1.9 CELL DIFFERENTIATION

Differentiation is the biological process whereby an unspecialized cell acquires the properties of a specialized cell (e.g., stem cells as described in chapter 2). It defines the specific structures and functions of a cell (Fig. 1.10). Mitosis produces daughter cells that are genetically identical but still the cells of multicellular organism are obviously not all identical in structures or functions. This is because of the regulation of the gene expression of various parts of the genome. The regulation of gene expression starts from the embryo level. When the embryo consists of only a few cells, each cell has the potential to develop in many different ways. As development proceeds, the possibilities available to individual cells gradually narrow, until each cells fate is fully determined and the cell has differentiated.

Differentiated cells are different from one another starting from their protein products to morphology. So the main cause is differential gene expression for the cellular differentiation process to happen. The fertilized egg or zygote has the ability to give rise to every type of cell in the adult body and hence, referred to as *totipotent*. The genomes of these cells carry instructions for all of the structures and the functions that will arise throughout

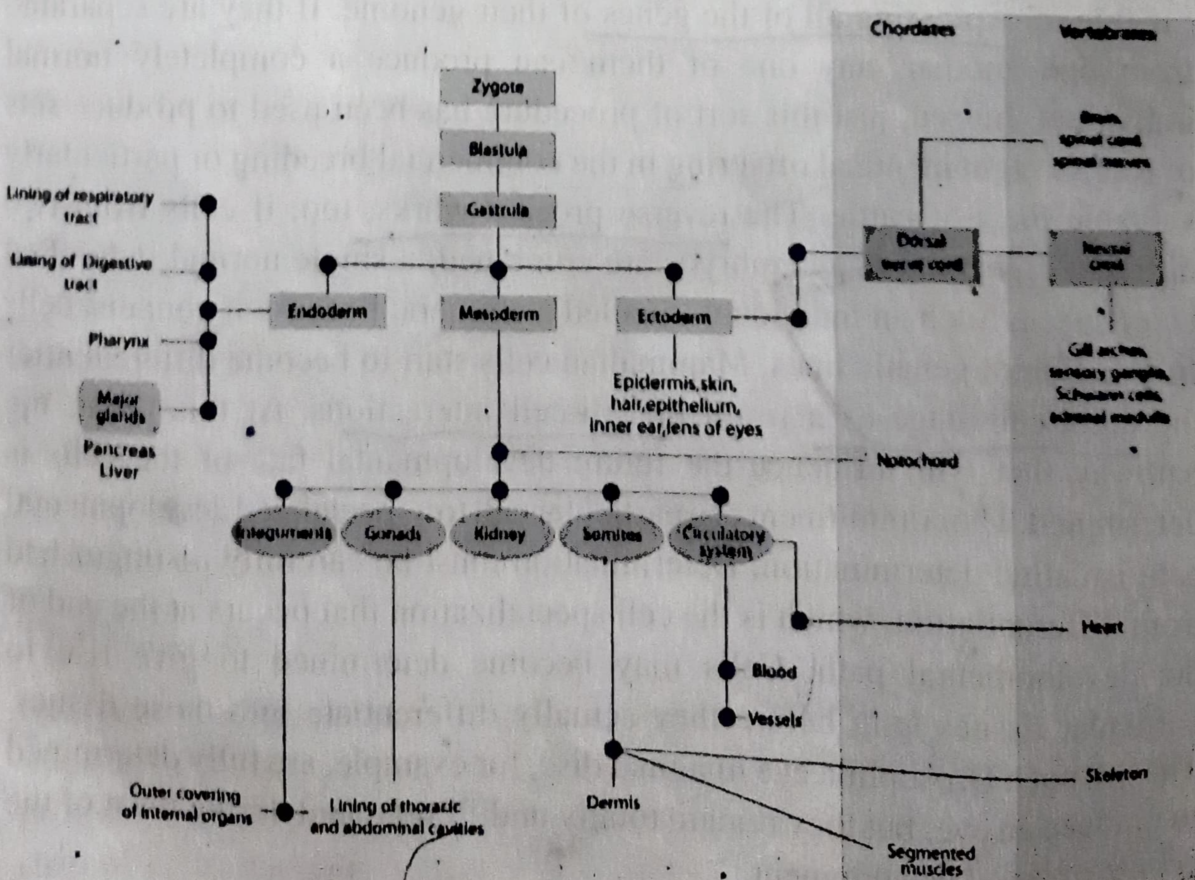

Fig. 1.10 *Development of various cellular and organ structures of the body from cellular differentiation during the fetal*

the life cycle. Later in the development of animals, the cellular descendents of the zygote lose their totipotency and become determined cells, then differentiate into specific types of cells.

