論文 / 著書情報
Article / Book Information

題目(和文)	
Title(English)	Engineering supramolecular peptide hydrogels for cell culture and drug delivery applications
著者(和文)	福永和人
Author(English)	Kazuto Fukunaga
出典(和文)	学位:博士(工学), 学位授与機関:東京工業大学, 報告番号:甲第10817号, 授与年月日:2018年3月26日, 学位の種別:課程博士, 審査員:三原 久和,小畠 英理,廣田 順二,小倉 俊一郎,堤 浩
Citation(English)	Degree:Doctor (Engineering), Conferring organization: Tokyo Institute of Technology, Report number:甲第10817号, Conferred date:2018/3/26, Degree Type:Course doctor, Examiner:,,,,
学位種別(和文)	博士論文
Category(English)	Doctoral Thesis
種別(和文)	論文要旨
Type(English)	Summary

（博士課程）
Doctoral Program

論 文 要 旨

THESIS SUMMARY

専攻： Department of	生物プロセス	専攻	申請学位（専攻分野）： Academic Degree Requested	博士 Doctor of	（ 工学 ）
学生氏名： Student's Name	福永 和人		指導教員（主）： Academic Supervisor(main)	三原 久和	
			指導教員（副）： Academic Supervisor(sub)	堤 浩	

要旨（英文 800 語程度）
Thesis Summary（approx.800 English Words ）

Self-assembling peptides have attracted interest as building blocks to construct functional materials for biomedical applications, such as tissue engineering and drug delivery system, because of their high biocompatibility, ability to form various nanostructures, and design flexibility to generate molecular diversity. A *de novo* designed self-assembling peptide, E1Y9, self-assembles into supramolecular networked nanofibers in water and forms cell-compatible hydrogels with desired shapes in response to calcium ion treatment. Therefore, E1Y9 hydrogels are useful as cell culture scaffolds with controlled shapes that provide three-dimensional structural supports for cells, and beneficial for tissue engineering applications. To construct complex tissues/organs using cell culture scaffolds, however, biological supports to promote cellular behaviors are also required. In this thesis, bioactivities to enhance cell adhesion and differentiation were conferred to E1Y9 materials by newly designed E1Y9 derivatives conjugated with bioactive peptides derived from extracellular matrices. In addition, disk- and string-shaped hydrogels were fabricated from E1Y9 and E1Y9 derivatives as functional cell scaffolds to regulate multiple cellular behaviors by the bioactive motifs and hydrogel structures. As a new application of E1Y9 hydrogels, they were also developed as injectable drug-releasing devices to locally deliver therapeutics.

In Chapter 2, E1Y9-derivatives for cell culture applications were designed and synthesized. RGDS sequence that is derived from fibronectin and known to promote cell adhesion, and IKVAV sequence that is derived from laminin and is reported to promote cell differentiation, were conjugated to C-terminus of E1Y9 to obtain E1Y9 derivatives, E1Y9-RGDS and E1Y9-IKVAV, respectively. These derivatives formed networked nanofibers in a similar manner to E1Y9, indicating the robust self-assembly of E1Y9 to form nanofibers with attached functional moieties. Cells were then cultured on polystyrene substrate coated with these peptide nanofibers to evaluate their bioactivities. 3T3-L1 cells cultured on the E1Y9-RGDS substrate exhibited enhanced cell adhesion compared to the cells on E1Y9. Neuronal differentiation of PC12 cells on the E1Y9-IKVAV substrate displayed longer neurites than the cells on E1Y9, indicating their promoted differentiation.

In Chapter 3, two types of shaped hydrogels were constructed from E1Y9/E1Y9-IKVAV mixed solutions. Disk-shaped hydrogels were fabricated by using a disk-shape mold. String-shaped hydrogels were formed by injecting the peptide solutions into medium containing calcium ions. PC12 cells were then cultured on these E1Y9/E1Y9-IKVAV mixed hydrogels with various E1Y9-IKVAV contents to investigate their cell differentiation activities. The neuronal differentiation was facilitated on hydrogels of both shapes that contained the IKVAV moieties, with the highest activity being observed on hydrogels with 25% E1Y9-IKVAV contents. This indicates that bioactivities of E1Y9/E1Y9-derivative mixed hydrogels can be controlled by changing the mixing ratios of the E1Y9-derivative. Moreover, long neurites extended from cells cultured on string-shaped hydrogels were aligned along the long axis of the string shape, suggesting the possibility of controlling cellular orientation by the structure of shaped hydrogels.

In Chapter 4, E1Y9 hydrogels were developed as injectable drug-releasing devices for local chemotherapy. An E1Y9 derivative conjugated with a hydrophilic moiety KGES, namely E1Y9-KGES, was designed and synthesized to control drug releasing profiles of E1Y9/E1Y9-KGES mixed hydrogels. Transmission electron microscopy revealed different nanostructures of E1Y9-KGES and E1Y9, suggesting the structural difference that could affect drug-releasing profiles of the hydrogels. E1Y9/E1Y9-KGES mixed hydrogels containing doxorubicin were formed via syringe injection, and they gradually released doxorubicin molecules with different releasing profiles depending on the E1Y9 derivative contents. E1Y9 formulation of doxorubicin was peri-tumorally injected to a syngeneic murine tumor model and significantly delayed tumor growth compared to free doxorubicin.

In summary, calcium-ion-responsive supramolecular peptide materials comprising E1Y9 and functional E1Y9-derivatives were developed and evaluated for cell culture and drug delivery applications, and are promising materials with multiple functions that can be easily modified for the biomedical applications.

備考 ： 論文要旨は、和文 2000 字と英文 300 語を 1 部ずつ提出するか、もしくは英文 800 語を 1 部提出してください。
Note : Thesis Summary should be submitted in either a copy of 2000 Japanese Characters and 300 Words (English) or 1copy of 800 Words (English).