

- 2) 株式会社シミックバイオリサーチセンター社内検討試験, マウス急性喘息モデルにおけるデキサメタゾンの効果 (試験番号.11V0131N)
- 3) Fujita H. et al. Production of both IL-27 and IFN- after the treatment with a ligand for invariant NK T Cells is responsible for the suppression of Th2 response and allergic inflammation in a mouse experimental asthma model. J. Immunol., 2009, 183: 254-260

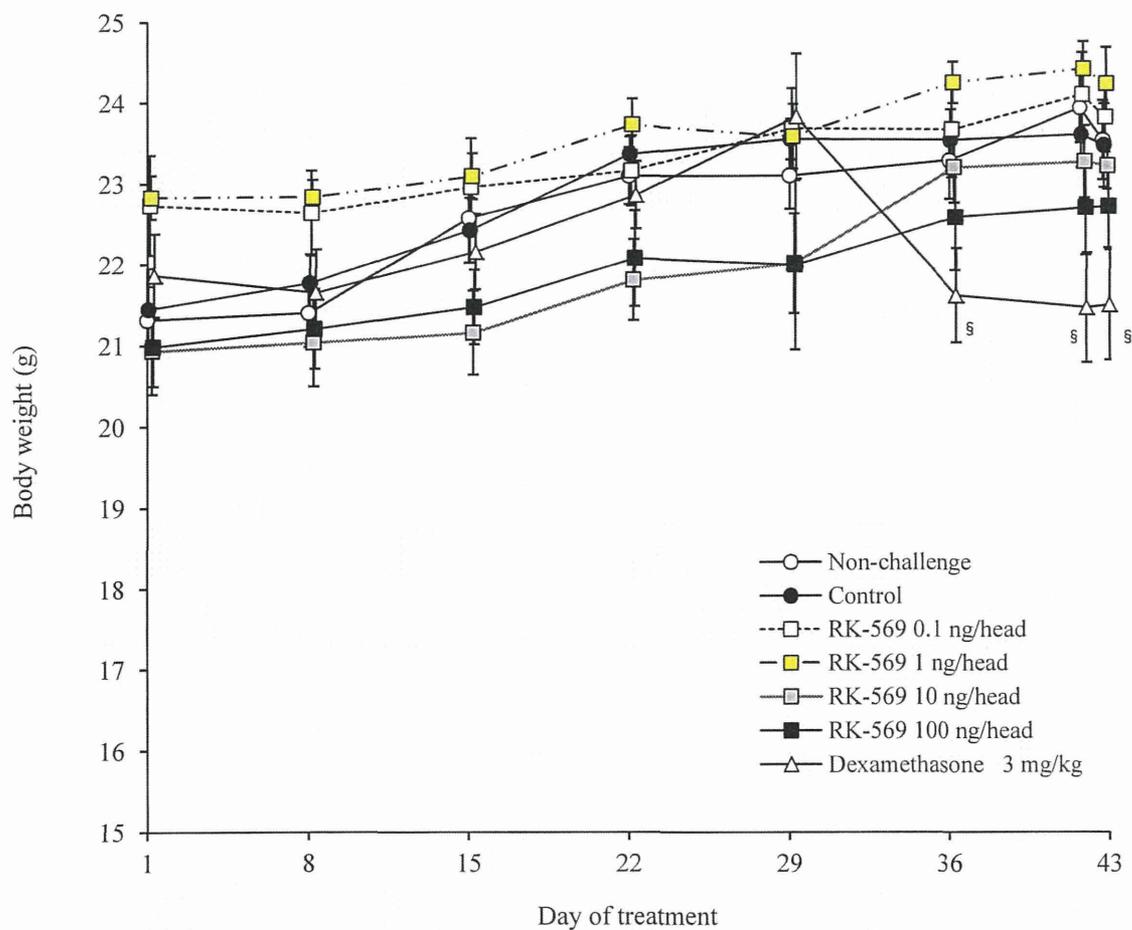


Fig. 1 Body weights in mice treated with RK-569 and Dexamethasone

Data are the mean \pm standard errors of 6 animals.

Student's *t*-test was performed to compare the non-challenge with control (not significant).

Dunnett's test was performed to compare the control with RK-569 groups (not significant).

Student's/Aspin-Welch's *t*-test was performed to compare the control with dexamethasone groups (^s $p < 0.05$).

