CELL–CELL INTERACTION

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11.3 CELL–CELL INTERACTION

In the last section we discussed the role of cell adhesion, cell motility and cell signalling as crucial processes in morphogenesis. We should also realise by now that from the early stages of embryogenesis, cells do not function in isolation or in a random manner. All cell behaviours like cell adhesion, cell migration, differentiation and cell division are regulated by signals being passed from one set of cells to another. These cell to cell interactions allow the embryo to get its form and shape. But how do organs develop in their proper place in the embryo? And how do cells "know" that they have to migrate and position themselves? **Pattern formation** is the process by which the cells find their positional information. There are two general modes of pattern formation: (i) through use of **morphogen** gradients and (ii) by **sequential induction**. Let us first take a look at the role of morphogen gradients.

11.3.1 Morphogen Gradients

Pattern formation in the embryo can involve gradient of chemical signals known as morphogens. This term was coined by Allen Turing in 1952 for substances whose distribution through diffusion would determine the development of cells which would respond to different threshold concentrations of the morphogen. This is a type of paracrine signalling in which the concentration of morphogen is high near the source of release and becomes lower as the distance of the responding cells increases from the source. Morphogens can consist of cytoplasmic proteins such as transcription factors that can form a concentration gradient in a single cell or syncytium as seen in early embryo of *Drosophila*, or secreted as signalling molecules that travel from cell to cell. In most cases, the responding cells find their positional information because of the different concentrations of morphogens along its gradient. Thus morphogens guide the formation of different cell types in a specific positional order by inducing transcription of genes in a dose

dependent manner. Let us understand this with a hypothetical example. In Figure 11.9 we see a plane of unspecified cells in a region of the developing embryo. Out of these cells type **A** cell have matured enough may be due to maternal cytoplasmic determinants (refer to Unit-10) so that their function is specified. **A** type cells begin to express a signalling protein that functions in this case as a morphogen. The other cells seen in the figure (B, C, and D) are still unspecified in their cell fate but are **competent** to respond to this particular morphogen as they have the receptors to bind to the morphogen. As the morphogen is secreted the cells closest to the signalling cells come in contact with the signal first. Over time the morphogen diffuses and a concentration gradient is formed as the cells closest to the source experience more ligand-receptor binding and for longer duration than the cells located farther away from the source. Cells show a differential response to the morphogen in term of the duration and the concentration of the morphogen they are experiencing. As a result they differentiate and mature by different pathways.

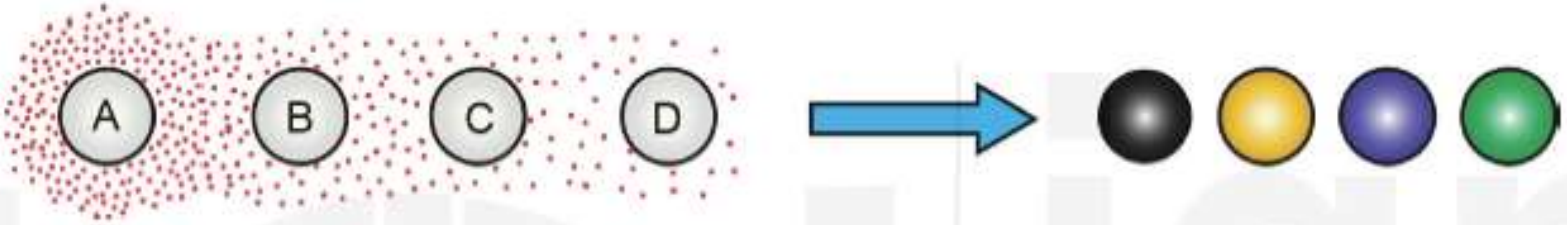

Fig. 11.9: Theoretical morphogen gradient induces different cell types. A type cells release the morphogen shown in red and depending on the concentration gradient and duration of exposure different cell fates are seen for cell type B, C, and D

