

The Ageing Human Lens

Wound-healing

Growth

Signalling

Stress

Age-related Signalling Capacities of the Human Lens

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The Investigation

Objectives

To identify age-related differences in signalling capacity through expression of signalling components and/or the ability to activate these pathways.

Background

Ageing phenomena are observed following cataract surgery. Wound healing responses leading to formation of posterior capsule opacification (PCO; Fig. 1A) are greater in the young (<40 years) than older people (>60 years). To study this problem we developed a human lens capsular bag culture system based on a sham cataract operation, which allows growth rates and matrix modification to be monitored. Using this model we observed that cells grow across the previously cell free posterior capsule in non-supplemented medium (EMEM). However, growth rate was markedly faster in the younger age group (Fig. 1B).

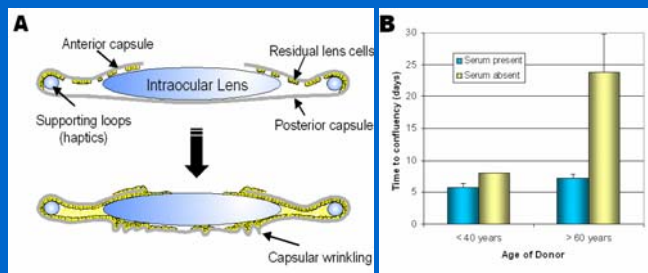


Figure 1. (A) A schematic representation of the post-surgical capsular bag followed by extensive growth and modification that gives rise to PCO (Wormstone 2002). (B) The effects of age and serum in time to confluence of cells on the posterior capsule (Wormstone et al 1997).

Experimental Plan

Preparations: Human lens capsular bags generated from young and aged donors \pm global stimulus (10% FCS).

Analysis: Protein expression level and activation status of signalling molecules will be determined using a suspended bead array BIO-PLEX system (www.bio-rad.co.uk).

References

- Wormstone I M. Posterior Capsule Opacification: A Cell Biological Perspective. *Exp. Eye Res.* 2002, 74:337-347.
Wormstone I M, Liu C S C, Rakic J-M, Maracantonio J M, Vresen G F J M and Duncan G. Human lens epithelial cell proliferation in protein-free medium. *Invest. Ophthalmol. Vis. Sci.* 1997, 38: 396-404.

Potential Benefits

Cataract renders millions blind worldwide and is a condition largely affecting older age groups (>60 years). The development of PCO following corrective surgery therefore impacts on the clinical outcome and most importantly can reduce the quality of life of an individual. Both cataract and PCO therefore impact on the quality of life of patients and are a major financial cost to the health service.

This one-year project will provide valuable baseline information concerning the levels of signalling molecules in young and aged lens cells. Furthermore, it will also provide information on the ability of lenses from different age groups to respond to stress. This information can then be related to natural ageing phenomena in the eye, such as susceptibility to cataract and age-related development of PCO.

Future applications

The work sets out to identify key systems involved in the development of lens pathologies. This information in turn could form a platform from which to develop future strategies to prevent PCO. Benefit can be gleaned from the inhibition of cell growth and/or matrix contraction. Many putative drugs to suppress signalling mechanisms are toxic to all cells, but recent advances in drug delivery enable general cytotoxic drugs to be delivered in a targeted manner to lens cells. This advance therefore increases the possibility that our laboratory findings can be translated to the clinic.



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