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Lens regeneration using endogenous stem cells for treatment of congenital cataract

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The repair and regeneration of tissues using endogenous stem cells represents an ultimate goal in regenerative medicine. However, tissue or organ regeneration using endogenous stem cells in human has not been demonstrated. Currently, the only treatment for cataracts, the leading cause of blindness worldwide, is to extract the cataractous lens and implant an artificial intraocular lens. This procedure poses significant risks of complications for young patients. Here we isolate lens epithelial stem/progenitor cells (LECs) in mammals and show that Pax6 and Bmi-1 are required for LEC renewal. We designed a surgical method of cataract removal that preserves endogenous LECs and achieved functional lens regeneration in rabbits and macaques, as well as in human infants with cataract. Compared with the traditional procedure, we move the anterior capsulorhexis from the center to the periphery, reducing the diameter to 1-1.5mm, preserving the capsule, sub-capsular cells, and the physiological barrier between the anterior and the posterior segment. For infants and young children, this procedure reduces post-operative inflammation and the incidence of postoperative complications such as iris adhesion and secondary ocular hypertension while protecting the local milieu required for lens regeneration. Our approach conceptually differs from current practice, as it maximally preserves endogenous LECs and their natural environment, and regenerates lenses with visual function. Our findings demonstrate a novel treatment strategy for cataract and provide a new paradigm for tissue regeneration using endogenous stem cells.

Recent Publications

1. Chen X, Xiao W, Chen W, Liu X, Wu M, Bo Q, Luo Y, Ye S, Cao Y, Liu Y*. MicroRNA-26a and -26b inhibit lens fibrosis and cataract by negatively regulating Jagged-1/Notch signaling pathway. *Cell Death Differ.* 2017 Nov;24(11):1990.
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4. Skowronska-Krawczyk D, Zhao L, Zhu J, Weinreb RN, Cao G, Luo J, Flagg K, Patel S, Wen C, Krupa M, Luo H, Ouyang H, Lin D, Wang W, Li G, Xu Y, Li O, Chung C, Yeh E, Jafari M, Ai M, Zhong Z, Shi W, Zheng L, Krawczyk M, Chen D, Shi C, Zin C, Zhu J, Mellon PL, Gao W, Abagyan R, Zhang L, Sun X, Zhong S, Zhuo Y, Rosenfeld MG, Liu Y*, Zhang K. P16INK4a Upregulation Mediated by SIX6 Defines Retinal Ganglion Cell Pathogenesis in Glaucoma. *Mol Cell.* 2015 Sep 17;59(6):931-40.
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Biography

Yizhi Liu's research focuses on ocular stem cells' self-renewal, differentiation and senescence, and the role of extracellular matrix and engineered biomaterials that surround both normal and degenerated cells in cornea, lens and retina. Dr. Liu has published or co-authored more than 80 peer reviewed manuscripts in top journals including *Nature*, *New England Journal of Medicine*, *Science*, *BMJ* and *PNAS*. He is recognized as one of the pioneer ophthalmologists in China who perform phacoemulsification and intraocular lens implantation. He has carried out approximately 200,000 surgical operations for cataract patients. He is serving as the Co-Editor-in-Chief of *Molecular Vision*, Associate Editor-in-Chief of *Current Molecular Medicine*. He has received grants from the National Basic Research Program of China, the Chinese Ministry of Health Key Clinical Program, the Chinese National Natural Science Foundation and the Natural Science Foundation's Key Program in Guangdong.

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