Title	組織工学応用のためのソフト生体適合性両性電解質高分子ハイドロゲル
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Citation	
Issue Date	2016-03
Type	Thesis or Dissertation
Text version	ETD
URL	http://hdl.handle.net/10119/13535
Rights	
Description	Supervisor:松村　和明，マテリアルサイエンス研究科，博士

Soft Biocompatible Polyampholyte Hydrogels For Tissue Engineering Applications

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Introduction

Regenerative medicine and human tissue engineering are the two newly developed fields in medicine. Tissue engineering has emerged from the field of biomaterials and involves the combination of scaffolds, cells and biologically active compounds in functional tissues. The wider goal of regenerative medicine is to restore the normal function of the body tissues, which can be successfully achieved by repairing or replacing dysfunctional tissues. Hydrogels are attractive substitutes for tissue engineering as they meet many of these requirements such as resemblance to natural extracellular matrix (ECM), ability to absorb large quantities of water, improving biocompatibility over bulk polymers. Due to the immense importance of hydrogels in the field of tissue engineering, in my doctoral research I developed various kinds of hydrogels based on polyampholytes. Previously in my group, cryoprotective property of poly-L-lysine based polyampholyte was elucidated. In my research, I developed new polymer-based cryoprotectants and also employed these polyampholytes as one of the components in the fabrication of hydrogels. Hydrogels were prepared by chemical and physical cross-linking. Each hydrogel so developed have very unique applications in the field of tissue engineering.

Results and Discussion

Firstly in **chapter 2**, I developed cryoprotective hydrogels based on dextran polyampholyte. Hydrogel was fabricated using Cu-free Click chemistry. Cu-free Click cross-linking made this system a good candidate for injectable hydrogels. Hydrogels with cryoprotective property are very essential in the current scenario for the preservation of 2D or 3D tissue engineered constructs.

In next **chapter 3**, I developed thixotropic hydrogel based on poly-L-lysine polyampholyte and laponite. It is a very simple and effective method to fabricate injectable hydrogel using physical cross-linking. My major target was to cryopreserve the cells using polyampholyte and formulates it into hydrogel (using laponite as cross-linker) after thawing without washing out cryoprotectant. These kinds of hydrogels are very important for tissue engineering applications, as firstly it eliminates the need of cell harvestment and cell maintenance and secondly, due to its thixotropic nature, it is very useful as an injectable hydrogel. Thixotropic nature of the hydrogel prevented the unnecessary loss of the effective biomaterials to the unaffected areas after injection.

After the development of this type of hydrogel, in **chapter 4**, I introduced chemical cross-linking in this system using 4-arm polyethylene glycol amine as a cross-linker. This led to the development of hydrogel with tuneable mechanical properties. Mechanical stiffness of the substrate plays a crucial role in regenerative medicine and tissue engineering. Substrate stiffness decides the fate of cell differentiation. The hydrogels so developed with varied mechanical properties can have potent applications.

The last material, which I developed in **chapter 5**, is based on dextran hydrogel, which incorporates the nano-assemblies. This hydrogel shows controlled codelivery of hydrophobic drug and growth factors. It is very useful for topical wound healing applications.

Conclusion

In conclusion, I believe I was able to successfully fabricate different hydrogels with various unique applications using polyampholytes. Besides their cryoprotective property, in my study I was able to utilize their behavior of charge tuneability for the development of hydrogels by the incorporation of laponite as a cross-linker. Due to the presence of charge on both the components, numerous combinations were obtained. To my knowledge, no such work has been reported before which describes the interaction of polyampholyte with laponite. The beautiful interaction of the two by changing various parameters has opened up new avenues in the field of tissue engineering. These systems can be potentially useful in the fields of stem cell based therapies (where substrate stiffness plays crucial role in cell differentiation), pH-triggered cell delivery, drug delivery applications, etc.

Keywords: Polyampholyte, hydrogels, laponite, cryopreservation, thixotropic.