Academic Program [Oral B] | 18. Polymer：Oral B

Thu. Mar 27, 2025 1:00 PM - 2:50 PM JST | Thu. Mar 27, 2025 4:00 AM - 5:50 AM UTC
[F]2501(2501, Bldg. 2, Area 4 [5F])

[[F]2501-2pm] 18. Polymer

Chair: Yuuki Hata, Tomonari Tanaka

Japanese
1:00 PM - 1:20 PM JST | 4:00 AM - 4:20 AM UTC
[[F]2501-2pm-01]

Fabrication of self-reinforced chitin composites by double crystalline blend approach and their cell adhesion propaty

○MASAYASU TOTANI[1], YUKO TANIHATA[1], YUSUKE EGI[1], HIROYUKI SHINCHI[1], JUN-ICHI KADOKAWA[1] (1. Kagoshima University)

English
1:20 PM - 1:40 PM JST | 4:20 AM - 4:40 AM UTC
[[F]2501-2pm-02]

Zwitterionic Polymer-Immobilized Chitosan Hydrogel: A Novel Platform for Enhanced Protein Protection and Delivery.

○ASHWIN RAJEEV[1], Kazuaki Matsumura[1] (1. Japan Advanced Institute of Science and Technology)

Japanese
1:40 PM - 2:00 PM JST | 4:40 AM - 5:00 AM UTC
[[F]2501-2pm-03]

Design of Artificial Membrane Proteins with Catalytic activity and Channel function using Amphiphilic Random Copolymers

○Chieri Inada[1], Tomoki Nishimura[2] (1. Grad. Sch. of Sci. Tech., Shinshu Univ., 2. Dept. Chem. Mater Sci., Shinshu Univ.)

2:00 PM - 2:10 PM JST | 5:00 AM - 5:10 AM UTC

Break

English
2:10 PM - 2:30 PM JST | 5:10 AM - 5:30 AM UTC
[[F]2501-2pm-04]

Anti-PEG Antibody Assays Using Designable Cello-oligosaccharide Assemblies as Solid-Phase Platforms

○Kai Sugiura[1], Koichiro Ishibashi[2], Yuuki Hata[1], Toshiki Sawada[1], Go Watanabe[2,3,4], Hiroshi Tanaka[1,5], Takeshi Serizawa[1] (1. School of Materials and Chemical Technology, Institute of Science Tokyo, 2. School of Science, Kitasato University, 3. School of Frontier Engineering, Kitasato University, 4. Kanagawa Institute of Industrial Science and Technology (KISTEC), 5. Faculty of Pharmacy, Juntendo University)

Japanese
2:30 PM - 2:50 PM JST | 5:30 AM - 5:50 AM UTC
[[F]2501-2pm-05]

Development of Vasohibin-2 targeted Chimeric Artificial Nucleic Acids for suppression of pancreatic cancer malignancy

Kosuke Machida[1], Masahito Inagaki[2], Mitsuyo Matumoto[1], Yasuyuki Araki[1], Yasufumi Sato[1], ○Takehiko Wada[1] (1. Tohoku University, 2. Nagoya University)

二重結晶ブレンド法による自己強化キチン複合体の構築と細胞接着特性の評価

（鹿児島大院理工）○戸谷 匡康・谷畑 優子・江木 優介・新地 浩之・門川 淳一

Fabrication of Self-reinforced Chitin Composites by Double Crystalline Blend Approach and their Cell Adhesion Property (*Graduate School of Science and Engineering, Kagoshima University*) ○Masayasu Totani, Yuko Tanihata, Yusuke Egi, Hiroyuki Shinchi, Jun-ichi Kadokawa

In this study, all-chitin composite films, named self-reinforced chitin composite (SR-ChC) films, were found to be fabricated from aqueous acetic acid dispersions of high-crystalline scaled-down chitin nanofibers (SD-ChNFs, crystalline index (CI) = 90.5%) and low-crystalline scaled-down chitin powder (SD-LC-Ch, CI =57.4%) (Figure 1(a,b)).[1] The tensile testing revealed that the SR-ChC film with the SD-ChNF/SD-LC-Ch weight ratio of 1/6.6 exhibited superior mechanical properties, including tensile strength of 64.0 MPa and elongation of 22.4% at break. On the other hand, the surface analysis of the SR-ChC revealed reorientation of the molecular chain assemblies with amino groups in the SD-LC-Ch components in water. Consequently, the increase of the number of hydrophilic amino groups on the film surfaces according to the weight ratios of the SD-LC-Ch components resulted in the efficiency of human-derived cancer cells adhesion and elongation (Figure 1(c)).[2]
Keywords : All-chitin composite; Double crystalline blend; Low crystalline chitin; Nanofiber; Self-reinforced composite

