Institute of Clinical Medicine and Research

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General Summary

The aim of our research is to bridge 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 separate radioactive compounds by means of magnetic basket-shaped nanocapsules containing decontaminants. We also made progress in gene technology, especially in the treatment of hepatitis C virus (HCV) infection and liver cancer. Two of our major research topics are the transporter of rivavirin 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 with our newly developed ion-exchange chromatography; last year we used this chromatography method to measure lipoprotein (a), a atherosclerotic lipoprotein, with a special apolipoprotein called apolipoprotein (a).

Research Activities

Transporter gene in the treatment of chronic hepatitis C virus infection
Combination therapy with pegylated interferon and ribavirin is the standard-of-care treatment for chronic infection with hepatitis C virus (HCV). In this treatment, exposure of HCV to ribavirin in hepatocytes is critical for virus eradication. Ribavirin is transported into hepatocytes by cell-membrane transporters. We are investigating the function of the transporters and the association of single nucleotide polymorphisms of the gene with treatment response.

Comprehensive gene expression profiling analysis of microRNA/messenger RNA in liver tissue
We are profiling and analyzing the expression of microRNA/messenger (m) RNA in the liver tissue of patients with chronic HCV infection who would receive standard-of-care treatment. We are analyzing whether the microRNA/mRNA candidates can be associated with treatment response in chronic HCV infection. When the candidates affect the treatment outcome, the function of the microRNA/mRNA will be investigated in detail.

The temporal and spatial manipulation of "basket-type organic/inorganic-hybrid structure" as a future theragnostic nanomedicine
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 and perfectly timed" diagnosis and treatment.

We aim to realize innovative nanomedicine in which we can remotely control the accumulation, release, and effects of drugs with nanocapsules 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 are 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 and biotechnology.

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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