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1 **Tolerance and resistance to a nematode challenge are not always mutually exclusive**

2

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24 Abstract

25 The relationship between the manifestations of tolerance (host's ability to reduce the impact of a
26 given level of pathogens) and resistance (host's ability to clear pathogens) has been assumed to be
27 an antagonistic one. Here we tested the hypothesis that mice from strains more resistant to
28 intestinal nematodes will experience reduced tolerance compared to less resistant mice. Three
29 inbred strains of mice were used: C57BL/6 mice have been characterised as susceptible, whereas
30 BALB/c and NIH mice have been characterised as resistant to *Heligmosomoides bakeri* infection.
31 Mice of each strain were either parasitized with a single dose of 250 L₃ *H. bakeri* (n=10) in water or
32 were sham-infected with water (n=10). Body weight, food intake and worm egg output were
33 recorded regularly throughout the experiment. Forty-two days post infection mice were
34 euthanized and organ weights, eggs in colon and worm counts were determined. C57BL/6 mice
35 showed significantly greater worm egg output (P<0.001), eggs in colon (P<0.05) and female worm
36 fecundity (P<0.05) compared to NIH and BALB/c. Parasitized BALB/c mice grew more whilst
37 parasitized C57BL/6 grew less than their sham-infected counterparts during the first two weeks
38 post challenge (P=0.05). Parasitism significantly increased liver, spleen, small intestine and
39 caecum weights (P<0.001), but reduced carcass weight (P<0.01). Average daily gain and worm
40 numbers were positively correlated in NIH mice (P=0.05); however, the relationship was reversed
41 when carcass weight was used as a measure for tolerance. BALB/c mice did not appear to suffer
42 from the consequences of parasitism, with carcass weight similar in all animals. Our hypothesis
43 that strains more resistant to the *H. bakeri* infection are less tolerant compared to less resistant
44 strains is rejected, as the two resistant strains showed variable tolerance. Thus, resistance and
45 tolerance to intestinal nematode infection are not always mutually exclusive.

46

47 Keywords: mice; genetic resistance; infection tolerance; nematodes; performance;

48 *Heligmosomoides bakeri*.

49

50 **1. Introduction**

51 The intestinal trichostrongyloid nematode *Heligmosomoides (polygyrus) bakeri* has been used as a
52 model of chronic intestinal nematode infection for over four decades (Behnke et al., 2006). *H.*
53 *bakeri* infection in mice induces a strongly polarized Th2 immune response, which has been shown
54 to be critical for worm control and expulsion (Reynolds et al., 2012). The mechanisms
55 underpinning helminth expulsion in mice are studied to facilitate predictions about the outcome
56 of similar interactions between helminths and the immune system in livestock and humans, to
57 enable the development of control strategies. The outcome of primary *H. bakeri* infection is
58 strongly influenced by the genetic background of mice, with strains differing in their susceptibility
59 to chronic infection (Reynolds et al., 2012). Whilst between-strain variation in nematode
60 resistance has been previously described (Behnke et al., 2006), there is no evidence of description
61 of variation in tolerance. Resistance describes the ability of the host to clear pathogens, whereas
62 tolerance describes the ability to reduce the health or fitness impact of a given infection intensity
63 (Ayres and Schneider, 2012; Raberg, 2014). Characterising the tolerance of mice strains that differ
64 in their resistance to *H. bakeri* infection will facilitate the selection of the most appropriate mouse
65 strain to model nematodiasis in human and livestock hosts.

66

67 The study of tolerance to parasites and its association with resistance has a long tradition in plant
68 science, but very limited evidence is available from animals. Recently, the individual variation in
69 tolerance to parasites has been described, in wild sheep and rodent populations (Hayward et al,
70 2014; Jackson et al, 2014). Haward et al (2014) observed a positive relationship between tolerance
71 and evolutionary fitness in sheep, with more tolerant animals having higher lifetime breeding
72 success. Jackson et al (2014) on the other hand observed a negative relationship between
73 tolerance and reproduction, with more tolerant animals having reduced reproductive effort. The

74 association between the manifestations of tolerance and resistance to nematodes in animals has
75 been previously assumed to be an antagonistic one (Doeschl-Wilson et al., 2009), although there is
76 no experimental evidence to support this view. Råberg (2014) argued that when analysed
77 simultaneously, tolerance and resistance should be under correlational selection; this implies
78 either a negative relationship between these traits, or the possibility they may be both at
79 intermediate levels.

