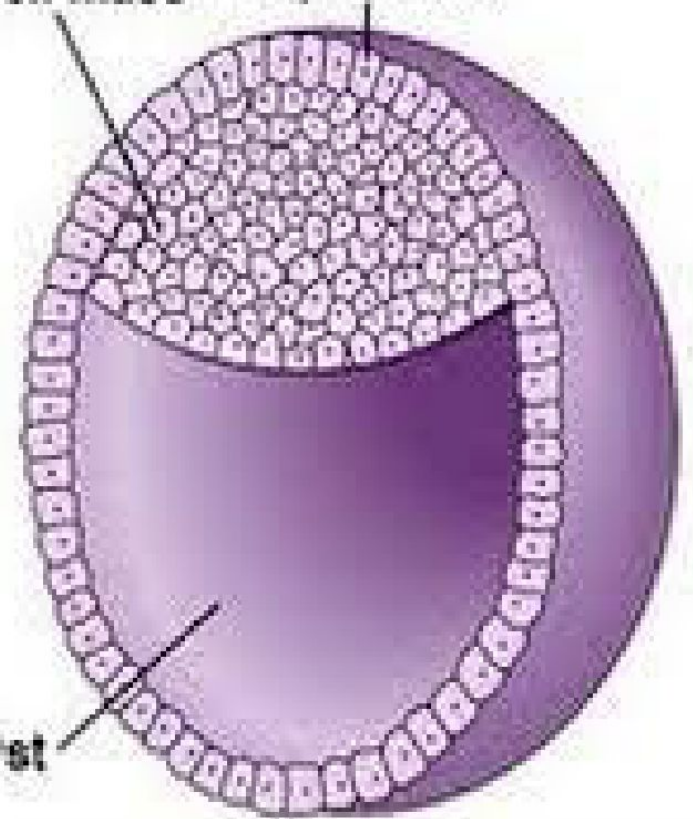


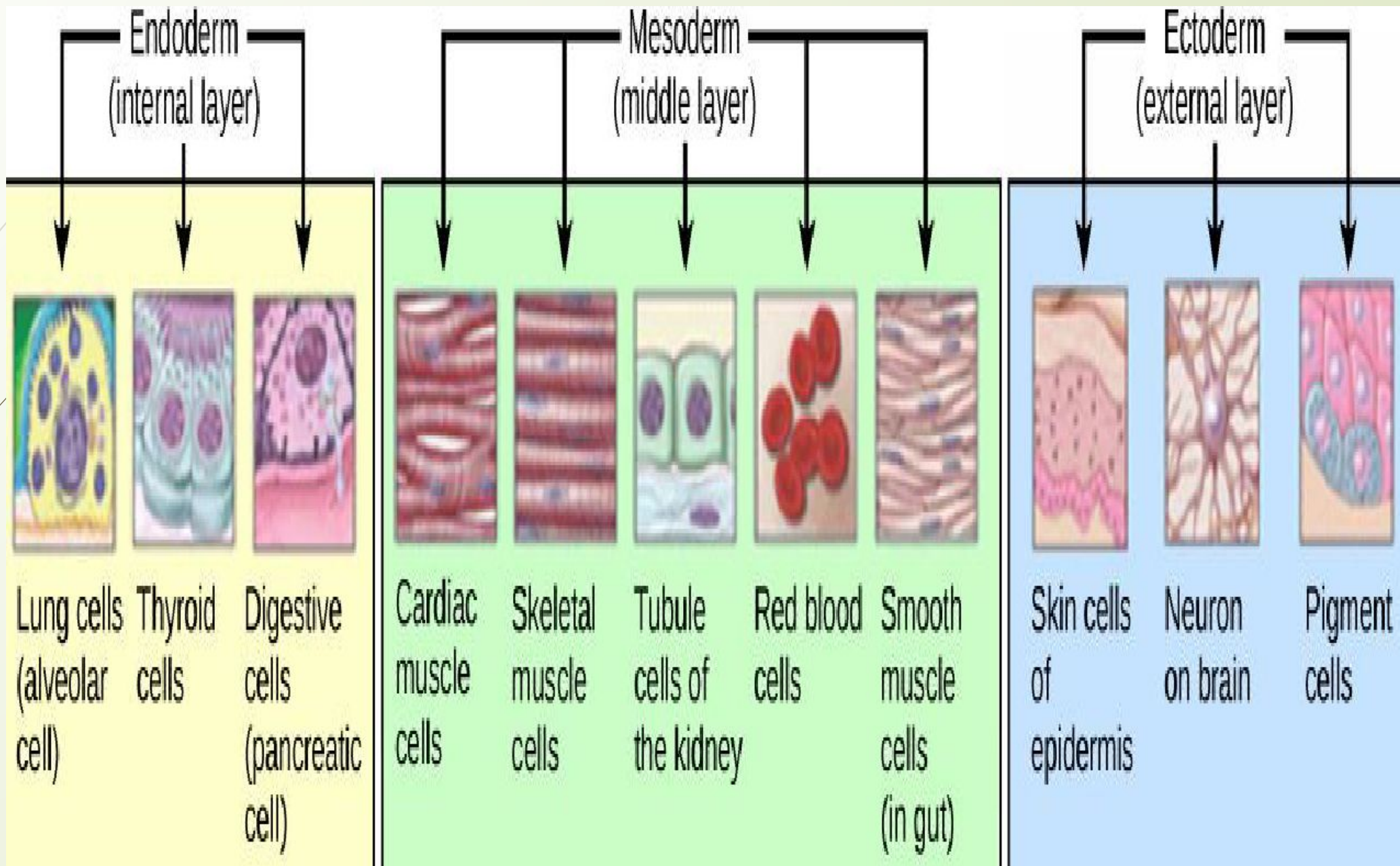
Embryonic Development — Blastocyst


inner cell mass trophoblast

Blastocyst:
hollow ball with
inner cell mass


blastocyst
cavity








Cells are not always restricted to a single activity and frequently perform two or more specialized functions, for example. Intestinal epithelial cells both absorb nutrients & synthesize digestive enzymes such as disaccharidases and peptidases



:Cellular Specialization


Cellular specialization is the ability of cell to become a distinct type of cells. All cells come from stem cells, and some of those will become RBC's, other will become muscle cells, or often .organs

Cell specialization is when a newly divided cell starts to change in shape, inner structure, cytoplasm and membrane composition so that it can carry out a specific function in one's body. Muscle cells, neurons, epidermal cells, they all have characteristics that .make them adapted to their functions



To consider how differentiation might be accomplished by an individual cell in order to differentiate during embryonic development, cells must make a series of **small shifts** in their potential, as for example, when a cell of (**blastocyst**) becomes a cell belonging to the endoderm, these then proliferate to make more cells of their own kind of **another shift** is made, and member of this group may become either part of the gut wall or the lung. If the former occurs then a **third shift** results, and the .cell becomes either absorptive or secretory

It is also generally agreed that the basic codes in the genetic material do not change with development, but that different regions of the genome are turned on and other turned off as cells develop. The genes are said to be differentially expressed, as the .cells are progressively determined



It is important, however, to recognize that a cell may have several functions and be a member of more than one cell group, **for example:**

:There are four groups of contractile cell

Muscle cells, muscle cells are the main type and comprise: striated -(1)
. (voluntary) muscle, cardiac & smooth (involuntary) muscle

Myoepithelial cells, cells are an important component of certain-(2)
. secretory glands

Myofibroblasts, have a contractile role in addition to being able to -(3)
. secrete collagen

Pericytes, are contractile cells that wrap around the endothelial—(4)
cells that are contractile cells that line the capillaries and venules
. throughout the body