アカデミックプログラム［B講演］ | 17. 生体機能関連化学・バイオテクノロジー：口頭B講演

2025年3月26日(水) 15:55 ~ 17:15 [A]D401(第3学舎 4号館 [4階] D401)

[[A]D401-1vn] 17. 生体機能関連化学・バイオテクノロジー

座長：朴 昭映、木村 康明

英語
15:55 ~ 16:15

[[A]D401-1vn-01]
蛍光チミジン類似体によるグアニン四重鎖の検出と応用

○熊谷 智孝[1]、杉山 弘[3]、朴 昭映[2] (1. 京都大学大学院理学研究科、2. 大阪大学免疫学フロンティア研究センター（iFReC）、3. 京都大学 物質-細胞統合システム拠点 (iCeMS))

英語
16:15 ~ 16:35

[[A]D401-1vn-02]
2種類の短鎖DNAをビルディングブロックとした階層的な集合体の形成

○牧野 哲直[1]、梶谷 孝[2]、田仲 真紀子[1] (1. 電気通信大学、2. 東京科学大学)

英語
16:35 ~ 16:55

[[A]D401-1vn-03]
tRNA-グアニントランスグリコシラーゼを用いたRNA内部への5’キャップ構造導入反応の開発

○河崎 泰林[1]、飯田 優実[5]、中嶋 裕子[1]、阿部 奈保子[1]、橋谷 文貴[2]、稲垣 雅仁[1]、阿部 洋[1,2,3,4] (1. 名古屋大学大学院理学研究科、2. 名古屋大学物質科学国際センター、3. 科学技術振興機構CREST、4. 東海国立大学機構糖鎖コア研究所、5. 名古屋大学理学部)

英語
16:55 ~ 17:15

[[A]D401-1vn-04]
核酸の糖部2'位への化学修飾によるsiRNAの標的特異性の向上

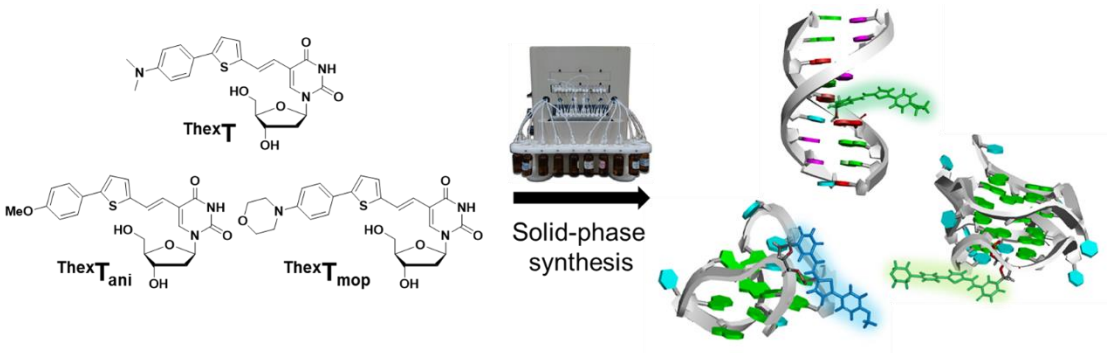
○野村 浩平[1]、安 成鎮[2]、村瀬 裕貴[1]、中本 航介[1]、木村 康明[1]、阿部 奈保子[1]、小林 芳明[3]、程 久美子[2,3]、近藤 次郎[4]、阿部 洋[1,5,6] (1. 名古屋大学大学院理学研究科、2. 東京大学大学院新領域創成科学研究科、3. 東京大学大学院理学研究科、4. 上智大学理工学部、5. JST CREST、6. iGCORE)

