

表22 MNU投与により誘発された胸腺リンパ腫のゲノムDNAを用いたaCGH解析によるTCRを含む6番染色体qB1の欠失

Genotype	No. of samples	Sample	Chr	Cytoband	Genes	Start	Stop	No. of probes	Amplification	Deletion	
Wt	6	AD0006_ReSet01	chr6	qB1	Tp4 1810048H199L, LOC438322	40,990,945	41,470,882	61	0	-1.93	
		AD0006_ReSet02	chr6	qB1	Tp4 1810048H199L, LOC438322	41,125,695	41,461,916	42	0	-2.02	
		AD0006_ReSet04	chr6	qB1	170073P139L, 1810009J069L, 2210010C04R	40,830,126	40,991,345	25	0	-0.92	
				chr6	qB1	Tp4 1810048H199L, LOC438322	40,999,261	41,461,916	59	0	-2.40
				chr6	qB1	LOC438322, Pns13, LOC438323	40,999,261	41,104,121	15	0	-3.77
				chr6	qB1	LOC438322	41,244,828	41,403,803	16	0	-1.37
				chr6	qB1	Tp4 1810048H199L, LOC438322	41,119,252	41,461,916	43	0	-1.69
				chr6	qB1	Tp4 1810048H199L, LOC438322	41,162,920	41,470,882	39	0	-0.75
				chr6	qB1	Tp4 1810048H199L, LOC438322	41,047,950	41,470,882	52	0	-3.42
	Rev1 Tg	6	AD0006_Set09	chr6	qB1	Tp4 1810048H199L, LOC438322	41,119,252	41,461,916	43	0	-2.55
			AD0006_Set14	chr6	qB1	Tp4 1810048H199L, LOC438322	41,060,190	41,378,649	38	0.71	0
			AD0006_Set15	chr6	qB1	Tp4 1810048H199L, LOC438322	41,155,364	41,461,916	39	0	-1.88
			AD0006_Set16	chr6	qB1	Tp4 1810048H199L, LOC438322	41,087,543	41,470,882	48	0	-1.31
			AD0006_Set17	chr6	qB1	Tp4 1810048H199L, LOC438322	41,119,252	41,461,916	43	0	-1.64
			AD0006_Set18	chr6	qB1	Tp4 1810048H199L, LOC438322	41,060,190	41,461,916	50	0	-2.39

表23 MNU投与により誘発された胸腺リンパ腫のゲノムDNAを用いたaCGH解析による*Bcl11b*を含む12番染色体qF1-qF2の欠失

Genotype	No. of samples	Sample	Chr	Cytoband	Genes	Start	Stop	No. of probes	Amplification	Deletion
Wt	2	ADD0006_ReSet01	chr12	qF1 - qF2	<i>Bcl11b, A130014H13Rik, Setd3...</i>	103,958,897	117,799,069	1493	0	-0.90
		ADD0006_Set43	chr12	qE - qF2	<i>Primal1, Ash2, Ouid2...</i>	100,611,540	117,799,069	1871	0	-0.75
Rev1 Tg	1	ADD0006_Set15	chr12	qF1 - qF2	<i>Setd3, Ccnk, Cypfa1...</i>	105,520,428	117,799,069	1409	0	-0.66

表24 MNU投与により誘発された胸腺リンパ腫のゲノムDNAを用いたaCGH解析による*Pten*を含む19番染色体qC1の欠失

Genotype	No. of samples	Sample	Chr	Cytoband	Genes	Start	Stop	No. of probes	Amplification	Deletion
Wt	2	ADD0006_ReSet03	chr19	qC1	<i>Aiad1, Pten, B430203M17Rik</i>	32,323,791	32,961,944	63	0	-3.09
		ADD0006_ReSet05	chr19	qC1	<i>B430203M17Rik</i>	32,457,164	33,023,708	54	0	-2.25
Rev1 Tg	1	ADD0006_Set16	chr19	qC1	<i>B430203M17Rik</i>	32,474,734	32,922,929	38	0	-2.60

表25 MNU投与により誘発された胸腺リンパ腫のゲノムDNAを用いたaCGH解析による14番染色体qC1の欠失

Genotype	No. of samples	Sample	Chr	Cytoband	Genes	Start	Stop	No. of probes	Amplification	Deletion		
Wt	10	AD0006_ReSet01	chr14	qC1	A13002M079, C92006C019, B23035F1	48,190,086	49,034,354	90	0	-0.37		
		AD0006_ReSet02	chr14	qC1	A63006A139A	48,749,088	49,056,003	41	0	-1.88		
		AD0006_ReSet03	chr14	qC1		48,942,388	49,056,003	16	0	-1.02		
		AD0006_ReSet04	chr14	qC1	B23035F089A, A63006A139A	48,589,831	49,069,040	68	0	-2.17		
		AD0006_ReSet05	chr14	qC1	A63006A139A	48,826,322	49,047,849	31	0	-1.19		
		AD0006_ReSet06	chr14	qC1	LOC434473, A430107P099A, A13002M079	47,910,127	49,047,849	107	0	-1.67		
			chr14	qC1	LOC434473, A430107P099A, A13002M079	47,910,127	48,444,218	35	0	-0.93		
			chr14	qC1		48,673,355	48,731,332	12	0	-2.91		
			chr14	qC1	B23035F089A, A63006A139A	48,556,504	49,047,849	68	0	-2.10		
		AD0006_ReSet07	chr14	qC1	LOC434473, A430107P099A, A13002M079	47,910,127	48,597,844	44	0	-0.74		
		AD0006_ReSet08	chr14	qC1		48,610,231	49,056,003	64	0	-2.59		
			chr14	qC1	B23035F089A, A63006A139A	48,826,322	49,047,849	31	0	-2.36		
		AD0006_Set43	chr14	qC1	A63006A139A	48,749,088	49,034,354	38	0	-3.05		
		AD0006_Set44	chr14	qC1		48,749,088	48,846,157	13	0	-2.00		
			chr14	qC1		48,896,237	48,988,041	13	0	-4.26		
		Rev1 Tg	9	AD0006_Set09	chr14	qC1	B23035F089A	48,443,818	48,762,352	36	0	-0.51
					chr14	qC1	A63006A139A	48,778,223	49,047,849	36	0	-1.79
				AD0006_Set11	chr14	qC1	B23035F089A, A63006A139A	48,643,090	49,069,040	63	0	-2.21
	chr14			qC1		48,836,780	48,902,821	10	0	-1.39		
	chr14			qC1		48,999,285	49,069,040	10	0	-3.46		
AD0006_Set12	chr14			qC1	B23035F089A	48,589,831	48,832,857	36	0	-0.70		
	chr14			qC1		48,836,780	48,980,619	20	0	-2.36		
	chr14			qC1	B23035F089A, A63006A139A	48,589,831	49,047,849	65	0	-1.68		
AD0006_Set13	chr14			qC1	B23035F089A, A63006A139A	48,647,041	49,056,003	60	0	-1.60		
AD0006_Set14	chr14			qC1	B23035F089A	48,647,041	48,744,143	19	0	-0.92		
	chr14			qC1	B23035F089A	48,589,831	48,877,822	43	0	-0.73		
AD0006_Set15	chr14			qC1		48,896,237	49,047,849	21	0	-2.04		
	chr14			qC1	A430107P099A, A13002M079A, C92006C0	48,158,291	49,047,849	97	0	-1.38		
AD0006_Set16	chr14			qC1		48,673,355	48,726,029	11	0	-2.50		
	chr14			qC1	B23035F089A, A63006A139A	48,643,090	49,047,849	60	0	-2.01		
AD0006_Set17	chr14			qC1	LOC434473, A430107P099A, A13002M079	47,903,376	48,506,126	37	0	-0.56		
AD0006_Set18	chr14			qC1	B23035F089A, A63006A139A	48,530,058	49,047,849	71	0	-2.46		
	chr14			qC1		48,530,058	48,833,051	11	0	-1.57		
	chr14	qC1		48,673,355	48,731,332	12	0	-3.73				

