Academic Program [Oral B] | 20. Materials Chemistry -Basic and Application-：Oral B

Fri. Mar 28, 2025 1:30 PM - 2:50 PM JST | Fri. Mar 28, 2025 4:30 AM - 5:50 AM UTC [G]3402(3402, Bldg. 3, Area 4 [4F])

[[G]3402-3pm] 20. Materials Chemistry -Basic and Application-

Chair: Keitaro Suyama, Toshinori Fujie

English
1:30 PM - 1:50 PM JST | 4:30 AM - 4:50 AM UTC
[[G]3402-3pm-01]

Preparation of SN-38-Based Prodrugs for Size-Dependent Development of Pancreatic Cancer Nano-prodrugs and Evaluation of The Therapeutic Effects in Pancreatic Cancer Treatment

○Mengheng Yang[1], Ryuju Suzuki[2], Yoshitaka Koseki[1], Hitoshi Kasai[1] (1. Tohuku University, 2. National Institute of Technology, Sendai College)

Japanese
1:50 PM - 2:10 PM JST | 4:50 AM - 5:10 AM UTC
[[G]3402-3pm-02]

Development of cell-encapsulated devices with porous nanosheets and their application to islet cell transplantation

○Mahiro Suzuki[1], Atena Endo[1], Nanami Zushi[1], Nobuaki Shiraki[1], Shoen Kume[1], Toshinori Fujie[1] (1. Institute of Science Tokyo)

English
2:10 PM - 2:30 PM JST | 5:10 AM - 5:30 AM UTC
[[G]3402-3pm-03]

Development of thermoresponsive biomaterials by condensation of short elastin-like peptide $(FPGVG)_n$ and proteins

○Keitaro Suyama[1], Reina So[2], Iori Maeda[3], Takeru Nose[1] (1. Faculty of Arts and Science, Kyushu University, 2. Department of Chemistry, Faculty and Graduate School of Science, Kyushu University, 3. Department of Physics and Information Technology, Kyushu Institute of Technology)

Japanese
2:30 PM - 2:50 PM JST | 5:30 AM - 5:50 AM UTC
[[G]3402-3pm-04]

Synthesis and characterization of supramolecular polymer gel with four-armed PEG cross-linked via the association of hemoglobin subunits

○Takashi Matsuhira[1], Hiromi Sakai[1] (1. Nara Medical University)

Preparation of SN-38-Based Prodrugs for Size-Dependent Development of Pancreatic Cancer Nano-prodrugs and Evaluation of The Therapeutic Effects in Pancreatic Cancer Treatment

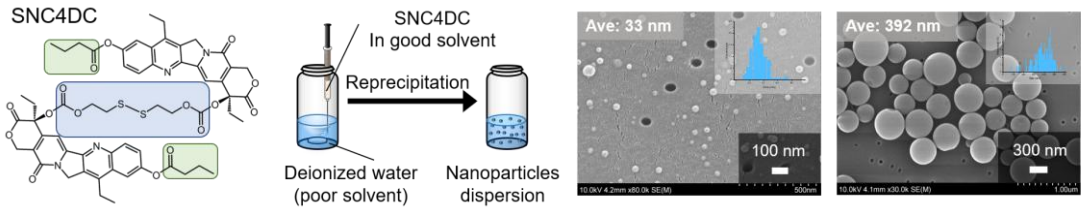
([1]*Institute of Multidisciplinary Research for Advanced Materials, Tohoku University*, [2]*National Institute of Technology, Sendai College School of Engineering,* [3]*Faculty of Bioresource Sciences, Prefectural University of Hiroshima*) ○Mengheng Yang[1], Ryuju Suzuki[2], Yoshitaka Koseki[3], and Hitoshi Kasai[1]

Keywords: cancer treatment; nano-prodrugs; size-dependent; reprecipitation; SNC4DC

