Fig. 3 Number and area of GST-P-positive foci for F344 *gpt* delta rats treated with furan for 4 weeks
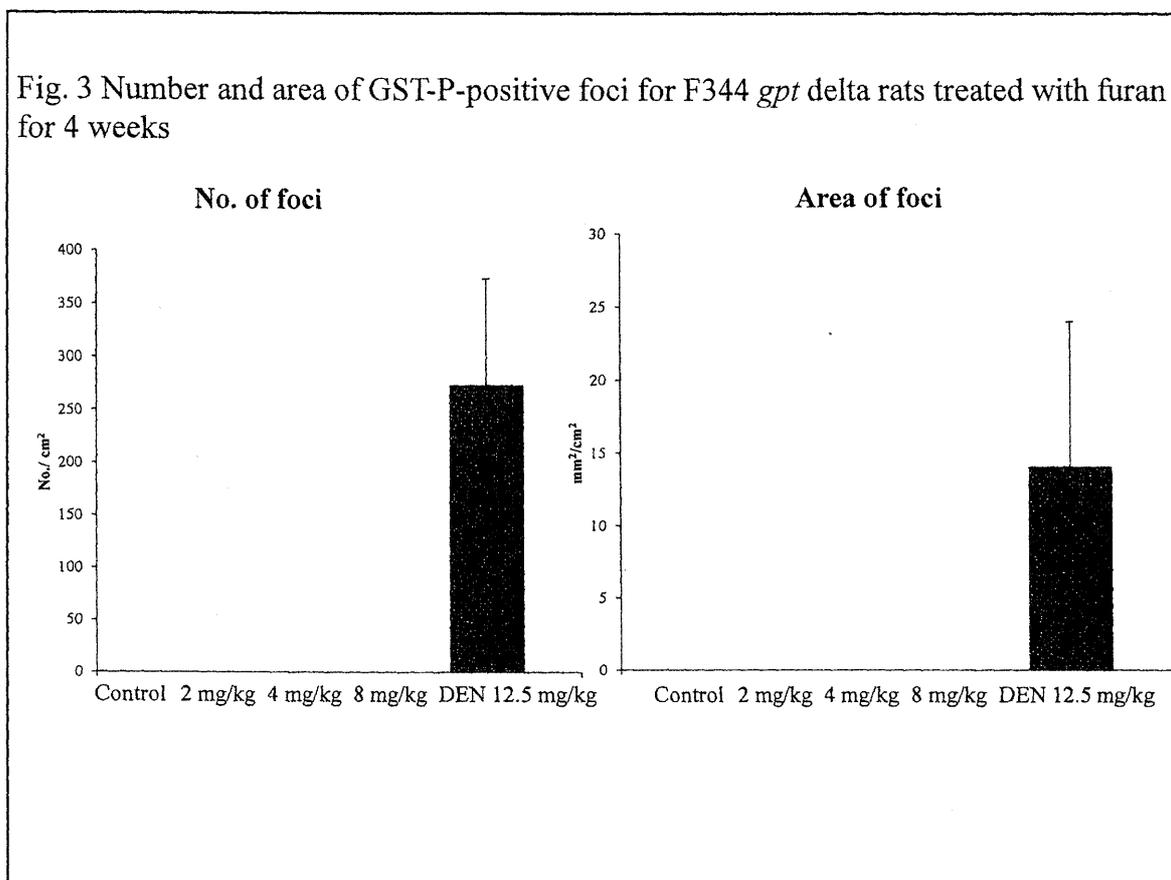
No. of foci

Area of foci

Table 1. Final body and organ weight of SD *gpt* delta rats treated with 2-MF for 13 weeks

Male

Absolute weight (g)

Item	0 mg/kg	1.2 mg/kg	6 mg/kg	30 mg/kg
Body weight	526.9 ± 40.0	547.6 ± 52.0	512.2 ± 35.5	456.3 ± 21.2**
Liver	14.41 ± 1.80	15.20 ± 2.41	15.02 ± 1.57	19.00 ± 1.49**