80

81 Here we tested the hypothesis that between-strain variation in resistance to *H. bakeri* infection
82 will correlate with between-strain variation in tolerance. The expectation was that mouse strains
83 more resistant to the *H.bakeri* infection will be less tolerant compared to less resistant strains.

84

85 **2. Materials and Methods**

86

87 *2.1. Experimental animals and housing*

88 This animal experiment was approved by SRUC's Ethical Review Committee (ED AE 06/2011) and
89 carried out under Home Office authorization (PPL 60/3626). A total of 60 5-wks-old male C57BL/6,
90 NIH and BALB/c mice (n=20 per strain), were housed in a room with an ambient temperature of
91 $21\pm 1^{\circ}\text{C}$ and a 12 h light cycle (07.00 to 19.00 h). Mice were individually housed in solid bottomed
92 cages with fresh sawdust and bedding material provided weekly. Shredded paper was added as
93 environmental enrichment. The three strains were selected based on variation in their
94 susceptibility to infection with *H. bakeri* as defined by their phenotype during the infection.
95 C57BL/6 mice have been characterised as poor responders to *H. bakeri*; they maintain a high
96 worm burden that can persist for over 30 weeks (Behnke et al., 2006). NIH mice have been
97 characterised as strong, early responders to *H. bakeri*; compared to C57BL/6 mice, worm

98 establishment is lower, and worm burdens are cleared out within seven weeks (Behnke *et al.*,
99 2006). BALB/c mice have also been characterised as strong responders, although worm expulsion
100 rate is slower than in NIH mice (Behnke *et al.*, 2006; Reynolds *et al.*, 2012).

101

102 *2.2. Infection protocol and experimental design*

103 The experiment was conducted over two consecutive blocks, balanced for all treatments, of 30
104 mice each. At day 0 of the experiment, mice of each strain received either a single dose of 250 *H.*
105 *bakeri* L₃ suspended in 0.2 ml of water (n=10) or a sham infection of 0.2 ml of water (n=10) via oral
106 gavage (Houdijk and Bunger, 2007). The *H. bakeri*, formerly known as *Heligmosomoides polygyrus*
107 *bakeri* and *Nematospiroides dubius* (Cable *et al.*, 2006), were cultured from mono-specifically
108 infected donor mice. The dose of *H. bakeri* was chosen to produce a subclinical level of infection
109 that has been shown to affect mice growth (Houdijk and Bunger, 2006; 2007).

110

111 Mice were fed *ad libitum* throughout the experiment a maintenance diet (14% crude protein;
112 Special Diet Services, Lillico Biotechnologies, UK). Mice were monitored for 42 days post
113 nematode infection. On day 42 they were euthanized for sample recovery.

114

115 *2.3. Measurements and sample collection*

116 Body weight and food intake: Mice and food refusals were weighed three times weekly
117 throughout the experiment. On each of these days food refusals were weighed out and fresh food
118 added weighed in. From these measurements, food intake was calculated per mouse per day.
119 Food intake and body weight of mice were used as indicators of growth performance.

120

121 Nematode egg counts: Mice were placed onto wire-bottomed cages and faecal samples were
122 collected on wetted cardboard on days 17, 24, 31, 38 post infection to assess faecal egg counts
123 (eggs per g faeces). This was carried out using a modified flotation technique (Christie and Jackson,
124 1982). Faeces were collected over a 12h period, during which a constant rate of egg production
125 was assumed. Egg output was expressed as eggs per 12h (EO) to account for possible dilution
126 effect on faecal egg counts attributed to variable faecal outputs as a consequence of different
127 food intake in different mice strains (Coltherd et al., 2009).

