Background data analysis of rasH2 mice produced by CLEA Japan over a 26-week experimental period (2020–2022)

○ **Masahiko Yasuda[1], Takuma Mizusawa[1], Chie Shimomura[2], Masahiro Wada[2], Yoko Kamai[1], Rui Nagakubo[2], Misa Mochizuki[1], Masaaki Handa[2], Riichi Takahashi[1], Kenji Kawai[1]**

[1] Central Institute for Experimental Medicine and Life Science
[2] CLEA Japan, Inc.

Background:

The CByB6F1-Tg(HRAS)2Jic (rasH2) mouse is commonly utilized in 26-week carcinogenicity studies, adhering to the ICH S1B guideline. The rasH2-Tg(tg/wt) mouse is a genetically engineered mouse containing the c-Ha-ras (HRAS) gene. This strain is produced through cross-breeding between C57BL/6JJic-Tg(HRAS)2Jic (B6-Tg) hemizygous males and BALB/cByJJic (BALB) females. The rasH2-Tg and rasH2-Wt(wt/wt) mice are supplied worldwide by CLEA Japan and Taconic Bioscience. This study investigated the most recent background data of rasH2 mice from the Breeding Facility of CLEA Japan.

Materials and Methods:

Animals:

8–10-week-old started, 26-week study

rasH2-Tg	male	n=181
	female	n=180
rasH2-Wt	male	n=45
	female	n=45

Breeding retired

B6-Tg	male	n=46	(51–60-week-old)
BALB	female	n=45	(36–42-week-old)

Results:

Table 1. Body weight of rasH2-Tg, rasH2-Wt, B6-Tg, and BALB mice (mean ± S.D.)

	rasH2-Tg (34–36w)		rasH2-Wt (34–36w)		B6-Tg (51–60w)	BALB (36–42w)
	Males (n=170)	Females (n=174)	Males (n=45)	Females (n=45)	Males (n=46)	Females (n=45)
Body weight (g)	33.7 ± 2.4	27.6 ± 2.4	40.6 ± 3.7	30.1 ± 2.3	25.8 ± 2.1	30.9 ± 2.1

Figure 1. Survival Ratio for rasH2-Tg and rasH2-Wt mice

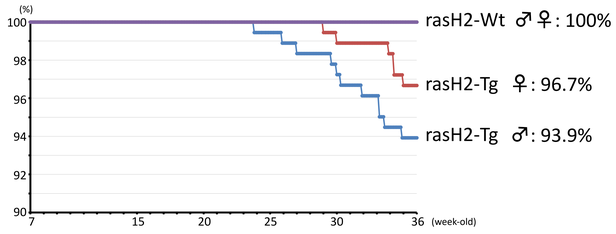

Table 2. Causes of Death of rasH2-Tg and rasH2-Wt mice

	rasH2-Tg		rasH2-Wt	
	Males (n=181)	Females (n=180)	Males (n=45)	Females (n=45)
	Average (Range)	Average (Range)	Average	Average
Survival ratio	93.9% (85–100%)	96.7% (80–100%)	100%	100%
Hemangiosarcoma	1.1%	2.8%	-	-
Bronchiolo-alveolar carcinoma	-	0.6%	-	-
Squamous cell papilloma (skin hemorrhage)	0.6%	-	-	-
Others (Non-tumor)	4.4%	-	-	-

-: none, Others: unknown or accidental causes.

Table 3. Incidence of Necropsy Findings in rasH2-Tg, rasH2-Wt, B6-Tg and BALB mice

		rasH2-Tg (24–36w)				rasH2-Wt (34–36w)				B6-Tg (51–60w)		BALB (36–42w)	
		Males (n=181)		Females (n=180)		Males (n=45)		Females (n=45)		Males (n=46)		Females (n=45)	
		Average (%)	Total Number of Animals	Average (%)	Total Number of Animals	Average (%)	Total Number of Animals	Average (%)	Total Number of Animals	Average (%)	Total Number of Animals	Average (%)	Total Number of Animals
Lung	Nodule	7.7	14	8.3	15	6.7	3	2.2	1	15.2	7	15.6	7
	Patchy	3.3	6	2.3	4	0	0	0	0	0	0	0	0
	Sclerosis	0	0	0.6	1	0	0	0	0	0	0	0	0
Heart	Mineralization	0	0	0	0	0	0	0	0	0	0	51.1	23
Teeth	Malocclusion	0.6	1	0.6	1	0	0	0	0	0	0	0	0
Salivary glands	Cyst	0	0	0.6	1	0	0	0	0	0	0	0	0
Stomach	Focus	0.6	1	0.6	1	0	0	0	0	0	0	0	0
	Thickening	0	0	0.6	1	0	0	0	0	0	0	0	0
Small intestine	Diverticulum	0	0	0.6	1	0	0	0	0	0	0	0	0
	Thickening	0	0	0	0	0	0	0	0	2.2	1	0	0
Liver	Cyst	0	0	0.6	1	0	0	0	0	0	0	0	0
	Focus	1.7	3	0	0	0	0	0	0	2.2	1	2.2	1
	Infarction	0	0	1.7	3	0	0	2.2	1	0	0	4.4	2
	Nodule	2.2	4	0.6	1	2.2	1	0	0	0	0	0	0
Pancreas	Cyst	0	0	0.6	1	0	0	0	0	0	0	2.2	1
Kidney	Cyst	0	0	0	0	0	0	0	0	2.2	1	0	0
	Hydronephrosis	0.6	1	0	0	0	0	0	0	0	0	0	0
	Nodule	0	0	0	0	0	0	0	0	2.2	1	0	0
Spleen	Enlargement	2.2	4	1.1	2	0	0	0	0	0	0	0	0
	Nodule	5.5	10	3.3	6	0	0	0	0	4.3	2	0	0
	Pigmentation	13.8	25	15.6	28	15.6	7	8.9	4	17.4	8	0	0
Lymph nodes	Enlargement	0	0	0.6	1	0	0	0	0	0	0	0	0
Testis	Enlargement	0.6	1	-	-	0	0	-	-	0	0	-	-
	Focus	0.6	1	-	-	0	0	-	-	0	0	-	-
Prostate gland	Enlargement	0.6	1	-	-	2.2	1	-	-	0	0	-	-
Uterus	Nodule	-	-	1.7	3	-	-	0	0	-	-	0	0
	Thickening	-	-	4.4	8	-	-	2.2	1	-	-	2.2	1
Harderian gland	Enlargement	0.6	1	0.6	1	0	0	0	0	0	0	0	0
Skin	Injury	1.1	2	0	0	0	0	0	0	0	0	0	0
	Polyp	1.1	2	1.1	2	0	0	0	0	4.3	2	0	0
	Thickening	0	0	0	0	0	0	0	0	0	0	2.2	1
Subcutis	Mass	2.8	5	3.9	7	0	0	0	0	2.2	1	0	0
Mammary gland	Cyst	0	0	0	0	0	0	0	0	0	0	2.2	1
Thoracic cavity	Chylothorax	1.1	2	0.6	1	0	0	0	0	0	0	0	0
Abdominal cavity	Ascites	0	0	0.6	1	0	0	0	0	2.2	1	0	0
Mesentery	Mass	0	0	0.6	1	0	0	0	0	0	0	0	0

