THE ROLE OF TGF-β IN NORMAL AND PATHOLOGICAL LENS DEVELOPMENT

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How the lens develops its highly ordered architecture and growth patterns is a major question in developmental biology. During embryogenesis, cells in the anterior and posterior segments of the lens vesicle, differentiate into the epithelial and fibre cells, respectively. Our research has aimed to identify the molecules and mechanisms that regulate the divergent fates of lens cells. We have studied the roles of various growth factors in regulating lens cell fates using rat lens epithelial explant cultures and transgenic and mutant mouse models. Our research has shown that members of the FGF growth factor family are key initiators of lens fibre differentiation in mammals and there is now compelling evidence that a gradient of FGF in the eye controls lens polarity and growth patterns. Recent evidence also supports a role for TGF-β signalling in this process and indicates that a cascade of growth factor signalling may be required for normal fibre differentiation. Less is known about the anterior segment; however, our recent studies point to an important role for the Wnt growth factor family in epithelial differentiation. Growth factor signalling can also cause pathological changes; e.g. TGF-β can destabilise the normal epithelial phenotype and induce aberrant growth and differentiation that mimics the epithelial-mesenchymal transition characteristic of some forms of cataract. These studies highlight the importance of growth factor signalling in regulating the ordered growth and differentiation of the lens. It is also clear that the bioavailabity of some growth factors needs to be tightly regulated so that they act in the appropriate cellular compartment. Some cataracts may be a consequence of disturbed growth factor, particularly TGF-β, regulatory mechanisms.

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