分子認識能を向上させる精密環状オリゴマーの合成

（九大工[1], 九大院工[2], 九大 CMS[3]）○和田宏之介[1]・多田隼人[2]・井福雅也[2]・森口ほの華[2]・辻爽太郎[2]・永井薫子[2]・星野友[2,3]

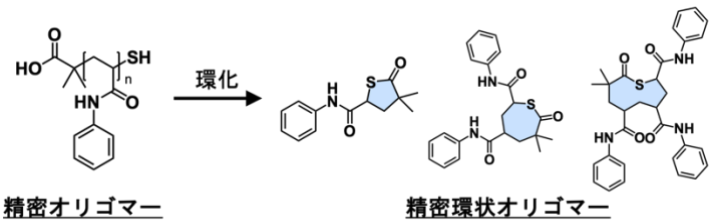
Synthesis of precision cyclic oligomers for improve molecular recognition ability

(*1. Kyushu Univ., 2. Grad. Sch. of Eng., Kyushu Univ., 3. Center for Molecular Systems (CMS), Kyushu Univ.*) ○Konosuke Wada[1], Hayato Tada[2], Honoka Moriguti[2], Masaya Ifuku[2], Sotaro Tuji[2], Yukiko Nagai[2], Yu Hoshino[2,3]

Precision oligomers have emerged as promising, cost-effective, and stable antibody alternatives[1]. However, their low binding constants with target molecules remain a significant limitation. We considered that the loss of binding constants is attributed to the high molecular mobility of linear oligomers, which results in substantial entropy loss upon binding. In this study, we synthesized precision cyclic oligomers with a cyclic backbone to investigate how topology influences molecular recognition and to improve their binding capabilities. Linear oligomers, functionalized with a carboxylic acid group at one terminus and a thiol group at the other terminus, were synthesized as monomers and dimers and subsequently cyclized via thiolactone formation. Hemolysis-neutralization assays using hemolytic peptides were conducted to compare the molecular recognition abilities of cyclic and linear oligomers. The results indicated that cyclic oligomers exhibited an enhanced neutralization ratio compared to their linear oligomers, highlighting the potential of cyclic oligomers to improve molecular recognition ability.

Keywords : Cyclic Molecule, Molecular Recognition, Precision Polymer, Oligomer, RAFT Polymerization

制御ラジカル重合とカラム分離によりモノマー配列と分子量が一義的に規定された『精密オリゴマー』は、抗体の安価で安定な代替品として注目される[1]。しかし、標的分子に対する結合定数は抗体と比較して顕著に低く、依然として大きな制限となっている。結合定数の低下は、直鎖オリゴマーの高い分子運動性によって結合時にエントロピーが失われることに起因する可能性を考えた。本研究では、分子認識能の向上を目指し、主鎖を環状構造にした精密環状オリゴマーの合成および分子認識における主鎖形状の影響の解明を目的とした。末端にカルボン酸、もう片末端にチオール基をもつ、直鎖状オリゴマー 1 量体と 2 量体を合成し、チオラクトンの形成により、環状オリゴマーを合成した。合成した直鎖状、環状オリゴマーの溶血毒性を示すペプチドの中和試験の結果から、環状 1 量体と環状 2 量体で溶血毒性の阻害率の向上が確認された。



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