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A focus on the human lens in vitro

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Abstract

The lens is a unique organ in that it is avascular and non-innervated, obtaining all nutrients from the aqueous and vitreous humours that bathe the lens. All lenses attempt to achieve the same goal, namely to maintain transparency and focus light on to the retina. However, the mechanisms by which these processes are maintained, or disrupted leading to a loss of transparency, are likely to differ in some cases between animals and humans. To allow comparison to take place, human in vitro models have been developed, ranging from whole organ culture to the generation of human lens cell lines. All have their merits and limitations, but as a whole, they permit extensive studies of lens cell behaviour and function to be carried out. Together, these in vitro methods allow the biological events of the lens to be further understood. Moreover, they could help identify the mechanisms that give rise to cataract and posterior capsule opacification, a problem that occurs following surgery, providing therapeutic targets for their prevention.

Keywords: Lens; Human; Cataract; Posterior capsule opacification; In vitro; Culture

1. Introduction

At first glance, the lens is a simple organ but its apparent simplicity disguises a wealth of cell biological sophistication and ingenuity. The level of complexity in our understanding of this organ is, however, increased when we consider species variation. All lenses attempt to achieve the same goal, namely to maintain transparency and focus light on to the retina. However, the mechanisms by which these processes are maintained, or disrupted leading to a loss of transparency, are likely to differ in some cases between animals and humans (Vrensen, 1994; Fougerousse et al., 2000; Rhodes et al., 2002). It is, therefore, important to identify the similarities and differences between human and animal species, such that meaningful advances in human biomedicine can be achieved. For comparison to be made, it is important to identify the different mechanisms driving similar cell biological events in the human lens. The review that follows will consider some of the techniques currently employed to study human lens cells in vitro.

2. The lens

The lens is a unique organ in that it is avascular and non-innervated, obtaining all nutrients from the aqueous and vitreous humours that bathe the anterior and posterior regions of the lens, respectively (Davson, 1984). All cells within the lens are derived from epithelial cells and the region where cell division and fibre differentiation take place is highly localised (Fig. 1). In the normal lens, these events only take place at the equatorial region while the central epithelium is in effect a non-dividing population. Identifying the processes controlling normal cell function is of great importance as modification of these highly regulated mechanisms can result in lenticular pathologies, namely cataract.

3. Cataract

Cataract is one of the major causes of blindness in the world and is a disease largely associated with the elderly (Thylefors et al., 1995). The incidence of cataract on a global scale is not uniformly distributed, with developing countries showing a far greater frequency than developed countries. Cataract is the term used to describe any opacification of the lens and this may be restricted to a localised region or can involve the entire lens

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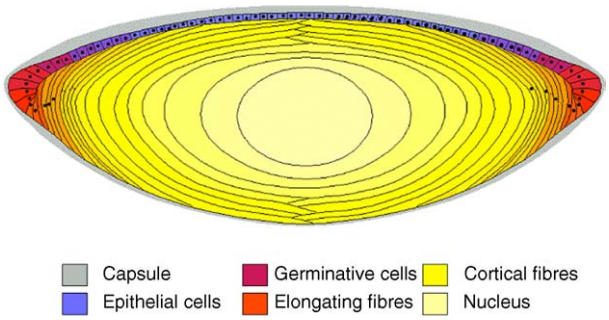

Fig. 1. A diagrammatic representation of a cross section of the human lens (Maidment et al., 2004).

substance preventing any light transmission through it (Davson, 1984). The induction of a cataract may be caused by a number of factors, such as senile changes or trauma where UV light, nutritional defects and osmotic imbalance have all been identified as important (Davies et al., 1984; Bunce et al., 1990; Hightower, 1994). At present, there is no prevention or cure for cataract with surgical intervention being the only means to resolve it. However, the relative success of this procedure is diminished by the development of a secondary loss of vision termed posterior capsule opacification (Wormstone, 2002).

