Institute of Clinical Medicine and Research

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General Summary

The aim of our research is to fill the gap between clinical medicine and basic medicine. We have made good progress in the development of a drug delivery system using nanotechnology. In addition, this year we developed methods to eliminate radioactive compounds using magnetic basket-shaped nanosized capsules containing decontaminants. We also made progress in gene technology, especially in the treatment of hepatitis C virus (HCV) infection and liver cancer. Other major research topics are a transporter of ribavirin into hepatocytes and the function of microRNA/messenger (m) RNA. In the field of lipid metabolism related to atherosclerosis, we have reassumed lipoprotein cholesterols separated using our newly developed ion-exchange chromatography; last year we used this chromatography method to measure lipoprotein (a), atherosclerotic lipoproteins with a special apolipoprotein called apolipoprotein (a).

Research Activities

Transporter gene in the treatment of chronic HCV infection
Ribavirin is the main component of the combination treatment for chronic HCV infection, even though great progress has been made in developing direct-acting antiviral agents against HCV. In ribavirin-combined treatment, exposure of HCV in hepatocytes to ribavirin is critical for virus eradication. Ribavirin is transported into hepatocytes by cell membrane transporters. We have discovered and are investigating the novel function of transporters and the association of single nucleotide polymorphisms of the gene with treatment response.

Comprehensive gene expression profiling analysis of microRNA/mRNA in liver tissue
We are profiling and analyzing the expression of microRNA/mRNA in the liver tissue of patients with chronic HCV infection who would receive pegylated interferon-alpha plus ribavirin combination treatment. We have analyzed whether the microRNA/mRNA candidates can be associated with treatment response in chronic HCV infection. We have found the novel interaction between microRNA and mRNA in the replication and lifecycle of HCV. Currently, the functions of microRNA/mRNA are being investigated in detail.

The fabrication of "3D organic/inorganic-hybrid structure" as a future theranostic (therapy + diagnostic) and preventive nanomedicine
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Free manipulation of the movement of drugs with remote-controlled light/magnetism/ultrasound used in cutting-edge medical technology is expected to be a next-generation technology. Remotely manipulating the speed and position of nanoparticles, which are mineral capsules that respond to various types of physical energy and are filled with organic drugs, will lead to an innovative technology that allows "pinpoint" prevention, diagnosis, and treatment.

We aim to realize innovative nanomedicine in which we can remotely control the accumulation, release, and effects of drugs with nanosized capsules that efficiently convert light, magnetic, and ultrasonic energies. This is unprecedented research in which we can apply Japan's world-leading nanotechnology to medicine. It will allow highly sensitive, rapid diagnosis and highly effective treatment that is gentle to the body for incurable diseases and for diseases that are difficult to diagnose. The realization of medical care that is gentle to the weak, such as elderly persons, will help promote a long and healthy life, reduce healthcare costs, and lead to the development of the healthcare industry. Moreover, because this technology can precisely control the behavior of drugs, it can be applied to diverse areas, such as pharmacology, biotechnology, agriculture, and environmental science.

Studies of lipid metabolism and atherosclerosis

The relationship between diet and the incidence of cardiovascular disease among Japanese was investigated exhaustively through large-scale cohort studies in Japan, and their results were published in the *Journal of Atherosclerosis and Thrombosis*. Effects of carbohydrate co-feeding with lipids on postprandial hyperlipidemia were investigated with the measurement of serum levels of apolipoprotein B48. An incubation study using bacteriophages was performed to examine the antiviral effects of plasma fractions, and the antiviral fraction was extracted from human plasma. We developed a new high-performance liquid chromatography (HPLC) method for measuring lipoprotein (a) (published in the *Journal of Lipid Research*). By measuring very low density lipoprotein cholesterol with this HPLC, we proved the benefit of therapeutic exercise for reducing remnant lipoproteins. The effects of carbohydrate co-feeding with lipids on postprandial hyperlipemia, with measurement of serum levels of apolipoprotein B48, in healthy Japanese subjects were investigated, and the results were reported at the scientific meeting of the International Symposium on Atherosclerosis.

Publications

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