本研究では、高結晶性キチンナノファイバー（SD-ChNF、結晶化度指数（CI）=90.5%）と低結晶性キチン粉末（SD-LC-Ch、CI=57.4%）の酢酸水分散液から、自己強化キチン複合体（SR-ChC）フィルムが得られることを見出した（Figure 1（a,b））[1]。引張試験の結果、SD-ChNF/SD-LC-Ch の重量比が 1/6.6 の SR-ChC フィルムは、引張強度 64.0 MPa、破断伸度 22.4%など、優れた力学的特性を示した。また、SR-ChC フィルムの表面分析から、水環境下においてはフィルム表面に SD-LC-Ch 成分中のアミノ基含有分子鎖が再配向していることが示唆された。このことから、SD-LC-Ch 成分中の重量比に応じてフィルム表面の親水性アミノ基が増加し、ヒト由来癌細胞接着数と細胞伸長に影響することが分かった（Figure 1（c））[2]。

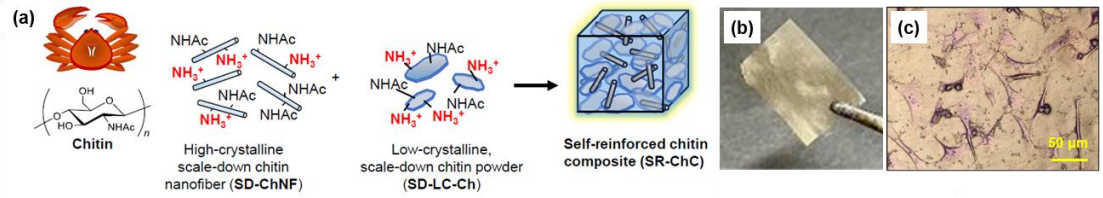


Figure 1. (a) Schematic illustration of self-reinforced chitin composite (SR-ChC), (b) photo-image of SR-ChC film, and (c) laser microscopic image of adherent human-derived cancer cells on SR-ChC film.

1) Fabrication of self-reinforced chitin composites by double crystalline blend approach. M. Totani, Y. Tanihata, Y. Egi, J. Kadokawa, *Int. J. Biol. Macromol.*, **2025**, 286, 138441.
2) Cancer cell adhesion property on all-chitin composite films with reduced crystallinity. M. Totani, H. Shinchi, J. Kadokawa, *Carbohydr. Res.*, **2025**, 549, 109373.

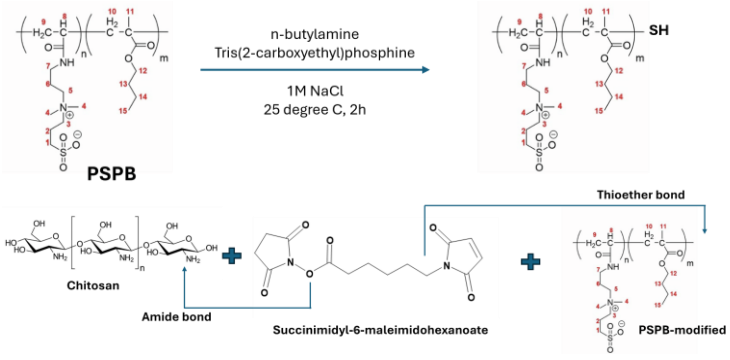
Zwitterionic Polymer-Immobilized Chitosan Hydrogel: A Novel Platform for Enhanced Protein Protection and Delivery

([1]*School of Materials Science, Japan Advanced Institute of Science and Technology*)
○Rajeev Ashwin,[1] Matsumura Kazuaki,[1]

