MERIT Internship Program (Domestic) Report

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【Outline】

In my doctoral researches, I have developed novel redox-active polymers to achieve growth suppression through modulation of the redox state in cancer cells. On the other hand, it is important not only to develop anticancer drugs based on novel mechanisms of action, but also to develop methods for delivering the drugs to tumor sites. In this internship, in order to obtain the viewpoint of material design for practical usages, I carried out research activities in the Ebara Laboratory in NIMS, where new medical materials have been developed using smart polymers that express diverse functions in response to various external stimuli.

【Research】

Hyperthermia is a type of cancer treatment that kills cancer cells by exposing certain parts of the body to high temperatures. Under high temperature conditions, cancer tissue can be damaged and killed with minimal damage to normal tissue. Thermotherapy is also known to enhance the effects of certain anticancer drugs, and the combination of thermotherapy and anticancer drugs is considered as a promising method for cancer treatment. Ebara Laboratory, the host of this internship, has developed a smart film as a local drug delivery platform to realize fusion of hyperthermia treatment and anticancer drugs. The film is composed of poly (ε-caprolactone) (PCL) containing anticancer drugs and magnetic nanoparticles (MNPs). Polymers based on PCL can control the melting point near body temperature by molecular design, and exhibit special properties such as drug releasing and shape memory properties by thermal stimulation. Thus, when an alternating magnetic field is applied to the film, the MNPs in the film generate local heat, causing a thermal effect and release of anticancer drugs, resulting in suppression of cancer cell growth. In order to realize the cancer treatment by the smart film, it is essential to investigate the basic physical properties of the film. Based on the above background, in this internship, I evaluated the basic physical properties of the smart film and examined the effect of hyperthermia treatment.

1. Development and evaluation of smart films

PCL films and PCL/MNPs films were prepared by polymerization of PCL macromonomer and MNPs. In order to evaluate the shape memory characteristics of the films, the films was stretched under heating conditions using a tensile testing machine, then the shape was fixed, and the recovery

rate of the film length by heating was measured. Three cycles of this experiment showed that the PCL films possessed complete recovery property after three cycles, whereas the PCL/MNPs films did not fully recover from the first cycle. Next, the Young's modulus at elongation was measured. The PCL/MNPs films showed larger Young's modulus than the PCL films. The Young's modulus of PCL/MNPs films tended to decrease with each cycle, whereas that of PCL films did not change significantly with each cycle. From these results, it can be inferred that in the PCL/MNPs films, the presence of MNPs prevents the polymer chain from returning to the initial state upon shape recovery, resulting in the decrease of Young's modulus. Furthermore, in order to investigate the heat generation characteristics of PCL/MNPs, the temperature change during the application of alternating magnetic field was tracked, and it was found that the heat generation temperature tended to increase depending on electric power of the magnetic field device.

2. Effect of hyperthermia on MCF -7 breast cancer cells

The effect of hyperthermia on breast cancer cell MCF -7 was investigated. The anticancer drug doxorubicin (DOX) was added to MCF-7 cell culture medium, and the cells were incubated under a hyperthermia condition of 45 °C for a certain period of time, followed by incubation for 24 hours in the incubator of 37°C. After the cultivation, cell viability was evaluated. As a result, it was confirmed that the cell growth inhibitory effect of DOX tended to be increased by heat treatment for 0.5 hours and 1 hour. On the other hand, the effect of DOX tended to decrease after 2 hours of heat treatment. This is considered to be due to the fact that the cell viability was drastically decreased even without DOX. These results suggest that 0.5 to 1 hour is a suitable heating time.

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