表26 Rev1ホモマウス体重(g)の推移(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

Sex	Group	Age					
Male		6W	7W	8W	9W	10W	11W
	0	16.77 ± 0.98 <sup>a</sup>	17.86 ± 1.07	19.52 ± 2.04	20.05 ± 1.16	21.04 ± 0.74	21.30 ± 0.88
	0.63	17.75 ± 0.78	18.96 ± 1.08	20.42 ± 0.93	21.30 ± 1.21	23.07 ± 0.92	23.37 ± 1.04
	1.25	17.18 ± 1.14	18.73 ± 1.23	20.33 ± 1.43	21.20 ± 1.29	22.71 ± 4.58	23.25 ± 4.31
	2.5	16.37 ± 0.69	17.55 ± 0.75	18.92 ± 0.89	20.46 ± 0.99	21.65 ± 0.52	21.86 ± 0.64
	5	15.94 ± 1.31	17.32 ± 1.19	18.92 ± 1.10	20.34 ± 1.07	21.19 ± 0.65	21.67 ± 0.64
		12W	13W	14W	15W	16W	17W
	0	22.39 ± 0.76	21.58 ± 0.63	22.47 ± 0.68	22.81 ± 0.21	24.14 ± 0.06	25.05 ± 0.30
	0.63	24.15 ± 0.79	25.22 ± 0.33	25.67 ± 0.72	25.99 ± 0.07	26.76 ± 0.13	28.19 ± 0.36
	1.25	23.99 ± 4.31	24.88 ± 4.32	25.61 ± 4.53	26.07 ± 4.52	26.75 ± 4.73	28.29 ± 5.02
	2.5	22.90 ± 0.75	24.14 ± 0.42	24.59 ± 0.70	24.82 ± 0.78	25.69 ± 0.56	27.17 ± 0.70
	5	22.30 ± 0.68	22.92 ± 0.76	23.83 ± 0.80	23.99 ± 1.36	24.47 ± 1.41	25.77 ± 1.38
		18W	19W	20W	24W	29W	34W
	0	26.44 ± 1.52	26.40 ± 1.97	27.10 ± 2.28	28.94 ± 2.55	35.86 ± 3.51	40.21 ± 3.59
	0.63	29.23 ± 1.26	29.89 ± 1.99	30.60 ± 1.98	32.98 ± 3.08	37.03 ± 4.42	41.06 ± 4.90
	1.25	29.12 ± 3.07	29.46 ± 3.08	29.42 ± 3.31	31.71 ± 4.36	35.99 ± 6.16	39.24 ± 7.73
	2.5	27.46 ± 1.86	28.56 ± 2.14	28.65 ± 2.30	30.31 ± 2.94	36.36 ± 2.56	40.30 ± 2.85
	5	26.37 ± 2.75	27.05 ± 2.89	27.41 ± 3.09	27.32 ± 4.14	32.62 ± 5.15	36.09 ± 5.48
		39W	44W	48W	52W	56W	60W
	0	42.45 ± 4.64	43.64 ± 4.27	43.92 ± 4.96	44.55 ± 4.79	44.24 ± 4.62	45.19 ± 4.76
	0.63	42.68 ± 4.51	43.51 ± 4.28	42.99 ± 4.38	44.31 ± 4.14	44.82 ± 4.13	43.77 ± 4.43
1.25	41.18 ± 6.90	41.71 ± 6.27	40.84 ± 6.19	42.49 ± 5.93	42.83 ± 6.02	41.49 ± 5.92	
2.5	41.90 ± 3.77	42.57 ± 4.18	42.22 ± 3.99	42.93 ± 4.38	43.27 ± 4.12	42.29 ± 4.12	
5	37.62 ± 5.68	38.94 ± 5.68	39.24 ± 5.30	40.82 ± 5.62	40.82 ± 5.51	38.69 ± 5.54	
Female		6W	7W	8W	9W	10W	11W
	0	15.69 ± 0.81	15.94 ± 0.67	17.02 ± 0.68	17.63 ± 0.36	18.07 ± 0.47	18.28 ± 0.46
	0.63	15.43 ± 0.71	15.38 ± 0.52	16.81 ± 1.14	17.11 ± 0.54	17.60 ± 0.11	17.77 ± 0.03
	1.25	14.83 ± 0.71	15.01 ± 0.77	16.17 ± 0.90	17.19 ± 0.56	17.48 ± 0.85	17.81 ± 0.90
	2.5	14.59 ± 0.99	14.72 ± 1.13	16.00 ± 1.00	17.20 ± 0.95	17.87 ± 0.55	18.16 ± 0.56
	5	14.28 ± 1.36	14.52 ± 1.24	15.75 ± 1.21	16.69 ± 1.16	17.30 ± 0.34	17.58 ± 0.19
		12W	13W	14W	15W	16W	17W
	0	18.25 ± 1.66	19.29 ± 0.22	18.61 ± 1.64	19.40 ± 0.44	20.23 ± 0.57	20.81 ± 1.09
	0.63	18.29 ± 0.08	18.50 ± 0.11	19.16 ± 0.36	19.16 ± 0.21	19.43 ± 0.41	20.22 ± 0.76
	1.25	17.91 ± 0.36	18.41 ± 0.31	18.76 ± 0.36	18.91 ± 0.14	19.16 ± 0.73	20.04 ± 0.76
	2.5	18.43 ± 0.57	18.99 ± 0.67	19.77 ± 0.90	19.94 ± 1.16	20.51 ± 1.37	21.12 ± 1.57
	5	17.72 ± 0.48	18.20 ± 0.69	18.94 ± 0.81	19.21 ± 1.21	19.45 ± 0.65	19.20 ± 1.49
		18W	19W	20W	24W	29W	34W
	0	21.82 ± 2.32	21.36 ± 1.99	21.62 ± 1.93	23.11 ± 2.86	26.55 ± 4.89	28.26 ± 5.58
	0.63	20.25 ± 2.05	20.67 ± 1.85	21.27 ± 1.82	22.54 ± 2.98	23.82 ± 4.41	26.74 ± 6.04
	1.25	20.43 ± 1.11	20.45 ± 1.24	21.10 ± 1.19	22.20 ± 1.92	25.05 ± 2.68	29.33 ± 3.54
	2.5	22.21 ± 1.96	21.97 ± 2.18	22.49 ± 2.75	24.60 ± 3.24	27.95 ± 3.86	31.38 ± 4.19
	5	20.73 ± 1.84	20.68 ± 1.91	20.05 ± 2.31	22.94 ± 2.88	24.27 ± 5.01	26.64 ± 6.91
		39W	44W	48W	52W	56W	60W
	0	29.95 ± 7.15	32.35 ± 7.63	34.90 ± 7.40	35.25 ± 8.36	36.44 ± 8.82	37.14 ± 8.92
	0.63	28.57 ± 6.43	28.63 ± 7.99	29.42 ± 7.73	30.92 ± 7.39	29.76 ± 7.38	30.52 ± 7.37
1.25	31.68 ± 3.65	34.40 ± 3.70	35.02 ± 4.46	36.81 ± 4.17	36.42 ± 4.61	36.63 ± 5.04	
2.5	31.95 ± 4.52	34.46 ± 4.69	35.18 ± 4.85	35.54 ± 5.73	34.31 ± 7.17	36.23 ± 6.40	
5	28.45 ± 7.47	29.75 ± 8.05	29.96 ± 8.43	31.39 ± 9.54	31.38 ± 9.84	31.86 ± 9.47	

a : Mean±SD

\*, \*\*: Significantly different from the untreated control value at the levels of p&lt;0.05, p&lt;0.01, respectively.