Changes in the genome during differentiation: Changes are of two types, either reversible or irreversible. Differentiation is irreversible in certain types of cells like mammalian RBC, It loses its nucleus during development and become specialized for oxygen uptake and transportation.

Genomic equivalence: No information is lost from the nucleus of cells as they pass through the early stages of embryonic developments.

The zygotic cells are regarded to be totipotent as they hold the ability to generate the whole organism. As the cell divides by responding to internal and external stimuli, its potency decreases. The cells at the blastula stage are then referred to as *pluripotent*, as they can generate all the cell types except the trophoectoderm. Further upon division, they become *more restricted* and give rise to *multipotent* stem cells like hematopoietic stem cell that can generate different blood cell types.

The mammalian egg is symmetrical in its contents as well as in shape, so that all of the cells of an early blastoderm are equivalent up to the eight cell stage. The cells are said to be totipotent, meaning that they are potentially capable of expressing all of the genes of their genome. If they are separated from one another, any one of them can produce a completely normal individual. Indeed, just this sort of procedure has been used to produce sets of four or eight identical offspring in the commercial breeding of particularly valuable lines of cattle. The reverse process works, too; if cells from two different eight-cell-stage embryos are combined, a single normal individual is produced. Such an individual is called a chimera, because it contains cells from different genetic lines. Mammalian cells start to become different after the eight-cell stage as a result of cell-cell interactions. At this point, the pathway that will influence the future developmental fate of the cells is determined. The commitment of a particular cell to a specialized developmental path is called determination. Determination must be carefully distinguished from differentiation, which is the cell specialization that occurs at the end of the developmental path. Cells may become determined to give rise to particular tissues long before they actually differentiate into those tissues. The cells of a Drosophila eye imaginal disc, for example, are fully determined to produce an eye, but they remain totally undifferentiated during most of the course of larval development.

After the development of three primary cell layers from the zygote, their transformation into body's tissue and organs starts. The process of tissue differentiation begins with the formation of two morphological features found only in chordates, the notochord and the hollow dorsal nerve cord. This development of the dorsal nerve cord is called neurulation.

The notochord is first visible soon after gastrulation is complete, forming from mesoderm along the dorsal midline of the embryo. It is a flexible rod located along the dorsal midline in the embryos of all chordates, although its function is replaced by the vertebral column when it develops from mesoderm in the vertebrates. After the notochord has been laid down, a layer of ectodermal cells situated above the notochord invaginates, forming a long crease, the neural groove, down the long axis of the embryo. The edges of the neural groove then move toward each other and fuse, creating a long hollow cylinder, the neural tube, which runs beneath the surface of the embryo's back. The neural tube later differentiates into the spinal cord and brain. The dorsal lip of the blastopore induces the formation of a notochord, and the presence of the notochord induces the overlying ectoderm to differentiate into the neural tube. While the neural tube is forming from ectoderm, the rest of the basic architecture of the body is being determined rapidly by changes in the mesoderm. On either side of the developing notochord, segmented blocks of mesoderm tissue called somites form; more somites are added as development continues.

Ultimately, the somites give rise to the muscles, vertebrae, and connective tissues. The mesoderm in the head region does not separate into discrete somites but remains connected as somitomeres and form the striated muscles of the face, jaws, and throat. Some body organs, including the kidneys, adrenal glands, and gonads, develop within another strip of mesoderm that runs alongside the somites. The remainder of the mesoderm moves out and around the endoderm and eventually surrounds it completely. As a result of this movement, the mesoderm becomes separated into two layers. The outer layer is associated with the body wall and the inner layer is associated with the gut. Between these two layers of mesoderm is the coelom which becomes the body cavity of the adult.

The Neural Crest

Neurulation occurs in all chordates, and the process in a lancelet is much the same as it is in a human. However, in vertebrates, just before the neural groove closes to form the neural tube, its edges pinch off, forming a small strip of cells, the neural crest, which becomes incorporated into the roof of the neural tube. The cells of the neural crest later move to the sides of the developing embryo. The appearance of the neural crest was a key event in the