128

129 Internal organ weights, eggs in colon and worm burdens: On day 42 mice were humanely killed
130 via CO₂ inhalation and dissected for sample recovery. The small intestine was weighed, opened up
131 and placed in a tube with PBS, which was then incubated at 37°C for 3 h to allow worms to migrate
132 out of the tissue. Tissue and recovered worms were stored in a 5% formalin solution. Male and
133 female worms were separated and counted. The colon contents were weighed and an egg count
134 was performed with the same floatation technique (Christie and Jackson 1982). The colon egg
135 count was then multiplied by colon contents weight to account for dilution effects arising from
136 variation in food intake and colon content volumes between the different strains. Resultant data
137 were expressed as number of eggs in colon (EIC, number of eggs). The EIC was divided by the
138 number of females counted to obtain an estimate for the *per capita* fecundity (eggs per female).
139 EO, EIC, *per capita* fecundity and total worm counts were used to confirm variation in resistance of
140 the strains. EIC and worm counts were used in tolerance estimates, as explained below.

141 Measures of tolerance: Individual tolerance was estimated in two different ways. Firstly, we
142 associated carcass weight at dissection (true reflection of performance) and worm burdens
143 recovered at dissection (accurate estimate of parasite load). We also associated average daily gain,
144 which is often used as an indirect indicator for performance and eggs in colon (EIC), as an indirect

145 indicator for parasite load. Our expectation was that tolerance estimates will be similar in both
146 cases.

147

148 *2.4. Statistical analysis*

149 Data were analysed in Genstat 11th Edition (VSN International LTD, 2008). Model assumptions
150 were tested on normality of means and residuals. Average daily body weight gain and food intake
151 during worm establishment (P1: days 0-16) and the established infection (P2: days 17-42) were
152 analysed through a 3 x 2 factorial ANOVA (3 strains x 2 levels of parasitism) with pre-infection
153 body weight used as covariate. Carcass and internal organ weights were analysed through the
154 same 3 x 2 factorial ANOVA, again with pre-infection body weight as covariate. EIC, EO, worm
155 counts and worm fecundity were analysed in parasitised animals by one-way ANOVA (3 strains).
156 The EO data were analysed in a repeated measure model. Due to the skewed nature of the data,
157 EO, EIC and *per capita* fecundity were log₁₀ (n) transformed. These are reported as back-
158 transformed least-square means, accompanied by lower and upper confidence intervals,
159 calculated from back-transforming least-square mean of transformed data (m), m–S.E. and m+S.E
160 respectively. Experimental round was included in both statistical models as block. Effects with P-
161 values less than 0.05 are considered significant whilst those with P-values between 0.05 and 0.10
162 are described as tendencies or trends. Pearson's correlations were performed between
163 aforementioned *a priori* selected parasitological and performance data to characterise the
164 tolerance of different mice strains to the *H. bakeri* infection.

165

166 **3. Results**

167 *3.1. H. bakeri* nematodes were more prolific in C57BL/6 than in NIH or BALB/c mice

168 There was a significant strain effect on EO ($P < 0.001$) with C57BL/6 mice excreting more eggs
169 compared to NIH and BALB/c. EO eggs/12h reached 48,000 (39,000-60,000) in C57BL/6 mice,
170 25,000 (20,000-31,000) in BALB/c mice and 24,000 (20,000-30,000) in NIH mice, day 38 post
171 challenge. There was a significant time effect, with EO increasing over time in all strains ($P = 0.004$).
172 The strain x time interaction was also significant, with the rate of increase being greater in
173 C57BL/6 mice compared to mice from the other strains (Figure 1).

174

175 <<Figure 1 here>>

176

177 EIC determined on day 42 was significantly affected by strain at the same direction as EO
178 ($P = 0.033$); C57BL/6 mice had significantly greater EIC compared to mice of the other two strains
179 (Figure 2).

180

181 <<Figure 2 here>>

182

183 There was no significant strain effect on total ($P = 0.189$), male ($P = 0.239$) or female ($P = 0.156$) worm
184 counts, although worm burdens were 40% greater in C57BL/6 mice compared to NIH (Figure 3).
185 Strain significantly affected *per capita* fecundity ($P = 0.045$), which averaged 535 (475-604), 338
186 (275-415) and 280 (230-341) eggs/female worm in C57BL/6, BALB/c and NIH mice, respectively.