表27 RevIホモマウスの平均摂餌量(g/day) (ばい煎ダイズ抽出物の1年間反復投与毒性試験)

Sex	Group	Age									
Male		6W	7W	8W	9W	10W	11W	12W	13W	14W	
	0	2.49	2.44	2.45	2.72	2.89	2.98	2.71	2.72	2.63	
	0.63	2.44	2.46	2.51	2.66	2.77	2.91	2.90	2.87	2.76	
	1.25	2.48	2.53	2.57	2.86	3.18	3.45	2.93	3.05	2.94	
	2.5	2.37	2.32	2.40	2.58	2.89	3.08	2.84	2.88	2.77	
	5	2.41	2.25	2.27	2.50	2.71	3.02	2.59	2.68	2.72	
		15W	16W	17W	18W	19W	20W	24W	29W	34W	
	0	2.95	2.74	2.38	2.71	2.89	2.76	2.95	2.89	3.03	
	0.63	2.83	2.44	2.52	2.75	2.91	2.80	2.58	3.12	3.07	
	1.25	3.20	3.08	2.77	3.31	3.03	2.80	2.90	3.27	3.20	
	2.5	3.01	2.94	2.56	2.74	3.04	2.77	2.71	3.05	2.97	
	5	2.78	2.72	2.40	2.62	2.80	2.61	2.47	2.93	2.94	
		39W	44W	48W	52W	56W	60W				
	0	2.76	2.81	2.68	2.66	2.71	3.08				
	0.63	2.96	2.88	2.82	2.69	2.70	3.21				
	1.25	3.14	3.05	2.81	2.78	2.72	3.00				
	2.5	2.83	2.67	2.76	2.91	2.63	2.60				
	5	2.82	2.66	2.70	2.58	2.44	2.67				
	Female		6W	7W	8W	9W	10W	11W	12W	13W	14W
		0	1.52	2.09	2.12	2.23	2.61	2.59	2.14	2.49	2.22
0.63		1.72	1.81	2.01	2.27	2.69	2.67	2.60	2.60	2.62	
1.25		1.92	1.86	2.03	2.18	2.62	2.59	2.58	2.42	2.33	
2.5		2.02	1.87	2.04	2.15	2.55	2.54	2.20	2.22	2.27	
5		1.70	1.70	1.85	1.99	2.50	2.53	2.17	2.30	2.27	
		15W	16W	17W	18W	19W	20W	24W	29W	34W	
0		2.76	2.60	2.18	2.54	2.40	2.50	2.11	2.65	2.40	
0.63		2.65	2.63	2.29	2.55	2.52	2.48	2.11	2.61	3.00	
1.25		2.53	2.52	2.28	2.37	2.50	2.60	2.32	2.53	3.06	
2.5		2.31	2.37	1.98	2.22	2.25	2.31	2.18	2.51	2.81	
5		2.19	2.27	2.00	2.15	2.19	2.19	2.20	2.44	2.66	
		39W	44W	48W	52W	56W	60W				
0		2.53	2.57	2.72	2.25	2.59	2.66				
0.63		2.76	2.64	2.47	2.26	2.35	2.76				
1.25		2.60	2.75	2.67	2.49	2.29	2.58				
2.5		2.53	2.66	2.51	2.10	2.23	2.54				
5		2.67	2.59	2.44	2.34	2.21	2.48				

表28 Rev1ホモマウスの平均摂水量(ml/day)(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

Sex	Group	Age									
Male		6W	7W	8W	9W	10W	11W	12W	13W	14W	
	0	3.15	3.38	3.44	3.79	4.20	3.73	3.33	3.17	3.38	
	0.63	3.67	3.94	4.95	3.99	4.68	4.10	3.99	3.76	4.17	
	1.25	3.93	3.97	4.49	4.44	6.17	5.11	6.37	5.70	5.09	
	2.5	3.39	3.79	4.03	4.25	5.36	4.20	4.32	3.82	4.45	
	5	3.18	4.66	4.97	4.48	6.31	5.39	5.35	4.85	5.21	
		15W	16W	17W	18W	19W	20W	24W	29W	34W	
	0	2.85	3.33	3.05	3.05	2.83	2.67	2.70	2.01	2.18	
	0.63	3.02	3.39	3.11	3.15	3.17	3.08	3.21	2.64	2.26	
	1.25	3.12	3.41	3.53	3.48	3.94	3.05	3.01	2.70	2.44	
	2.5	3.00	3.48	3.41	3.42	3.59	3.07	3.73	2.88	2.37	
	5	3.32	3.71	3.64	3.43	3.99	3.91	3.22	2.53	2.99	
		39W	44W	48W	52W	56W	60W				
	0	1.84	2.03	2.25	2.67	2.59	2.91				
	0.63	1.91	2.17	2.33	3.49	2.81	3.40				
	1.25	2.10	2.46	2.22	4.40	4.25	3.73				
	2.5	2.00	2.23	2.54	3.86	3.10	3.07				
	5	1.96	2.33	2.80	4.16	3.43	3.88				
	Female		6W	7W	8W	9W	10W	11W	12W	13W	14W
		0	1.23	2.62	2.83	3.07	2.48	2.67	2.35	2.52	2.75
0.63		1.37	3.12	2.56	3.15	2.91	3.17	3.65	3.66	4.04	
1.25		2.14	3.15	3.84	4.21	3.24	4.81	4.61	4.40	4.58	
2.5		1.55	3.06	3.10	3.03	2.24	3.28	3.23	4.02	3.51	
5		1.56	3.37	3.10	2.86	2.51	3.76	4.13	4.23	3.88	
		15W	16W	17W	18W	19W	20W	24W	29W	34W	
0		2.50	3.04	2.87	2.79	2.71	2.63	2.46	2.30	1.91	
0.63		2.98	3.64	3.24	3.29	3.18	3.07	2.74	2.86	2.70	
1.25		2.97	3.50	3.22	2.83	2.90	2.96	3.45	2.53	2.37	
2.5		2.45	2.76	2.62	2.61	2.70	2.70	2.73	2.51	2.46	
5		3.04	3.22	3.31	3.13	3.44	3.00	3.27	3.08	2.96	
		39W	44W	48W	52W	56W	60W				
0		2.12	2.35	2.42	2.30	2.78	2.81				
0.63		2.34	2.72	2.44	3.60	3.40	3.39				
1.25		2.57	2.16	2.32	3.60	3.37	3.68				
2.5		2.50	2.50	2.61	2.86	2.92	3.17				
5		2.31	2.72	2.94	3.93	3.45	3.29				

表29 Rev1ホモマウスの平均被験物摂取量(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

Sex	Group	Diet intake	Water consumption	Soybean extracts intake
		(g/rat/day)	(ml/rat/day)	(g/kg/day)
Male	0	2.75 ± 0.19 <sup>a</sup>	2.94 ± 0.60	0.00 ± 0.00
	0.63	2.77 ± 0.21	3.35 ± 0.78	0.78 ± 0.37
	1.25	2.96 ± 0.25	3.88 ± 1.19	1.81 ± 0.89
	2.5	2.76 ± 0.22	3.47 ± 0.78	3.34 ± 1.52
	5	2.64 ± 0.20	3.90 ± 1.08	7.85 ± 3.70
Female	0	2.39 ± 0.28	2.52 ± 0.39	0.00 ± 0.00
	0.63	2.46 ± 0.31	3.05 ± 0.56	0.92 ± 0.26
	1.25	2.44 ± 0.26	3.31 ± 0.79	1.98 ± 0.82
	2.5	2.31 ± 0.23	2.80 ± 0.48	3.18 ± 1.13
	5	2.25 ± 0.27	3.19 ± 0.59	7.69 ± 2.33

a : Mean±SD

\*: Significantly different from the untreated control value at the levels of p<0.01

