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Functions of crystallins in and out of lens: Roles in elongated and post-mitotic cells

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ABSTRACT

The vertebrate lens evolved to collect light and focus it onto the retina. In development, the lens grows through massive elongation of epithelial cells possibly recapitulating the evolutionary origins of the lens. The refractive index of the lens is largely dependent on high concentrations of soluble proteins called crystallins. All vertebrate lenses share a common set of crystallins from two superfamilies (although other lineage specific crystallins exist). The α-crystallins are small heat shock proteins while the β- and γ-crystallins belong to a superfamily that contains structural proteins of uncertain function. The crystallins are expressed at very high levels in lens but are also found at lower levels in other cells, particularly in retina and brain. All these proteins have plausible connections to maintenance of cytoplasmic order and chaperoning of the complex molecular machines involved in the architecture and function of cells, particularly elongated and post-mitotic cells. They may represent a suite of proteins that help maintain homeostasis in such cells that are at risk from stress or from the accumulated insults of aging.

1. Introduction. Evolution of lens and crystallins: an elongation connection?

The vertebrate lens is an avascular cellular structure composed mainly of highly elongated, terminally differentiated fiber cells, most of which lack all organelles (Bassnett et al., 2011; Kuszak et al., 2004). In many species it survives and functions for decades, maintaining transparency and a gradient of refractive index (RI) to produce clear focused images on the light sensitive cells of the retina. Optical adaptation for a particular habitat is generally achieved by the shape of the gradient in ways that reduce spherical aberration (Kroger et al., 1994) or optimize chromatic aberration (Gustafsson et al., 2008; Kroger and Fernald, 1994). The RI of the lens is largely due to high concentrations of soluble proteins generically known as crystallins (Bloemendal et al., 2004; Slingsby et al., 2013; Wistow, 2012). The lens and its contents evolved at some early point in the history of vertebrates, but long after the evolution of light sensitive cells, the photoreceptors, that perform the key step in vision of transducing photons into neural impulses.

Although fossils are lacking, there are many examples of existing simple eyes, particularly in invertebrates, that have photosensitive patches or organized retinas with no lens (Ayala, 2007; Land and Fernald, 1992; Land and Nilsson, 2002; Shimeld et al., 2005). From the ontogeny of the eye and from the parallel example of existing simple eyes a simple, staged process can be imagined that led to the evolution of the modern lens in discrete steps that all produced a useful, evolutionary selected structure. Indeed, modeling has suggested that such an evolutionary process could be relatively rapid (Nilsson and Pelger, 1994). A layer of cells overlying the retinal anlagen gives rise to a lens in both vertebrates and cephalopods (Harris, 1997). Elongation of these cells, which is an early step in the formation of lens placode in mammals and continues throughout development (Fig. 1), gives rise to a structure capable of gathering light. In a remarkable parallel example in vertebrates the parietal or median eye found in reptiles and amphibians acquires a “lens” of a single layer of elongated transparent cells (Fig. 1) by a completely different mechanism from that in the familiar lateral eyes (Eakin, 1973; McDevitt, 1972), emphasizing again the connection between cell elongation and lens formation (In mammals, the ancestral parietal eye is represented only by light sensitive structures in the pineal gland).

Elongation of cells to produce a convex surface is a common feature of cellular lenses, but this alone would not produce an effective lens. The lens needs to be transparent, but also needs an increased refractive index (RI) to diffract and concentrate incoming

