THE SUMMARY OF Ph. D. DISSERTATION

Major Biomedical Engineering		SURNAME, Firstname NAGAO, Tomokazu

Title

A study on mechanism of cytotoxic effect induced by photodynamic therapy

Abstract

In the aging society where elderly people die of cancer, establishment of a low invasive treatment for cancer is expected in consideration of a patient's Quality Of Life. Since photodynamic therapy (PDT) using laser light and photosensitizer can treat cancer with endoscope and selectively eradicate neoplastic tissue, it is the low invasive cancer therapy with little injury to normal tissue. However, the cytotoxic effect, that is a central effect of this therapy, was not investigated in detail. In this dissertation, factors influencing the cytotoxic effects are analyzed with a novel quantitative method for assessing intracellular photosensitizer, and then the mechanism of the cytotoxic effect by PDT was revealed.

In Chapter 1, basic information about PDT is described as a new cancer treatment that meets the requirements for low invasive therapy. Then new approaches to solve many problems in previous studies of PDT are described.

In Chapter 2, excitation light sources and photosensitizers used in PDT are introduced in terms of the history of PDT. And cytotoxicity of reactive oxygen species (ROS) is mentioned as basic mechanisms of PDT.

In Chapter 3, ability of Zn CP-III to generate ROS is demonstrated by measuring the optical property of Zn CP-III and the generation of ROS from Zn CP-III. In Chapter 4, photochemically induced cytotoxicity to malignant cells was investigated, and then dependence of the cytotoxicity on parameters of Zn CP-III and light was presented.

In Chapter 5, quantitative method for determination of intracellular concentration of Zn CP-III is developed using confocal laser scanning microscope and image analysis. This chapter shows that photobleaching of Zn CP-III and cell activation effect was induced by laser irradiation, and that these phenomena reduce the cytotoxicity.

Chapter 6 proposes the extended method for determination of the Zn CP-III concentration of individual subcellular region. The relationship between the intracellular content of Zn CP-III and the cytotoxicity is obtained by this method.

Chapter 7 shows that PDT induces apoptotic cell death in malignant cells. The apoptotic pathway is analyzed, and applicability of PDT for leukemia treatment is revealed.

Finally, Chapter 8 summarizes the results of each chapter and concludes this dissertation.