The sister chromatid exchange (SCE) assay is sensitive, simple method for measurement of damage to DNA. We have investigated the potential use of the SCE assay to determine the in vitro chemosensitivity by comparing results obtained with SCE assay and xenografts in nude mice.

In this study, NUE-1 (endometrial carcinoma cell line) and NUC-1 (choriocarcinoma cell line) were used and drugs were ADM, CDDP and MMC, and CDDP and MTX, respectively. The maximum drug concentration was chosen in accordance with the human tumor clonogenic assay. Cells were treated with graded concentrations of drugs for 1 hr and then bromodeoxyuridine was added. Cultures were allowed to replicate for 48 hr, harvested by addition of Colcemid, hypotonic treated and fixed. Sister chromatids were differentially stained by acridine orange. Anticancer agents at 1/3 LD_{50} dosage for mice were administered intraperitoneally on a schedule of 3 doses for 4 days. For the antitumor evaluation of effects, the method of Battelle Columbus Institute was employed.

ADM was judged to be most sensitive from the SCE doseresponse curves in NUE-1 and CDDP was more sensitive in NUC-1. In xenografts in nude mice, ADM was effective in NUE-1 and CDDP in NUC-1.

The SCE assay has potential clinical use for the analysis of the response of human tumors.

23. (Abstract is not available)

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24. Isolation of Cisplatin-resistant Subline from Human Ovarian Cancer Cell Line and Analysis of its Cell-biological Characteristics

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Cisplatin-resistant subline, TYK-ntu (R), has been developed by culturing TYK-ntu (human ovarian cancer cell line in vitro) with exposure to cisplatin in stepwise increasing concentrations. The characteristics of both cell lines were compared, the results were as follows; 1) Both cell lines formed monolayer in a pavement-like arrangement and large cells were occasionally present in TYK-ntu (R) rather than TYK-ntu. The population doubling time of TYK-ntu and TYK-ntu (R) was 43 hr and 48 hr, respectively. 2) IC_{50} (\mu g/ml) in 96 hr treatment with cisplatin and carboplatin was 0.035 and 0.5 in TYK-ntu and 0.62 and 2.0 in TYK-ntu (R), respectively. Thus, compared to TYK-ntu, TYK-ntu (R) was 17.7 fold more resistant to cisplatin and 4 fold to carboplatin. 3) In intracellular cisplatin concentration, there was no significance between TYK-ntu and TYK-ntu (R) after cisplatin (2.0 \mu g/ml) treatment in 2 hrs. 4) After treatment with cisplatin (0.2 \mu g/ml) and carboplatin (2.0 \mu g/ml), a decrease of S and G2+M compartments was observed in the pattern of DNA histogram of TYK-ntu, but not in that of TYK-ntu (R). 5) The majority of chromosome in both cell lines was in hyperdiploid area and the mode of TYK-ntu and TYK-ntu (R) was 56 and 51~52, respectively. The karyotype of TYK-ntu (R) showed deletion of chromosome 7q.

25. Intra-peritoneal Cisplatin Chemotherapy (CDDP-ip) in Patients with Ovarian Cancer

—Report III, Peritoneal Clearance and Needlessness of PSTS Rescue—

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Understanding the in vivo pharmacokinetics of CDDP-ip is very important not only with regard to the manifestation of the effects, but also the side effects. We have studied the kinetics of CDDP in the ascites and blood after CDDP-ip by means of the compartment model and moment analysis.

After CDDP-ip, a high concentration of free-CDDP was reached in the ascites. The AUC (area under the curve), MRT (mean residence time), and VRT (variance of residence time) showed obviously high values and direct effects on the tumor cells in the abdominal cavity.

The AUC, MRT and VRT of free-CDDP, having entered the blood, showed values nearly equal to or higher than those by intravenous administration (iv), and it has been demonstrated that there are also sufficient effects on the tumor blood vessels. These