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## Developmental Biology

Volume 248, Issue 2, 15 August 2002, Pages 265-280

Regular Article

### The Homeobox Gene Six3 Is a Potential Regulator of Anterior Segment Formation in the Chick Eye

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#### Abstract

The anterior segment of the vertebrate eye consists of highly organized and specialized ocular tissues critical for normal vision. The periocular mesenchyme, originating from the neural crest, contributes extensively to the anterior segment. During chick eye morphogenesis, the homeobox gene *Six3* is expressed in a subset of periocular mesenchymal cells and in differentiating anterior segment tissues. Retrovirus-mediated misexpression of *Six3* causes eye anterior segment malformation, including corneal protrusion and opacification, ciliary body and iris hypoplasia, and trabecular meshwork dysgenesis. Histological and molecular marker analyses demonstrate that *Six3* misexpression disrupts the integrity of the corneal endothelium and the expression of extracellular matrix components critical for corneal transparency. *Six3* misexpression also leads to a reduction of the periocular mesenchymal cell population expressing *Lmx1b*, *Pitx2*, and *Pax6*, transcription factors critical for eye anterior segment morphogenesis. Moreover, elevated levels of *Six3* attenuate proliferation of periocular mesenchymal cells *in vitro* and differentiating anterior segment tissues *in vivo*. These results suggest that, in addition to its function in eye primordium determination, *Six3* plays a role in regulating the development of the vertebrate eye anterior segment.

#### Keywords

eye; development; anterior segment; mesenchyme; *Six3*; misexpression; chick

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