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論　文　内　容　要　旨

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学位論文題目	Study on the impact of physical treatment on tumors and testicular tissues （腫瘍および精巣組織に対する物理的処置の影響に関する研究）		

Although, using physical stimuli is accepted in the area of oncology, it may be harmful to normal tissue. So this study was conducted to investigate the effects of two different physical treatments (weak electric current (WEC) and hyperthermia) on tumor and testicular tissues, respectively. In the first section of this thesis, I investigated the effects of WEC on tumor. I postulated that WEC amplifies the enhanced permeability and retention (EPR) effect in solid tumors by dissociating intercellular junctions based on a previous study that reported that WEC triggers an intracellular signaling pathway in the skin, which opens the intercellular space apparatus. Based on this premise, I tested the antitumor activity of WEC treatment in combination with PEG-modified doxorubicin encapsulated nanoparticles (DOX-NP) or alone in B16-F1 melanoma bearing mice. I found that WEC treatment enhanced the EPR effect of DOX-NP. Also, WEC treatment alone prevented tumor growth. To clarify the mechanism of the tumor growth prevention effect of WEC, I examined the effect of WEC treatment on B16-F1 melanoma cells in vitro. I found that WEC treatment prevented the proliferation, but no cytotoxic effect was observed. Furthermore, WEC treatment suppressed cyclin B1 protein expression, which is considered a key regulatory protein involved in mitosis. In the second section of this thesis, I evaluated the impact of thermal treatment on testicular cells. Previous researchers have found that hyperthermia impairs testicular function through a variety of mechanisms, including apoptosis, oxidative stress, and induction of heat shock proteins, but the exact mechanism is unknown. Here, I studied the effect of thermal treatment on male fertility, focusing on the CatSper channel (cation channel of sperm) as a new mechanism of hyperthermia-induced testicular injury and examined the time dependent change of this cation channel after heat treatment. I found that thermal treatment caused notable downregulation of CatSper1 and-2 gene expression on day 1, day 14 and day 35. I also found a reduction in testis weight and a deterioration of sperm motility in heat stressed rats, which was correlated with reduced CatSper gene expression. In conclusion, physical treatment by WEC and heat reduced the tumor and testis size, respectively, by two distinct mechanisms.