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Functional assessment of bioengineered corneal keratocyte spheroids fabricated on high-molecular-weight hyaluronic acid coatings

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Recent progress in biomaterial science has greatly contributed to rapid development of corneal stromal tissue engineering. Although tissue-engineered scaffolds have been investigated for cultivation of keratocytes, the transplantation of cell/polymer constructs usually involves the creation of large-sized incision wound, which may restrict rehabilitation process. In order to overcome the drawbacks, we propose a minimally invasive surgical technique to reconstruct corneal stromal tissue defects by injection of multicellular spheroids. Hyaluronic acid (HA) with a high molecular weight (MW ≥ 360 kDa) was used to generate a microenvironment for the formation of keratocyte spheroids. Similar to those of keratocytes in vivo, the spheroidal cell aggregates could maintain the mitotically quiescent state and proper phenotype. In addition to a high prevalence of elevated extracellular matrix production, the bioengineered cell spheroids grown on these high MW HA coatings presented good viability without hypoxia-induced death. An animal model of bacterial keratitis was further used for evaluation of therapeutic efficiency of cultivated keratocyte spheroids. Results of clinical observations (i.e., slit-lamp biomicroscopy, intraocular pressure measurements, and corneal thickness determinations) and morphological studies (scanning and transmission electron microscopy) showed that when compared to the isolated cell suspensions, the multicellular transplants were more beneficial to corneal stromal tissue reconstruction. At 2 weeks of post-injection, the rabbit cornea receiving cell spheroids also demonstrated better optical and biomechanical characteristics than their suspension counterparts. It is concluded that the bioengineered keratocyte spheroids fabricated on high MW HA coatings may have potential for use in corneal stromal tissue repair.

Biography

Dr. Jui-Yang Lai obtained his Ph.D. in Chemical Engineering in 2006 from the National Tsing Hua University, Taiwan. Currently, he is working as an Associate Professor of Institute of Biochemical and Biomedical Engineering, Chang Gung University, Taiwan. Dr. Lai's primary research activities are centered on the development of functional biomaterials for ophthalmic use, particularly on tissue engineering and drug delivery. He has published 4 book chapters and 30 international peer review journal papers. Dr. Lai also serves as an editorial board member for 8 international journals and a peer reviewer for 27 international journals.

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