Akimitsu Okamoto, Professor

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2012-Present	Professor, The University of Tokyo
2006-2012	Unit Leader, RIKEN
1999-2006	Research Associate, Kyoto University
1998-1999	PostDoc, MIT
1998 PhD	Kyoto University
1995 MS	Kyoto University
1993 BS	Kyoto University

Research Interests:

1. Synthesis of 'superbiopolymers' containing functional nucleotides and amino acids for elucidation of gene expression function.
2. Construction of new chemical platforms for collecting specific cells and analyzing cell-cell interactions at the single cell level.
3. Drug design, cell introduction, and functional analysis based on new chemical ideas.

Selected Publications:

1. Morihiro, K.; Morita, S.; Harada, N.; Baba, M.; Yum, J.; Naito, M.; Miyata, K.; Nagae, G.; Okamoto, A. RNA Oncological Therapeutics: Intracellular Hairpin RNA Assembly Enables MicroRNA-Triggered Anticancer Functionality. *J. Am. Chem. Soc.* **2024**, *146*, 1346-1355.
2. Takatsu, M.; Morihiro, K.; Watanabe, H.; Yuki, M.; Hattori, T.; Noi, K.; Aikawa, K.; Noguchi, K.; Yohda, M.; Okazoe, T.; Okamoto, A. Cellular Penetration and Intracellular Dynamics of Perfluorocarbon-Conjugated DNA/RNA as a Potential Means of Conditional Nucleic Acid Delivery. *ACS Chem. Biol.* **2023**, *18*, 2590-2598.
3. Morihiro, K.; Tomida, Y.; Fukui, D.; Hasegawa, M.; Okamoto, A. Nucleic Acid-to-Small Molecule Converter through Amplified Hairpin DNA Circuits. *Angew. Chem. Int. Ed.* **2023**, *62*, e202306587.
4. Furuhata, T.; Racheal, P. A. D.; Murayama, I.; Toyoda, U.; Okamoto, A. One-Pot, Photocontrolled Enzymatic Assembly of the Structure-Defined Heterotypic Polyubiquitin Chain. *J. Am. Chem. Soc.* **2023**, *145*, 11690-11700.
5. Morihiro, K.; Osumi, H.; Morita, S.; Hattori, T.; Baba, M.; Harada, N.; Ohashi, R.; Okamoto, A. Oncolytic Hairpin DNA Pair: Selective Cytotoxic Inducer through MicroRNA-Triggered DNA Self-Assembly. *J. Am. Chem. Soc.* **2023**, *145*, 135-142.

Cell Regulation by Oligonucleotide Aggregation Control

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Abstract

1. Assembly of hairpin DNA

We have developed a hairpin DNA assembly technology that enables cancer-selective immune activation to induce cytotoxicity. The designed artificial DNA hairpins assemble into long nicked double-stranded DNA triggered by intracellular microRNA-21 (miR-21), which is overexpressed in various types of cancer cells. The products from the hairpin DNA assembly selectively kill miR-21-abundant cancer cells in vitro and in vivo based on innate immune activation. Our approach is the first to allow selective oncolysis derived from intracellular DNA self-assembly, providing a powerful therapeutic modality to treat cancer.

2. Catalytic hairpin assembly

DNA decoys inhibit cellular transcription factors and are expected to be among the nucleic acid drugs used to downregulate the transcription process. To reduce undesired decoy function in normal cells, we adopted catalytic hairpin assembly (CHA) to produce a DNA duplex from a hairpin DNA pair in response to miR-21. We designed the DNA hairpin pairs to form a DNA decoy that binds to NF-κB, whose overexpression is related to many diseases, including cancer. The transformation of the DNA hairpin pair to the NF-κB DNA decoy was catalyzed by miR-21, which is expressed in various types of cancers. Intracellular CHA progression and the inhibitory effect against NF-κB were observed only in miR-21 overexpressing cancer cells. The intracellular miR-21-catalyzed production of the NF-κB DNA decoy has the potential to reduce side effects on normal cells, thereby strengthening the therapeutic profile of the CHA-decoy system.