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論　文　内　容　要　旨

報告番号	甲　先　第　275　号	氏　名	多田　竜
学位論文題目	Design, Synthesis and Evaluation of Boron – Containing Drug Having Pharmacological Activity and Physical Destructive Activity (薬理活性及び物理的破壊能を有するホウ素含有医薬品の設計・合成及び評価)		

内容要旨

Boron neutron capture reaction (BNCR) that is the non-radioactive isotope B-10 reacts with thermal neutron and then generates α-particle, Li nuclei and prompt gamma-ray. This reaction is used in cancer therapy, that is known as Boron neutron capture therapy (BNCT). However, conventional BNCT agents have no pharmacological activity themselves. There, we focused on boron containing drug which have pharmacological activity by drug scaffold and physical destructive activity and traceable by BNCR as well as. This multifunctional drug was named boron tracedrug.

In chapter 1, I evaluated the destructive effect of a boron tracedrug UTX-51 for glycated BSA as a advanced glycated-end product (AGE) model. AGE is aggregated protein and have been implicated in diabetes, Alzheimer's disease, and heart disease. The combination of UTX-51 with neutron irradiation showed a decreased of target protein. This result suggests that boron tracedrug UTX-51 can be used for the treatment of AGE related disease.

In chapter 2, I reported that designed and synthesized a series of boron containing PARP (poly (ADP-rybose) polymerase) inhibitors as a novel boron tracedrug. PARP is a nuclear enzyme, and involved in DNA repair. In *BRCA1* gene mutated cancer, inhibiting PARP activity led to tumor cell death. I showed that the inhibitory activity of PARP-targeted boron tracedrugs against PARP was enhanced 10 min neutron irradiation. Moreover, the PARP-targeted boron tracedrugs showed radiosensitize activity and neutron sensitizing activity against human breast cancer cells MDA-MB-231. These results suggest that the novel PARP inhibiting boron tracedrugs can be used for the treatment of BRCA mutated cancer.