

Molecular Genetic Mechanisms of Axial Patterning: Mechanistic Insights into Generation of Axes in the Developing Eye

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The hallmark of development of all multicellular organisms is transition of the organ primordium cells into a three-dimensional adult organ. Most tissues are derived from epithelial cell sheets that form highly organized structures. These structures exhibit polarization of apical–baso–lateral axes along with planar polarity. During organogenesis, many genetically programmed events that are sensitive to environmental cues play major roles. Various models like yeast (*Saccharomyces cerevisiae*), worm (*Caenorhabditis elegans*), fruit fly (*Drosophila melanogaster*), newts (*Notophthalmus viridescens*), mouse (*Mus musculus*), rabbit (*Oryctolagus cuniculus*), guinea pig (*Cavia porcellus*), etc. are being used to understand the genetic basis of organogenesis. Studies in different model systems have revealed that the process of organogenesis involves important events of specification, determination, and differentiation. Any deviation in these events can impair the processes of axes specification, cell proliferation, cell death, and cell differentiation. These cell biological processes work in tandem like part of a genetic orchestra, which results in final sculpting of the organ. Any perturbation in these processes leads to growth and patterning defects. During organogenesis, the determination of antero-posterior (AP), dorso-ventral (DV), and proximo-distal (PD) axes is referred to as axial patterning. We will focus on contributions from the *Drosophila* eye model to understand these important questions of developmental biology.

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Axial Patterning: Means to Generate Third Dimension to an Organ Primordium

Axial patterning marks a lineage restriction event that results in the generation of AP, DV, and PD domains in the developing organ primordium (Cohen et al. 1993; Cohen 1993). These domains are an outcome of progressive restriction of cell fates due to subdivision of the developing field into smaller fields with a more or less rigid developmental potential. These smaller fields within a larger developing field are referred to as compartments (Blair 2001; Curtiss et al. 2002; Dahmann et al. 2011; Held 2002b; Singh et al. 2012). Thus, compartments are unique territories within a bigger developing field (Blair 2001; Curtiss et al. 2002). The cells within a compartment commonly follow looser edicts such as “*You may make any portion of region ‘R’ but nothing outside it*” (Held 2002a; Wilkins 1993). The compartment boundaries are defined by the spatiotemporal expression or function of cell fate selector genes (Blair 2001; Curtiss et al. 2002; Dahmann et al. 2011). Therefore, “Selector” genes are responsible for attributing a unique property to the cells within their expression/functional domains. In the wing imaginal disc, *engrailed* (*en*) expressed in the posterior compartment and *apterous* (*ap*) expressed in the dorsal compartment (Brower 1986; Cohen et al. 1992; Held 2002b; Hidalgo 1998) serve as the selector for the posterior and dorsal fate, respectively (Table 1). The boundary between the cell populations of two compartments is the site for initiation of the signaling center that regulates patterning, growth, and differentiation of the developing field (Blair 2001; Meinhardt 1983). Activation of the signaling centers at these developmental boundaries are responsible in maintaining the downstream patterning events (Blair 2001; Curtiss et al. 2002; Dahmann et al. 2011; Singh et al. 2012). This leads to an important question: How are these boundaries generated and maintained during the development of a patterning field or an organ? In this chapter, we will provide an overview of recent advances on the genetic circuitry involved in generation of the boundary between the dorsal and ventral compartments, and its significance on the development of an organ using the *Drosophila* eye model. In this chapter, we will focus on the role of axial patterning genes in *Drosophila* eye development.

Drosophila Eye Model to Study Axial Patterning

The power of *Drosophila* as a model organism for patterning and disease lies in its large repertoire of genetic tools, making it a highly tractable model organism (Bier 2005; Singh and Irvine 2012). The *Drosophila* eye has been extensively used (a) to investigate tissue patterning, growth, cell–cell communication, cell survival, and cell death mechanisms during organogenesis and (b) to understand the genetic mechanism responsible for positional fate restrictions within a developing field that leads to formation of compartments (Dominguez and Casares 2005; Singh and Irvine 2012; Singh et al. 2005b; Singh et al. 2012). Interestingly, the eye as an organ has evolved independently as many as 40 different times (Land and Fernald 1992).