蛍光チミジン類似体によるグアニン四重鎖の検出と応用

（京大院理[1]・大阪大学免疫学フロンティア研究センターiFReC[2]・京都大学物質- 細胞統合システム拠点 iCeMS[3]）○熊谷 智孝[1]・杉山 弘[3]・朴 昭映[2]
Detection and Application of G-Quadruplexes by Fluorescent Thymidine Analogues ([1]*Graduate School of Science, Kyoto University*, [2]*Immunology Frontier Research Center (iFReC), Osaka University,* [3]*Institute for Integrated Cell-Material Sciences (iCeMS), Kyoto University*) ○Tomotaka Kumagai,[1] Hiroshi Sugiyma,[3] and Soyoung Park[2]

Fluorescent nucleobases have received considerable attention as versatile probes for studying the structure and dynamics of nucleic acids. Building on our previous development of ^{Thex}**T**, a fluorescent thymidine analogue with molecular rotor properties, we have synthesized two new derivatives, ^{Thex}**T**$_{ani}$ and ^{Thex}**T**$_{mop}$. By modifying the donor moiety of the ^{Thex}**T**, these derivatives demonstrate enhanced environmental responsiveness and increased fluorescence intensity. In this study, we evaluated the fundamental properties of ^{Thex}**T** derivatives and utilized their environmentally responsive fluorescence to detect guanine quadruplex (G4) structures.
Keywords : Fluorescent nucleoside; Thymidine analogue; Fluorescent molecular rotor; G-Quadruplex

蛍光性核酸塩基は、核酸の構造やダイナミクスを分析するためのプローブとして注目を集めている。近年、我々は分子ローターとしての特性を備えた蛍光性チミジン類縁体 ^{Thex}**T** を新たに開発し、その性質を報告した[1]。本研究では、^{Thex}**T** の骨格を基に、そのドナー部位の構造を改変することで、より高い環境応答性と蛍光強度を示す２つの新規誘導体 (^{Thex}**T**$_{ani}$, ^{Thex}**T**$_{mop}$)を開発した。本発表ではこれらの ^{Thex}**T** 誘導体の基本的性質についての評価と、環境応答性を利用したグアニン四重鎖(G4)構造の検出について報告する。



1) Thiophene-Extended Fluorescent Nucleosides as Molecular Rotor-Type Fluorogenic Sensors for Biomolecular Interactions. T. Kumagai, B. Kinoshita, S. Hirashima, H. Sugiyama, S. Park *ACS Sens.* **2023**, *8*, 923-932.

Formation of Hierarchical Assemblies Using Two Kinds of Short DNAs as Building Blocks

([1]*Graduate School of Informatics and Engineering, The University of Electro-Communications*, [2]*Research Infrastructure Management Center, Institute of Science Tokyo*) ○ Tetsunao Makino,[1] Takashi Kajitani,[2] Makiko Tanaka[1]

Keywords: DNA; Self-assembly; DNA Nanotechnology; Liquid Crystal

Double-stranded DNA (dsDNA) has the feature of self-assembling into the liquid crystalline phase under the environments with high concentrations of crowders.[1] We have previously reported that dsDNA, consisting of 25-mer oligonucleotides, assembles into a hexagonal plate-like liquid crystal with widths exceeding 10 μm in aqueous salt solutions containing high concentrations of poly(ethylene glycol) (PEG).[2] The dsDNA has two base overhangs AA/TT that promotes end-to-end stacking between dsDNAs. Hexagonal platelets form through the process of heating to 80°C and subsequent slow cooling to 25°C.

To our surprise, the addition of shorter dsDNA to the solution containing a pair of 25-mer oligonucleotides dramatically changed the morphology of the DNA assembly. Such changes in the morphology of the assemblies depended on the terminal sequences of shorter dsDNA (Fig. 1). Adding shorter dsDNA with AA/TT overhangs resulted in tube-like assemblies (molecular tube). On the other hand, the addition of shorter dsDNA with GG/CC overhangs formed hexagonal frames. Small angle X-ray scattering revealed hexagonal columnar phase diffraction peaks in both assemblies. This result shows that the molecular tube has a significantly elongated hexagonal edge structure, similar to the hexagonal frame, even though its appearance differs from that of hexagonal assemblies.[3] In this presentation, we will discuss the mechanisms underlying hierarchical DNA assembly.