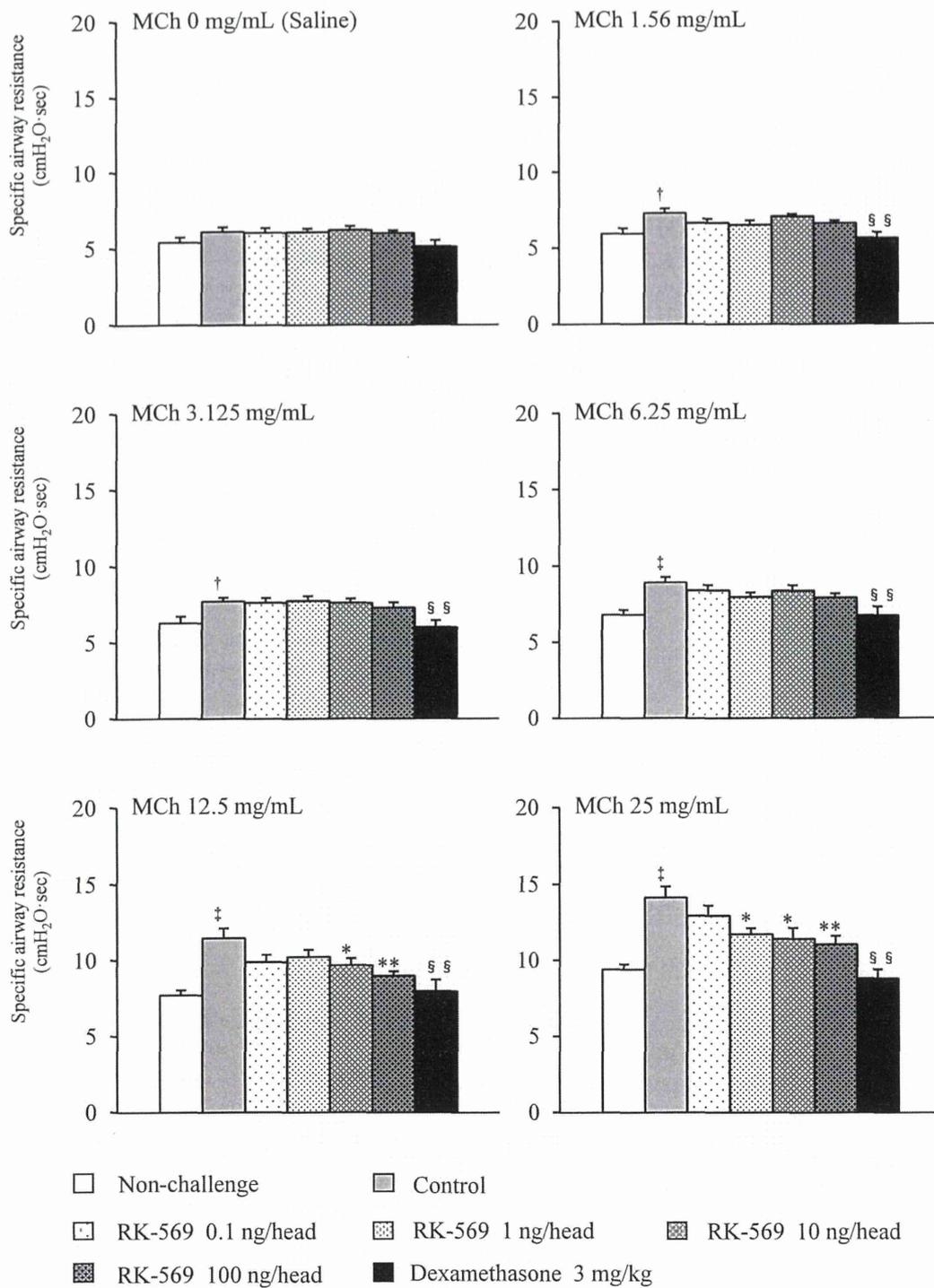


Fig. 2-1 Effects of RK-569 and Dexamethasone on airway hyperresponsiveness induced by ovalbumin in mice

Data are the mean ± standard errors of 6 animals.

Student's *t*-test was performed to compare the non-challenge group with the control group († *p* < 0.05, ‡ *p* < 0.01).

Dunnett's test was performed to compare the control group with the RK-569 groups (* *p* < 0.05, ** *p* < 0.01).

Student's *t*-test was performed to compare the control group with the dexamethasone group (§§ *p* < 0.01).

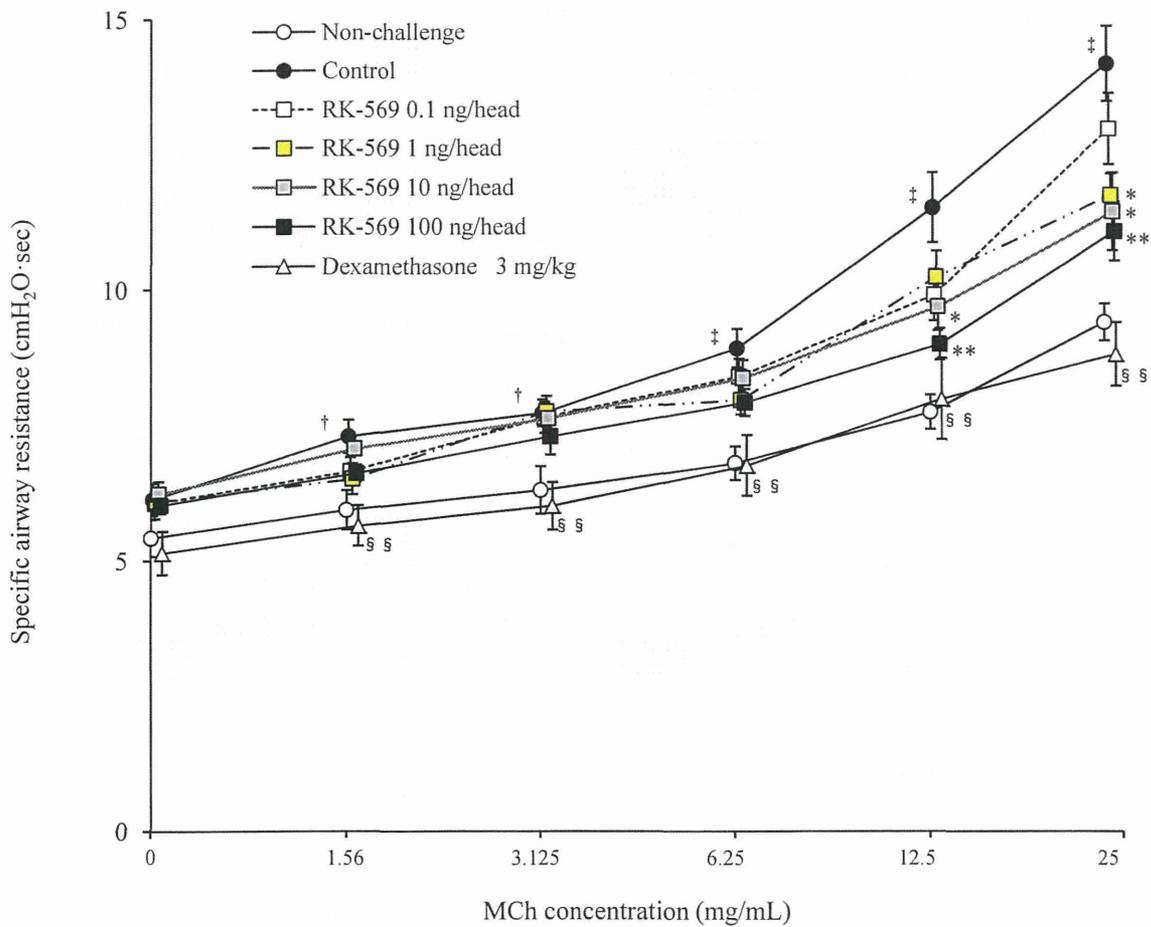


Fig. 2-2 Effects of RK-569 and Dexamethasone on airway hyperresponsiveness induced by ovalbumin in mice

Data are the mean ± standard errors of 6 animals.