Relative weight (g%)

Liver	2.73 ± 0.21	2.76 ± 0.23	2.93 ± 0.14	4.16 ± 0.23**

Female

Absolute weight (g)

Item	0 mg/kg	1.2 mg/kg	6 mg/kg	30 mg/kg
Body weight	302.9 ± 26.1	303.6 ± 22.0	286.5 ± 33.2	255.3 ± 18.5**
Liver	7.76 ± 1.19	7.56 ± 0.67	8.46 ± 1.07	10.80 ± 0.89**

Relative weight (g%)

Liver	2.56 ± 0.32	2.49 ± 0.18	2.96 ± 0.21**	4.24 ± 0.24**

*,**: $p < 0.05, 0.01$ vs Control

Table 2. Serum biochemistry of SD *gpt* delta rats treated with 2-MF for 13 weeks

Male

Item	Unit	Control	1.2 mg/kg	6 mg/kg	30 mg/kg
ALP	IU/L	428.6 ± 40.8	485.6 ± 64.8	486.8 ± 89.8*	566.2 ± 38.9**
T-Bil	mg/dL	0.0 ± 0.1	0.0 ± 0.0	0.1 ± 0.1	0.1 ± 0.0*
γ-GTP	IU/L	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	4.2 ± 0.8
Glucose	mg/dL	154.0 ± 26.5	144.8 ± 21.0	124.2 ± 27.2	101.8 ± 16.5**
T-Cho	mg/dL	61.8 ± 6.7	64.0 ± 12.5	67.8 ± 12.0	84.0 ± 7.1**

Female

Item	Unit	Control	1.2 mg/kg	6 mg/kg	30 mg/kg
ALP	IU/L	232.7 ± 60.1	256.5 ± 92.6	198.6 ± 63.9	303.9 ± 85.8
T-Bil	mg/dL	0.1 ± 0.1	0.0 ± 0.1	0.0 ± 0.1	0.1 ± 0.0
γ-GTP	IU/L	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	2.7 ± 0.9
Glucose	mg/dL	140.3 ± 20.9	147.8 ± 17.1	124.8 ± 25.7	114.9 ± 12.2*
T-Cho	mg/dL	118.0 ± 24.6	101.3 ± 13.9	105.3 ± 12.8	110.2 ± 20.6

*,**: $p < 0.05, 0.01$ vs Control

Table 3 Histopathological findings of SD *gpt* delta rats treated with 2-MF for 13 weeks

		Male				Female			
		Control	1.2 mg/kg	6 mg/kg	30 mg/kg	Control	1.2 mg/kg	6 mg/kg	30 mg/kg
Organs	Findings	10	10	10	10	10	10	10	10
Liver	Apoptosis, hepatocyte	0	0	0	6	0	0	1	6
	Foci of cellular alteration	0	0	0	10	0	0	0	10
	Bile duct proliferation	0	0	1	8	0	0	1	8
	Oval cell proliferation	0	0	0	2	0	0	0	0
	Cholangiofibrosis	0	0	0	9	0	0	0	9
	Cell infiltration, subcapsular	0	0	7	10	0	0	2	10
	Phagocytosis, macrophage	0	0	4	5	1	0	5	5
	Microgranuloma	0	0	0	0	1	0	0	0

Table 4. Final body and organ weight of F344 *gpt* delta rats treated with furan for 4 weeks

Absolute weight (g)				
Item	Control	2 mg/kg	4 mg/kg	8 mg/kg
Final body weight	227.5 ± 14.8	215.5 ± 4.8	221.4 ± 16.0	203.4 ± 9.0*
Liver	7.96 ± 0.54	7.86 ± 0.23	8.73 ± 0.89	8.84 ± 0.43
Relative weight (g%)				
Liver	3.5 ± 0.05	3.65 ± 0.09	3.94 ± 0.16**	4.35 ± 0.11**

