CARCINOGENIC COMPARATIVE STUDY ON CB6F1 TG RASH2 MICE PRODUCED BY TWO BREEDING FACILITIES

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Introduction:
Ras oncogene, which is closely related to malignancy, has been identified in human cancers and animal models. CB6F1-Tg(HRAS)2Jic mice (hereinafter rasH2 mice) have been validated by a large number of certification studies (Yamamoto, 1998; Usui et al., 2001). At present, this strain of mouse is produced by two breeding facilities, Taconic (Germantown, NY) and CLEA Japan, Inc. (Shizuoka, Japan), and supplied all over the world. Although genetic and microbiological monitoring has been performed periodically to maintain a quality of breeding parents, and also all mice used for commercial purpose were checked to determine whether they have the genetic background, variations were obtained due to differences in environmental factors such as temperature, microenvironment, diet, bedding and social order. To confirm phenotypic conformity of both mice produced at CLEA Japan, Inc. and Taconic, a 26-week carcinogenicity test was performed under the same protocols and environmental conditions in our facility.

Material & Method:
1. Animals
One hundred and twenty rasH2 mice from CLEA Japan and Taconic were divided into eight groups, as shown in Table 1. Mice in vehicle group were injected with saline buffer at pH 4.5 once intra-peritoneally (10 ml/kg) and mice in MNU group were injected with MNU (N-methyl-N-nitrosourea, 75 mg/kg) once intra-peritoneally.

2. Survival rate
Clinical observation was performed daily in all animals just after group formation to check for dead animals.

3. Pathological examination
All animals were necropsied at 26 weeks after administration, or at the time of death or emergency sacrifice. Liver, kidney, spleen, lung, thymus, lymph nodes, stomach (stomach and glandular stomach), bone marrow, skeletal muscle, skin, reproductive organs and sites of visual abnormalities were subjected to a histopathologic examination.

4. Statistical analysis
Differences in the incidences of each lesion between the two breeding facilities were tested by Fisher’s exact test with p < 0.05 taken as significant.

Table 1: Group composition at present study

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<th>Vehicle</th>
<th>MNU</th>
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Results:
A survival rate (Figure 1)
The survival rate of the vehicle group was maintained at 100% for mice from both facilities at the completion of test. In the MNU group, MNU induced tumor death occurred from 1-2 weeks after administration, and the final survival rate was 6.7%.

Pathological examination
Neoplastic changes (Table 2)
In the vehicle group, only benign tumors in lungs, spleen, fore-stomach and skin were observed in a few mice in both facilities. In the MNU group, the incidence of benign papillomas in mice from CLEA or Taconic was 100% (15/15) in males and 86.7% (13/15) in females, or 100% (15/15) in males and 93.3% (14/15) in females, respectively. The incidence of malignant lymphoma in both sexes were 86.7% (14/15 in males and 12/15 in females) and 93.3% (14/15 in both sexes), and no significant difference in the incidence of tumors was observed. There was also no significant difference in the incidence of major MNU-induced tumors (keratoacanthoma) in both sexes. A significant difference in males for oral cavity papilloma was indicated due to all multi-site changes.

Neoplastic changes (Table 3)
In the vehicle group, no significant differences were observed between the mice produced from the two breeding facilities. However, when specific changes in lungs, kidneys and thymus were observed, it was observed to a large number. A high incidence of internal myopathy was observed in all groups, but there was no significant differences between mice from both facilities. A high incidence of internal myopathy was observed in all groups, but there was no significant difference between mice from both facilities. Malignant changes were found in fore-stomach, lungs and skin where MNU-induced tumors occurred, but there was no significant difference between mice from both facilities. A high incidence of internal myopathy was observed in all groups, but there was no significant difference between mice from both facilities.

Conclusion:
A significant difference was observed in oral cavity papillomas in females due to all multi-site changes.

Comparison with historical data at CIEA

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