time sequence. Blood counts were daily evaluated for each blood cell and were compared with bone marrow findings from sequential bone marrow trephine biopsy at 30minutes, 18 hours, 3 days, 7 days, and 14 days after whole body irradiation. Gastrointestinal changes were evaluated by sequential endoscopic biopsies from stomach, jejunum, and rectum.

Results

Mini-pigs irradiated by 12Gy died due to sepsis and GI syndrome with bowel perforation at the period of 8 days to 11 days. Deaths by 7Gy irradiation might be attributed to hemorrhage and sepsis. In both 7Gy and 12Gy, E. coli was cultured from postmortem blood. Animals irradiated by 2Gy and 4 Gy survived. Blood cell counts showed quite similar pictures to humans according to time sequence. Mini-pigs irradiated by 7Gy and 12Gy showed abrupt decrease of WBCs from 30 minutes until 14 hrs after irradiation, with following slow decrease to less than 500/μl. RBC counts abruptly decreased until 14hrs and were slowly recovered. Platelet counts abruptly decreased until 36hrs with subsequent transient recovery and finally decrease to bottom. With 2Gy and 4Gy, WBCs showed relatively slow decline. In the serial observation of bone marrow section, CD34+ progenitor cells and Ki67+ proliferating cells were well correlated with radiation dose. In gastrointestinal system, jejunal mucosa was the most vulnerable and exhibited similar histologic changes to humans. Both hematopoietic and intestinal findings of minipigs were quite similar to those of humans.

Conclusion

These observations suggest that mini-pig model would be appropriate as an animal model corresponding to humans. It might be effective in therapeutic trials for better survival on victims of radiation accidents and nuclear terrorism.

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P#25

Suppression of Azoxymethane-Induced Colorectal Tumors in *iNOS* -/- C57BL/6J Mice.

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Nitric oxide (NO) is known to be involved in the pathogenesis of colorectal cancer in both rodents and humans. iNOS is responsible for the over production of NO in a variety of parenchymal cells and macrophage. In the present study we utilized iNOS gene knockout mice to investigate the role of iNOS on chemically-induced colorectal polyposis. Azoxymethane (AOM) at a dose of

10mg/kg body wt was administered to male and female iNOS-/- or iNOS wt C57BL/6J mice once a week for six weeks. The mice were sacrificed and examined with the incidence and multiplicities of colorectal polyps at the age of 30 weeks. The incidence of colorectal tumors were significantly reduced in iNOS gene knockout mice (22 9%). compared to that of control mice (59 1%). The multiplicity in colorectal polyps in iNOS knockout mice were 0 370.77 (n=35). being significantly smaller than the value of wild type mice (1.021.15. n=44). The sizes of the polyps in the iNOS gene knockout mice were also decreased Therefore, overproduced NO by iNOS plays an important role in mice colorectal carcinogenesis

Key words · azoxymethane, colorectal cancer, iNOS gene knockout mice. polyps

P#26

β-Estradiol 3-Benzoate Induces Rat Spermatogenic Germ Cells Apoptosis

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Estrogens play critical roles in spermatogenesis. We investigated the effects of sustained delivery of β-estradiol 3-benzoate (EB) on spermatogenesis and mechanisms involved in germ cell injuries with an emphasis on the germ cell apoptosis. Ten-week-old Sprague-Dawley rats were implanted subcutaneously with a pellet containing of 0.5 mg β-estradiol 3-benzoate (EB) fused to cholesterol and were sacrificed in 12 hr, 24 hr, 48 hr, 72 hr, 1 week, 2 weeks, 4 weeks and 6 weeks of EB implantation. We found that body weights and weights of testis and epididymis were significantly decreased in 2 weeks of EB treatment. Degeneration of germ cells was first found in pachytene spermatocytes in spermatogenic stages VII-VIII in 48 hr of EB treatment and progressively increased in a time-dependent manner. Severe degeneration and depletion of germ cells in seminiferous tubules was observed in 2 weeks of EB treatment. After 4 weeks, massive degeneration of the seminiferous epithelium exhibiting characteristics of epithelial structural disorganization, the formation of multinucleated giant cells, and decrease of interstitial cell numbers were noted. Severe atrophy and necrosis of seminiferous tubules was observed in 6 weeks of EB treatment. Apoptosis of germ cells was observed in pachytene spermatocytes in their developmental stages VII-VIII in48 hr. Mean incidence of apoptotic germ cells after EB treatment progressively increased until 2 weeks. Western blot analysis revealed an increase in Fas and Fas lignad (Fas-L) protein levels in the testis of EB-treated rats. While estrogen receptor α(ER α) expression was not changed until 2 weeks, significant decrease of ER in 4 and 6 weeks