Table 4. Incidence of Spontaneous Tumors in rasH2-Tg, rasH2-Wt, B6-Tg and BALB mice

		rasH2-Tg (24–36wks)				rasH2-Wt (34–36wks)				B6-Tg (51–60wks)		BALB (36–42wks)	
		Males (n=181)		Females (n=180)		Males (n=45)		Females (n=45)		Males (n=46)		Females (n=45)	
		Average (%)	Total Number of Animals	Average (%)	Total Number of Animals	Average (%)	Total Number of Animals	Average (%)	Total Number of Animals	Average (%)	Total Number of Animals	Average (%)	Total Number of Animals
Lung	Adenoma, bronchiolo-alveolar	11.6	21	11.1	20	8.9	4	2.2	1	10.9	5	15.6	7
	Carcinoma, bronchiolo-alveolar	0	0	0.6	1	0	0	0	0	0	0	0	0
Stomach	Hemangiosarcoma	0.6	1	0	0	0	0	0	0	0	0	0	0
Small intestine	Hemangioma	0	0	0	0	0	0	0	0	2.2	1	0	0
	Hemangiosarcoma	2.2	4	0	0	0	0	0	0	0	0	0	0
Liver	Adenoma, hepatocellular	0.6	1	0	0	2.2	1	0	0	0	0	0	0
	Hemangioma	3.9	7	0	0	0	0	0	0	0	0	0	0
Kidney	Hemangioma	0	0	0	0	0	0	0	0	2.2	1	0	0
Spleen	Hemangiosarcoma	4.4	8	3.3	6	0	0	0	0	4.3	2	0	0
Testis	Hemangiosarcoma	1.1	2	-	-	0	0	-	-	0	0	-	-
Prostate gland	Hemangiosarcoma	0.6	1	-	-	0	0	-	-	0	0	-	-
Uterus	Hemangioma	-	-	0.6	1	-	-	0	0	-	-	0	0
	Hemangiosarcoma	-	-	1.1	2	-	-	0	0	-	-	0	0
Harderian gland	Adenoma	0.6	1	0	0	0	0	0	0	0	0	0	0
Skin	Papilloma, squamous cell	1.1	2	1.1	2	0	0	0	0	4.3	2	0	0
Subcutis	Hemangioma	0.6	1	0	0	0	0	0	0	0	0	0	0
	Hemangiosarcoma	2.2	4	2.8	5	0	0	0	0	2.2	1	0	0
Mammary gland	Adenocarcinoma	0	0	0.6	1	0	0	0	0	0	0	0	0
Thoracic cavity	Hemangioma	0.6	1	0	0	0	0	0	0	0	0	0	0
Mesentery	Hemangiosarcoma	0	0	0.6	1	0	0	0	0	0	0	0	0

Conclusion:

Our results indicate that our recent background data regarding rasH2 mice showed no significant phenotypic changes from previously reported findings [1, 2] and instilling confidence in conducting 26-week carcinogenicity studies. Further, this study demonstrated the robustness and minimal drift in this animal model.

References:

1. Kanno H, et al. Histological background data in CB6F1-Tg-*ras*H2 mice and CB6F1-nonTg-*ras*H2 mice over a 26-week experimental period. J Toxicol Pathol. 16: 267–274. 2003.
2. Paranjpe MG, et al. Historical control data of spontaneous tumors in transgenic CByB6F1-Tg(HRAS)2Jic (Tg.rasH2) mice. Int J Toxicol. 32: 48–57. 2013.

Please scan the QR code to download the PDF.

CLEA Japan, Inc.'s website regarding rasH2 mice

Name of presenting author: Masahiko Yasuda
Organization: Central Institute for Experimental Medicine and Life Science (CIEM)

I have no COI regarding this presentation.