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2006- Present Professor, Tohoku University
2003-2006 Associate Professor, Kyusyu University
2001-2002 Post Doctoral Fellow, NIA (National Institute of Aging, Baltimore)
1989-2002 Assistant Professor, Kyusyu University
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Research Interests:
Nucleic Acid Chemistry, Chemical Biology

Selected Publications:

1. Soemawisastra, N.; Okamura, H.; Abdelhady, A. M.; Onizuka, K.; Ozawa, M.; Nagatsugi, F. Uracil-Selective Cross-Linking in RNA and Inhibition of miRNA Function by 2-Amino-6-vinyl-7-deazapurine Deoxynucleosides. *Chembiochem* **2024**. DOI: 10.1002/cbic.202400417.

2. Okamura, H.; Yao, T.; Nagatsugi, F. Reversible Control of Gene Expression by Guest-Modified Adenosines in a Cell-Free System via Host-Guest Interaction. *J. Am. Chem. Soc* **2024**. DOI: 10.1021/jacs.4c04262.

3. Nagasawa, R.; Onizuka, K.; Komatsu, K. R.; Miyashita, E.; Murase, H.; Ojima, K.; Ishikawa, S.; Ozawa, M.; Saito, H.; Nagatsugi, F. Large-scale analysis of small molecule-RNA interactions using multiplexed RNA structure libraries. *Commun. Chem.* **2024**, *7* (1). DOI: 10.1038/s42004-024-01181-8.

4. Okamura, H.; Iida, M.; Kaneyama, Y.; Nagatsugi, F. o-Nitrobenzyl Oxime Ethers Enable Photoinduced Cyclization Reaction to Provide Phenanthridines under Aqueous Conditions. *Org. Lett.* **2023**, *25* (3), 466-470. DOI: 10.1021/acs.orglett.2c04015.

5. Nagatsugi, F.; Onizuka, K. Selective Chemical Modification to the Higher-Order Structures of Nucleic Acids. *Chemical Record* **2022**, e202200194 DOI: 10.1002/tcr.202200194.

Development of the Selective Reactions to Target RNA

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Abstract

RNA, in particular, is a promising drug discovery target because of its diverse functions, including not only gene-coding mRNA but also non-coding RNA and selective reactions targeting RNA could be an important chemical tool for control gene expression. We have developed the selective alkylation to the target RNA with sequence selectively using the oligonucleotides containing the crosslinkable base (Fig.1). We have also applied these reactive oligonucleotides to inhibit the miRNA function in cells.[1] In addition, the higher-order structure of nucleic acids, especially RNA, has the important role for the control of gene expression and is one of the candidates for therapeutic targets. Due to the therapeutic potentials, efforts on the development of small molecule binders to specifically target the higher-order structures of nucleic acids have been intensely carried out. The selective alkylation using small molecules targeting the higher-order structures of nucleic acids have also been pursued. However, most of the alkylating agents have drawbacks of their efficiency under physiological conditions. We have developed reactive OFF-ON type alkylating agents, vinyl-quinazolinone (VQ) precursors (Fig.2).[2]

In this presentation, we summarize the selective alkylation to the target RNA.

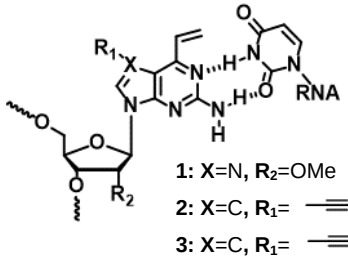

Fig. 1 The reactive oligonucleotides containing the crosslinkable base

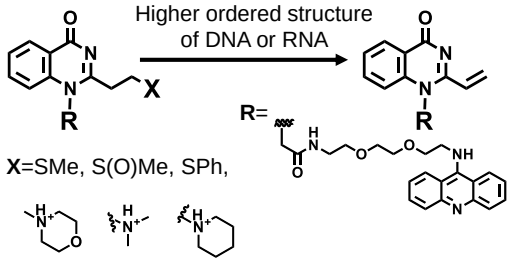

Fig. 2 The reactive OFF-ON type alkylating agents

References

1. Soemawisastra, N.; Okamura, H.; Abdelhady, A. M.; Onizuka, K.; Ozawa, M.; Nagatsugi, F.. *Chembiochem* **2024**. DOI: 10.1002/cbic.202400417.
2. Chen, Y. T.; Onizuka, K.; Hazemi, M. E.; Nagatsugi, F. *Bioconjugate Chem.* **2022**, *33*, 2097