Table 1 Gene involved in axial patterning in developing imaginal discs of *Drosophila melanogaster*

Imaginal disc	Axis	Time	Selector genes	Reference
Wing	AP	L1	Anterior: <i>cubitus interruptus</i> Posterior: <i>engrailed</i> , <i>invected</i>	Lawrence and Morata 1976; Morata and Lawrence 1975; Sanicola et al. 1995
	DV	L2	Dorsal: <i>apterous</i> , <i>Capricious</i> , <i>tartan</i> , <i>fringe</i> , <i>Serrate</i> Ventral: <i>Delta</i> , <i>wingless</i>	Blair et al. 1994; Cohen et al. 1992; Cohen et al. 1993; Cohen 1993; Diaz-Benjumea and Cohen 1993
	PD	L3	Proximal: <i>homothorax</i> , <i>teashirt</i> Distal: <i>nubbin</i> , <i>elbow</i> , <i>no ocelli</i>	Blair et al. 1994; Cohen et al. 1992; Cohen et al. 1993; Diaz-Benjumea and Cohen 1993; Zirin and Mann 2007
Leg	AP	L1	Anterior: <i>cubitus interruptus</i> Posterior: <i>engrailed</i> , <i>invected</i>	Dominguez et al. 1996; Eaton and Kornberg 1990; Kornberg et al. 1985; Masucci et al. 1990; Raftery et al. 1991; Zecca et al. 1995
	DV	L2	Dorsal: <i>decapentaplegic</i> Ventral: <i>wingless</i>	Baker, 1988a, b; Couso et al. 1993; Irvine and Vogt 1997; Zirin and Mann 2007
	PD	L3	Proximal: <i>teashirt</i> , <i>homothorax</i> Distal: <i>Distalless</i>	Diaz-Benjumea et al. 1994; Irvine and Vogt 1997; Lecuit et al. 1996
Eye	DV	L2	Ventral: <i>Lobe</i> , <i>Serrate</i> Dorsal: <i>pannier</i> , <i>Iroquois-Complex (araucan, caupolican and mirror)</i> , <i>wingless</i>	Maurel-Zaffran and Treisman 2000; Oros et al. 2010; Singh and Choi 2003
	AP	L3	Anterior: <i>eyeless</i> Posterior: <i>hedgehog</i>	Dominguez and Casares 2005; Halder et al. 1995; Lee and Treisman 2001
	PD	L3	Proximodistal: Not fully understood	

AP anteroposterior, DV dorsoventral, PD proximodistal

Despite the differences in the structure of the *Drosophila*'s compound eye and a vertebrate eye of a single lens and a retina with multiple layers of neurons, there is similarity in the underlying genetic pathways controlling eye fate specification and differentiation. Thus, the genetic machinery involved in eye development is highly conserved and exhibits structural and functional similarity between insects and humans (Erclik et al. 2009; Gehring 2005; Hartenstein and Reh 2002; Kumar 2009; Wawersik and Maas 2000). This suggests that information generated in the fly eye can be extrapolated to higher organisms. Therefore, *Drosophila* has proved to be an excellent model system for identifying new genes that are conserved in vertebrate retinal development (Singh et al. 2012).

Embryonic Eye Primordium Develops Into the Larval Eye Disc in *Drosophila*

Drosophila, a dipteran, is a holometabolous insect (Anderson 1972b; Miall and Hammond 1892) where the primordia for all adult structures are first specified during embryonic development. The embryonic precursors grow asynchronously from the rest of the developing embryo (Anderson 1972a, b; Cohen et al. 1993; Cohen 1993; Crick and Lawrence 1975; Held 2002b; Kumar 2011; Singh et al. 2012). These embryonic primordia grow inside the larva as epidermal invaginations called imaginal discs (Atkins and Mardon 2009; Bodenstein 1950; Ferris 1950; Held 2002b). The *Drosophila* embryonic eye primordium originates from five embryonic head segments and the acron (Jurgens and Hartenstein 1993; Younossi-Hartenstein and Hartenstein 1993), and is specified by expression of *twin of eyeless* (*toy*) and *eyeless* (*ey*), a *Drosophila* homolog of human PAX6 (Quiring et al. 1994). The embryonic eye primordium begins as an antero-dorsal sac comprising of approximately 20 cells that are set aside during mid-embryogenesis (Garcia-Bellido and Merriam 1969; Held 2002b; Poulson 1950; Tsachaki and Sprecher 2012; Yamamoto 1996).