Student's *t*-test was performed to compare the non-challenge group with the control group († $p < 0.05$, ‡ $p < 0.01$).

Dunnett's test was performed to compare the control group with the RK-569 groups (* $p < 0.05$, ** $p < 0.01$).

Student's *t*-test was performed to compare the control group with the dexamethasone group (†† $p < 0.01$).

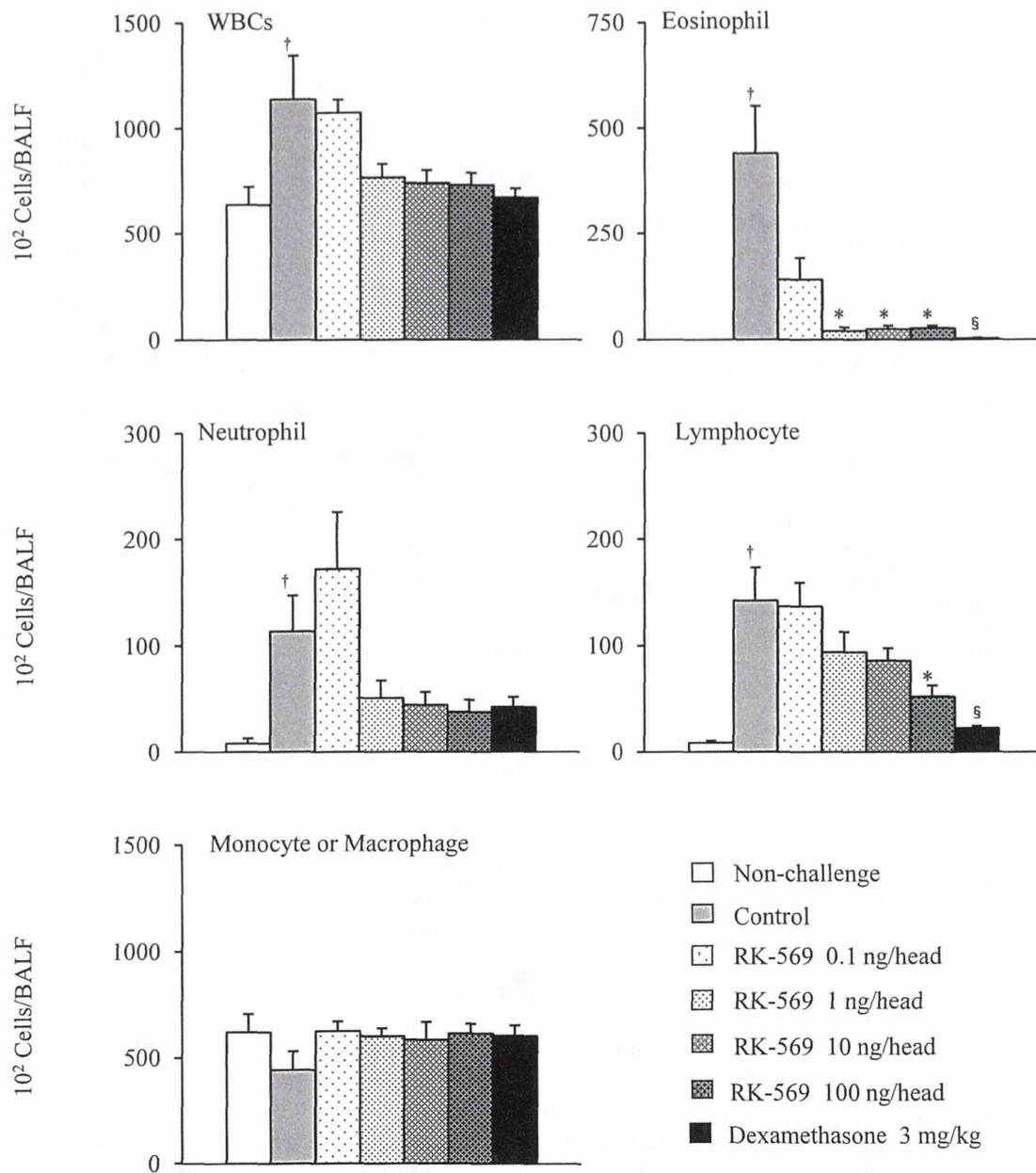


Fig. 3 Effects of RK-569 and Dexamethasone on the changes of bronchoalveolar lavage fluid induced by ovalbumin in mice

Data are the mean \pm standard errors of 5 or 6 animals.

Student's/Aspin-Welch's *t*-test was performed to compare the non-challenge group with the control group ([†] $p < 0.05$).

Dunnett's/Steel's test was performed to compare the control group with RK-569 groups (* $p < 0.05$).

Student's/Aspin-Welch's *t*-test was performed to compare the control group with the dexamethasone group ([§] $p < 0.05$).