Keywords: Hydrogel; Chitosan; Zwitterionic polymer; Polysulfobetaine; Protein

In the current healthcare settings, majority of the drugs have a broad-spectrum effect, which is undesirable, and have adverse side-effects.[1] It is high time to adopt precision medicine techniques, such as that of targeted drug delivery, using naturally obtained non-toxic materials with enhanced drug stability. This study involves the development of a drug delivery system using chitosan hydrogel as the carrier[2] and incorporating polysulfobetaine (PSPB) polymers into this hydrogel for potential long-term stability of the loaded therapeutic protein that has various cellular targets.[3]

1.5% (w/v) chitosan hydrogel beads were prepared by dissolving chitosan powder in 0.2M acetic acid. The PSPB polymers of DP = 100 were synthesized by following the already established protocol from previous reports.[4] The synthesized PSPBs were covalently attached to the chitosan hydrogels using succinimidyl-6-maleimidohexanoate as an immobilizer (Scheme 1). Characterizations were propelled using techniques such as ^{1}H-NMR of PSPBs, SEM, TEM, and FT-IR analysis of the obtained hydrogels to confirm the chemical linkage, and zeta potential analysis, and cytotoxicity studies are to be followed. The 1.5% (w/v) chitosan hydrogel microspheres synthesized were found to be more stable with a defined surface and structure. The PSPBs were found to have similar properties to the ones synthesized in previous studies from NMR analysis. The protein protecting ability of the hydrogel is expected to increase many-fold after PSPB incorporation, thereby increasing the efficiency of the drug-delivery system.



Scheme 1: Modification of chitosan hydrogel using succinimidyl-6-maleimidoh exanoate as an immobilizer for covalently attaching PSPB to chitosan.

1) R. Rajan, T. Furuta, D. Zhao, K. Matsumura, *Cell Rep. Phys. Sci.*, **2024**, *19*, 5. 2) W. Song, J. Xu, L. Gao, *Appl. Sci*, **2021**, *11*, 4217. 3) J. Vimali, Y.K. Yong, A. Murugesan, *Front. Med.*, **2022**, *9*,1019230. 4) J. Zhou, J. Zheng, Y. Zhang, *ACS Omega*, **2019**, *4*, 10185.

両親媒性ランダムコポリマーを基盤とした触媒能とチャネル能を有する人工膜タンパク質の創製

(信州大院総理工[1]・信州大繊維[2]) ○稲田 智理[1]・西村 智貴[2]

Creation of Artificial Membrane Proteins with Catalytic activity and Channel function Based on Amphiphilic Random Copolymers ([1]*Graduate School of Science and Technology, Shinshu University*, [2]*Dept. Chem. Mater. Sci., Shinshu University*) ○Chieri Inada,[1] Tomoki Nishimura[2]

膜タンパク質は、シグナル伝達や分子輸送、酵素反応などの機能を担う。このような機能を持つ人工膜タンパク質を細胞に導入することで、新たな細胞機能制御が期待できる。実際に Deng らは、銅触媒を配位させた高分子を細胞膜に組み込むことで、分子変換能を付与することに成功している[1)]。しかし、積極的な分子透過性の付与は行われておらず、生成分子の細胞内取り込みが不十分なため、十分な機能制御は困難である。

我々の研究室では、poly(propyrene oxide)を疎水鎖に有する両親媒性高分子がリン脂質二分子膜へ組み込まれ、人工分子チャネルとして機能することを見出している。[2)]本研究では、この知見を基に分子変換能と分子透過能を兼ね備えた人工膜タンパク質の開発を目的とした(Fig. 1)。

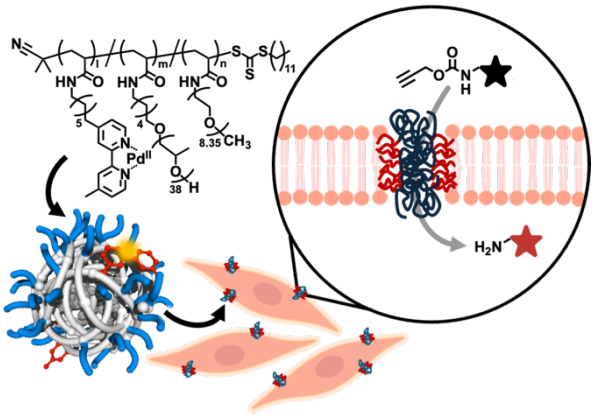


Fig. 1 Schematic illustration of artificial membrane protein and chemical structure of the random copolymers