表30 Rev/ホモウスの尿検査(ばい菌ダイズ抽出物の1年間反復投与毒性試験)

Sex	Group	WBC			Urobilinogen			Protein			pH			Occult blood			Specific gravity			Ketone body			Glucose																											
		-	±	1+	2+	3+	0	1	2	-	±	1+	2+	3+	4+	5.0	6.0	6.5	7.0	7.5	8.0	8.5	-	±	1+	2+	3+	4+	5+	-	±	1+	2+	3+	4+	5+														
Male	0	No. of animals	4	2	3	0	0	9	0	0	0	3	4	1	1	0	0	6	3	0	0	0	6	0	1	0	1	0	0	0	0	1	0	0	0	8	9	0	0	0	9	0	0							
			9					9				9				9							9																											
	0.63	No. of animals	3	4	3	0	0	10	0	0	0	0	8	1	1	0	0	10	0	0	0	0	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	9	10	0	0	0	10	0	0				
			10					10				10				10							10																											
	1.25	No. of animals	5	1	2	1	0	9	0	0	0	0	5	1	3	0	0	5	2	2	0	0	5	0	0	2	0	2	0	0	0	0	0	1	8	9	0	0	0	9	0	0	9	0	0					
			10					10				10				10							10																											
	2.5	No. of animals	4	4	2	0	0	10	0	0	0	0	6	4	0	0	0	9	1	0	0	0	9	0	0	0	0	1	0	0	0	0	0	0	0	0	0	10	0	0	0	10	0	0	0	10	0	0		
			19					19				19				19							19																											
	5	No. of animals	15	4	0	0	0	19	0	0	0	0	11	6	2	0	1	15	0	3	0	0	16	0	0	0	0	3	0	0	0	0	1	17	19	0	0	0	19	0	0	19	0	0						
			9					9				9				9							9																											
	Female	0	No. of animals	4	3	0	2	0	9	0	0	0	1	5	3	0	0	7	1	0	0	1	6	0	0	0	0	3	0	0	0	0	0	0	0	0	1	8	9	0	0	0	9	0	0					
				8					8				8				8						8																											
0.63	No. of animals	6	1	1	0	0	8	0	0	0	0	5	3	0	0	0	2	4	1	1	0	0	8	0	0	0	0	0	0	0	0	0	2	0	6	8	0	0	0	8	0	0								
		10					10				10				10							10																												
1.25	No. of animals	6	0	3	1	0	10	0	0	0	2	4	4	0	0	0	9	1	0	0	0	7	0	0	1	0	2	0	0	0	0	0	0	2	8	10	0	0	0	10	0	0								
		8					8				8				8							8																												
2.5	No. of animals	7	0	1	0	0	8	0	0	0	2	4	1	1	0	0	4	3	1	0	0	5	0	0	0	3	0	0	0	0	1	1	6	8	0	0	0	8	0	0										
		18					18				18				18							18																												
5	No. of animals	13	3	2	0	0	18	0	0	0	1	11	6	0	0	0	16	1	0	0	1	13	1	0	0	1	0	0	0	0	1	1	16	18	0	0	0	18	0	0										
		18					18				18				18							18																												



表31 *Rev1*ホモマウスの血液学的検査(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

	Group				
	0	0.63	1.25	2.5	5
<b>Male</b>					
RBC count ( $10^4/\text{mm}^3$ )	900	956	951.5	939	966.75
Hb (g/dl)	13.55	13.4	13.05	13.3	14
Ht (%)	40.2	41	42.45	41.85	42.6
Plt count ( $10^4/\text{mm}^3$ )	120.05	137.65	123.9	112.05	150.3
MCV (fl)	44.55	42.9	44.55	44.75	44.1
MCH (pg)	15.2	14	13.75	14.2	14.5
MCHC (g/dl)	34.15	32.7	30.8	31.75	32.875
WBC count (/ $\text{mm}^3$ )	15285	11605	13520	13325	15567.5
Neutrophils (%)	8.7	13.65	14.9	18.4	8.333333
Lymphocytes (%)	88.55	84.15	80.2	81.9	89.55
Monocytes (%)	2.05	2.2	4.85	4.05	1.725
Eosinophils (%)	0	0	0.05	0	0.033333
Basophils (%)	0.05	0	0	0.1	0.05
<b>Female</b>					
RBC count ( $10^4/\text{mm}^3$ )	921.5	944	905	988.5	988
Hb (g/dl)	13	13.25	13.25	13.7	13.95
Ht (%)	41.5	40.35	39.85	41.35	43.05
Plt count ( $10^4/\text{mm}^3$ )	83.35	93.8	101.1	118.8	98.6
MCV (fl)	45	42.75	44.05	41.8	43.55
MCH (pg)	14.1	14.05	14.65	13.85	14.1
MCHC (g/dl)	31.35	32.75	33.3	33.15	32.45
WBC count (/ $\text{mm}^3$ )	8005	9765	17855	12010	12785
Neutrophils (%)	8.75	11.45	6.5	9.25	8.05
Lymphocytes (%)	89.35	86.6	91.3	89.2	89.15
Monocytes (%)	1.9	1.9	2.15	1.5	2.75
Eosinophils (%)	0	0	0	0	0
Basophils (%)	0	0.05	0.05	0.05	0.05

表32 Rev1ホモマウスの血液生化学的検査(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

	Group				
	0	0.63	1.25	2.5	5
<b>Male</b>					
TP (g/dl)	5.4	5.6	5.6	5.0	5.5
Alb (g/dl)	3.6	3.6	3.6	3.4	3.6
A/G	1.9	1.8	1.9	2.1	1.9
GOT (IU/l)	104.0	116.5	106.5	92.0	112.5
GPT (IU/l)	60.5	54.0	34.0	73.5	45.8
ALP (IU/l)	278.0	251.5	288.0	226.0	285.8
γ-GTP (IU/l)	1.0	1.0	1.0	1.0	1.0
CRE (mg/dl)	0.2	0.2	0.1	0.1	0.1
BUN (mg/dl)	26.3	31.8	24.1	22.8	24.0
Glu (mg/dl)	145.5	141.0	139.0	134.5	147.0
TG (mg/dl)	143.5	143.0	100.5	129.0	107.5
T-Cho (mg/dl)	120.5	110.5	94.5	98.0	100.3
Na (mEq/l)	147.5	148.0	148.5	150.0	149.3
K (mEq/l)	8.4	8.7	7.7	9.0	
Cl (mEq/l)	114.0	114.5	114.5	117.0	113.5
Ca (mg/dl)	9.1	9.3	9.1	9.1	9.3
IP (mg/dl)	6.3	6.8	7.5	6.6	7.7
T-Bil (mg/dl)	0.1	0.1	0.1	0.1	0.1
<b>Female</b>					
TP (g/dl)	5.4	5.3	5.4	5.3	5.5
Alb (g/dl)	3.7	3.6	3.5	3.7	3.7
A/G	2.1	2.2	1.9	2.2	2.1
GOT (IU/l)	179.5	162.0	105.0	145.5	140.8
GPT (IU/l)	68.0	60.0	38.5	39.5	38.3
ALP (IU/l)	484.0	505.0	501.5	514.0	527.8
γ-GTP (IU/l)	1.0	1.0	1.0	1.0	1.0
CRE (mg/dl)	0.1	0.1	0.1	0.1	0.1
BUN (mg/dl)	32.0	28.2	27.7	22.2	24.0
Glu (mg/dl)	139.5	119.5	128.5	139.5	139.0
TG (mg/dl)	75.5	41.0	72.5	43.0	46.0
T-Cho (mg/dl)	84.0	76.5	90.5	84.5	85.3
Na (mEq/l)	148.5	147.0	149.0	148.5	148.5
K (mEq/l)		8.4	7.2	6.8	6.5
Cl (mEq/l)	116.5	115.5	115.0	114.0	115.0
Ca (mg/dl)	9.0	9.2	9.1	9.1	9.1
IP (mg/dl)	6.0	5.8	6.0	6.3	6.1
T-Bil (mg/dl)	0.1	0.1	0.1	0.1	0.1