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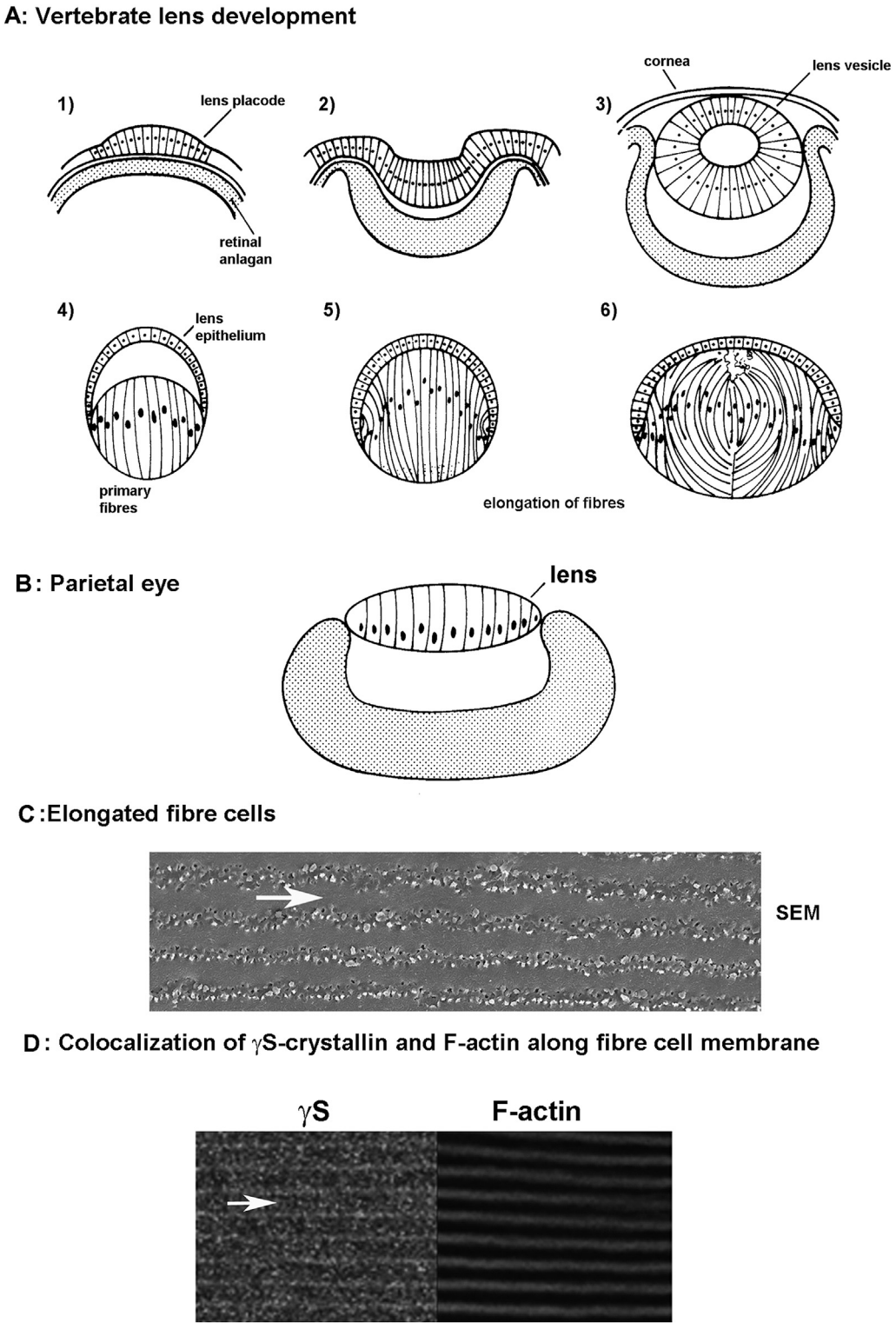

Fig. 1. Lens formation is associated with cell elongation. A: Steps in the embryonic development of the vertebrate lens (adapted from Wistow (1993)). 1) Epithelial cells overlying the retinal anlagen elongate to form the lens placode, 2) Elongation continues as the optic vesicle invaginates, 3) Formation of the lens vesicle and cornea, 4) Within the lens vesicle, primary fiber cells elongate, 5) Fibres fill the lens, 6) New layers of secondary fibres form throughout life through differentiation and elongation of equatorial epithelial cells. B: Schematic structure of the lizard parietal eye (adapted from Eakin (1973)). A monolayer of elongated cells forms the simple cellular lens. C: Elongation and intercalation of mature fiber cells. Scanning electron micrograph of fiber cells from adult mouse lens. Arrow indicates the longitudinal axis of a fiber cell. Extensive cell–cell contacts are formed through intercalation of complex junctions. (For methods, see Fan et al. (2012)). D: Co-localization of γS-crystallin and F-actin along the plasma membranes of mature mouse fiber cells (adapted from Fan et al. (2012)).