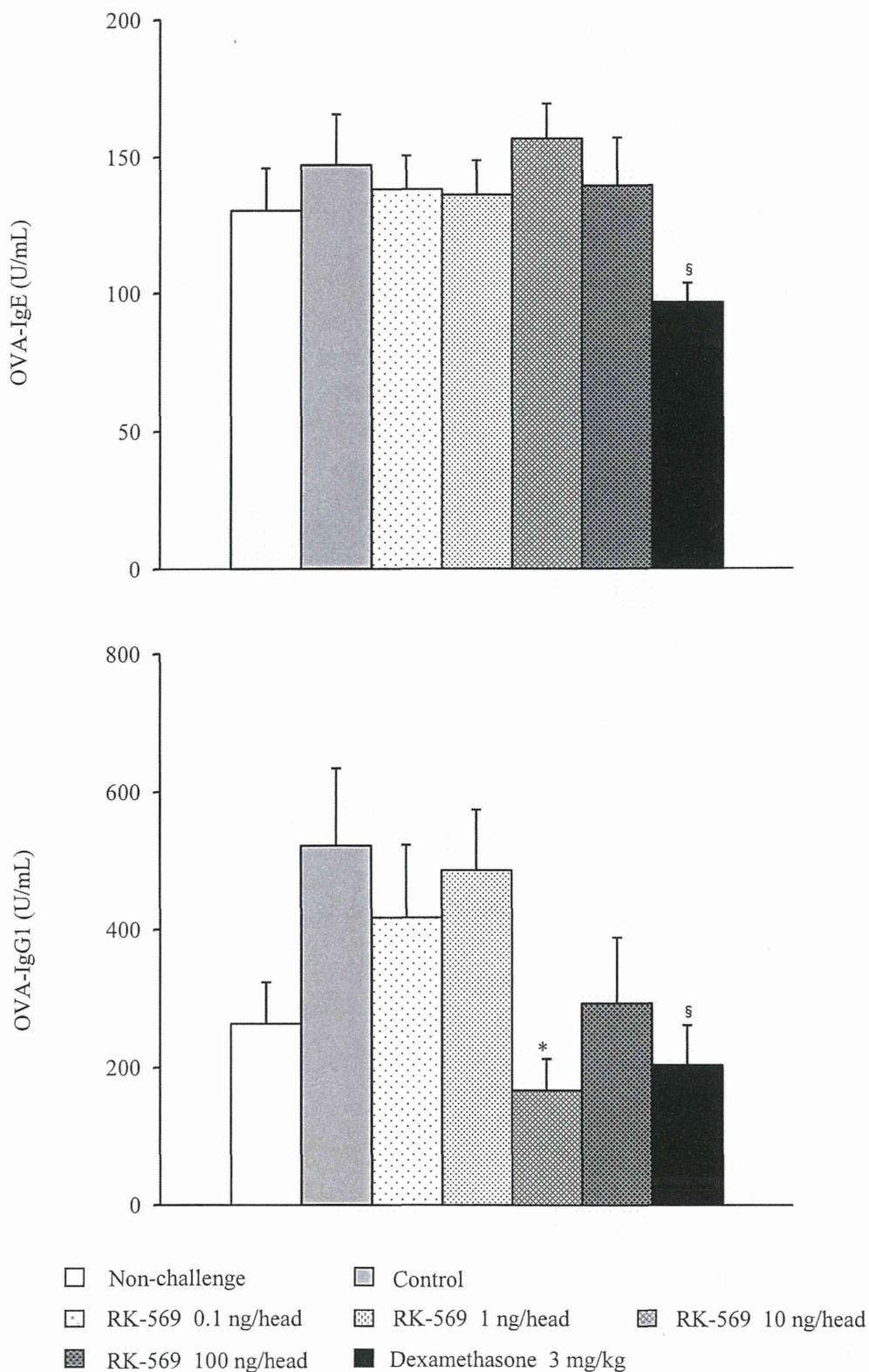


Fig. 4 Effects of RK-569 and Dexamethasone on the changes of OVA-IgE and OVA-IgG1 induced by ovalbumin in mice

Data are the mean \pm standard errors of 6 animals.

Student's *t*-test was performed to compare the non-challenge group with the control group (not significant).

Dunnett's test was performed to compare the control group with the RK-569 groups (* $p < 0.05$).

Student's *t*-test was performed to compare the control group with the dexamethasone group ([§] $p < 0.05$).

