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. Recently, we have also applied polymeric materials 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. Additionally, some of our research studies combine ultrasound and polymeric biomaterials. One example is ultrasound-assisted targeting of polymeric drug carrier systems.

Research Activities

Medical application of ultrasound
We have applied ultrasound for a transcranial therapy against brain ischemic stroke. Against this serious disease, injection of tissue plasminogen activator (t-PA) has been the only effective therapy. However, significant increases in therapeutic effects are strongly wanted. Transcranial ultrasound can enhance the thrombolytic activity of t-PA. Our technology features the use of medium-frequency ultrasound, which is known to enhance thrombolysis more than does the ordinal ultrasound. However, the medium-frequency ultrasound is believed to be associated with a high risk of brain hemorrhage. To resolve the hemorrhage risk problem, we control both the irradiation period and the interval of irradiation; we have shown in models of hypertensive brain ischemia that, the ultrasound irradiation is both safe and effective. Furthermore, we have found that the modulation of ultrasound reduced unfavorable reflections of the applied ultrasound. 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, Japan.

Polymeric micelle drug carrier systems
Polymeric micelles are assemblies of synthetic polymers, and have been actively applied for drug targeting. Associate 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 the polymeric micelle systems. We are studying the immunological properties of polymeric micelles. Curiously, the polymeric micelle carriers are very different from liposome systems. Although both the surfaces of carrier systems possess poly(ethylene glycol), the polymeric micelle carriers induced no or low immunological responses of the accelerated blood clearance phenomenon. This low immunogenicity presents a great advantage of the polymeric micelle systems. We are also studying basic chemistry to analyze, through the use of the Super Photon Ring 8 Gigaelectronvolt facility, the drug-incorporated inner core and to prepare polymeric micelles with cross-linked inner cores through photochemistry. These cross-linked micelles are extremely useful for determination of the in vivo fates of polymeric micelles.

Polymer-based contrast agents for image diagnosis

We have developed new polymeric micelle contrast agents for magnetic resonance imaging (MRI). These contrast agents were proven to be targeted at solid tumor sites and to exhibit clear magnetic resonance images of very small tumors. Therefore, the polymeric micelles can be used for the "theranostics" of tumors because the polymeric micelles can target both drugs and contrast agents to solid tumors. Furthermore, we are studying a novel application of the polymeric carrier system for diagnosing brain ischemic stroke. We observed that a polymeric micelle MRI contrast agent was successfully targeted 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 may be extremely useful for both the diagnosis and the therapy of ischemic stroke.

Publications

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