

[PA3-8] [ 2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function ]

### **Chronic Effects of Hair, Blood And Testis In Black Mouse With Neutron Irradiation By Lying Flat Pose**

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The purpose of this study is to investigate the biological effects in black mouse by neutron irradiation at HANARO reactor in KAERI. Neutrons readily penetrate the charged field of an atomic nucleus because they are electrically neutral. And so it can fight cancer with the radiation released when an atom of the element boron absorbs a neutron. The main patient in BNCT facility is brain cancer and sometimes skin cancer in foreign countries until now. Therefore, mice were laid flat and so irradiated at the direction of the front. Six-week-old black male mice were irradiated with neutron (flux:  $1.036739E+09$ ) for 1 hr or 2 hrs. After irradiation, life span and hair color in mice were investigated and then on day 80 the mice a part were sacrificed for measuring the blood cell ratios of blood and weight, volume and sperm count of testis. All experimental mice survived over 90 days after neutron irradiation. In hair, mice with neutron irradiation for 2 hrs only were changed white color on center of the back. In blood, WBC, RBC, Hb, Hct, MCH, MCV and MCHC was almost normal but platelet was half value compared to the control group. In testis, testis wt. in experimental groups were almost same but testis volume and sperm count were reduced a little compared to the control group. In conclusion, the mice with neutron irradiation by lying flat pose for 1hr or 2hrs without administration of boron compounds were not reduced the life span. Among blood cell, platelet were not recovered and the others were recovered after long time with neutron irradiation. Black mice hair color on the center of the back with irradiation of high dose in this experiment were changed white color and testis volume and number of sperm were reduced by chronic effect in response to neutron irradiation.

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### **Role of the de novo Ceramide and Arachidonic Acid in Paclitaxel-Induced Apoptosis**

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Recently, several reports suggest that ceramide formation has been implicated in the apoptosis signaling in response to chemotherapeutic agents. In this study, to enhance paclitaxel-mediated cytotoxicity and endogenous ceramide levels, we blocked ceramide metabolism using an inhibitor of glucosylceramide synthase, 1-phenyl-2-dacanylamino-3-morpholino-1-propanol (PDMP) and SM synthase, D609. Exposure of human breast cancer cells to paclitaxel accumulated de novo ceramide synthesis by enhancement of SPT activity 1.2-fold, whereas ceramide synthase activity was not altered. Activation of SPT seemed to be mediated via a posttranscriptional mechanism because levels of human LCB<sub>1</sub> and LCB<sub>2</sub> mRNAs were not changed. An inhibitor of glucosylceramide synthesis (PDMP) accumulated ceramide production and increased cytotoxicity when used in combination with paclitaxel. The effect of D609, a xanthate derivative that inhibits SM synthase or PC-PLC, on the paclitaxel-induced cytotoxicity was investigated. Interestingly, the combination of D609 and paclitaxel partially attenuated the cytotoxic action of MCF-7 cells and was not significant increase of ceramide levels. Also, paclitaxel caused enhancement of 1,2-diacylglycerol levels, probably by activation of a PC-PLC. Taken together, this data suggest that GC synthesis has been thought to be the main pathway for clearance in paclitaxel-induced ceramide formation. Furthermore, the addition of paclitaxel or PDMP resulted in the accumulation of ceramide, which was followed by a prolonged arachidonic acid release. Participation of ceramide de novo pathway in arachidonate signaling was detected since L-cycloserine, an inhibitor of de novo synthesis, was able to inhibit the PDMP or paclitaxel-induced AA release and cytotoxicity. This result suggest that the production of ceramide in response to de novo synthesis appears to be related with in arachidonic acid release, probably cytotoxicity.

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