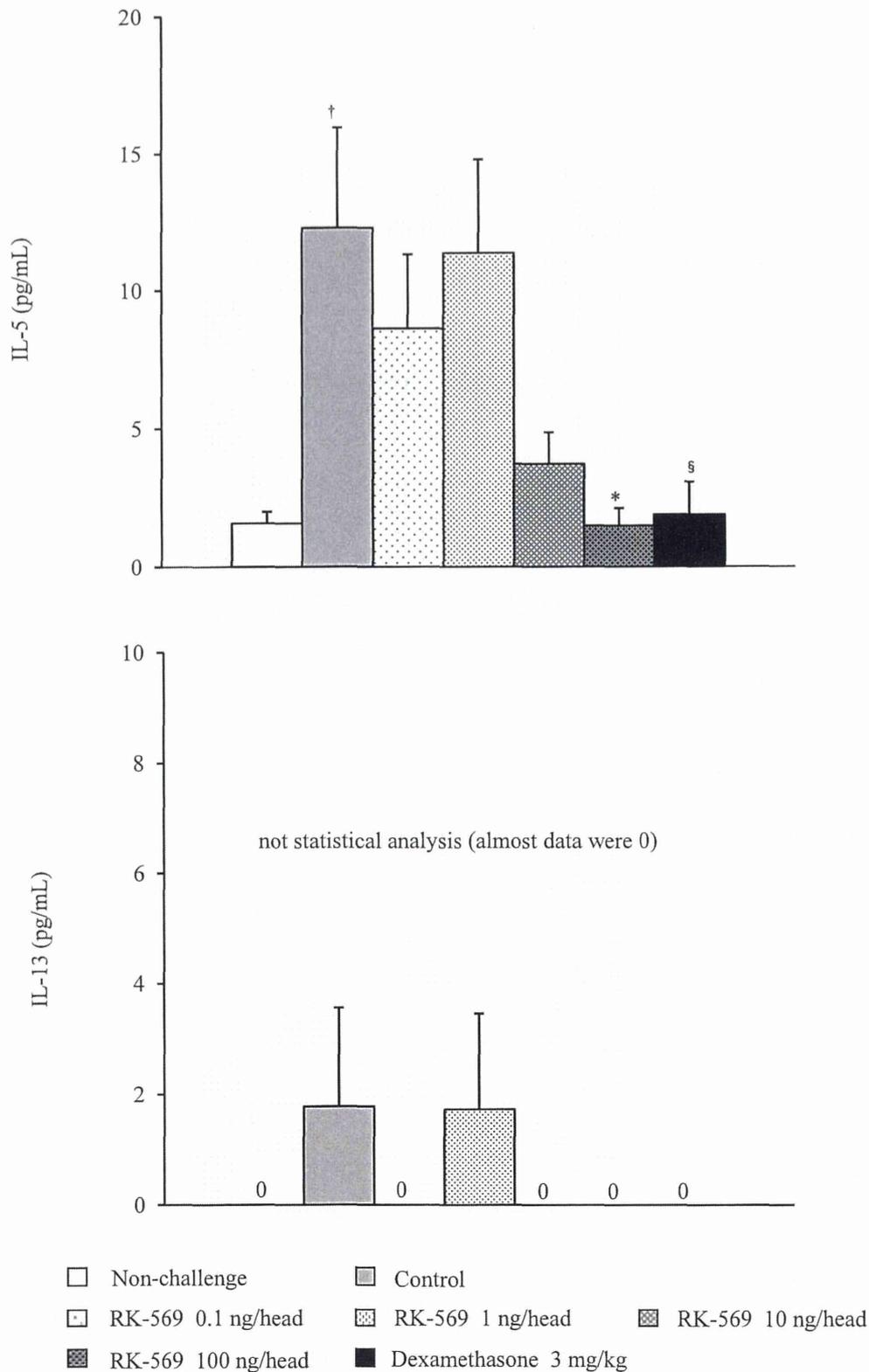


Fig. 5 Effects of RK-569 and Dexamethasone on the changes of interleukin (IL) -5 and -13 induced by ovalbumin in mice

Data are the mean \pm standard errors of 6 animals.

Aspin-Welch's *t*-test was performed to compare the non-challenge group with the control group ([†] $p < 0.05$).

Steel's test was performed to compare the control group with RK-569 groups (^{*} $p < 0.05$).

Aspin-Welch's *t*-test was performed to compare the control group with the dexamethasone group ([§] $p < 0.05$).

Table 1-1 Clinical signs in mice during study periods
Day 1 - 14

Test substance	Route	Dose (ng/head)	Animal No.	Day of treatment														
				1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Non-challenge	i.v.	0	2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Control	i.v.	0	2201	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2202	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2203	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2204	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2205	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2206	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RK-569	i.v.	0.1	2301	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2302	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2303	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2304	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2305	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2306	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	i.v.	1	2401	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2402	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2403	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2404	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2405	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2406	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
i.v.	10	2501	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2502	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2503	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2504	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2505	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2506	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
i.v.	100	2601	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2602	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2603	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2604	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2605	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2606	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Dexamethasone	p.o.	3 mg/kg	2701	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2702	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2703	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2704	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2705	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2706	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormalities.

Table 1-2 Clinical signs in mice during study periods
Day 15 - 28

Test substance	Route	Dose (ng/head)	Animal No.	Day of treatment														
				15	16	17	18	19	20	21	22	23	24	25	26	27	28	
Non-challenge	i.v.	0	2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Control	i.v.	0	2201	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2202	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2203	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2204	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2205	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2206	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RK-569	i.v.	0.1	2301	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2302	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2303	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2304	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2305	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2306	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	i.v.	1	2401	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2402	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2403	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2404	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2405	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2406	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
i.v.	10	2501	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2502	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2503	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2504	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2505	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2506	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
i.v.	100	2601	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2602	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2603	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2604	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2605	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2606	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Dexamethasone	p.o.	3 mg/kg	2701	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2702	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2703	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2704	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2705	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2706	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormalities.

Table 1-3 Clinical signs in mice during study periods
Day 29 - 43

Test substance	Route	Dose (ng/head)	Animal No.	Day of treatment														
				29	30	31	32	33	34	35	36	37	38	39	40	41	42	43
Non-challenge	i.v.	0	2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Control	i.v.	0	2201	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2202	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2203	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2204	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2205	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2206	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RK-569	i.v.	0.1	2301	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2302	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2303	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2304	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2305	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2306	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	i.v.	1	2401	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2402	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2403	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2404	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2405	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2406	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
i.v.	10	2501	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
		2502	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
		2503	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2504	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2505	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2506	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
i.v.	100	2601	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
		2602	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
		2603	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2604	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2605	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2606	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Dexamethasone	p.o.	3 mg/kg	2701	-	-	-	-	-	-	-	-	-	-	-	-	-		
			2702	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
			2703	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2704	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2705	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			2706	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormalities.