During larval development, the embryonic eye primordium develops into a monolayer epithelium called the eye–antennal imaginal disc (Fig. 1a). The monolayer epithelium does not accurately reflect the sac-like anatomy of the imaginal discs (Gibson and Schubiger 2001). *Drosophila* imaginal discs are a contiguous cell sheet of flattened epithelial cells with two opposing surfaces comprising a columnar epithelium called the disc proper (DP) and a squamous epithelium called the peripodial membrane (PM) (Atkins and Mardon 2009; McClure and Schubiger 2005). Fate map studies have revealed that the DP of the eye–antennal imaginal disc gives rise to the retina, whereas the PM forms the adult head structures (Atkins and Mardon 2009; Haynie and Bryant 1986; Milner et al. 1983; Singh et al. 2012). Earlier, it was postulated that the PM is required during metamorphosis events of eversion and fusion. However, recent findings suggest that the PM is involved in sending signals to the DP and is required for cell survival and proliferation in the DP (Atkins and Mardon 2009). The eye–antennal imaginal disc upon differentiation gives rise to the adult eye, antenna, head cuticle, and other head structures (Cohen 1993; Held 2002b). In the second instar larva, the division of the complex eye–antennal disc into the eye and antennal field occurs due to restriction of developmental potentials. This division occurs due to activation of the genetic circuitry required to initiate specification followed by differentiation of the eye and antenna (Atkins and Mardon 2009; Dominguez and Casares 2005; Kenyon et al. 2003; Kumar and Moses 2001). The developing eye field gives rise to the eye proper, head cuticle, and the ocelli, whereas the antennal field develops into the antenna and head cuticle (Haynie and Bryant 1986).

Drosophila, like other dipteran insects, has compound eyes for vision (Fig. 1d). The compound eye of the adult fly develops from the larval eye imaginal disc (Garcia-Bellido and Merriam 1969; Haynie and Bryant 1986). The growth spurt occurs during early larval (first and second instar) eye development. During this stage, the undifferentiated cells of the eye–antennal imaginal disc cells divide and undergo rapid proliferation. During late second or early third larval instar stage, a synchronous