*: p<0.05, **: p<0.01 vs. Control

Table 4. Histophatological findings for the liver of F344 *gpt* delta rats treated with furan for 4 weeks

Liver	Male			
	Control	2 mg/kg	4 mg/kg	8 mg/kg
No. of animals	5	5	5	5
Apoptosis, hepatocyte	0	0	3	4
Oval cell proliferation	0	0	1	2
Cholangiofibrosis	0	0	0	1
Cell filtration, subcapsular	0	0	3	4

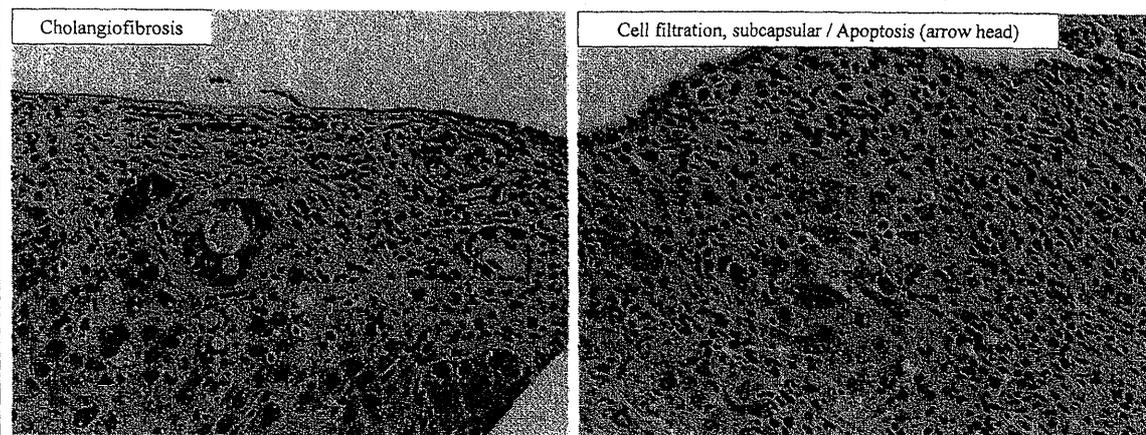Cholangiofibrosis

Cell filtration, subcapsular / Apoptosis (arrow head)

Table 5. *gpt* mutant frequencies of F344 *gpt* delta rats treated with furan for 4 weeks

Group	Animal No.	Cm^R colonies $(\times10^5)$	6-TG^R and Cm^R colonies	Mutant Frequencies $(\times10^{-5})$	Mean $\pm$ SD
Control	1	8.9	5	0.56	
	2	6.9	6	0.87	
	3	6.7	5	0.75	0.91$\pm$0.53
	4	7.3	4	0.55	
	5	4.9	9	1.83	
2 mg/kg	6	6.3	12	1.90	
	7	7.8	7	0.90	
	8	8.1	5	0.62	0.95$\pm$0.55
	9	6.7	5	0.75	
	10	7.2	4	0.55	
4 mg/kg	11	6.4	6	0.94	
	12	5.9	6	1.01	
	13	7.1	6	0.85	0.99$\pm$0.11
	14	7.0	8	1.14	
	15	7.9	8	1.02	
8 mg/kg	16	8.0	5	0.62	
	17	6.9	5	0.73	
	18	4.3	6	1.39	1.06$\pm$0.37
	19	7.7	11	1.42	
	20	4.4	5	1.13	
DEN 12.5 mg/kg[a]	21	1.0	178	171.98	
	22	0.6	56	97.22	
	23	1.1	97	90.57	148.54$\pm$50.57**
	24	0.3	57	191.92	
	25	0.5	98	191.03	

a: For rats treated with DEN, *gpt* mutants were analyzed only on one selected plate whose colony numbers were closest to the average number of 5 plates, and MFs were calculated using the packaging efficacy values divided by 5.