表33 Rev1ホモマウスの臓器重量(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

	Group				
	0	0.63	1.25	2.5	5
<b>Male</b>					
Body weight (g)	45.19 ± 4.76 <sup>a</sup>	43.77 ± 4.43	40.34 ± 5.92	42.29 ± 4.12	38.69 ± 5.54
<b>Tissue</b>					
Brain (g)	0.43 ± 0.03	0.42 ± 0.04	0.41 ± 0.04	0.41 ± 0.04	0.41 ± 0.03
Thymus (mg)	99.56 ± 32.27	72.70 ± 27.45 <sup>*</sup>	61.00 ± 15.27 <sup>**</sup>	70.10 ± 24.22 <sup>*</sup>	64.47 ± 21.28 <sup>**</sup>
Heart (g)	0.18 ± 0.02	0.19 ± 0.06	0.18 ± 0.03	0.19 ± 0.02	0.17 ± 0.02
Lung (g)	0.18 ± 0.04	0.16 ± 0.05	0.16 ± 0.03	0.16 ± 0.02	0.17 ± 0.02
Liver (g)	1.88 ± 0.51	1.77 ± 0.34	1.52 ± 0.46	2.38 ± 1.55	1.48 ± 0.28
Spleen (mg)	73.11 ± 25.08	78.40 ± 41.11	86.44 ± 30.30	90.50 ± 45.77	62.79 ± 12.84
Kidney (g)	0.43 ± 0.03	0.69 ± 0.80	0.44 ± 0.03	0.45 ± 0.03	0.78 ± 1.43
Testis (g)	0.16 ± 0.02	0.16 ± 0.02	0.14 ± 0.01	0.13 ± 0.03 <sup>**</sup>	0.14 ± 0.02
Adrenal (mg)	7.22 ± 2.33	7.20 ± 3.55	7.33 ± 2.78	10.40 ± 5.10	8.53 ± 2.39
Pituitary (mg)	1.90 ± 0.36	1.81 ± 0.72	2.01 ± 0.72	1.85 ± 0.32	1.87 ± 0.46
Thyroid (mg)	3.95 ± 1.08	4.74 ± 1.03	4.98 ± 1.59	4.98 ± 1.54	4.94 ± 0.79
<b>Female</b>					
Body weight (g)	37.14 ± 8.92	30.52 ± 7.37	36.63 ± 5.04	36.23 ± 6.40	31.86 ± 9.47
<b>Tissue (g)</b>					
Brain (g)	0.44 ± 0.03	0.42 ± 0.02	0.44 ± 0.03	0.43 ± 0.04	0.41 ± 0.04
Thymus (mg)	72.89 ± 27.03	69.25 ± 54.16	69.90 ± 23.02	63.63 ± 24.78	55.44 ± 20.73
Heart (g)	0.14 ± 0.02	0.12 ± 0.02	0.13 ± 0.01	0.13 ± 0.01	0.12 ± 0.02
Lung (g)	0.19 ± 0.04	0.18 ± 0.04	0.19 ± 0.06	0.15 ± 0.02	0.17 ± 0.05
Liver (g)	1.16 ± 0.25	1.16 ± 0.36	1.25 ± 0.31	1.07 ± 0.13	1.08 ± 0.33
Spleen (mg)	97.56 ± 17.27	177.38 ± 292.47	79.80 ± 36.42	62.25 ± 11.07	67.83 ± 29.44
Kidney (g)	0.35 ± 0.04	0.33 ± 0.02	0.40 ± 0.23	0.32 ± 0.04	0.32 ± 0.04
Ovary (mg)	27.89 ± 18.96	18.25 ± 8.38	22.40 ± 17.35	18.63 ± 6.91	20.00 ± 7.23
Uterus (g)	0.12 ± 0.05	0.12 ± 0.05	0.12 ± 0.07	0.27 ± 0.45	0.12 ± 0.07
Adrenal (mg)	11.78 ± 4.79	8.00 ± 2.07	12.90 ± 5.82	8.00 ± 3.85	10.28 ± 3.68
Pituitary (mg)	2.35 ± 0.60	1.91 ± 0.55	2.34 ± 0.74	1.77 ± 0.58	2.10 ± 0.66
Thyroid (mg)	4.80 ± 2.01	5.15 ± 1.07	4.36 ± 2.00	3.87 ± 2.25	3.69 ± 1.05

a : Mean±SD

\*,\*\* : Significantly different from the untreated control value at the levels of p&lt;0.05, p&lt;0.01, respectively.

表34 Rev1ホモマウスの相対的臓器重量比(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

	Group				
	0	0.63	1.25	2.5	5
<b>Male</b>					
Brain	8.43 ± 3.23 <sup>a</sup>	9.52 ± 0.85	10.12 ± 1.00	9.62 ± 0.98	10.63 ± 0.72 <sup>**</sup>
Thymus	2.20 ± 0.71	1.66 ± 0.63	1.51 ± 0.38	1.66 ± 0.57	1.67 ± 0.55 <sup>**</sup>
Heart	4.04 ± 0.50	4.33 ± 1.27	4.54 ± 0.76	4.44 ± 0.47	4.31 ± 0.62
Lung	3.98 ± 0.97	3.58 ± 1.07	4.03 ± 0.70	3.86 ± 0.46	4.29 ± 0.59
Liver	41.68 ± 11.38	40.46 ± 7.83	37.79 ± 11.36	56.22 ± 36.70	38.15 ± 7.36
Spleen	1.62 ± 0.56	1.79 ± 0.94	2.14 ± 0.75	2.14 ± 1.08	1.62 ± 0.33
Kidney	9.56 ± 0.67	15.87 ± 18.37	10.86 ± 0.83	10.57 ± 0.78	20.28 ± 36.84
Testis	3.50 ± 0.42	3.58 ± 0.43	3.44 ± 0.32	2.96 ± 0.78	3.63 ± 0.52
Adrenal	0.16 ± 0.05	0.16 ± 0.08	0.18 ± 0.07	0.25 ± 0.12	0.22 ± 0.06
Pituitary	0.04 ± 0.01	0.04 ± 0.02	0.05 ± 0.02	0.04	0.01
Thyroid	0.09 ± 0.02	0.11 ± 0.02 <sup>*</sup>	0.12 ± 0.04	0.12 ± 0.04	0.13 ± 0.02 <sup>**</sup>
<b>Female</b>					
Brain	11.94 ± 0.91	13.75 ± 0.80 <sup>**</sup>	11.95 ± 0.83	11.83 ± 1.12	12.90 ± 1.23 <sup>*</sup>
Thymus	1.96 ± 0.73	2.27 ± 1.77	1.91 ± 0.63	1.76 ± 0.68	1.74 ± 0.65
Heart	3.87 ± 0.55	4.02 ± 0.54	3.49 ± 0.33	3.50 ± 0.38	3.78 ± 0.68
Lung	5.02 ± 0.98	5.84 ± 1.29	5.27 ± 1.59	4.22 ± 0.54	5.39 ± 1.43
Liver	31.22 ± 6.74	37.89 ± 11.64	34.06 ± 8.57	29.52 ± 3.68	33.77 ± 10.33
Spleen	2.63 ± 0.47	5.81 ± 9.58	2.18 ± 0.99	1.72 ± 0.31	2.13 ± 0.92
Kidney	9.55 ± 1.06	10.88 ± 0.80	10.84 ± 6.16	8.75 ± 1.02	9.98 ± 1.29
Ovary	0.75 ± 0.51	0.60 ± 0.27	0.61 ± 0.47	0.51 ± 0.19	0.63 ± 0.23
Uterus	3.34 ± 1.38	3.98 ± 1.74	3.37 ± 1.79	7.58 ± 12.54	3.90 ± 2.09
Adrenal	0.32 ± 0.13	0.26 ± 0.07	0.35 ± 0.16	0.22 ± 0.11	0.32 ± 0.12
Pituitary	0.06 ± 0.02	0.06 ± 0.02	0.06 ± 0.02	0.05 ± 0.02	0.07 ± 0.02
Thyroid	0.13 ± 0.05	0.17 ± 0.04	0.12 ± 0.05	0.11 ± 0.06	0.12 ± 0.03

a : Relative organ weight was calculated as follows: (organ weight/ body weight)×1000. Value are means ±S.D..