In this way a morphogen gradient describes a mechanism by which cells of one part of the embryo can determine the location, differentiation and fate of many surrounding cells and provide a basis for understanding many patterning processes. The role of these signals range from establishment of initial polarity of embryos to specification of cell identity in particular tissues, notably in limb appendages and nervous system of both vertebrates and *Drosophila*. The best

11.3.2 Embryonic Induction

The embryonic process during which the close range influence of one cell or group of cells on adjacent cell/cells resulting in the change of cell behaviour like change in shape, mitotic rate, cell fate is called **embryonic induction.** There are at least two components to every inductive interaction-the **inducer,** which is the tissue that produces a signal or signals that change the cell behaviour of the receiving tissue or **responder**. Not all tissues are capable of responding to the signals produced by the inducer, only the tissues that have the ability to respond can be induced. This ability to respond is called **competence** which is an acquired condition.

Let us understand this phenomenon by taking the example of the development of the vertebrate eye. When the development of eye is initiated, two bulges are seen in the brain that approach the surface ectoderm in the head region. The head ectoderm is competent to respond to the paracrine factors released by the brain bulges that are the **optic vesicles**. The head ectoderm cells are induced to form the **lens** tissue of the eye that is, the genes for expressing the lens protein are activated. The prospective lens cells in turn secrete another paracrine factor that instructs the optic vesicle to form the retina. *Note that the two cell types that co-construct the eye induce each other*. The important part is that the head ectoderm is the only region in the embryo that is competent to respond to the instructions from the optic vesicle signals. Experiments done with *Xenopus laevis* embryo show that if the optic vesicle is placed in another part of the head ectoderm it still can induce lens tissue but if the optic vesicle is implanted anywhere else say underneath the trunk ectoderm it will fail to induce the lens tissue, showing that only the head ectoderm is competent to respond to the inducing signal (see fig.11.10).