合成したポリマーは、リン脂質リポソームに自発的に組み込まれ、分子チャネル能を有することを明らかにした。また、金属触媒を担持させることで、分子変換能も導入できることを見出している。さらに、生細胞膜上でも同様の機能を保持することを明らかにした。

Membrane proteins play essential roles in signal transduction, molecular transport, and enzymatic reactions. Artificial membrane proteins with similar functions are expected to enable new ways to control cellular functions. Herein, we aimed to develop artificial membrane proteins with both molecular transformation and transport abilities, and successfully synthesized amphiphilic polymers that integrate into lipid bilayers, exhibit molecular channel activity, and retain their functions, including metal-catalyzed transformation, in live cell membranes.

1) Y. Deng *et al.*, *J. Am. Chem. Soc.*, 2023, 145, 2, 1262–1272.
2) T. Nishimura *et al.*, *J. Am. Chem. Soc.*, 2020, 142, 1, 154–161.

Anti-PEG Antibody Assays Using Designable Cello-oligosaccharide Assemblies as Solid-Phase Platforms

([1]*School of Materials and Chemical Technology, Institute of Science Tokyo*, [2]*School of Science, Kitasato University*, [3]*School of Frontier Engineering, Kitasato University*, [4]*Kanagawa Institute of Industrial Science and Technology*, [5]*Faculty of Pharmacy, Juntendo University*) ○Kai Sugiura,[1] Koichiro Ishibashi,[2] Yuuki Hata,[1] Toshiki Sawada,[1] Go Watanabe,[2,3,4] Hiroshi Tanaka,[1,5] Takeshi Serizawa[1]

Keywords: Cello-oligosaccharide; Enzyme-catalyzed oligomerization; Click reaction; Anti-PEG antibody; ELISA

Recent studies have shown that some of polyethylene glycol (PEG)-conjugated proteins and nanoparticles can induce the production of anti-PEG antibodies. The antibodies can reduce the therapeutic efficacy and clinical safety of the PEG-conjugated protein and nanoparticle drugs. Therefore, analyzing the binding characteristics and levels of anti-PEG antibodies is crucial for improving the therapeutic efficacy and clinical safety of PEGylated drugs.

In our recent study, we demonstrated that oligo(ethylene glycol) (OEG)-tethering cello-oligosaccharide assemblies could be used to detect a monoclonal anti-PEG antibody via enzyme-linked immunosorbent assay (ELISA) method.[1] The assemblies were synthesized through enzyme-catalyzed oligomerization reactions. However, controlling OEG conjugation rates and introducing long OEG chains onto cello-oligosaccharide assemblies were difficult, and consequently, few species of anti-PEG antibodies were detectable using the assemblies.

In this study, we present propargylated cello-oligosaccharide assemblies to conjugate OEG chains for ELISAs of anti-PEG antibodies (Figure 1). OEG chains with various lengths were chemically conjugated onto the assemblies via the click reactions while controlling the conjugation rates. ELISAs using the OEG-conjugated assemblies allowed for detecting three kinds of monoclonal anti-PEG antibodies. Notably, it was revealed that one anti-PEG antibody exhibited binding characteristics distinct from the already accepted ones. Furthermore, the quantification of anti-PEG antibodies was successfully demonstrated in the presence of serum.

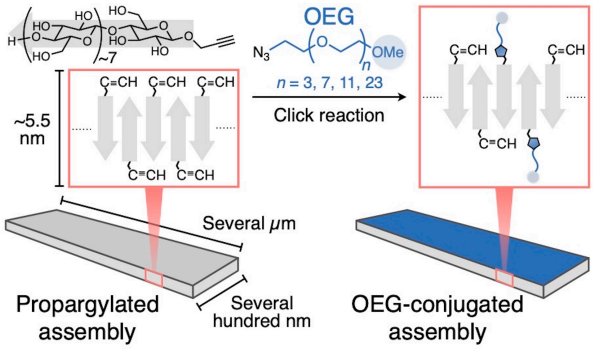


Figure 1. Construction of OEG-conjugated cello-oligosaccharide assemblies via click reactions.

