Development of new functional nucleic acids having nuclease-resistant properties being included in a multi-functional envelope type nano device

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【Outline of survey】

It is possible now to diagnose a number of diseases on the genome level from results of the Human Genome Project. However, there are still a number of disease without efficacious therapies, including genetic diseases. Although nucleic acid drugs such as antisense and ribozyme molecules were greatly expected to be effective for the treatment of these diseases, only one drug (Vitravene) for the treatment of human cytomegalovirus retinitis in people with AIDS has been approved to use in clinics in U. S. A. Vitravene only works in the eye in which it is injected, but not for systemic uses. Several problems of these molecules have been thought in early days for the clinical developments, such that these molecules 1) did not have enough stability against widely-distributed endo- and exonucleases, 2) did not have enough cell-penetration properties, and 3) mainly contains a phosphorothioate linkage instead having a phosphodiester linkage, which binds randomly to many proteins in serum. Therefore, we became interested in developing new functional nucleic acids for being used for systemic therapy. The prerequisite properties for new modified nucleic acids should be 1) both endo- and exonuclease resistant, 2) formed a highly thermaly stable complex with target molecules, 3) applicable to aptamers as being expected to be a next-generation antibody, siRNAs and nuclease resistant vectors encoded these functional molecules. Moreover, the development of a multi-functional envelop-type nano-device as vehicles to deliver the functional nucleic acids to cytosol or nucleus effectively, will also be carried out.

【Expected results】

Now many biotechnology companies in worldwide are competing to develop new functional nucleic acids that can be used in systematic therapy. However, on going clinical trials using siRNAs and aptamers directed towards local uses such as the eye-injection. Therefore, if it should be worth developing not only new nuclease-resistant nucleic acids but also new drug delivery systems to carry them.

【References by the principal researcher】

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【Term of project】 FY2006－2010	【Budget allocation】 25,200,000 yen

【Homepage address】 http://www.pharm.hokudai.ac.jp/shoukai/yakka.html