A major goal of cancer research is to develop effective drug delivery systems with minimal side effects. Nano-prodrugs have emerged as a promising approach in cancer therapy due to their unique advantages over conventional drug delivery systems. By encapsulating therapeutic agents within nanocarriers, nano-prodrugs offer several key advantages that enhance their efficacy and reduce systemic toxicity. Liposomes and nanoparticle carriers with diameters of approximately 100 nm have been widely utilized for improving the distribution and accumulation of cancer drugs, primarily effective against highly permeable tumors. However, recent studies have shown that micelles with a size of 30 nm can penetrate low-permeability pancreatic tumors, demonstrating antitumor effects.[1]

This study focuses on preparing SNC4DC nano-prodrugs of varying particle sizes (33–392 nm) *via* a reprecipitation method, which controls particle size by modifying preparation conditions.[2] SNC4DC consists of two SN-38 molecules linked by a disulfide bond and modified with butyric acid (C4), enhancing nano-dispersibility and reducing degradation in the bloodstream.[3] *In vitro* toxicity experiments revealed size-dependent effects of SNC4DC nano-dispersions on BxPC-3 pancreatic cancer cells, while *in vivo* testing confirmed tumor growth inhibition in a BxPC-3 mouse model.

These findings highlight the potential of SNC4DC as a candidate for pancreatic cancer therapy. Further studies are planned to explore the impact of particle size on therapeutic efficacy and optimize this nano-prodrug system for clinical applications.



1) H. Cabral, *et al*. *Nat. Nanotechnol*, (**2011**), 6(12): 815-23. 2) H. Kasai, *et al*. *Angew. Chem. Int. Ed.*, (**2012**), 51(41): 10315-8. 3) K. Tanita, *et al*. *Nanoscale*, (**2024**), 16(32): 15256-64.

多孔質ナノシートを搭載した細胞封入デバイス開発と膵島細胞移植への応用

(東京科学大学 生命理工学院 [1]) ○鈴木麻紘 [1], 遠藤貴南 [1], 圖師菜々美 [1], 白木伸明 [1], 粂昭苑 [1], 藤枝俊宣 [1]

Development of cell-encapsulated devices with porous nanosheets and their application to islet cell transplantation ([1]*School of Life Science and Technology, Institute of Science Tokyo*) ○ Mahiro Suzuki[1], Atena Endo[1], Nanami Zushi[1], Nobuaki Shiraki[1], Shoen Kume[1], Toshinori Fujie[1]

Implantable encapsulated devices with beta cells have been developed for the treatment of type 1 diabetes[1]. Device-based cell transplantation protects cells from autoimmunity and provides a stable supply of insulin. In this study, porous polymeric nanosheets (PPN) composed of polycarbonate (PC) were fabricated to develop cell-encapsulated devices that can rapidly secrete insulin. PPN were made from a mixture of PC and polystyrene (PS) (2 wt% PC:PS = 1:1 or 3:1 in weight ratio dissolved by tetrahydrofuran (THF)) with selectively etching of the PS island region, which was then observed using atomic force microscopy (AFM). Next, insulin-producing cells were encapsulated inside a silicone ring and covered with triple-layered PPN (PC:PS=1:1, 1:1, 3:1 layered by each) to fabricate the cell-encapsulated device, and glucose-stimulated insulin secretion (GSIS) performance was evaluated with an indicator of glucose stimulation index (GSI). Compared to a commercially available membrane with a thickness of 10 μm, the thickness of the triple-layered PPN was 303 ± 21.7 nm (**Fig. 1**), more than 30 times thinner. The GSIS assay showed that the PPN-equipped device held the same level of GSI (PPN: 8.1 ± 5.8) as control groups (Pristine cells: 8.1 ± 5.8 and commercial membrane: 11.4 ± 10.9), suggesting the potential applicability of PPN for the implantable device.

Keywords : Cell-encapsulated device, Porous polymer nanosheet, Polycarbonate, Glucose-stimulated insulin secretion, Islet transplantation

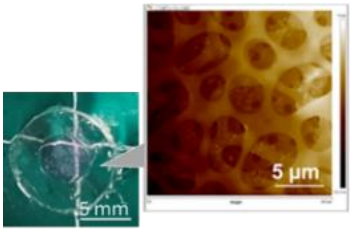


Figure 1. A cell-encapsulated device and an AFM image of triple-layered PPN equipped in the device.