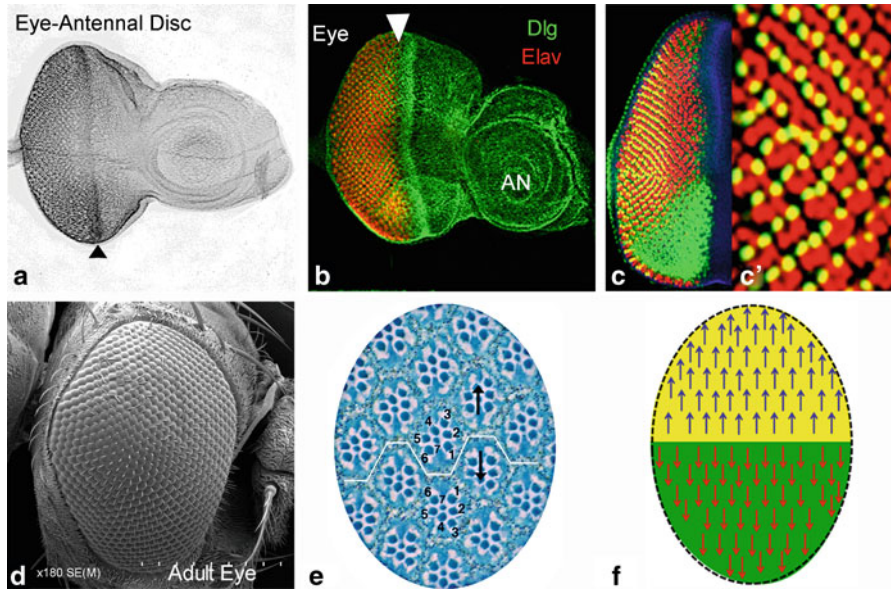


Fig. 1 Dorsoventral (DV) patterning of the *Drosophila* compound eye begins in larval eye imaginal disc. **a–c** Eye–antennal imaginal disc of a third instar larva. **a** Eye imaginal disc. **b** Eye–antennal imaginal disc stained for membrane-specific marker disc large (*Dlg*, green), and pan-neural marker *Elav* (red). *Elav* marks the photoreceptor neurons in the eye. Arrowhead in **a** and **b** marks the position of the morphogenetic furrow. **c**, **c'** Photoreceptor neurons exhibit DV polarity in the eye imaginal disc indicated by staining of Bar (B) antibody (green). **d** Scanning electron micrograph (SEM) of a wild-type adult *Drosophila* eye. The adult compound eye of *Drosophila* is made up of 750–800 unit eyes, each referred to as an ommatidium (Ready et al. 1976). All ommatidia are arranged in mirror image symmetry along the DV axis. **e** Each ommatidium consists of eight rhabdomeres, which are organized as an asymmetric hexagonal structure. The DV polarity is determined by two different orientations of the ommatidia based on the orientation of R3 rhabdomere. R3 pointing upward represents a dorsal ommatidium, whereas R3 pointing downward represents a ventral ommatidium. White line marks the equator. **f** Cartoon representing the mirror image symmetry of the ommatidia along the DV margins in the adult eye. Blue arrows in the yellow background mark the dorsal ommatidia, whereas red arrows in the green background mark the ventral ommatidia. Orientation of all images is dorsal up, ventral down, anterior right, and posterior left. AN: antenna

wave of retinal differentiation is initiated in the eye imaginal disc. This progressive pattern of differentiation results in the transition of an undifferentiated epithelium of retinal precursor cells to differentiated cell types comprising regularly spaced photoreceptor clusters (Ready et al. 1976; Wolff and Ready 1993). The differentiating cells undergo an apical constriction and apico-basal contraction, which results in an indentation in the eye imaginal disc. This indentation corresponds to the wave of retinal differentiation, which initiates on the posterior margin of the eye disc and moves anteriorly and is referred to as the morphogenetic furrow (MF, Fig. 1a, b, arrowhead). The photoreceptor clusters are generated posterior to the furrow by a sequence of events including the selection of the R8 founder neuron and recruitment

of additional photoreceptor precursors in the order of R2/5, R3/4, and R1/6/7 (Kumar 2011; Wolff and Ready 1993). The compound eyes in the adult fly consist of 750–800 unit eyes called ommatidia (Fig. 1d). Each ommatidium is made up of approximately 20 cells. Of these, eight are distinct photoreceptor neurons (Fig. 1e) that project axons to the optic lobe of the brain. The remaining non-neuronal cells in an ommatidium are pigment cells, cone cells, and mechanosensory bristles (Fig. 1d, e) (Held 2002b; Kumar 2011; Roignant and Treisman 2009; Singh et al. 2012; Wolff and Ready 1993).

The photoreceptor neurons are arranged in an asymmetric trapezoid or a hexagonal facet (Ready et al. 1976; Wolff and Ready 1993). The ommatidia within a compound eye are polarized in opposite directions. The orientation of one group of ommatidia is the mirror image of the other group (Fig. 1e, f). Furthermore, their orientation serves as a marker to distinguish the dorsal and ventral compartment-specific fate in the larval eye imaginal disc (Fig. 1c, c') as well as the adult compound eye (Fig. 1d–f). The ommatidia in the adult eye possess mirror image symmetry along the DV axis. These dorsal and ventral domains are referred to as the dorsal (D) and ventral (V) compartments. The border between these D and V compartments is referred to as an equator. Since photoreceptor differentiation initiates at the intersection of the DV midline of the eye imaginal disc from the posterior margin (Lee and Treisman 2002; Moses 2002), the delineation of DV midline or equator is crucial for differentiation of photoreceptors. Thus, DV patterning is an important facet of axial patterning during organogenesis. The DV polarity has been attributed to play a role in targeting of the retinal axons to the brain. This ommatidial configuration along with the targeting of the axons from the retina to the brain is a masterpiece of microoptics and microcircuitry, and enhances visual acuity and thereby forms the equator a sensitive “fovea” (Held 2002b). Interestingly, the eye imaginal disc is largely undifferentiated until second instar of development. It raises an interesting issue of how and when the compartments are established in the *Drosophila* eye imaginal disc.