Table 2 Body weights in mice treated with RK-569 and Dexamethasone

Test substance	Route	Dose (ng/head)	Animal No.	Day of treatment							
				1	8	15	22	29	36	42	43
Non-challenge	i.v.	0	2101	20.1	20.4	20.8	21.7	21.5	21.8	22.7	22.1
			2102	21.3	21.1	22.1	23.3	23.0	22.5	23.8	23.0
			2103	22.3	22.1	24.0	23.8	23.2	23.4	25.3	24.9
			2104	21.5	22.7	23.8	23.5	23.4	24.1	23.8	24.4
			2105	22.5	22.0	23.4	23.8	24.6	25.0	25.0	24.4
			2106	20.2	20.1	21.3	22.4	22.8	22.8	22.9	22.3
			N	6	6	6	6	6	6	6	6
Mean	21.3	21.4	22.6	23.1	23.1	23.3	23.9	23.5			
S.E.	0.4	0.4	0.6	0.3	0.4	0.5	0.4	0.5			
Control	i.v.	0	2201	22.4	22.4	22.8	23.6	23.4	24.7	25.3	25.3
			2202	21.4	21.6	22.1	23.8	23.0	23.3	23.1	22.1
			2203	22.5	22.8	22.9	23.5	24.4	24.7	23.9	24.7
			2204	22.5	22.3	23.9	23.7	24.2	22.8	23.8	23.3
			2205	19.8	20.8	21.6	22.4	23.0	22.9	22.5	22.6
			2206	20.1	20.7	21.2	23.1	23.2	22.7	22.9	22.7
			N	6	6	6	6	6	6	6	6
Mean	21.5	21.8	22.4	23.4	23.5	23.5	23.6	23.5			
S.E.	0.5	0.4	0.4	0.2	0.3	0.4	0.4	0.5			
RK-569	i.v.	0.1	2301	20.8	20.5	20.2	21.3	21.7	21.7	22.0	22.4
			2302	21.9	22.2	22.8	22.8	22.8	25.5	25.6	25.3
			2303	21.6	22.4	23.5	23.3	24.3	22.3	24.1	23.8
			2304	23.9	23.4	22.9	23.2	23.7	24.2	24.2	24.2
			2305	23.6	23.0	24.0	24.3	24.9	24.7	25.1	24.3
			2306	24.6	24.3	24.3	24.0	24.6	23.5	23.5	22.8
			N	6	6	6	6	6	6	6	6
	Mean	22.7	22.6	23.0	23.2	23.7	23.7	24.1	23.8		
	S.E.	0.6	0.5	0.6	0.4	0.5	0.6	0.5	0.4		
	i.v.	1	2401	22.1	22.2	22.0	22.5	22.1	23.7	24.1	24.2
			2402	22.7	22.4	23.5	23.7	23.9	24.4	24.5	24.3
			2403	22.5	22.6	23.6	24.6	23.6	24.3	25.9	26.2
			2404	23.1	23.2	22.6	23.1	23.1	23.4	23.5	22.9
			2405	22.6	23.1	23.0	24.3	23.6	24.4	24.4	24.0
			2406	24.0	23.5	23.8	24.1	25.1	25.2	24.0	23.7
N			6	6	6	6	6	6	6	6	
Mean	22.8	22.8	23.1	23.7	23.6	24.2	24.4	24.2			
S.E.	0.3	0.2	0.3	0.3	0.4	0.3	0.3	0.4			
i.v.	10	2501	18.9	19.0	19.4	20.5	21.2	22.0	22.5	22.5	
		2502	21.0	20.9	22.1	22.6	21.6	23.5	23.5	23.3	
		2503	20.2	20.6	20.7	21.6	22.1	23.1	22.6	23.0	
		2504	21.1	20.9	20.1	20.3	19.8	21.9	21.9	22.4	
		2505	22.8	23.0	22.6	23.4	24.0	24.5	24.4	24.1	
		2506	21.6	21.8	22.0	22.4	23.3	24.1	24.6	23.9	
		N	6	6	6	6	6	6	6	6	
Mean	20.9	21.0	21.2	21.8	22.0	23.2	23.3	23.2			
S.E.	0.5	0.5	0.5	0.5	0.6	0.4	0.4	0.3			
i.v.	100	2601	19.8	20.5	20.4	21.2	19.7	21.1	20.7	21.0	
		2602	19.8	19.8	20.5	20.8	20.1	20.9	21.2	21.4	
		2603	21.4	21.2	21.5	22.4	23.2	23.5	23.6	23.1	
		2604	21.5	21.9	22.0	22.9	23.8	23.4	23.4	23.6	
		2605	20.5	20.6	21.0	20.7	19.5	21.6	22.9	22.9	
		2606	22.9	23.2	23.4	24.4	25.6	24.9	24.3	24.2	
		N	6	6	6	6	6	6	6	6	
Mean	21.0	21.2	21.5	22.1	22.0	22.6	22.7	22.7			
S.E.	0.5	0.5	0.5	0.6	1.0	0.7	0.6	0.5			

Unit: g.

Student's *t*-test was performed to compare the non-challenge group with the control group (not significant).

Dunnett's/Steel's test was performed to compare the control group with RK-569 groups (not significant).

Table 2 Body weights in mice treated with RK-569 and Dexamethasone (continued)

Test substance	Route	Dose (mg/kg)	Animal No.	Day of treatment							
				1	8	15	22	29	36	42	43
Dexamethasone	p.o.	3	2701	21.1	20.6	21.1	21.4	21.5	21.1	21.7	21.2
			2702	22.4	22.8	23.2	23.7	23.3	21.1	20.4	20.6
			2703	19.8	20.0	20.5	21.7	22.0	19.6	19.1	19.4
			2704	23.0	23.4	23.2	23.5	25.6	22.7	22.4	22.7
			2705	23.1	21.9	22.8	23.5	26.2	23.7	23.9	24.1
			2706	21.8	21.2	22.1	23.3	24.3	21.4	21.2	20.9
			N	6	6	6	6	6	6	6	6
Mean	21.9	21.7	22.2	22.9	23.8	21.6	21.5	21.5			
S.E.	0.5	0.5	0.5	0.4	0.8	0.6 [§]	0.7 [§]	0.7 [§]			

Unit: g.

Student's/Aspin-Welch's *t*-test was performed to compare the control group with the dexamethasone group ([§] $p < 0.05$).

