A Tet-Regulated Mouse Model for Cataract

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Technology description

Summary

Cataract is the most common cause of blindness worldwide, with an estimated 25 million blind and 119 million visually impaired individuals worldwide. Over 20 million adults in the US alone are currently diagnosed with cataracts making this disease a major health concern. The incidence of cataract increases with age and a number of etiologic factors have been proposed in the pathogenesis of age-related cataract in humans including genetic factors, environmental factors and metabolic and biochemical changes in the crystalline lens. Ultraviolet radiation exposure and oxidative injury to the lens has been considered by some to be one of the most important factors in cataractogenesis. The present therapy of choice for cataract is laser surgery.

Experimental investigation of human age-related cataract is hindered by a lack of available animal models of cataract. Several laboratory mice strains with heritable cataracts have been studied including the Nakona, Frasier and the Philly mouse strains. An animal model with a predictable phenotype of cataract, particularly one with a pathogenesis relating to oxidative injury to the lens (the proposed central factor in human-related cataract) would be of great value to ophthalmic researchers and in the development of pharmacological agents for delaying or preventing cataract.

Researchers at the NIEHS have developed a transgenic mouse model in which the DNA repair gene DNA polymerase ß (ß-pol) is highly over-expressed in the lens epithelial cells of the eye (DNA Repair (2003) 609-622). A bicistronic tetracycline-responsive transgenic system was used to over-express ß-pol in mice. Over-expression of ß-pol in the lens epithelium results in the early onset of severe cortical cataract with cataractogenesis beginning within 4 days after birth. In utero and post-natal suppression of transgenic Flag-ß-pol-expression by doxycycline administration completely prevents cataract formation through adulthood, yet cataract is subsequently observed following removal of doxycycline and re-expression of the transgene. This predictable and regulated onset of cataract make this mouse an ideal animal model both for evaluating new therapeutics for delaying or preventing cataract as well as for understanding the mechanisms responsible for cataract formation.

Institution

NIH - National Institutes of Health

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com