Sequence of Events During Axis Determination

The sequence of events during axial patterning of the wing and the leg imaginal discs first involves the division of a field into anterior and posterior compartments of independent cell lineages, which is defined by selector genes (Table 1). Generation of AP lineage is followed by subdivision of the wing and leg imaginal discs into dorsal and ventral compartments (Blair 2001; Singh et al. 2012). However, this sequence of division is not followed in the eye imaginal disc. The AP axis is generated with the onset of differentiation marked by the MF in early third instar of larval development. The MF sweeps across the eye imaginal disc from the posterior margin toward anterior, resulting in the formation of posterior fate behind the furrow. The entire early eye primordium is ventral in fate and on which the dorsal fate is established in early second instar of larval eye development (Singh and Choi 2003). Therefore, Dorso-Ventral (DV) patterning, which is established during early second instar of eye development, is the first lineage restriction in the eye imaginal disc

(Singh and Choi 2003; Singh et al. 2005b; Singh et al. 2012). Although there are differences in the sequence of events, evidence suggests that some aspects of the DV patterning mechanism are highly conserved in the developing eye and the wing. One of the common features among all these organ primordia is the generation of the DV boundary, which serves as the site for activation of the signaling pathways to trigger growth and patterning of the imaginal disc. Here our emphasis will be on the genetic mechanism of the generation of DV domains and how it regulates growth and patterning in the developing eye.

Generation of Dorsal and Ventral Compartments in the Developing Eye Disc

The *Drosophila* eye is a polarized tissue. The polarity in *Drosophila* eye is reflected by mirror image arrangement of ommatidia across the DV midline or equator (Fig. 1f). The relation between the equator and DV compartmental boundary has been a matter of debate for a long time. The equator was first reported by Wilhelm Dietrich (Dietrich 1909). In many insect eyes, the equator has been described as the boundary between the photoreceptor neurons of the dorsal and ventral compartments (Dietrich 1909). The equator is generated upon specification of dorsal and ventral compartments and serves as the signaling centre, which is crucial for cell proliferation and differentiation of the eye as an organ. The *Drosophila* eye model has been extensively used to unravel the molecular genetic mechanisms underlying this crucial process of generation of DV compartments in the eye (Singh et al. 2005b; Singh et al. 2012). Since the developmental mechanisms underlying the DV pattern are not fully understood, it raises an interesting question of how the dorsal and ventral pattern is established in the developing eye.

Earlier studies employed the genetic mosaic approach to study the generation of the DV pattern in the developing eye. Hans Becker reported that clones respect the equator and do not cross the DV lineage boundary (Becker 1966; Held 2002b). The pioneering studies authored by Donald Ready, Thomas Hansen, and Seymour Benzer (1976) entitled “Development of the *Drosophila* retina, a neurocrystalline lattice,” provided insights into patterning of the *Drosophila* eye (Ready et al. 1976). They rejected the clonal analysis model of ommatidial lineage (Kankel et al. 1980). They employed a genetic mosaic approach to generate mitotic recombination between the *white*⁺ (*w*⁺) wild type and *w*⁻ mutant chromosomes. Their aim was to generate two new cell populations *w*⁻/*w*⁻ and *w*⁺/*w*⁺ clones in a *w*⁺/*w*⁻ paternal heterozygous background. The *w*⁺ gene is essential for red eye pigment uptake in the cells and serves as an excellent cell autonomous marker for photoreceptors and pigment cells (Lawrence and Green 1979; Ready et al. 1976). They found that in genetic mosaic, *w*⁻ clones generated in the dorsal half of the eye can cross a few cells into the ventral half and vice versa. The results from these studies in the *Drosophila* eye suggested that the equator is not determined as the boundary between the D and V cell lineages (Ready et al. 1976). Although the result from this study does not exclude

the possibility that the dorsal and the ventral domains of the eye derive from two independent cell lineages, the lineage boundary may not precisely correspond to the equator (Netter et al. 1998).

