



Preface

Controlling the function of genes and biologically active nucleic acids

Nucleic acids, DNA and RNA, are among the most important molecules for life. It is thought that the last universal common ancestor, or LUCA, had DNA and RNA, and therefore, all living organisms on the Earth share nucleic acids. Except that in RNA viruses, in other organisms, the genetic information is stored in DNA, transcribed into RNA, and translated into proteins. Proteins and RNAs, including micro RNAs, are involved in various physiological and pathological events. Regulation of these molecules is an important mode of treatment of various diseases. Therefore, compounds that regulate gene expression can be drug candidates, which include both nucleic acid- and non-nucleic acid-based compounds. Non-nucleic acid-based compounds regulate gene functions through specific interactions with genomic DNA. Nucleic acid drugs, which are typical nucleic acid-based compounds, have attracted increasing attention, and the number of approved nucleic acid drugs is rapidly increasing.

In this milieu, we have organized this special issue: *Controlling the Function of Genes and Biologically Active Nucleic Acids*. It covers the following aspects of the recent approaches to control the function of genes and biologically active nucleic acids: (i) the importance of the structural properties of nucleic acids for their interaction with other molecules, including nucleic acids and proteins; (ii) the structure-dependent activity of biologically active nucleic acids; and (iii) the novel compounds selectively regulating the gene functions.

A major topic covered in this issue is the application of DNA nanotechnology for regulating the functions of biologically active nucleic acids and other bioactive molecules. Since the original proposal by Nadrian C. Seeman [1], DNA nanotechnology has been used in various research fields, including the design and construction of DNA-based nanostructures as delivery vehicles of bioactive compounds [2]. Jiang et al. [3] focusses on the applications of DNA-based nanometer-sized materials for molecular imaging and drug delivery in cancer treatment. They elucidate a variety of DNA-based nanostructures and summarize their applications in the delivery of payloads, including functional nucleic acids, chemotherapeutic agents, and radioactive isotopes. Zuo and Mao [4] review a symmetric approach for the construction of DNA-based nanostructures using DNA tiles, which can minimize the number of different DNA strands. They applied these nanostructures for the delivery of small interfering RNA. Nishikawa et al. [5] demonstrate the structural and physicochemical properties of DNA-based nanostructures, with an emphasis on the interaction of DNA-based nanostructures and cells.

The following two articles focus on RNA. Seya et al. [6] review the recognition of RNA by RNA sensors, including Toll-like receptor 3 (TLR3), and the subsequent immune stimulation. They describe the properties of a synthetic TLR3 agonist, which can be used as an immune adjuvant in cancer immunotherapy. Tomoike and Abe [7] elucidate the detection

of intracellular RNA using molecular beacons, hybridization-sensitive probes, and other chemical probes. In this case, both targets and compounds used are nucleic acids and nucleic acid-based compounds.

The last two articles deal with the compounds that regulate the functions of genomic DNA. Tsuji and Imanishi [8] describe the properties and functions of transcription activator-like effectors, or TALEs, which specifically and sensitively recognize DNA containing 5-methylcytosine. They also discuss TALE-based epigenome editing and oxidized methylated cytosine recognition. Yu et al. [9] focus on pyrrole-imidazole polyamides, which are a major class of DNA minor groove-binding compounds. They can be designed to recognize specific DNA sequences, in order to modulate the functions of specific genes.

The review articles compiled in this issue provide an overview of recent approaches to control the functions of genes and biologically active nucleic acids. Because nucleic acids are essential to life and are involved in the most important processes occurring in our body, the topics covered can help develop new therapeutic strategies for various diseases.

References

- [1] N.C. Seeman, DNA in a material world, *Nature* 421 (2003) 427–431.
- [2] M. Nishikawa, S. Rattanakit, Y. Takakura, DNA-based nano-sized systems for pharmaceutical and biomedical applications, *Adv. Drug Deliv. Rev.* 62 (2010) 626–632.
- [3] Q. Jiang, S. Zhao, J. Liu, L. Song, Z.G. Wang, B. Ding, Rationally designed DNA-based nanocarriers, *Adv. Drug Deliv. Rev.* 147 (2019) 2–21.
- [4] H. Zuo, C. Mao, A minimalist's approach for DNA nanoconstructions, *Adv. Drug Deliv. Rev.* 147 (2019) 22–28.
- [5] M. Nishikawa, M. Tan, W. Liao, K. Kusamori, Nanostructured DNA for the delivery of therapeutic agents, *Adv. Drug Deliv. Rev.* 147 (2019) 29–36.
- [6] T. Seya, Y. Takeda, M. Matsumoto, A Toll-like receptor 3 (TLR3) agonist ARNAX for therapeutic immunotherapy, *Adv. Drug Deliv. Rev.* 147 (2019) 37–43.
- [7] F. Tomoike, H. Abe, RNA imaging by chemical probes, *Adv. Drug Deliv. Rev.* 147 (2019) 44–58.
- [8] S. Tsuji, M. Imanishi, Modified nucleobase-specific gene regulation using engineered transcription activator-like effectors, *Adv. Drug Deliv. Rev.* 147 (2019) 59–65.
- [9] Z. Yu, G.N. Pandian, T. Hidaka, H. Sugiyama, Therapeutic gene regulation using pyrrole-imidazole polyamides, *Adv. Drug Deliv. Rev.* 147 (2019) 66–85.

Makiya Nishikawa

Faculty of Pharmaceutical Sciences, Tokyo University of Science, Japan

Hiroshi Sugiyama

Department of Chemistry, Graduate School of Science, Kyoto University,
Japan

Institute for Integrated Cell-Material Sciences (WPI-iCeMS), Kyoto University,
Japan