\*,\*\* : Significantly different from the untreated control value at the levels of p&lt;0.05, p&lt;0.01, respectively.

表35 Rev1ホモマウスの各実験群に認められた肉眼的所見(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

Organ	Finding	Male					Female				
		0% (n=9)	0.63% (n=10)	1.25% (n=9)	2.50% (n=10)	5% (n=19)	0% (n=9)	0.63% (n=8)	1.25% (n=10)	2.50% (n=8)	5% (n=18)
Harderian gland	enlargement					1				1	1
Thyroid gland	enlargement	1									1
Lymph node	enlargement	1				1	1	1	1		
Thymus	atrophy					1					
	enlargement							1			
Lung	congestion										1
	white nodule					1		1			
Heart	enlargement		1								
Liver	enlargement					3		1			
	white nodule	2						2		1	
Spleen	bleeding	1	1	3	1	2	1				1
	enlargement							1			
	white nodule				1			1			
Stomach	white nodule	1				1		1			1
	hypertrophy								1		
Pancreas	white nodule	1	1				1				
Kidney	cyst			1				1			1
	hydronephrosis		2		2	3		1			3
	atrophy										1
	bleeding										1
Others	lipoma				1	1	2	1	1		1
	white nodule							1			
	red nodule								1		1
<b>Male</b>											
Testis	atrophy					1					
Prostate	atrophy	1									
	white nodule					1					
<b>Female</b>											
Ovary	cyst								2		
Uterus	cyst									1	

表36-1 Rev/ホモマウスの各実験群に認められた病理学的所見 I (ばい煎ダイズ抽出物の1年間反復投与毒性試験)

Organ	Finding		Male					Female				
			0% (n=9)	0.63% (n=10)	1.25% (n=9)	2.50% (n=10)	5% (n=19)	0% (n=9)	0.63% (n=8)	1.25% (n=10)	2.50% (n=8)	5% (n=18)
salivary gland	atrophy	+	2			1						
	cell infiltration	+	2	3	5	4	5	5	1	1	2	4
	fatty degeneration	+	1			2	1	1		2	1	1
	hyperplasia	+		1								
	metastasis of neoplasm	+								1		
Thymus	fibrosis	+	1									
	fatty degeneration	+	2	1	2		4	3	2	1	1	2
Lymph node	bleeding	+	1									
	metastasis of neoplasm	+								1		
Heart	arteritis					1						
	atrophy	+			1	1						
	cell infiltration	+			1							
	metastasis of neoplasm	+										1
Lung	bleeding	+			1		1					
	cell infiltration	+	4	7	6	2	7	5	6	8	5	11
	congestion	+	7	9	8	10	18	7	8	9	7	16
		++			1							
	fibrosis	+									1	
	alveolar epithelial hyperplasia	+		2	1		1		1	1	1	1
	metastasis of neoplasm	+					1	2	1	1	1	1
Liver	hepatoma					3				1	1	1
	foci		1									
	bile duct proliferation	±	1	2	3	1	11	2	2	1		2
		+	4	4	5	4	4	5	3	4	5	14
		++									2	
		+++	1									
	cell infiltration	±		1								
		+				2	1	3		3		
		++				1				1		
	fatty liver	±					1					1
	+		3	1	4		1		1			
	++	3	1	4	3	6						
	+++	4	3		2	2						
	metastasis of neoplasm						2	1	1		1	
	necrosis	±				1				1		
Spleen	atrophy	+	1	5	3	1		4	1	2	4	3
	bleeding	+	1			1				1		
		++	1									
	cell infiltration	+	1			1						
	hemosiderin deposition	+	2	1	3	1	1	1			1	
	metastasis of neoplasm				1				1			
Stomach	papilloma					1						
	atrophy	+	3	1		2	2	2		2	2	
	eosinophilic degeneration	+	1	1	1		1					
	cell infiltration	+	2	1	1	3	1	1	1	3	3	
	edema	+	2	2			1	1		1	5	
		++	1									
	hyperplasia	+	3		3		1	2	2	4	3	

±; minimal, +; mild, ++; moderate; +++severe

表36-2 Rev1ホモマウスの各実験群に認められた病理学的所見Ⅱ(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

Organ	Finding	Male					Female				
		0% (n=9)	0.63% (n=10)	1.25% (n=9)	2.50% (n=10)	5% (n=19)	0% (n=9)	0.63% (n=8)	1.25% (n=10)	2.50% (n=8)	5% (n=18)
Kidney	cyst				1						
	papilloma									1	
	squamous cell hyperplasia	+				1		1			
	squamous cell metaplasia	+							1		
	atrophy	+							1	3	
	bleeding	+								1	
	cast	±	2	1							
		+				1			1	1	
	cell infiltration	+	5	7	5	2	8	6	1	2	3
		++					1				8
		+			1					1	1
	fibrosis	+			2	5		1	1	1	5
	hydronephrosis	+		2				2			1
	metastasis of neoplasm	±					1				
regenerative epithelium	+	1	5	5	3	7	1	2	1	4	
	+									3	
Adrenal	cell infiltration	+		1						1	
	fatty degeneration	+				1		1			
Bladder	hyperplasia	+				1					
Pituitary	cyst									1	
	hyperplasia	+								2	
Thyroid	c-cell hyperplasia	+		1		1				1	
	cell infiltration	+	1		1				1		
	fatty degeneration	±	1								
		+	4	6	5	8	5	7	8	10	6
										13	
parathyroid	cyst					1					
	fatty degeneration	+				1					
Pancreas	adenocarcinoma							1			
	sarcoma								1		
	atrophy	+	4	6	5	8	12	6	7	4	
		++							1	1	
		+++	1								
		±			1						
	+	6	5	5	6	14	9	6	8	7	
	++	2	5	1	3	3			1	1	
	cell infiltration	+	2	2			2	3	2	1	
									1	2	
others	sarcoma								1		
	lipoma			1	1	2	1		1		
	non-thymic lymphoma					1		2	1	2	
										1	
<b>Male</b>											
Prostate	atrophy	+				1					
	fibrosis	+			1						
	hyperplasia	+		1	1		3				
Testis	atrophy	+	2	8	9	10	19				
		++		1							
	seminiferous tubule vacuol	+	9	8	8	10	18				
<b>Female</b>											
Ovary	bleeding	+							1	1	
	squamous cell metaplasia	+							1		
	stromal fibrosis	+								1	
Uterus	sarcoma									1	
	cyst						9	8	10	7	
	cell infiltration	+	1	1	4	1				1	