一型糖尿病の治療法では、埋込型のβ細胞封入デバイスの開発が進められている[1]。デバイスを用いた細胞移植により、自己免疫から細胞を保護し、インスリンの安定的な供給が可能となる。本研究では、polycarbonate (PC) からなる多孔質高分子ナノシート (PPN) を作製し、迅速にインスリンを分泌できる細胞封入デバイスの開発を目指した。PC と polystylen (PS)の混合溶液 (2 wt%, PC:PS = 1:1 or 3:1 in weight rate, 溶媒: THF) を製膜し、相分離後の PS 相を溶解除去することで PPN を作製し、原子間力顕微鏡 (AFM) にて観察した。次に、シリコーンリング内部にインスリン産生細胞を封入後に、triple-layered PPN (PC:PS=1:1, 1:1, 3:1 の順で積層) を被せて細胞封入デバイスを作製し、glucose stimulation index (GSI)を指標として、glucose-stimulated insulin secretion (GSIS) を実施した。Triple-layered PPN は膜厚 303 ± 21.7 nm であり(**Fig. 1**)、厚さ 10 μm の市販膜と比較して 30 倍以上薄かった。GSIS 試験より、PPN 搭載デバイスの GSI (PPN: 8.1 ± 5.8) は、対照群(細胞のみ: 8.1 ± 5.8, 市販膜: 11.4 ± 10.9)と同程度であったことから、PPN 搭載デバイスの埋め込み型デバイスへの有用性が示唆された。

1) C. Nyitray et al., *ACS Nano*, **9**, 5675 (2015).

Development of thermoresponsive biomaterials by condensation of short elastin-like peptide $(FPGVG)_n$ and proteins

([1] *Faculty of Arts and Science, Kyushu University*, [2] *Department of Chemistry, Faculty and Graduate School of Science, Kyushu University*, [3] *Department of Physics and Information Technology*) ○Keitaro Suyama,[1] Reina So,[2] Iori Maeda,[3] Takeru Nose[1,3]
Keywords: Elastin-like peptide; Self-assembly; Temperature-responsive molecules

Elastin-like peptides (ELPs) are synthetic peptides that exhibit temperature-responsive and reversible self-assembly ability. ELPs are composed of characteristic repetitive sequences of hydrophobic amino acids, such as Val-Pro-Gly-Val-Gly (VPGVG), derived from tropoelastin. These repeating sequences are considered crucial for their reversible self-assembly ability. Owing to their thermoresponsive behavior and excellent biocompatibility, ELPs have been regarded as promising candidates for thermoresponsive biomaterials that are applicable to protein purification and drug delivery. Previously, we reported that a short ELP composed of $(FPGVG)_n$ sequence, which contains a phenylalanine residue in each repetitive sequence, exhibited strong self-assembly ability.[1] In addition, it was revealed that $(FPGVG)_n$ (n=1–2), which shows quite weak self-assembly, could achieve self-assembly through multimerization using other molecules as scaffolds.[2] From these findings, it was hypothesized that protein-based thermoresponsive biomaterials could be developed by conjugating multiple short-chain ELPs to a non-thermoresponsive protein.

In this study, to impart temperature-responsiveness to proteins, ELP-protein conjugates were synthesized by conjugating short-chain ELPs to bovine serum albumin (BSA), selected as a non-thermoresponsive model protein. The short-chain ELPs, $(FPGVG)_2$, $(FPGV)_2$, and (FPGVG) were synthesized and subsequently conjugated with BSA using DMT-MM as a condensing agent in a basic aqueous solution. As a result, ELP-protein conjugates containing multiple ELPs were successfully obtained. The self-assembling ability of the ELP-BSA conjugates was evaluated by turbidity measurement. Upon increasing temperature, BSA formed insoluble gels irreversibly, likely due to denaturation, with no decrease in turbidity observed upon subsequent cooling. In contrast, ELP-BSA conjugates showed temperature-dependent self-assembly and gradually redissolved upon cooling. The self-assembly behavior of the ELP-BSA conjugates varied depending on both the number and the self-assembly ability of short ELPs introduced. These results suggest that short-chain ELPs can be utilized as tags to impart temperature responsiveness to other proteins.