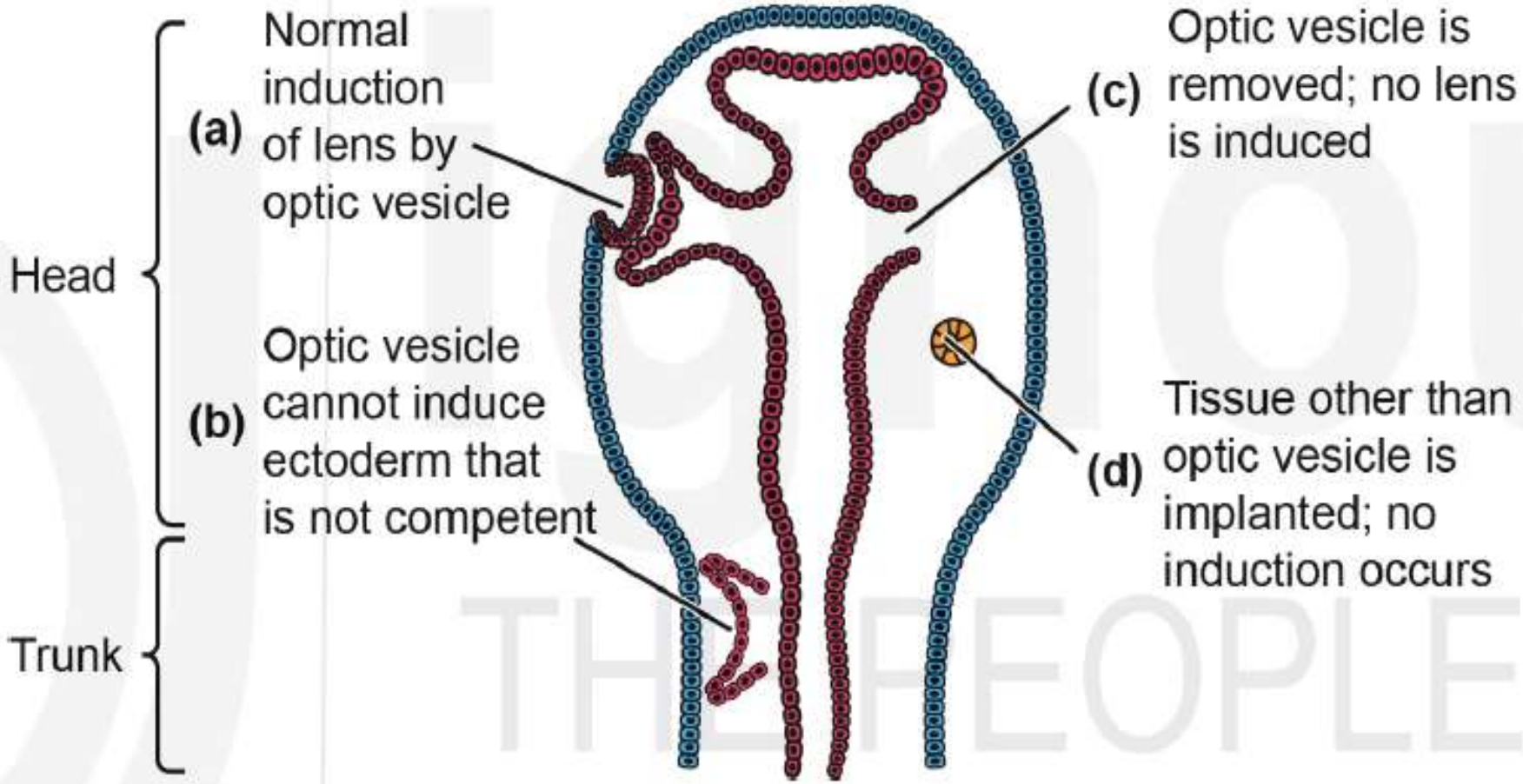

Fig. 11.10: Ectoderm's ability to respond to the optic vesicle inducer in *Xenopus* is due to competence of ectodermal cells in the head region. The optic vesicle is able to induce lens formation in the anterior portion of the head ectoderm a); b) but not in the presumptive trunk region; c) If the optic vesicle is removed no lens is formed by the overlying head ectoderm; d) most of the other tissues implanted under the head ectoderm are not able to substitute for the optic vesicle.

Another important feature of embryonic induction is that an inducer tissue is often induced by the receiver tissue as well. For example once the lens is formed it induces the optic vesicle to become the optic cup and the walls of the optic cup become distinguished to form two layers one, the neural retina and second, the pigmented retina. Such induction is called **reciprocal induction.** At the same time the lens also induces the ectoderm above it to form the cornea. The cornea forming ectoderm also acquires its competence to respond to the signals from the lens tissue. Under the influence of the lens the corneal ectoderm becomes columnar and secretes multiple layers of collagen. The mesenchyme cells from the neural crest use this collagen matrix to enter the area and secrete proteins that further differentiate the cornea. A third signal which is hormonal, dehydrates the tissue and the makes it transparent. Thus we can see that there is a sequence of induction events as shown in the development of eye in Fig.11.11.

