Medical Engineering Laboratory

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General Summary

Medical engineering is an essential foundation for developments in medicine. In our laboratory, there are 2 key technologies: ultrasound and polymeric biomaterials. We have developed ultrasound technology for a new thrombolytic treatment for acute ischemic stroke. Our ultrasound research is characterized by the use of medium-frequency ultrasound and close collaborations with clinical departments and basic science departments, both in our university and hospital and others'. For the other key technology, polymeric biomaterials, we have applied these materials mainly for drug delivery systems. We have also recently applied polymeric biomaterials to imaging diagnosis through the synthesis of new polymeric contrast agents. In particular, we study polymeric micelle systems that can deliver both drugs and contrast agents. Therefore, these systems are called "theranostic" systems because of the dual functions of therapy and diagnostics.

Research Activities

Medical application of ultrasound

We have applied transcranial ultrasound therapy to the treatment of ischemic stroke. For this condition, injection of tissue plasminogen activator has been the only effective treatment. However, significant increases in therapeutic effects are desperately needed. Transcranial ultrasound can enhance the thrombolytic activity of tissue plasminogen activator. Our technology features the use of medium-frequency ultrasound, which enhances thrombolysis more than does ordinary ultrasound. However, medium-frequency ultrasound is believed to be associated with a high risk of brain hemorrhage. To minimize the risk of hemorrhage, we control both the period and interval of irradiation; we have shown in an animal model of high-blood-pressure brain ischemia (spontaneously hypertensive rat) that ultrasound irradiation is both safe and effective. Furthermore, we have found that modulation of the ultrasound reduced nonuniformity of the applied ultrasound. We have developed a new instrument that can rapidly determine the sonothrombolytic effect through the absorption of blood clots. We have been developing this new therapy through a "super special consortium for supporting the development of cutting-edge medical care" program supported by the Ministry of Health, Labour and Welfare of Japan.

Polymeric micelle drug carrier systems

Polymeric micelles are assemblies of synthetic polymers, which have been used for drug targeting. Professor Yokoyama, director of this laboratory, is an international pioneer in

the development of polymeric micelle targeting systems. Currently, 4 formulations of polymeric micelle anticancer drugs are undergoing clinical trials in Japan, Europe, and the United States. We are trying to establish the next-generation science technology in polymeric micelle systems. We are studying the polyethylene glycol (PEG)-related immune response, which is called the accelerated blood clearance (ABC) phenomenon, of the polymeric micelles. Curiously, the polymeric micelle carriers are very different from liposome systems. Although the surfaces of both carrier systems possess PEG, polymeric micelle carriers induced no or low immune responses of the ABC phenomenon. This avoidance of the immune response is a great advantage of polymeric micelle carrier systems for drug targeting. In this immune response, we have found that the generated anti-PEG antibody does not bind to the PEG main chain but does bind to the interface between PEG and hydrophobic blocks.
We are also performing basic chemistry studies to analyze the drug-incorporated inner core of polymeric micelles by use of synchrotron radiation (Super Photon Ring 8 Giga electron volt facility, Hyogo Prefecture). The precise measurement accurately determines the structure of polymeric micelles, and this knowledge can be used to better understand polymeric micelles in biological systems.

Polymer-based contrast agents for diagnosis
We have developed new polymeric micelle magnetic resonance imaging (MRI) contrast agents for the diagnosis of diseases. These contrast agents were proven to target sites of solid tumors and to exhibit clear MR images of extremely small tumors. Therefore, the polymeric micelles can be used for "theranostics" of tumors because the polymeric micelles can deliver both drugs and contrast agents to solid tumors. Furthermore, we are studying a novel application of the polymeric carrier system for diagnosing ischemic stroke. We observed that a polymeric micelle MRI contrast agent was successfully directed to a specific site in the ischemic hemisphere and provided high-contrast images that were not obtained with a conventional low molecular weight MRI contrast agent. This high contrast was obtained in a short time, such as 20 to 60 minutes, after the contrast agent was injected intravenously. Therefore, the polymeric micelle carrier system and polymer biomaterials may be extremely useful for both the diagnosis and treatment of ischemic stroke. This new challenge may lead to beneficial treatments.

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