1) I. Maeda, S. Taniguchi, N. Watanabe, A. Inoue, Y. Yamasaki, T. Nose, *Protein Pept. Lett.* **2015**, *22*, 934.
2) N. Tanaka, K. Suyama, K. Tomohara, I. Maeda, T. Nose, *J. Pept. Sci.* **2023**, *29*, e3499.

四分岐PEGをヘモグロビンのサブユニット会合により架橋した超分子ポリマーゲルの合成と性質

（奈良医大化学）○松平 崇・酒井 宏水

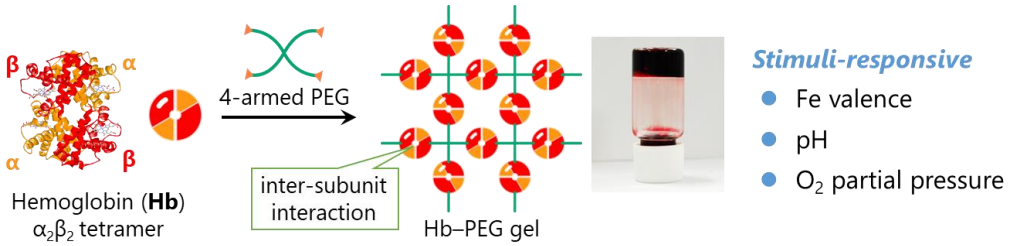
Synthesis and characterization of supramolecular polymer gel with four-armed PEG cross-linked via the association of hemoglobin subunits

(*Department of Chemistry, Nara Medical University*) ○Takashi Matsuhira, Hiromi Sakai

Supramolecular polymer gels including self-assembled proteins have attracted considerable attention in recent years.[1] Hemoglobin (Hb) has a stable $\alpha_2\beta_2$ tetrameric structure comprising two αβ heterodimers associated through non-covalent interactions. We previously synthesized a linear supramolecular polymer by conjugating the two termini of polyethylene glycol (PEG) to each of the two β subunits of hemoglobin.[2,3] The resulting supramolecular polymer has an alternating Hb−PEG structure in which linear PEGs are bound through the interactions between the two αβ subunits. In this study, we synthesized a supramolecular polymer gel (Hb−PEG gel) with a network structure by replacing the linear PEG with a four-armed PEG. The viscoelasticity of the Hb−PEG gel changed in response to external stimuli such as changes in the iron ion valence, pH, and oxygen partial pressure.

Keywords: Association-dissociation equilibrium; Hemoprotein; PEGylation; Stimuli-responsive; Rheology

自己組織化するタンパク質を構成成分とする超分子ポリマーゲルが、近年盛んに研究されている[1]。私たちはこれまでに、ヘモグロビン(Hb)のβ鎖を直鎖PEGで化学架橋することで、Hbが安定な$\alpha_2\beta_2$四量体構造を形成することを利用した鎖状の超分子ポリマーを合成してきた[2,3]。本研究では、直鎖PEGの代わりに四分岐PEGを使用することで、Hbのサブユニット会合により網目状に架橋された、超分子ポリマーゲルHb−PEG gelを合成した。Hb−PEG gelに対し、ヘム部分の構造を変化させる刺激(鉄イオンの酸化、pH変化、酸素分圧変化)を加えて動的粘弾性測定を行った。その結果、緩和時間τとゼロずり粘度η_0は、Fe^{2+}からFe^{3+}への酸化や生理的pH (7.4)からの逸脱によって低下した。一方、低酸素分圧下ではヘム鉄からのO_2の解離によりτとη_0は増大した。この結果は、粘性緩和が$\alpha_2\beta_2$構造の結合解離平衡により支配されていることを示唆している。



1) Li, Y.; Xue, B.; Cao, Y. ACS *Macro Letters* **2020**, *9*, 512–524.
2) Matsuhira, T.; Sakai, H. *Biomacromolecules* **2021**, *22*(5), 1944–1954.
3) Matsuhira, T.; Yamamoto, K.; Sakai, H. *Biomacromolecules* **2019**, *20*(4), 1592–1602.