Table 3 Effects of RK-569 and Dexamethasone on airway hyperresponsiveness induced by ovalbumin in mice

	Specific airway resistance (cmH ₂ O·sec)						Dexamethasone 3 mg/kg n=6
	Non-challenge n=6	Control n=6	RK-569				
			0.1 ng/head n=6	1 ng/head n=6	10 ng/head n=6	100 ng/head n=6	
MCh concentration (mg/mL)							
0 (Saline)	5.421 ± 0.338	6.131 ± 0.294	6.061 ± 0.288	6.091 ± 0.219	6.229 ± 0.227	6.025 ± 0.155	5.144 ± 0.397
1.56	5.936 ± 0.363	7.286 ± 0.304 †	6.644 ± 0.255	6.506 ± 0.286	7.063 ± 0.132	6.612 ± 0.154	5.644 ± 0.371 §§
3.125	6.293 ± 0.437	7.712 ± 0.246 †	7.630 ± 0.290	7.738 ± 0.287	7.616 ± 0.246	7.282 ± 0.341	6.003 ± 0.436 §§
6.25	6.786 ± 0.308	8.904 ± 0.356 †	8.382 ± 0.328	7.949 ± 0.269	8.352 ± 0.333	7.899 ± 0.247	6.740 ± 0.558 §§
12.5	7.719 ± 0.316	11.484 ± 0.638 †	9.882 ± 0.476	10.214 ± 0.481	9.669 ± 0.438 *	8.976 ± 0.290 **	7.966 ± 0.748 §§
25	9.377 ± 0.341	14.147 ± 0.697 †	12.934 ± 0.660	11.708 ± 0.391 *	11.408 ± 0.710 *	11.046 ± 0.536 **	8.786 ± 0.589 §§

Each value represents the mean ± standard error.

Student's *t*-test was performed to compare the non-challenge group with the control group († *p* < 0.05, ‡ *p* < 0.01).

Dunnett's test was performed to compare the control group with RK-569 groups (* *p* < 0.05, ** *p* < 0.01).

Student's *t*-test was performed to compare the control group with the dexamethasone group (§§ *p* < 0.01).

Table 4 Effects of RK-569 and Dexamethasone on the changes of bronchoalveolar lavage fluid induced by ovalbumin in mice

	Cell number (cells/BALF)						
	Non-challenge	Control	RK-569				Dexamethasone 3 mg/kg
			0.1 ng/head	1 ng/head	10 ng/head	100 ng/head	
	n=6	n=5	n=6	n=6	n=6	n=6	n=6
WBCs	638 ± 85	1140 ± 204 [†]	1075 ± 63	765 ± 64	738 ± 61	729 ± 57	671 ± 42
Eosinophil	0 ± 0	441 ± 112 [†]	141 ± 50	20 ± 7 [*]	24 ± 7 [*]	26 ± 5 [*]	3 ± 1 [§]
Neutrophil	8 ± 4	114 ± 33 [†]	172 ± 53	51 ± 16	44 ± 12	38 ± 11	43 ± 9
Lymphocyte	9 ± 2	142 ± 31 [†]	137 ± 22	94 ± 18	86 ± 11	52 ± 10 [*]	22 ± 2 [§]
Monocyte or Macrophage	621 ± 86	444 ± 87	625 ± 45	600 ± 37	584 ± 82	614 ± 45	604 ± 48

Each value represents the mean ± standard error.

BALF: bronchoalveolar lavage fluid.

Student's/Aspin-Welch's *t*-test was performed to compare the non-challenge group with the control group ([†] *p* < 0.05).

Dunnett's/Steel's test was performed to compare the control group with RK-569 groups (^{*} *p* < 0.05).

Student's/Aspin-Welch's *t*-test was performed to compare the control group with the dexamethasone group ([§] *p* < 0.05).

Table 5 Effects of RK-569 and Dexamethasone on the changes of OVA-IgE and OVA-IgG1 induced by ovalbumin in mice

	Non-challenge n=6	Control n=6	RK-569				Dexamethasone 3 mg/kg n=6
			0.1 ng/head n=6	1 ng/head n=6	10 ng/head n=6	100 ng/head n=6	
OVA-IgE	130.4 ± 15.5	147.0 ± 18.4	138.2 ± 12.2	136.1 ± 12.4	156.6 ± 12.6	139.4 ± 17.4	96.4 ± 7.1 [§]
OVA-IgG1	263.8 ± 59.6	521.5 ± 112.5	417.1 ± 105.3	485.6 ± 87.9	166.2 ± 45.9 *	292.8 ± 94.8	202.9 ± 58.1 [§]

Each value represents the mean ± standard error.

Student's *t*-test was performed to compare the non-challenge group with the control group (not significant).

Dunnnett's test was performed to compare the control group with RK-569 groups (* *p* < 0.05).

Student's *t*-test was performed to compare the control group with the dexamethasone group ([§] *p* < 0.05).

Table 6 Effects of RK-569 and Dexamethasone on the changes of interleukin (IL) -5 and -13 induced by ovalbumin in mice

	Non-challenge n=6	Control n=6	RK-569				Dexamethasone 3 mg/kg n=6
			0.1 ng/head n=6	1 ng/head n=6	10 ng/head n=6	100 ng/head n=6	
IL-5	1.575 ± 0.424	12.297 ± 3.648 †	8.617 ± 2.699	11.377 ± 3.412	3.726 ± 1.129	1.485 ± 0.635 *	1.891 ± 1.180 §
IL-13	0.000 ± 0.000	1.780 ± 1.780	0.000 ± 0.000	1.728 ± 1.728	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000

Each value represents the mean ± standard error.

IL-13: not statistical analysis (almost data were 0).

Aspin-Welch's *t*-test was performed to compare the non-challenge group with the control group († $p < 0.05$).

Steel's test was performed to compare the control group with RK-569 groups (* $p < 0.05$).

Aspin-Welch's *t*-test was performed to compare the control group with the dexamethasone group (§ $p < 0.05$).