±: minimal, +: mild, ++: moderate; +++severe

図1-1 雄ラット体重の推移(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

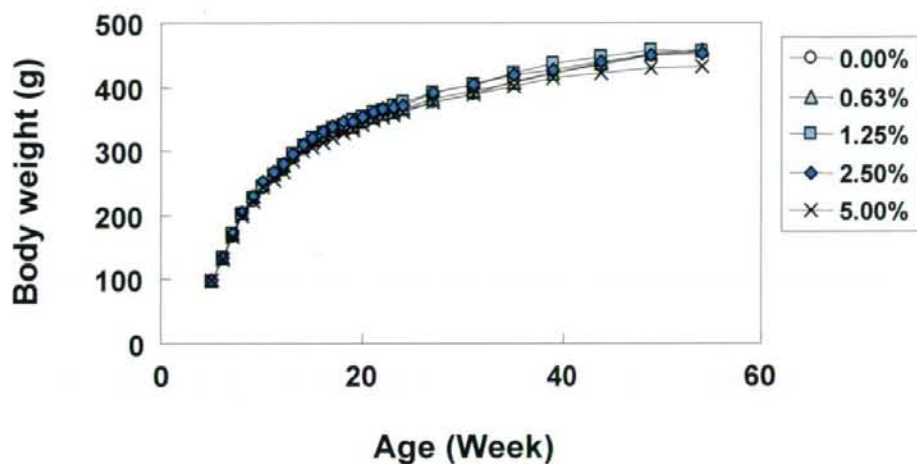


図1-2 雌ラット体重の推移(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

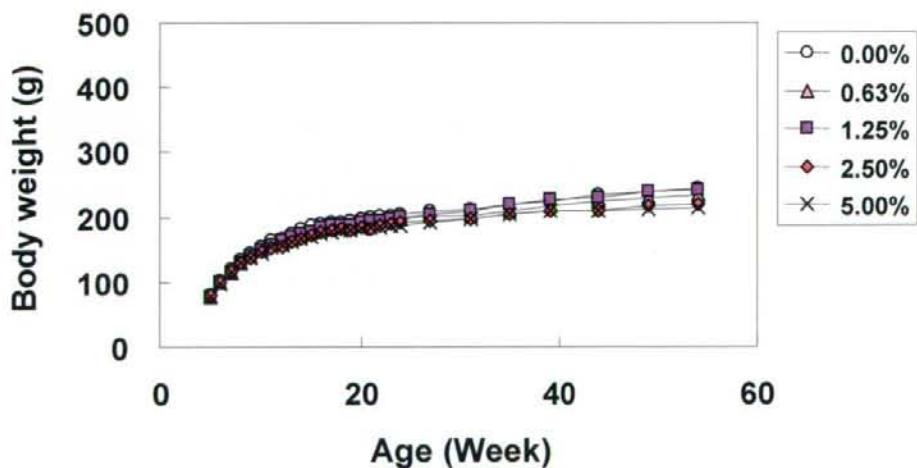


図2-1 雄ラットの平均摂餌量(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

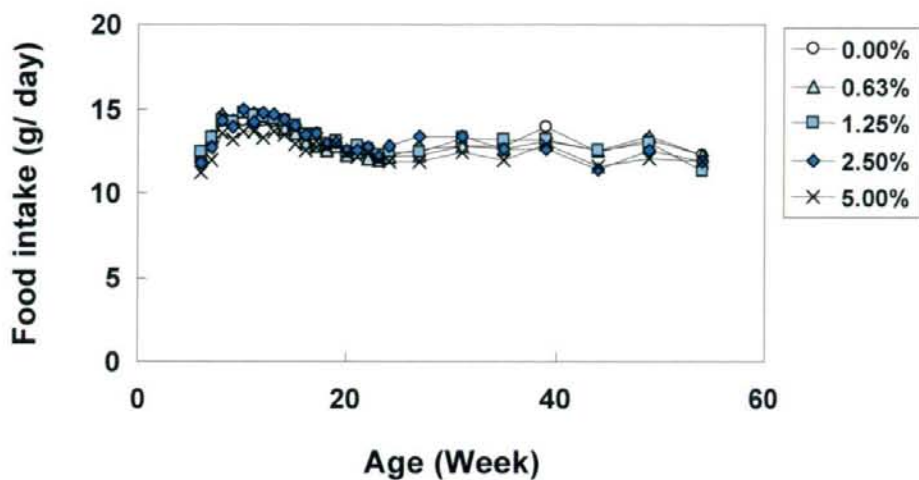


図2-2 雌ラットの平均摂餌量(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

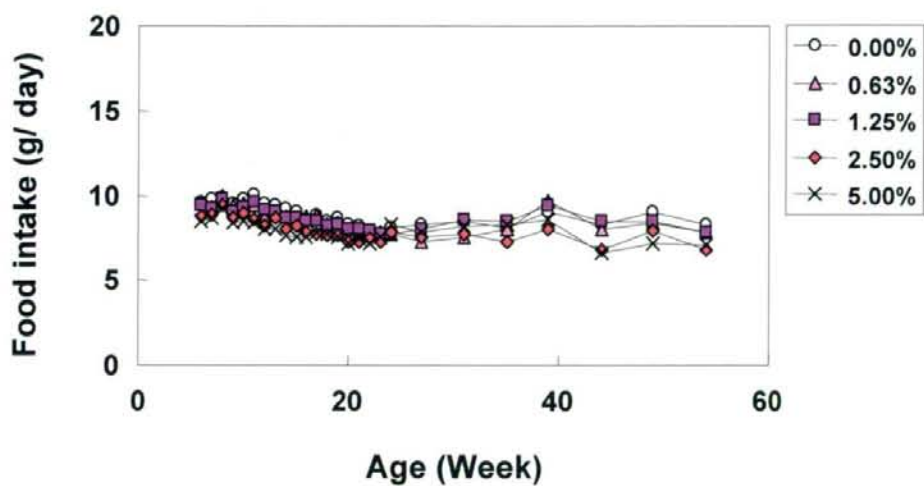




図3-1 雄ラットの平均摂水量(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

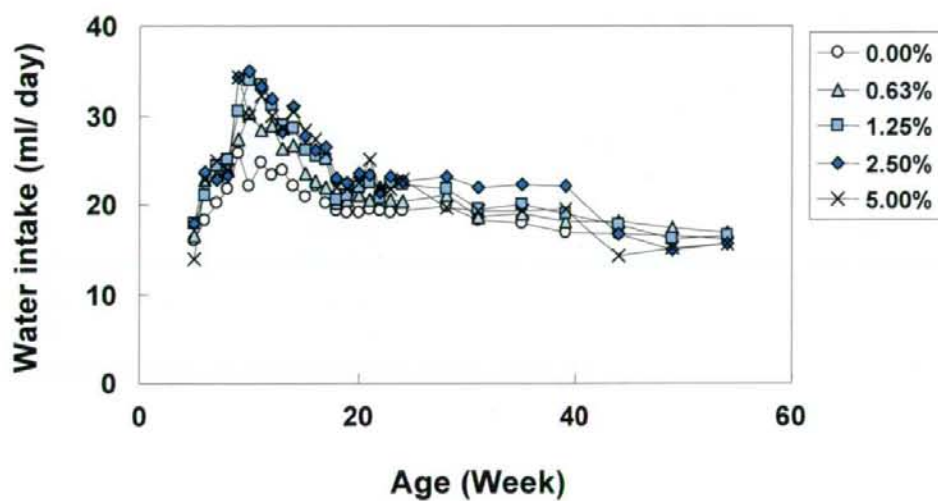


図3-2 雌ラットの平均摂水量(ばい煎ダイズ抽出物の1年間反復投与毒性試験)