In a series of elegant genetic analysis experiments involving a large number of mosaic clones in the adult eye, Baker (1978) demonstrated that clones strictly follow the DV boundary and do not intermingle near the DV border (Held 2002b; Singh et al. 2012). These studies validated the hypothesis that the *Drosophila* eye is derived from D and V compartments. To analyze whether the eye and the head are also subdivided into different domains by sequential compartmentalization, a mosaic analysis was carried out. Nearly all clones (96 %) respected the DV boundary (did not cross the boundary) and were restricted to either dorsal or ventral domain of the eye. A few clones (4 %) did cross the DV border, which is probably because of the fact that such clones may have been induced prior to formation of dorsal and ventral compartment boundary. Alternatively, two independent dorsal and ventral clones may have juxtaposed at the equator region, thereby giving a false notion of a single clone not respecting the DV boundary (Baker 1978; Singh et al. 2005b; Singh et al. 2012). The DV lineage restriction observed in the adult eye was also confirmed in the developing eye imaginal disc where large clones did not cross the DV midline in the larval eye imaginal disc. These clones showed a sharp outline along the DV midline, and the clones located within the dorsal or ventral domain had wiggly borders (Dominguez and de Celis 1998). Later, it was established that DV lineage specification is the first event that occurs during organogenesis of the eye (Singh et al. 2012). Therefore, identification of the major developmental landmarks along the temporal axis is important to understand patterning and growth of this organ.

Genesis of the Eye

Activation of Notch (N) signaling at equator, the boundary between dorsal and ventral compartments, has been shown to promote growth, in establishing planar polarity, in spacing of ommatidial clusters, and in cell fate specification and differentiation (Baonza and Garcia-Bellido 2000; Cagan and Ready 1989; de Celis et al. 1996; Go et al. 1998; Singh et al. 2012). However, this argument of DV patterning being crucial for growth, does not fit the timeline of developmental events (Singh et al. 2012). If ommatidial orientation corresponds to the generation of the DV axis, then on the basis of the time point when ommatidial rotation occurs, the majority of the growth and cell proliferation of the developing eye field is already accomplished. The ommatidial orientation of the photoreceptors occurs in the pupal retina, and growth spurt occurs during early larval instars of eye imaginal disc development. Based on the earlier notion, if DV patterning occurs in the pupal retina, then its role in growth and differentiation cannot be explained as majority of both growth and differentiation occurs prior to it during imaginal disc development, and not in the adult eye. Thus, efforts were channeled toward investigating the timeline and the genetic control that initiates DV patterning during eye development. Therefore, efforts were directed to (a) understand the time point of generation of DV axis in the developing eye or (b)

identify the developmental event that corresponds to the onset of N signaling in the developing eye (Singh et al. 2012).

Three different groups provided evidences in their independent publications that DV lineage restriction takes place earlier in the larval eye imaginal disc because of domain-specific expression of the genes. These genes are referred to as the DV patterning genes (Cho and Choi 1998; Dominguez and de Celis 1998; Papayannopoulos et al. 1998). These genes may be involved in assigning, generating, and maintaining the DV lineage in the developing eye imaginal disc. A new timeline assigned the time window of initiation of DV patterning to early larval development. This hypothesis also fits with the logic of a growth spurt. They identified the domain-specific expression of these genes whose function also follows the DV domain constraint that is established during early larval stages of development (Cho et al. 2000; Cho and Choi 1998; Dominguez and de Celis 1998; Papayannopoulos et al. 1998; Singh et al. 2012).

These studies raised a new question: if DV patterning occurs so early in the developing eye disc, then what is the default state of the early eye primordium? During embryonic development, the eye primordium begins as a homogenous group of cells that continue to grow during first larval instar to form the eye imaginal disc. Several studies have reported the genes that are expressed in the early larval eye primordium. It is known that the generation of MF marks the formation of AP axis in early third instar of larval eye imaginal disc development (Ready et al. 1976; Wolff and Ready 1993). However, the DV axis is determined as early as late first instar of larval development by domain-specific expression of genes along the DV axis (Cho and Choi 1998; Dominguez and de Celis 1998; Papayannopoulos et al. 1998; Singh and Choi 2003; Singh et al. 2012). Another interesting outcome from the Singh and Choi (2003) studies was that early eye primordium begins from a default ventral state (Fig. 2), which depends on the function of ventral genes like *Lobe* (*L*) and its downstream target *Serrate* (*Ser*) (Kumar 2011; Singh et al. 2005a; Singh and Choi 2003; Singh et al. 2005b). It has been shown that loss of function of *L/Ser* results in preferential loss of ventral eye (Figs. 2, 3b, c). *L* is expressed uniformly in the entire eye imaginal disc (Figs. 2, 3a). The loss-of-function studies suggested that the requirement of *L* function evolves along the temporal axis (Singh and Choi 2003; Singh et al. 2005b; Singh et al. 2012). During early eye development, the loss-of-function of *L* results in the complete loss of the eye field (Figs. 2, 3b). However, loss of the *L* gene function later during eye development causes selective loss of the ventral half of the eye (Fig. 2) (Singh et al. 2012). Loss of function of *Ser* also results in the similar loss of ventral eye phenotype (Kumar and Moses 2001; Singh and Choi 2003; Singh et al. 2005b; Singh et al. 2012). Interestingly, the timing of restriction of the *L/Ser* functional domain from the entire developing eye field (Fig. 3e, f) to only the ventral half of eye (Fig. 3c, d) corresponds to the onset of *pannier* (*pnr*) gene expression along the dorsal margin of the eye (Table 2, Fig. 2). During late first instar larval eye development, the entire homogenous population of the ventral cells of the eye primordium transitions into two distinct dorsal and ventral lineages with the onset of *pnr* expression on the dorsal eye margin (Singh and Choi 2003; Singh et al. 2012). This suggests that the ventral fate is the ground state of the larval

