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Review

An eye on eye development ☆

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ABSTRACT

The vertebrate eye is composed of both surface ectodermal and neuroectodermal derivatives that evaginate laterally from an epithelial anlage of the forming diencephalon. The retina is composed of a limited number of neuronal and non-neuronal cell types and is seen as a model for the brain with reduced complexity. The eye develops in a stereotypic manner building on evolutionarily conserved molecular networks. Eye formation is initiated at the onset of gastrulation by the determination of the eye field in the anterior neuroectoderm. Homeobox transcription factors, in particular *Six3* are crucially involved in the establishment and maintenance of retinal identity. The eye field expands by proliferation as gastrulation proceeds and is initially confined to a single retinal primordium by the differential activity of specifying transcription factors. This central field is subsequently split in response to secreted factors emanating from the ventral midline. Concomitant with medio-lateral patterning at the onset of neurulation, morphogenesis sets in and laterally evaginates the optic vesicle. Strikingly during this process the neuroectoderm in the eye field transiently loses epithelial features and cells migrate individually. In a second morphogenetic event, the vesicle is transformed into the optic cup, concomitant with onset and progression of retinal differentiation. Accompanying optic cup morphogenesis, neural differentiation is initiated from a retinal signalling centre in a stereotypic and species specific manner by secreted signalling factors. Here we will give an overview of key events during vertebrate eye formation and highlight key players in the respective processes.

Contents

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1. Establishment of the eye field

Eye formation in vertebrates is tightly interconnected with the patterning of the forming neuroectoderm at the onset of gastrulation. Controlled by factors patterning the neural plate, the eye field is determined in the anterior neuroectoderm soon after neural induction (Chow and Lang, 2001) by a series of inductive signals. These are sub-divided into three major steps: neural induction in the presumptive ectoderm, anterior–posterior subdivision of the neural plate and specification of the eye field in the diencephalic territories (Fig. 1).

Neural induction follows a molecular mechanism that likely applies to all vertebrates (Wilson and Houart, 2004). Factors of the fibroblast growth factor family (Fgf) are secreted prior to the onset of gastrulation (Gamse and Sive, 2001; Itoh et al., 2002; Wessely et al., 2001; Wilson et al., 2000) and trigger neural fate, when Wnt-signalling is suppressed (Niehrs, 1999; Stern, 2006). To establish and maintain neural fate, bone morphogenetic proteins (BMPs) must be repressed by antagonists such as Follistatin, Noggin, Chordin and Cerberus (Bouwmeester et al., 1996; Hemmati-Brivanlou et al., 1994; Niehrs, 2001) which are specifically expressed in organising centres such as the Spemann organiser (amphibia), Hensen's node (birds) or the mouse node.

Fates along the anterior–posterior axis of the neural plate are determined by posteriorising factors such as retinoic acid, or secreted proteins of the Wnt, Fgf, BMP or Nodal family (Agathon et al., 2003; Munoz-Sanjuan and Brivanlou, 2001). The role of Wnt-signalling becomes obvious when members of the Wnt-pathway are mutated. Enhancement of Wnt-signalling results in the absence of head structures in the zebrafish mutant *headless (hdl/Tcf3)*, a negative Wnt-modulator (Kim et al., 2000). The opposite phenotype is observed in mutants affected in Nodal-signalling. Here the telencephalon is massively expanded as observed in the zebrafish mutant *one-eyed pinhead (oep)* (Gritsman et al., 1999; Kim et al., 2000)

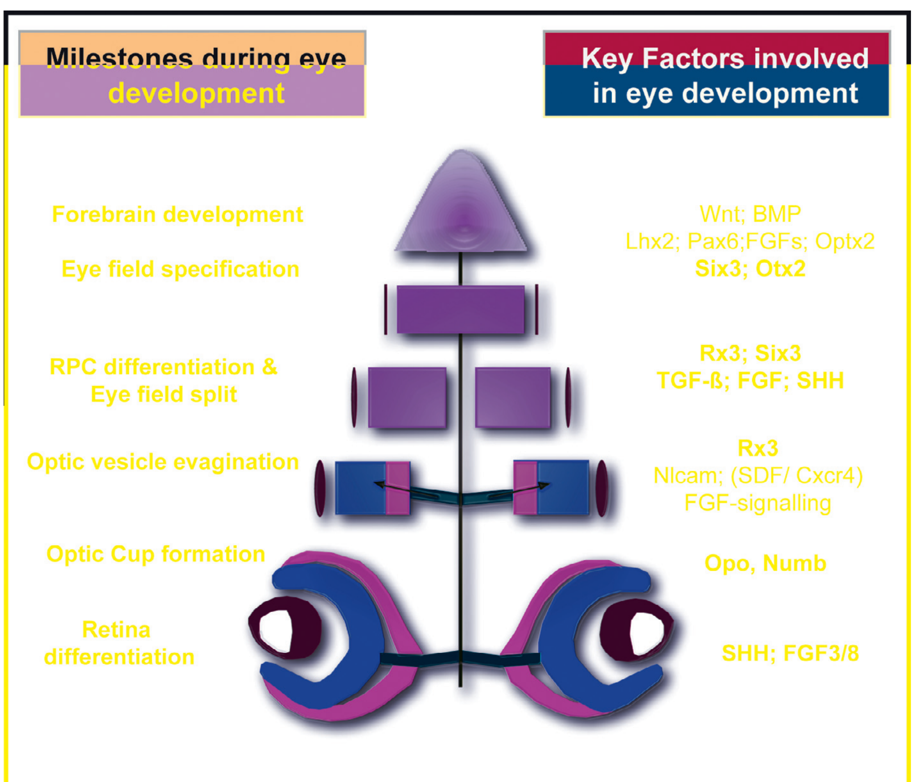

Fig. 1 – Christmas tree scheme of vertebrate eye development. The central trunk of the tree represents both, temporal axis as well as ventral midline. Orange indicates neuroectodermal parts fated to become retina during stages prior to neurulation. Concomitant with neurulation optic vesicles undergo the first morphogenetic transition: they evaginate and get sub-patterned into optic stalk (blue), pigmented retinal epithelium (yellow) and prospective neuroretina (red). In the subsequent second morphogenetic transition, the formation of the optic cup, retinal differentiation triggered by a Fgf signalling centre, spreads over the entire retina. The lens (green) forms from surface ectodermal derivatives. Adapted from (Wittbrodt et al., 2002) with permission.