



学際物質科学研究センター(TIMMS)セミナー

題目： 『New Approach in Bioengineering. I. TISSUE ENGINEERING FOR CORNEAL ENDOTHELIAL RECONSTRUCTION. II. NOVEL MIXED MICELLAR SYSTEM IN INTRACELLULAR DRUG DELIVERY.』

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日時： 5月31日(水曜日) 16:00-17:00

場所： 総合研究棟 B 0110 公開講義室

概要：

(1) Tissue Engineering for Corneal Endothelial Reconstruction.

Along with the recent advance of regenerative medicine, functional biomedical materials have received much attention in relation to diverse research fields such as tissue engineering, cell therapy, drug delivery, and gene delivery. Corneal endothelial reconstruction is an attractive research field in tissue engineering since it is of high clinical importance. The purpose of this study was to develop a novel technology for harvesting and transplanting the cultured adult human corneal endothelial cell (HCEC) sheets by utilizing multi-functional biomaterials.

For fabrication of transplantable corneal endothelial equivalents, the thermo-responsive PNIPAAm-grafted culture supports were prepared by plasma chemistry and characterized via surface and chemical analyses. Bioengineered HCEC sheets were harvested by a mechanism of temperature-controlled cell adhesion/detachment. The results of ex vivo assessments showed that the HCEC sheets are viable monolayers and have intact barrier and pump functions. Moreover, biodegradable and cell-adhesive hydrogel discs made from gelatins with high molecular weight and negative charge was used as cell sheet carriers for intraocular delivery. After transplantation of gelatin-HCEC sheet constructs into the anterior chamber of rabbit eyes, the follow-up clinical observations and histopathological examinations showed the laminated HCEC sheets were successfully integrated onto rabbit corneas denuded with endothelial cells. These data indicate that the methodology of HCEC sheet transplantation as a cell therapy has great potential for corneal endothelial cell loss.

(2) Novel Mixed Micellar System in Intracellular Drug Delivery.

Well-defined and with a core-shell structure, polymeric micelles have been comprehensively studied, owing not only to their morphology, but also to their applications in separation and the biomedical field. In the recent year, we proposes a novel mixed micelle structure with a functional inner core and hydrophilic outer shells self-assembled from a graft copolymer and two diblock copolymers. Unlike other mixed micelles from the tri-triblock copolymer system, tri-diblock copolymer system or the di-diblock copolymer system, this nano-structure can completely screen one component of the graft copolymer and exhibits multi-functions. To the best of our knowledge, this study presents the first example of self-assembly from diblock and graft copolymers, not only by particle modification to hide their inner structure, but also by a new means of preparing multi-functional micelles.

The mixed micelle in this structure can be extended for many applications by manipulating and carefully designing each component. Combining the advantages of each copolymer, the mixed micelles perform many functions. One such application is as an anticancer drug carrier. From our design, the mixed micelle had a multi-functional inner core of P(NIPAAm-co-MAAc)-g-PLA to enable intracellular drug delivery and an extended hydrophilic outer shell of mPEG to screen the inner core. A change in pH deformed the structure of the inner core and induced the release of a significant quantity of doxorubicin (Dox) from mixed micelles. Clear differences between free Dox and Dox-mixed micelles were observed using confocal laser scanning microscopy (CLSM). Additionally, the efficiency of screening feature also displayed in the cytotoxicities; mixed micelles exhibited higher drug activity and lower material cytotoxicity than micelles from graft copolymer.

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