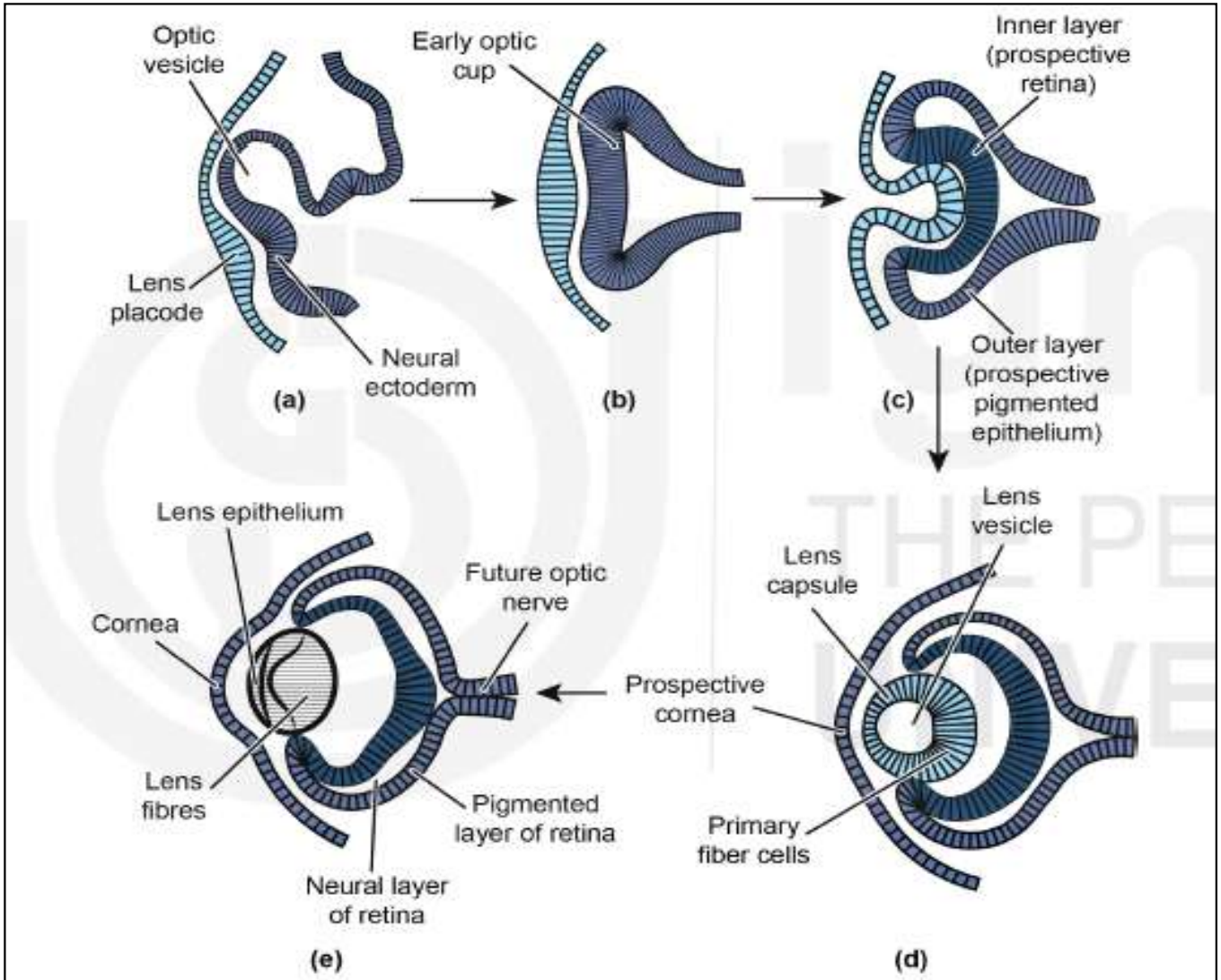

Fig. 11.11: Induction of lens in mouse. a) the optic vesicle extends toward the surface ectoderm from the forebrain. The lens placode (the prospective lens) appears as a local thickening of the surface ectoderm near the optic vesicle b) the lens placode enlarges and the optic vesicle has formed an optic cup; c) the central portion of the lens-forming ectoderm invaginates, while the two layers of the retina become distinguished; d) the lens vesicle has formed; e) the lens consists of anterior cuboidal epithelial cells and elongating posterior fiber cells. The cornea develops in front of the lens. The whole process takes about 4 days starting from day 9 in the embryo.

Induction interactions are called **instructive** if the signal from the inducing cell causes *a new gene expression in the responding cell*. In this case without the inducer cell the responding cell is not capable of differentiation into a particular cell type. Example of instructive interaction is when the optic vesicle of *Xenopus* is placed in another part of the body's ectoderm and it fails to induce the lens**. Permissive** interactions during induction are seen when the responding tissue is already specified but needs the environment to express its tissue characteristics. A good example of permissive interaction is the extracellular matrix that is often required by tissues to develop. The matrix itself does not alter the tissue type but allows the already specified tissue to express the traits of the tissue they are supposed to be. Thus, permissive interactions lend to regulate the degree of expression of the remaining developmental potential of the already specified cells.