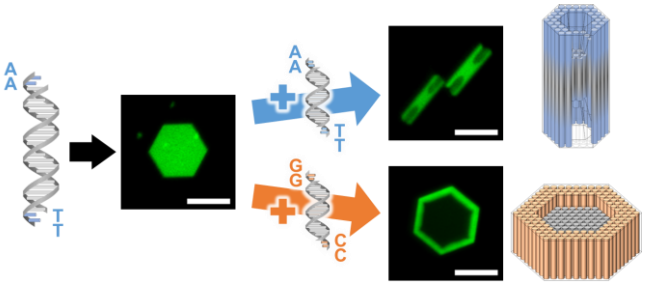


Fig.1 Fluorescence images and schematic illustration of DNA assemblies. Scale bars, 10 μm.

1) Y. M. Yevdokimov, *et al.*, *J. Biol. Phys.*, **2017**, *43*, 45.
2) T. Makino, *et al.*, *ChemBioChem*, **2022**, *23*, e202200360.
3) T. Makino, *et al.*, *Small*, **2024**, 2410243.

tRNA-グアニントランスグリコシラーゼを用いた RNA 内部への 5’ キャップ構造導入反応の開発

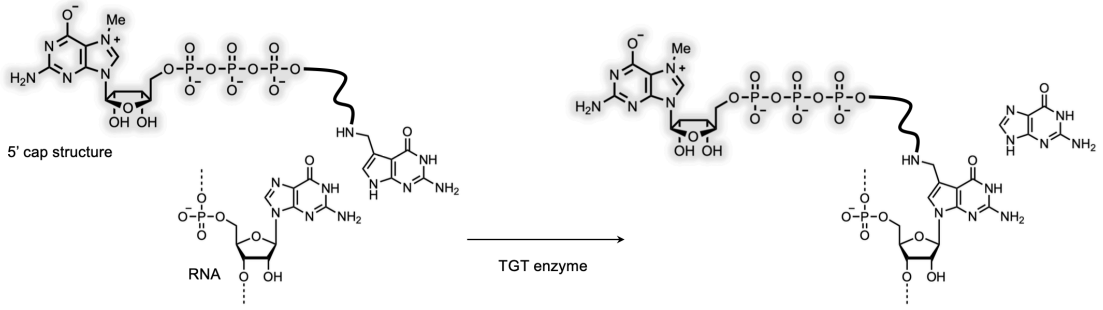
（名大院理[1]・RCMS[2]・CREST[3]・iGCORE[4]・名大理[5]）○河﨑 泰林[1]・飯田 優実[5]・中嶋 裕子[1]・阿部 奈保子[1]・橋谷 文貴[2]・稲垣 雅仁[1]・阿部 洋[1234]

5’ Cap Incorporation to Internal Site of RNA with tRNA-Guanine Transglycosylase ([1] *Graduate School of Science, Nagoya University*, [2] *Research Center for Materials Science, Nagoya University*, [3] *CREST, Japan Science and Technology Agency*, [4] *Institute for Glyco-core Research (iGCORE)*, [5] *Faculty of Science, Nagoya University*) ○Tairin Kawasaki,[1] Yumi Iida,[5] Yuko Nakashima,[1] Naoko Abe,[1] Fumitaka Hashiya,[2] Masahito Inagaki,[1] Hiroshi Abe[1234]

This study reports a method for directly incorporating a 5’ cap structure into an internal site of RNA using tRNA-guanine transglycosylase. The incorporated 5’ cap structure enhances protein expression from a downstream genetic sequence. Canonically, the 5’ cap structure resides at the 5’ terminus of eukaryotic mRNA, where it signals translation initiation. This study reveals that an internal cap, positioned non-canonically, also promotes protein expression. The developed cap-incorporation method enables the preparation of capped circular mRNA by directly introducing a cap structure into a simple circular RNA encoding a protein. This incorporation enhances protein production from the circular RNA.

