I. Project Research

Project 11

PR11 Project Research on a Study on Biological Character and Use of the Particle Induced by the Boron Neutron Capture Reaction

Y. Kinashi

Research Reactor Institute, Kyoto University

Objectives and Participating Research Subjects

In this project, we are intending to develop the new application using the characteristics of the particles from the neutron capture reaction. Our project researchers were not able to carry out own experiments because KUR has been stopping during this year.

PRS-1 Analysis of mutation in the mammalian cells induced by BNCR (boron neutron capture reaction)
(Y. Kinashi *et al.*)

PRS-2 Analysis of double strand breaks in the mammalian cells induced by BNCR
(S.Takahashi *et al.*)

PRS-3 Development of the PARP repressor reinforced in its function by BNCR
(Y.Uto *et al.*)

PRS-4 Development of the model animal shouing the blood vessel damage by BNCR
(R. Wate *et al.*)

Main Results and Contents

PRS-1 could not carry out the experiment of the mutation in the mammalian cells induced by BNCR because KUR (Kyoto University Research Reactor) has been stopping during this year.

Using the gamma-ray irradiation facility, biological effects of the combination of the gamma-ray irradiation and Temozolomide(TMZ) that is DNA alkylating agent on the T98G human glioblastoma cells were investigated. The result suggested that TMZ treatment has the sensitization effect of radiation in CHO cells with low MGMT(methylguanine methyltransferase) gene expression that is the DNA repair enzyme, whereas that T98G cells with MGMT gene expression were resistance to TMZ. The enhancement effect of the combination of radiation and TMZ treatment was not found in T98G cells.

PRS-2 was not able to carry out its experiments because KUR has been stopping during this year.

PRS-3 was not able to carry out its experiments because KUR has been stopping during this year.

PRS-4 was not able to carry out its experiments because KUR has been stopping during this year.

PR11-1

Biological Effects of DNA Alkylating Agents on the Cell Lethal Effects of Ionizing Radiation

Y. Kinashi, T. Ikawa and S. Takahashi

Research Reactor Institute, Kyoto University

INTRODUCTION: Most BNCT (boron neutron capture therapy) patients have already received chemotherapy. Especially many brain tumor patients are taking temozolomide(TMZ) treatment. TMZ is a DNA-alkylating agents and particularly effective cancer drug for glioblastoma. The purpose of this study is to investigate the biological effects of the combination of TMZ and ionizing radiation by the study of the cell lethal effects.

MATERIALS & METHODS: T98G human glioblastoma tumor cells and CHO (Chinese hamster ovary) cells are purchased from Riken BRC Cell Bank. T98G cells are resistance to TMZ because they have MGMT(methylguanine methyltransferase) gene expression that is the DNA repair enzyme. TMZ solution prepared by the medium, and removal washing with phosphate buffered saline after 23 hours incubation. In the experiment exposed with TMZ, T98G cells showed TMZ resistance about 4 times higher than CHO cells. The concentration of TMZ with γ-ray radiation was 100 μm in CHO cells and 400 μm in T98G cells, respectively. The gamma-rays irradiation for cells was carried out using Co-60 gamma-ray facility of KURRI. After gamma-ray irradiation, cells were seeded on a Petri dish and incubated for 14 days. The survival curve creates a Plating Efficiency of each treatment and control groups compared survival rate.

RESULTS and DISCUSSION: Figure 1 shows the survival data observed differences in sensitivity of the between two cells. D0 values are T98G 5.03 Gy, CHO: 5.21 Gy after gamma-ray irradiation. In the combination study of gamma-rays and TMZ, D0 value of T98G was 5.40 Gy. D0 value of CHO was 3.38 Gy. In CHO cells, D0 value was decreased 1.83 Gy. There was no apparent change in the D0 value of T98G cells by gamma-ray irradiation with TMZ treatment. D10 value also decreased 1.81 Gy after the gamma-ray and TMZ in CHO cells. These results show that TMZ treatment has the sensitization effect of radiation in CHO cells.

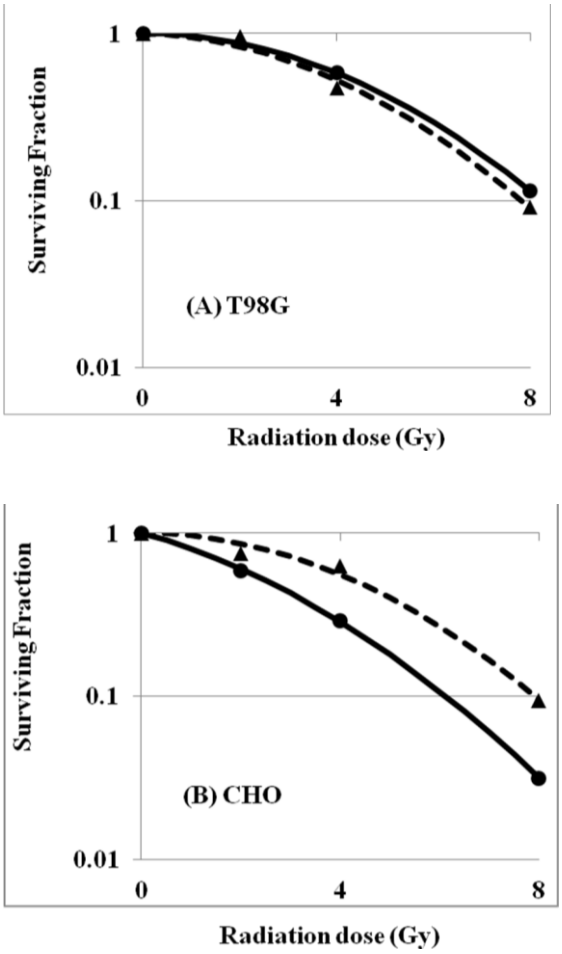

Fig. 1 Survival curves of gamma-ray irradiation with TMZ(—●—)compared without TMZ (- -▲- -)
(A)T98G cell study, (B) CHO cell study

The CHO cells that alkylation repair activity is low and cells have high susceptibility to TMZ. TMZ concluded that further enhance the cell-killing effect of radiation. It is generally known that patients with glioblastoma with MGMT gene silencing have the benefit from TMZ and survival benefit for the chemoradiotherapy[1]. Further studies will be needed to analyze whether synergy effect of the combination of BNCT and TMZ in various brain tumors showing low TMZ expression to aim the clinical effect improvement of BNCT.

[1] M.E.Hegi *et al.*, N. Engl. J. Med., **352**(2005)997-1003.