Table 7 Organ weights in mice treated with RK-569 and Dexamethasone

Test substance	Route	Dose (ng/head)	Animal No.	Lung (mg)	Spleen (mg)	Kidneys (mg)	Liver (mg)
Non-challenge	i.v.	0	2101	221	96	224	889
			2102	206	97	262	1001
			2103	235	113	256	1122
			2104	213	88	247	1083
			2105	211	88	279	1055
			2106	196	90	249	953
			N	6	6	6	6
			Mean	214	95	253	1017
S.E.	5	4	7	35			
Control	i.v.	0	2201	259	92	270	1082
			2202	330	89	251	1034
			2203	281	86	287	1252
			2204	273	96	256	1168
			2205	250	106	242	1080
			2206	225	89	249	1018
			N	6	6	6	6
			Mean	270	93	259	1106
S.E.	14	3	7	36			
RK-569	i.v.	0.1	2301	233	101	251	1070
			2302	291	114	248	1302
			2303	293	120	273	1231
			2304	268	105	267	1084
			2305	291	116	290	1209
			2306	255	116	264	926
	N	6	6	6	6		
	Mean	272	112	266	1137		
	S.E.	10	3	6	56		
	i.v.	1	2401	253	113	262	1174
			2402	267	122	278	1101
			2403	270	117	286	1321
			2404	258	91	273	1144
			2405	278	100	282	1238
			2406	237	118	256	962
	N	6	6	6	6		
	Mean	261	110	273	1157		
	S.E.	6	5	5	50		
i.v.	10	2501	227	132	243	1094	
		2502	252	132	261	1179	
		2503	226	105	237	1142	
		2504	228	91	260	1122	
		2505	290	127	270	1135	
		2506	231	121	273	1053	
N	6	6	6	6			
Mean	242	118	257	1121			
S.E.	10	7	6	18			
i.v.	100	2601	228	153	230	880	
		2602	255	148	251	1018	
		2603	229	119	258	1115	
		2604	226	142	265	1104	
		2605	193	118	263	1151	
		2606	257	143	299	1143	
N	6	6	6	6			
Mean	231	137	261	1069			
S.E.	10	6	9	42			

Student's *t*-test was performed to compare the non-challenge group with the control group ($^{\dagger} p < 0.01$).

Dunnett's test was performed to compare the control group with RK-569 groups ($* p < 0.05$, $** p < 0.01$).

Table 7 Organ weights in mice treated with RK-569 and Dexamethasone (continued)

Test substance	Route	Dose (mg/kg)	Animal No.	Lung (mg)	Spleen (mg)	Kidneys (mg)	Liver (mg)
Dexamethasone	p.o.	3	2701	231	41	240	897
			2702	225	44	250	865
			2703	212	45	225	864
			2704	243	47	289	1171
			2705	210	48	280	1101
			2706	212	39	250	910
			N	6	6	6	6
			Mean	222	44	256	968
			S.E.	5	1	10	54
				^s	^{ss}		

Student's/Aspin-Welch's *t*-test was performed to compare the control group with the dexamethasone group (^s $p < 0.05$, ^{ss} $p < 0.01$).

Table 8 Gross pathological findings in mice treated with RK-569 and Dexamethasone

Test substance	Route	Dose (ng/head)	Animal No.	Findings
Non-challenge	i.v.	0	2101	N
			2102	N
			2103	N
			2104	N
			2105	N
			2106	N
Control	i.v.	0	2201	N
			2202	N
			2203	N
			2204	N
			2205	N
			2206	N
RK-569	i.v.	0.1	2301	N
			2302	N
			2303	Liver: Yellow-green plaque, left lobe surface
			2304	N
			2305	N
			2306	N
	i.v.	1	2401	N
			2402	N
			2403	N
			2404	N
			2405	N
			2406	N
	i.v.	10	2501	Spleen: Large size
			2502	Liver: Yellow-green plaque, left lobe surface Spleen: Large size
			2503	N
			2504	Liver: Yellow-green plaque, left lobe surface
			2505	Spleen: Large size
			2506	N
i.v.	100	2601	Liver: Yellow-green plaque, left lobe surface Spleen: Large size	
		2602	Liver: Yellow-green plaque, left lobe surface Spleen: Large size	
		2603	N	
		2604	Liver: Yellow-green plaque, left lobe surface Spleen: Large size	
		2605	Liver: Yellow-green plaque, left lobe surface	
		2606	Liver: Yellow-green plaque, left lobe surface Spleen: Large size	
Dexamethasone	p.o.	3 mg/kg	2701	Spleen: Small size Thymus: Atrophy
			2702	Spleen: Small size Thymus: Atrophy
			2703	Spleen: Small size Thymus: Atrophy
			2704	Spleen: Small size Thymus: Atrophy
			2705	Spleen: Small size Thymus: Atrophy
			2706	Spleen: Small size Thymus: Atrophy

N: No abnormalities.

Table 9 Histopathological findings in mice treated with RK-569 and Dexamethasone

Test substance	Non-challenge					Control					RK-569 0.1 ng/head					RK-569 1 ng/head					RK-569 10 ng/head				
	i.v. n=6					i.v. n=6					i.v. n=6					i.v. n=6					i.v. n=6				
Grade	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4
Bronchus																									
Mononuclear cell infiltration	4	2	0	0	0	0	2	4	0	0	0	2	4	0	0	1	4	1	0	0	0	4	2	0	0
Hyperplasia, goblet cell	6	0	0	0	0	0	2	4	0	0	0	5	1	0	0	2	4	0	0	0	1	4	1	0	0
Lung																									
Mononuclear cell infiltration around the bronchioles and blood vessels	6	0	0	0	0	0	0	3	3	0	0	2	4	0	0	0	5	1	0	0	1	3	2	0	0
Hyperplasia, goblet cell	5	1	0	0	0	0	0	1	2	3	0	0	1	3	2	0	0	3	3	0	1	0	2	3	0

Test substance	RK-569 100 ng/head					Dexamethasone 3 mg/kg				
	i.v. n=6					p.o. n=6				
Grade	0	1	2	3	4	0	1	2	3	4
Bronchus										
Mononuclear cell infiltration	1	3	2	0	0	3	3	0	0	0
Hyperplasia, goblet cell	0	6	0	0	0	5	1	0	0	0
Lung										
Mononuclear cell infiltration around the bronchioles and blood vessels	1	4	1	0	0	5	1	0	0	0
Hyperplasia, goblet cell	0	0	5	1	0	5	1	0	0	0

Grade 0: No change, 1: Very slight, 2: Slight, 3: Moderate, 4: Marked.