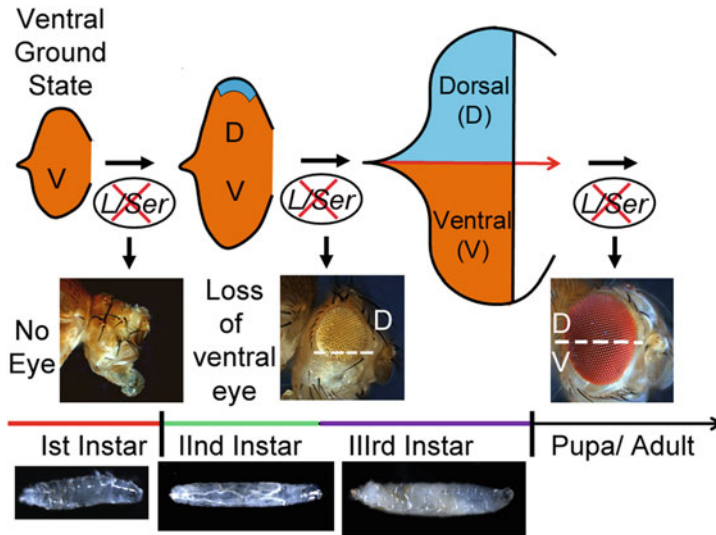


Fig. 2 Ventral is the default state of the developing *Drosophila* eye. Larval eye primordium begins with a default ventral state where all the cells of the eye primordium require ventral genes *L/Ser* function for growth and proliferation (Singh and Choi 2003; Singh et al. 2012). Loss-of-function phenotype of *LobelSerrate* (*L/Ser*) in the developing eye imaginal disc evolves progressively along the temporal scale. During early first instar of larval development, loss-of-function of *L/Ser* results in complete loss of the eye field. During early second instar of larval eye development, a few cells start expressing *pannier* (*pnr*) and the dorsal fate is specified. By the end of the second instar stage, DV lineage is established, and at this stage, loss of *L/Ser* results in loss of only the ventral half of the eye. In the late third instar stage of development, when retinal differentiation is almost complete, loss of *L/Ser* does not have significant effect on the overall adult eye morphology. These results clearly indicate that the entire early eye primordium, prior to onset of *pnr* expression, is ventral in fate (Singh and Choi 2003). DV dorsoventral

eye imaginal disc, and *L* and *Ser* are essential for survival and/or maintenance of this ventral state (Singh and Choi 2003; Singh et al. 2005b; Singh et al. 2006). In the subsequent parts of this chapter, we will focus on specific functions of DV patterning genes responsible for patterning of the in the developing eye.

DV Patterning During Imaginal Disc Development

The DV axis is determined by domain-specific expression or function of DV patterning genes. However, their localization may not be identical in all the imaginal discs. Unlike the wing imaginal disc where *Ser* and *Delta* (*Dl*) are preferentially expressed in the dorsal and ventral domains, respectively, their expression domains are reversed in the eye imaginal disc (Table 1). In the wing imaginal disc, the LIM homeodomain protein Apterous (*Ap*) acts as a dorsal fate selector (Table 1) (Blair et al. 1994; Cohen et al. 1992). It is known that *Ap* can induce *Fringe* (*Fng*) and *Ser* in the dorsal compartment of wing imaginal disc (Bachmann and Knust 1998; Cohen

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