1) K. Sugiura, T. Sawada, Y. Hata, H. Tanaka, T. Serizawa, *J. Mater. Chem. B* **2024**, *12*, 650.

癌治療薬を指向した高効率触媒的標的 RNA 切断機能付与型人工核酸の開発：Vasohibin-2 発現抑制による膵臓癌悪性化抑制への展開

（東北大多元研[1]・名大院理[2]・東北大 NICHE[3]・東北大 INGEM[3]）
○町田 光翼・稲垣 雅仁[2]・松本 光代[1]・荒木 保幸[1]・佐藤 靖史[3]・和田 健彦[1,4*]

Development of Vasohibin-2 targeted Chimeric Artificial Nucleic Acids for suppression of pancreatic cancer malignancy ([1]*IMRAM, Tohoku Univ.*, [2]*Grad. Sch. Sci., Nagoya Univ.*, [3]*NICHE, Tohoku Univ.*, [4]*INGEM, Tohoku Univ.*) ○ Kosuke Machida,[1] Masahito Inagaki,[2] Mitsuyo Matsumoto,[1] Yasuyuki Araki,[1] Masafumi Sato,[3] Takehiko Wada[1,4*]

To apply oligonucleotide therapeutics as promising pharmaceuticals, the following three issues should be improved: I) Off-target effects, II) Low cellular uptake capability, and III) Low therapeutic potency mainly due to extremely low intracellular concentrations. We have proposed and demonstrated a novel design strategy to improve these issues by enhancing the RNase H mediated target RNA cleavage efficiency by the Chimeric Artificial Nucleic Acids (CANAs), which consist of 5'-terminus modified DNA moiety conjugated with non-ionic peptide backbone artificial nucleic acid moiety such as PNA. In this study, we targeted the mRNA sequence of Vasohibin-2, a factor involved in the metastasis of pancreatic cancer, an intractable disease discovered by Prof. Sato et al. The structural design and synthesis of CANA, which contributes to the inhibition of pancreatic cancer malignant transformation, as well as its ability to form complexes with target mRNAs in vitro, complex stability, and catalytic RNA cleavage using RNase H, were investigated and reported.

Keywords : Chimera Artificial Nucleic Acid; Oligonucleotide Therapeutics; Pancreatic Cancer; Vasohibin-2; Catalytic cleavage of target RNA

次世代分子標的薬モダリティーとして期待される核酸医薬の実用化において、“オフターゲット効果の低減”と、主に細胞内極低濃度に起因する“低治療効果の向上”が喫緊の解決課題とされている。我々は両課題解決を目指し、RNase H を活用した標的 RNA 触媒的切断戦略に焦点を当て、標的 RNA の位置選択的切断による触媒回転数の向上に基づく極低濃度でも高い治療効果を実現し得る新規核酸医薬として、リン酸アニオン骨格 DNA/LNA（架橋型核酸）と PNA など負電荷を有しないアミド骨格人工核酸を融合したキメラ人工核酸（CANA：図 1）を提案し、その有効性を報告してきた。

本研究では、佐藤らが見出した難治性疾患である膵臓癌の悪性化に関与する Vasohibin-2 の mRNA 配列を標的とし、膵臓癌悪性化抑制に資する CANA の構造設計・合成ならびに標的 mRNA との複合体形成能・複合体安定性や RNase H を活用した触媒的 RNA 切断機能、特にジャンクション構造ならびに複合体安定性が切断効率におよぼす影響を詳細に検討したので報告する。

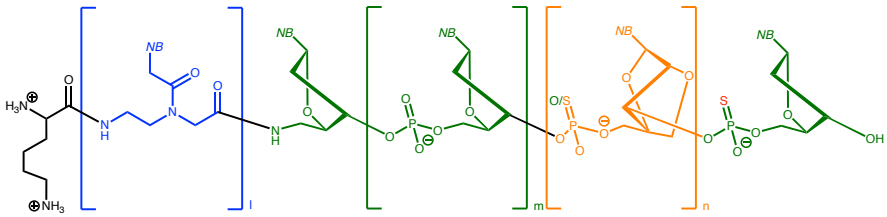


Fig. 1. Structure of Chimeric Nucleic Acids (CANAs). (*NB: Nucleobase*)