4. Posterior capsule opacification (PCO)

Cataract surgery initially restores high visual quality, but unfortunately, a significant proportion of patients develop PCO (Wormstone, 2002). A modern cataract operation generates a capsular bag (Fig. 2A), which comprises a proportion of the anterior and the entire posterior capsule. The bag remains in situ, partitions the aqueous and vitreous humours and in the majority of cases, houses an intraocular lens. The production of a capsular bag following surgery permits a free passage of light along the visual axis through the transparent intraocular lens and thin acellular posterior capsule. However, on the remaining anterior capsule, lens epithelial cells stubbornly reside despite enduring the rigours of surgical trauma. This resilient group of cells then begin to re-colonise the denuded regions of the anterior capsule, grow on to the intraocular lens surface, occupy regions of the outer anterior capsule and most importantly of all, begin to colonise the previously cell-free posterior capsule. Cells continue to divide, begin to cover the posterior capsule and can ultimately encroach on the visual axis (Fig. 2B). Although a thin cover of cells is insufficient to affect the light path, subsequent changes to the matrix and cell organisation can give rise to light scattering properies (Fig. 2C). If these changes are sufficiently severe, vision becomes seriously impaired and corrective laser surgery is required (Moisseiev et al., 1989; Sudhakar et al., 1989; Sundelin and Sjostrand, 1999) which is both expensive and not without some risk to the patient (Ranta and Kivela, 1998).

5. In vitro methods

Our knowledge of lens cell biology can be greatly enhanced from a study of lens cells in vitro. A number of in vitro model

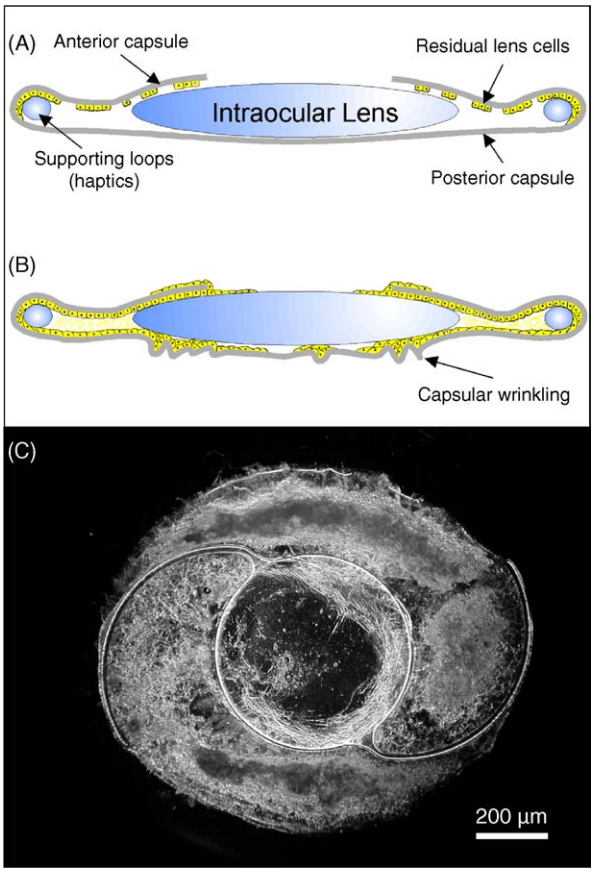

Fig. 2. A schematic representation of: (A) the post surgical capsular bag; (B) the extensive growth and modification that gives rise to postertior capsule opacification; (C) a dark-field micrograph of a capsular bag removed from a donor eye that had undergone cataract surgery prior to death that exhibits light scattering regions beneath an intraocular lens (Wormstone, 2002).

systems are available and these include: whole lens culture (Sanderson et al., 2000), capsular bag cultures (Liu et al., 1996) and cell lines (Andley et al., 1994; Ibaraki et al., 1998; Wormstone et al., 2004). All have their merits and limitations, but as a whole, they permit extensive studies of lens cell behaviour and function to be carried out. These methods will now be discussed with respect to the human lens and its cells.

6. Whole organ culture

Lenses can be isolated from the eye and remain transparent when maintained in culture. This technique has been used for lenses from a number of species, including mouse (Spector et al., 2001), rat (Hales et al., 1995), pig (Tamiya et al., 2000), bovine (Marcantonio and Duncan, 1983) and human (Marcantonio and Duncan, 1987). Although, all lenses from all these species appear to behave similarly, it is becoming increasingly obvious that the controlling mechanisms exhibit variation between different species. This could potentially have significant consequences for drug development and confuse our true understanding of normal tissue and pathological development if this fact is ignored.

Organ culture of the human lens has many advantages. One interesting benefit of using human donors is the considerable