

**表1** 最終体重、肝重量および2-AAFの摂取量

| Group | Patial<br>hepatectomy | Treatment | 2-AFF intake<br>(mg/kg bw/day) | Final body weight<br>(g) | Liver weight |             |            |
|-------|-----------------------|-----------|--------------------------------|--------------------------|--------------|-------------|------------|
|       |                       |           |                                |                          | Absolute (g) | Relative(%) |            |
| 1     | gpt delta             | +         | DEN                            | 0                        | 270 ± 17     | 7.4 ± 0.8   | 2.8 ± 0.3  |
| 2     | gpt delta             | +         | DEN+2-AAF                      | 15.0 ± 0.8               | 248 ± 18*    | 8.3 ± 0.9*  | 3.3 ± 0.4* |
| 3     | F344                  | +         | DEN                            | 0                        | 280 ± 10     | 7.3 ± 0.5   | 2.6 ± 0.2  |
| 4     | F344                  | +         | DEN+2-AAF                      | 13.9 ± 0.7               | 264 ± 12*    | 8.8 ± 1.1*  | 3.4 ± 0.4* |
| 5     | gpt delta             | -         | Non-treatment                  | 0                        | 278 ± 18     | 8.0 ± 0.5   | 2.9 ± 0.1  |
| 6     | gpt delta             | -         | 2-AAF                          | 16.3 ± 0.3               | 271 ± 7      | 8.6 ± 1.1   | 3.2 ± 0.2  |

\*significantly different DEN alone group

**表2 肝臓における *gpt* assay の結果 (点突然変異の頻度)**

| Treatment     | Animal ID | Total number of colonies | Number of 6TGr mutants | Mutant frequency ( $\times 10^{-6}$ ) | Average mutant frequency ( $\times 10^{-6}$ ) |
|---------------|-----------|--------------------------|------------------------|---------------------------------------|---|
| Non-treatment | 511       | 738,000                  | 12                     | 16.3                                  | 11.4 $\pm$ 2.8                                |
|               | 512       | 216,000                  | 2                      | 9.3                                   |   |
|               | 513       | 646,000                  | 7                      | 10.8                                  |   |
|               | 521       | 489,000                  | 5                      | 10.2                                  |   |
|               | 522       | 283,000                  | 3                      | 10.6                                  |   |
| 50 ppm 2-AAF  | 611       | 131,000                  | 16                     | 122.1                                 | 67.9 $\pm$ 35.6 **                            |
|               | 612       | 622,000                  | 51                     | 82                                    |   |
|               | 613       | 200,000                  | 7                      | 35                                    |   |
|               | 621       | 712,000                  | 43                     | 60.4                                  |   |
|               | 622       | 651,000                  | 26                     | 39.9                                  |   |

\* significantly different from Non-treatment group

表3 肝臓における *Spi*<sup>-</sup> assayの結果 (欠失変異の頻度)

| Treatment     | Animal ID | Total number of plaques | Number of <i>Spi</i> <sup>-</sup> mutants | Mutant frequency ( $\times 10^{-6}$ ) | Average mutant frequency ( $\times 10^{-6}$ ) |
|---------------|-----------|-------------------------|---|---------------------------------------|---|
| Non-treatment | 511       | 852,600                 | 7   | 8.2                                   | 9.6 $\pm$ 5.9                                 |
|               | 512       | 527,000                 | 8   | 15.2                                  |   |
|               | 513       | 986,400                 | 1   | 1                                     |   |
|               | 521       | 364,500                 | 5   | 13.7                                  |   |
|               | 522       | 615,250                 | 9   | 14.6                                  |   |
| 50 ppm 2-AAF  | 611       | 270,000                 | 25  | 92.6                                  | 79.7 $\pm$ 22.9**                             |
|               | 612       | 300,625                 | 18  | 59.9                                  |   |
|               | 613       | 360,100                 | 27  | 75                                    |   |
|               | 621       | 346,800                 | 19  | 54.8                                  |   |
|               | 622       | 119,250                 | 14  | 117.4                                 |   |

\* significantly different from Non-treatment group

**表4 マウスおよびハムスターの生存率、最終体重および肝臓重量**

| Treatment          | Initial no. of animal | Final no. of animal | Final body weight (g) | Absolute liver weight (g) | Relative liver weight (%) |
|--------------------|-----------------------|---------------------|-----------------------|---------------------------|---------------------------|
| <b>B6C3F1 mice</b> |                       |                     |                       |                           |                           |
| Control            | 5                     | 5                   | 28.2 ± 1.5            | 1.20 ± 0.12               | 4.25 ± 0.25               |
| DCM                | 5                     | 5                   | 27.9 ± 0.5            | 1.17 ± 0.02               | 4.17 ± 0.12               |
| DCP                | 5                     | 4 <sup>a</sup>      | 27.3 ± 1.9            | 1.23 ± 0.05               | 4.53 ± 0.51               |
| <b>Hamster</b>     |                       |                     |                       |                           |                           |
| Control            | 5                     | 5                   | 119.9 ± 7.2           | 5.24 ± 0.19               | 4.37 ± 0.14               |
| DCM                | 5                     | 5                   | 125.0 ± 4.7           | 5.45 ± 0.31               | 4.36 ± 0.21               |
| DCP                | 5                     | 4 <sup>b</sup>      | 106.6 ± 5.5*          | 5.19 ± 0.96               | 4.91 ± 1.17               |

<sup>a</sup> one mouse died at day 2

<sup>b</sup> one hamster died at day 3

\* significantly different from control hamster group

表5 マウスおよびハムスターの肝臓における病理学的所見と GSTT1 の発現

|                     | Treatment | No. of animal | Centrilobular necrosis | Expression of GSTT1 |            |                      |
|---------------------|-----------|---------------|------------------------|---------------------|------------|----------------------|
|                     |           |               |                        | Hepatocyte          |            | Bile duct epithelial |
|                     |           |               |                        | Centrilobular       | Periportal |                      |
| <b>B6C3F1 mouse</b> |           |               |                        |                     |            |                      |
|                     | Control   | 5             | 0                      | +                   | +++        | +++                  |
|                     | DCM       | 5             | 0                      | +                   | ++/+++     | +++                  |
|                     | DCP       | 5             | 4 (80%)                | +                   | ++         | +++                  |
| <b>Hamster</b>      |           |               |                        |                     |            |                      |
|                     | Control   | 5             | 0                      | +                   | +          | -                    |
|                     | DCM       | 5             | 0                      | +                   | +          | -                    |
|                     | DCP       | 5             | 5 (100%)               | + / ++              | ++ / +++   | -                    |

-: negtive; +: weak; ++: moderate; +++: strong