



Title	がん細胞におけるミトコンドリア由来活性酸素を介した3-Methyl pyruvateによる放射線感受性の増強 [論文内容及び審査の要旨]
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学位論文内容の要旨

博士の専攻分野の名称：博士（獣医学）

氏名 西 田 直 哉

学位論文題名

がん細胞におけるミトコンドリア由来活性酸素を介した
3-Methyl pyruvate による放射線感受性の増強

Considerable interest has recently been focused on the special characteristics of cancer metabolism, and several drugs designed to modulate cancer metabolism have been tested as potential anticancer agents. To date, however, very few studies have been conducted to investigate the combined effects of anticancer drugs and radiotherapy. In this study, to evaluate the role of mitochondria-derived reactive oxygen species (ROS) in the radiation-induced cell death of tumor cells, we have examined the effect of 3-methyl pyruvate (MP). MP is a membrane-permeable pyruvate derivative that is capable of activating mitochondrial energy metabolism, on human lung carcinoma A549 cells and murine squamous carcinoma SCCVII cells. Pretreatment with MP significantly enhanced radiation-induced cell death in both cell lines, and also led to increases in the mitochondrial membrane potential, intracellular adenosine triphosphate content, and mitochondria-derived ROS production following the exposure of the cells to X-rays. In A549 cells, MP-induced radiosensitization was completely abolished by vitamin C. In contrast, it was partially abolished in SCCVII cells. These results therefore suggest that the treatment of the cells with MP induced radiosensitization via the production of excess mitochondria-derived ROS in tumor cells.