Keywords : RNA Modification; Translation; 5’ Cap Structure; Circular mRNA; Enzymatic Modification

tRNA 修飾酵素である tRNA-グアニントランスグリコシラーゼの反応性を利用して、RNA 内部に位置特異的に 5’キャップ構造を導入する手法を開発した。通常 5’キャップ構造は直鎖 mRNA の 5’末端に存在しており、真核生物の細胞内でタンパク質合成をシグナルする。開発した手法により導入された 5’キャップ構造は、末端ではなく内部に存在しながらも、下流にある遺伝子情報にもとづくタンパク質発現を促すことが認められた。開発した手法を応用して、例えば、タンパク質の遺伝子情報をコードした環状 RNA に対して直截的にキャップ構造を導入した。キャップ構造が付与されることで、環状 RNA からの翻訳が促進されることが明らかになった。



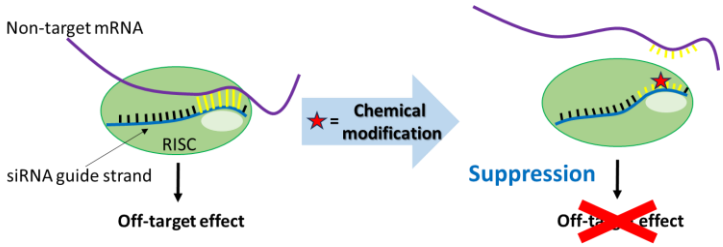
Improvement of siRNA target specificity by chemical modification to the 2' position of the sugar moiety of nucleic acids

([1]*Graduate School of Science, Nagoya University*, [2]*Graduate School of Frontier Science, the University of Tokyo,* [3]*Graduate School of Science, the University of Tokyo,* [4]*Faculty of Science and Technology, Sophia University,* [5]*JST CREST,* [6]*iGCORE*) ○Kohei Nomura,[1] Seongjin An,[2] Hirotaka Murase,[1] Kosuke Nakamoto,[1] Yasuaki Kimura,[1] Naoko Abe,[1] Yoshiaki Kobayashi,[3] Kumiko Tei,[2,3] Jiro Kondo,[4] Hiroshi Abe[1,5,6]

Keywords: siRNA; off-target effect; chemically modified nucleic acid

siRNA associates with various proteins in the cell to form a complex known as RISC, which targets and cleaves mRNAs with complementary sequences. This process, referred to as RNA interference, effectively inhibits the expression of genes linked to disease, and used as siRNA drugs. Despite its potential, siRNA-mediated gene silencing faces several obstacles, including limited stability in vivo, poor cell membrane permeability, and off-target effects due to interactions with unintended mRNAs. To address these challenges, siRNAs used in therapeutic applications have been chemically modified with groups such as 2'-OMe, 2'-F, and phosphorothioate. Nevertheless, these modifications alone are insufficient to fully eliminate off-target effects.

To address the suppression of off-target effects on non-target mRNAs, we developed a novel chemically modified nucleic acid and evaluated the siRNA with the modification. Off-target effects arise when the seed region of siRNA, 2nd to 8th nucleotides of guide strand, binds to non-target mRNAs through partial complementarity. Introducing chemical modifications to the seed region that destabilize base pair formation is considered an effective strategy to mitigate these effects (Figure 1). In this study, we designed, synthesized, and incorporated nucleic acid derivatives with a novel functional group at the 2' position into siRNA. This modification significantly reduced the RNA duplex stability. Subsequently, we evaluated the activity of siRNA containing the modification. The results demonstrated successful suppression of off-target activities while preserving on-target silencing by incorporating a single analog into the seed region. Overall, this novel analog represents a promising modification for siRNA therapeutics, offering effective suppression of off-target activity[1].



1) K. Nomura, S. An, Y. Kobayashi, J. Kondo, T. Shi, H. Murase, K. Nakamoto, Y. Kimura, N. Abe, K. Ui-Tei, H. Abe, *Nucleic Acids Res.*, **2024**, *52*, 10754–10774.