**: $p < 0.01$ vs. Control

Table 6. Spi⁻ mutant frequencies of F344 *gpt* delta rats treated with furan for 4 weeks

Group	Animal No.	Plaques within XL-1 Blue MRA (x 10^5)	Plaques within WL95 (P2)	Mutant Frequency (x 10^{-5})	Mean ± SD
Control	1	11.2	18	1.61	
	2	11.9	4	0.34	
	3	10.2	12	1.18	0.89±0.51
	4	12.0	7	0.58	
	5	13.2	10	0.76	
2 mg/kg	6	6.8	5	0.73	
	7	10.8	5	0.46	
	8	9.7	6	0.62	0.60±0.10
	9	9.8	6	0.61	
	10	8.5	5	0.59	
4 mg/kg	11	6.8	5	0.73	
	12	8.8	4	0.45	
	13	7.3	7	0.96	0.71±0.21
	14	6.2	9	1.45	
	15	10.0	7	0.70	
8 mg/kg	16	11.1	4	0.36	
	17	8.9	3	0.34	
	18	4.9	1	0.21	0.64±0.46
	19	6.8	8	1.19	
	20	5.5	6	1.09	
DEN 12.5 mg/kg	21	6.1	155	25.33	
	22	3.2	52	16.51	
	23	4.6	38	8.28	12.59±8.26*
	24	4.7	32	6.84	
	25	5.9	35	5.98	

* : $p < 0.05$ vs. Control

Table 7. Liver micronucleus assay of F344 *gpt* delta rats treated with furan for 4 weeks

Group	Animal No.	Hepatocytes	MNHEPs (cells)	MNHEPs (%)	Mean ± SD
	1	2124	2	0.094	
	2	2015	0	0.000	
Control	3	2002	2	0.100	0.058±0.041
	4	2100	1	0.048	
	5	2086	1	0.048	
	6	2005	1	0.050	
	7	2037	1	0.049	
2 mg/kg	8	2001	1	0.050	0.059±0.023
	9	2002	2	0.100	
	10	2066	1	0.048	
	11	2001	0	0.000	
	12	2004	2	0.100	
4 mg/kg	13	2078	1	0.048	0.109±0.096
	14	2003	5	0.250	
	15	2002	3	0.150	
	16	2018	0	0.000	
	17	2050	4	0.195	
8 mg/kg	18	2079	0	0.000	0.049±0.084
	19	2070	0	0.000	
	20	2000	1	0.050	
	21	2002	33	1.648	
	22	2001	37	1.849	
DEN 12.5 mg/kg	23	2001	32	1.599	1.886±0.376**
	24	2014	51	2.532	
	25	2000	36	1.800	

MNHEPs: micronucleated hepatocytes

$**: p < 0.01$ vs. Control

Ⅲ. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

書籍

発表者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
	該当無し						

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Kohei Matsushita, Ken Kuroda, Yuji Ishii, Shinji Takasu, Aki Kijima, Hiroaki Kawaguchi, Noriaki Miyoshi, Takehiko Nohmi, Kumiko Ogawa, Akiyoshi Nishikawa, Takashi Umemura	Improvement and validation of a medium-term *gpt* delta rat model for predicting chemical carcinogenicity and underlying mode of action. *Exp. Toxicol. Pathol.*	*Exp. Toxicol. Pathol.*	66	313-321	2014
Kohei Matsushita, Yuji Ishii, Shinji Takasu, Ken Kuroda, Aki Kijima, Takuma Tsuchiya, Hiroaki Kawaguchi, Noriaki Miyoshi, Takehiko Nohmi, Kumiko Ogawa, Akiyoshi Nishikawa, Takashi Umemura	A medium-term *gpt* delta rat model as an *in vivo* system for analysis of renal carcinogenesis and the underlying mode of action	*Exp. Toxicol. Pathol.*	67	31-39.	2015