Institute of Clinical Medicine and Research

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General Summary

This year is the 10th anniversary of the founding of the Institute of Clinical Medicine and Research in a corner of Kashiwa Hospital. Listed below are major works of the institute in clinical microbiology, liver disease and oxidative stress, the treatment of viral infections and cancer, the development of drug delivery systems, and lipid metabolism related to atherosclerosis.

Research Activities

Clinical microbiology

Blood stream infections and respiratory tract infections in children and adults with febrile neutropenia were studied with a magnetic filtration system for DNA/RNA extraction (Magtration, Precision System Science, Co., Ltd., Chiba, Japan), dual priming oligonucleotide polymerase chain reaction, and DNA microchip electrophoresis (MultiNA, Shimadzu Corp., Kyoto, Japan). Multiple infectious agents have been identified in both cases. Bioremediation of dioxins with thermophilic bacteria has been established for contaminated soil and has achieved reductions of 90% (W/W). Methods have been developed for treating infectious waste and chemical hazardous materials in hospitals and other institutions. Epidemiological studies were performed with the DNA diagnosis of pathogens.

Liver disease and oxidative stress

1. Gene expression profiling analysis for oxidative stress-induced liver carcinogenesis

Our group investigated how continuous exposure to reactive oxygen species produced in the oxidation-reduction reaction would affect carcinogenesis in chronic liver damage, using an animal model with naturally occurring and oxidative stress-induced hepatotumorigenesis. On the basis of our experiments, we have narrowed down numerous candidates to 2 signatures. Our gene expression profiling data have been uploaded to the National Center for Biotechnology Information's Gene Expression Omnibus Website.

2. Development of a novel antioxidant agent

We have verified the antioxidant activity of lactoferrin and proposed its mechanism of antioxidant action. We have completed a clinical randomized trial for chronic hepatitis C virus (HCV) infection and are analyzing treatment outcomes. We are planning to develop a new type of pegylated lactoferrin and to apply it to clinical practice.

Hepatitis C virus- and host-related factors associated with treatment outcome in pegylated interferon plus ribavirin combination therapy for chronic HCV infection

1. Analysis of factors predictive of treatment outcome in chronic HCV infection

To develop more rational and effective treatments for chronic HCV infection, we are improving antiviral treatment regimen and developing new agents by analyzing viral factors, such as kinetics and the HCV genome, and host-related factors, such as single nucleotide polymorphisms, in cooperation with the Division of Gastroenterology and Hepatology, Kashiwa Hospital.

Development of drug delivery systems

The aim of our research is to develop methods of anticancer drug release and magnetically guided nanostructures. To deliver sufficient amounts of therapeutic agents to deep internal tumor lesions with minimum drug doses, the combination of magnetic nanostructures and transplantable magnets are now being developed. We devised a new self-assembled nanoparticle formulation that can be magnetically delivered to silence genes in cells and tumor tissues (described in *Nature Nanotechnology* in 2009). This work has been supported by an Industrial Technology Research Grant, Program 08C46049a, in 2008 from the New Energy and Industrial Technology Development Organization of Japan, Grants-in-Aid for Scientific Research (B) from the Ministry of Education, Cultures, Sports, Science and Technology of Japan, the Life Science Foundation in 2009, the Futaba Electronics Memorial Foundation in 2008, the Takeda Science Foundation in 2007, and the Tsuchiya Foundation in 2006.

Studies of lipid metabolism and atherosclerosis

1. We studied the effects of carbohydrate feeding on postprandial hyperlipidemia by measuring serum levels of apolipoprotein B-48.
2. We are performing an incubation study using bacteriophages to examine the antiviral effects of plasma fractions. This work will investigate the connection between lipid metabolism and susceptibility to viral infection.
3. With our newly developed method of high-performance liquid chromatography (reported in Clinical Biochemistry in 2007 and in Lipids in Health and Disease in 2008) we established a method for measuring lipoprotein A, and a manuscript presenting this method was accepted for publication in the Journal of Lipid Research.

Publications

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