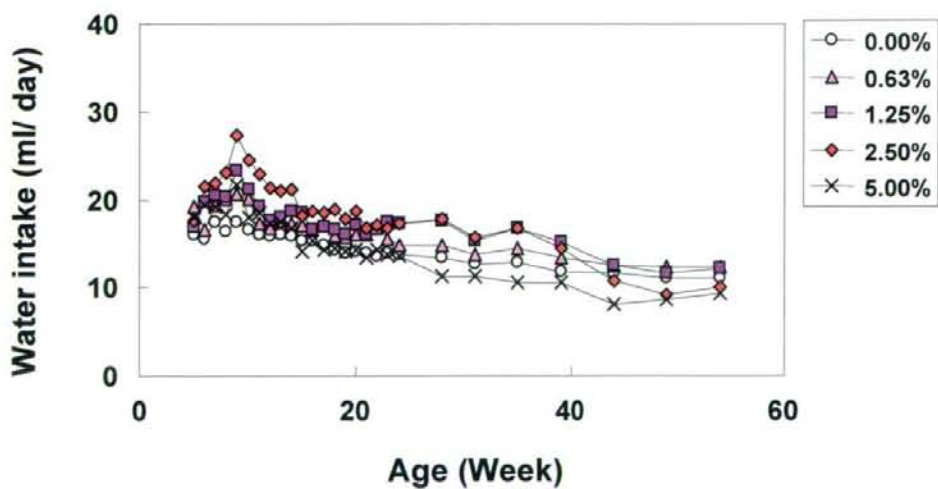


図4 *Rev1*ホモマウスに誘発された小腸腺癌

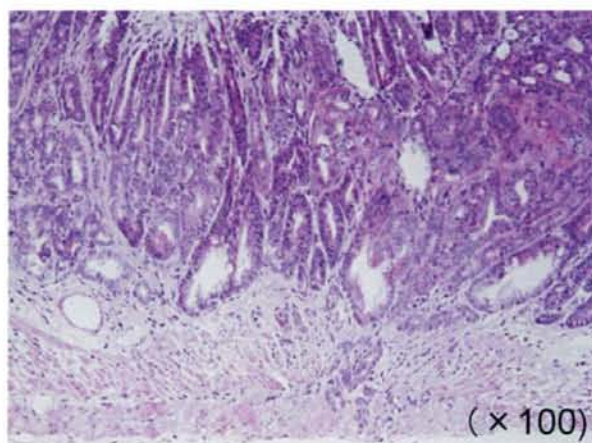


図5 *Rev1*ホモマウスの小腸での*Rev1* mRNAの発現

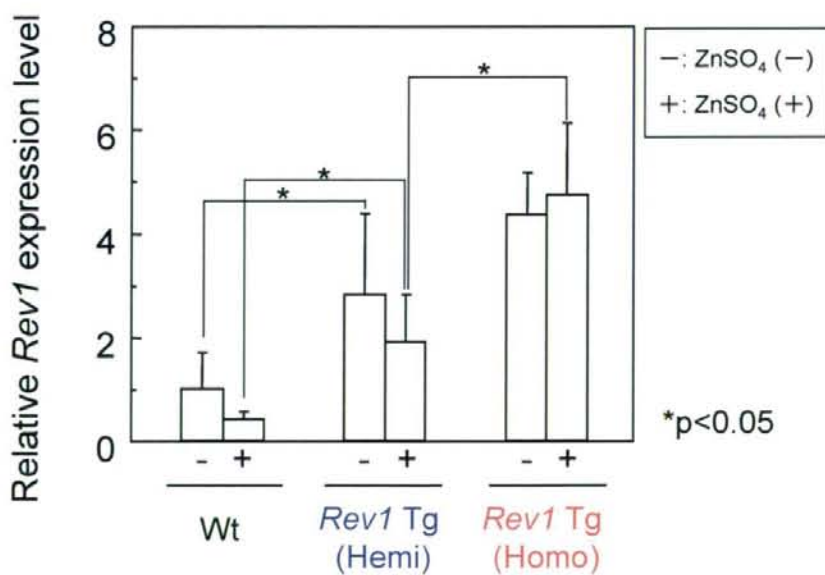
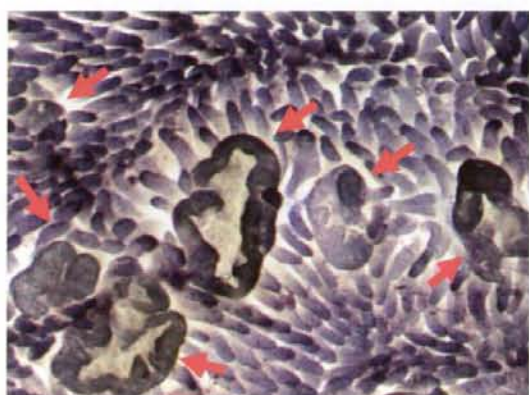
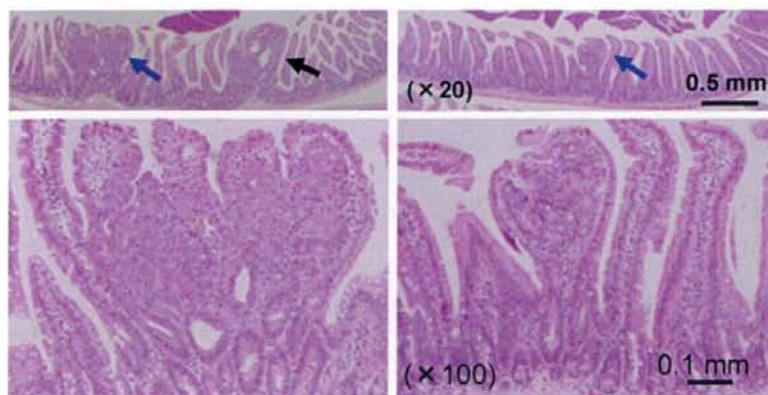


図6 *Rev1* マウスの小腸に誘発されたmicro-adenoma (I)



アルカリフォス  
ファターゼ染色

図7 *Rev1* マウスの小腸に誘発されたmicro-adenoma (II)



HE染色

図8 *Rev1* ホモマウスの1ヶ月間発がん試験

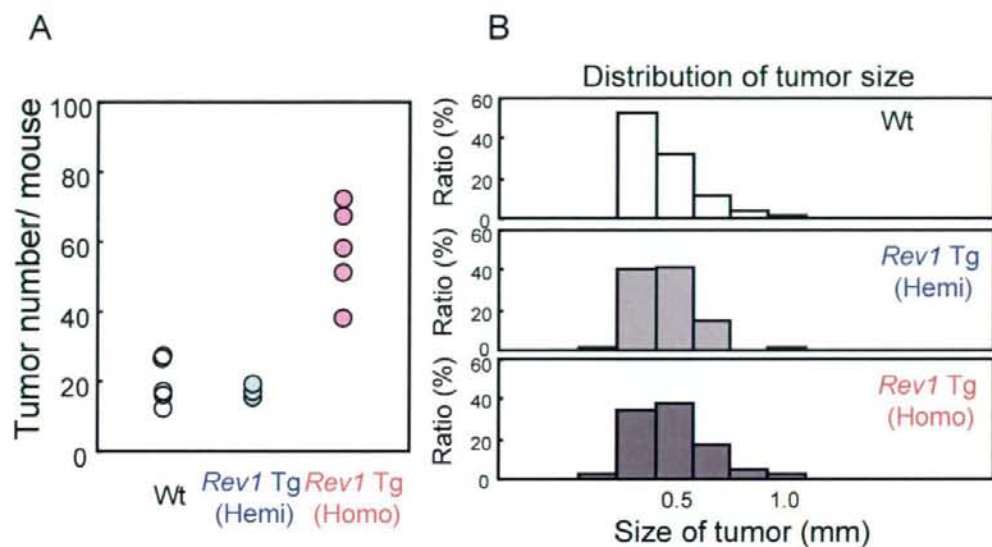


図9 *Rev1* ホモマウスの2ヶ月間発がん試験

