Current Topics

Biological and Pharmaceutical Aspects of Nucleic Acids Chemistry

Foreword

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Last year, 2003, marked two major milestones in genomics. It was the 50th anniversary of the Watson–Crick double-helix structure of DNA, and the sequencing of the human genome was successfully completed. With the completion of the human genome project, we now expect the development of genome-based drug discovery and administration, and the identification of new genes responsible for many diseases, including cancer.

Nowadays, nucleic acids are the molecules being pursued by many molecular biologists, biochemists, and chemists, and they are being recognized as pharmaceutically important compounds. Genetic and epigenetic analyses will be necessary to understand the mechanisms of both diseases and drug effects. Synthetic oligonucleotides on DNA chips will lead to the discovery of important genes involved in diseases. Synthetic nucleic acids may potentially become useful genome-based drugs, as antisense and antigene oligonucleotides, (deoxy)ribozymes, and small interference RNAs. Moreover, synthetic oligonucleotides containing a DNA lesion are essential experimental tools for analyses of induced mutations, which are deeply related to carcinogenesis and possibly involved in aging and many diseases, such as neurodegeneration. DNA lesion repair, which is an important mechanism to prevent mutagenesis, is also being extensively studied with synthetic oligonucleotides. The development of nucleic acids chemistry is thus profoundly important in pharmaceutical sciences as well as in biology. The ‘current topics’ in this

issue will briefly summarize several aspects of nucleic acids chemistry, in both pharmaceutical sciences and biology.

Koizumi will describe the properties of newly developed 2'-O,4'-C-ethylene-bridged nucleic acids (ENA), and their applications as antisense and antigene oligonucleotides. Komatsu will describe a new type of ribozyme, which can be regulated by a specific oligonucleotide. These allosteric ribozymes could be useful for properly regulating gene expression. Nagatsugi and Sasaki will summarize targeted mutagenesis by reactive triple-helix forming oligonucleotides. This strategy could be an alternative form of gene therapy, to correct or knock out a disease-causing mutated gene.

Murty and Sugiyama will discuss the sequence-specific recognition ability of low molecular weight compounds, polyamides, for studying various DNA-protein interactions. These compounds could be used to regulate the expression of specific gene(s) in antigene therapy.

Kamiya will summarize the mutagenicities of two oxidative DNA lesions in living cells. Ide and Kotera will summarize the recent progress in the research field of human DNA glycosylases involved in the repair of oxidative DNA lesions. These types of studies have been facilitated by the progress in nucleic acids chemistry.

This organizer hopes that these minireviews will help the readers to understand several aspects of nucleic acids chemistry, and its valuable potential in both basic biology and pharmaceutical sciences.