187

188 <<Figure 3 here>>

189

190 *3.2. The impact of parasitism on performance was short-lived and strain-dependant*

191 Infection reduced food intake in each strain during the first 16 days post challenge (P1); across
192 strains, food intake of parasitized and sham-infected mice averaged 4.23 and 4.64 g/day,
193 respectively ($P<0.001$; Table 1). NIH mice consumed the most and C57BL/6 consumed the least
194 food ($P<0.001$). Between days 17-42 post infection (P2), the strain effect on food intake was
195 sustained with C57BL/6 mice consistently eating the least and NIH mice eating the most food
196 ($P<0.001$). However, the effect of parasitism disappeared during this period; across strains, food
197 intake of parasitized and sham-infected mice averaged 4.40 and 4.32 g/day, respectively.

198

199 <<Table 1 here>>

200

201 During P1, body weight gain did not differ between parasitized and sham-infected mice across
202 strains ($P=0.540$), whilst NIH mice grew faster than C57BL/6 mice, with BALB/c being intermediate
203 ($P<0.001$; Table 1). However, an interaction demonstrated that parasitized BALB/c mice grew
204 more and parasitized C57BL/6 grew less than their sham-infected counterparts ($P=0.056$). During
205 P2, there was no significant difference in body weight gain between parasitized and sham-infected
206 mice ($P=0.432$). The strain effect on body weight gain remained significant, with NIH mice growing
207 faster compared to C57BL/6 and BALB/c mice ($P<0.001$).

208

209 *3.3. Parasitism and mouse strain had an impact on internal organs weight*

210 Strain significantly affected the weight of most internal organs measured (Table 2). The weight of
211 liver, spleen, small intestine and caecum were significantly greater in parasitized mice compared
212 to non-parasitized ones ($P<0.01$). However, the interaction between parasitism and strain was
213 significant for caecum and spleen weight; the caecum weighed significantly more in parasitized
214 C57BL/6 mice ($P=0.030$) compared to parasitized mice from the other strains, whereas the spleen

215 of parasitized NIH mice weighed significantly more compared to parasitized mice from the other
216 strains ($P < 0.001$). Across strains, spleen weight was negatively correlated with total number of
217 worms recovered and with EIC; mice with heavier spleens had fewer worms ($r = -0.46$; $P = 0.01$) and
218 EIC ($r = -0.63$; $P = 0.001$)

219

220 Final body weight at dissection was affected by strain; NIH mice weighed the most and C57BL/6
221 the least, with BALB/c weighing intermediate ($P = 0.028$). Carcass weight followed a similar pattern
222 across strains ($P < 0.001$). Parasitism did not affect the final BW of mice but significantly reduced
223 carcass weight ($P = 0.003$).

224

225 <<Table 2 here>>

226 <<Table 3 here>>

227

228 *3.4. Using body weight gain to estimate tolerance may underestimate the impact of parasitism on*
229 *performance*

230 Table 3 shows that for NIH mice only, there was a significant positive correlation between
231 averaged daily gain (ADG) and worm numbers ($r = 0.62$; $P = 0.05$). However, when carcass weight
232 was used to calculate tolerance, this relationship was reversed; the greater the number of worms
233 recovered at dissections, the lower the carcass weight of NIH mice ($r = -0.48$; $P > 0.05$). Although the
234 correlations between carcass weight and worm counts in BALB/c mice were not significant, BALB/c
235 mice appear to be the least affected by the infection compared to the other strains.

236

237 **4. Discussion**

238 This is the first study, where the tolerance to a nematode infection was quantified in strains of
239 mice that differ in their degree of resistance to *H. bakeri*. Three major outcomes were delivered
240 from the study. Firstly, we demonstrated that resistance and tolerance to a nematode parasite
241 infection are not necessarily mutually exclusive. The resistant BALB/c mice appear to be more
242 tolerant and least affected by the infection compared to the other strains. Secondly, we
243 demonstrated variation in tolerance between different strains of mice, which emphasizes the
244 importance of selecting the appropriate strain as a model of chronic nematode infection in
245 different mammalian hosts. Thirdly, we have clearly shown that body weight gain may not be the
246 best performance indicator to estimate the tolerance to parasitic challenge. Carcass
247 measurements revealed that the impact of parasitism was underestimated when based on body
248 weight gain measurement, as a consequence of an increase in the weight of internal organs in
249 parasitized mice, including spleen, liver, small intestine and caecum.

250

251 We used four measurements, namely EO, EIC, *per capita* fecundity and total worm counts to
252 confirm variation in resistance, i.e. the ability of the host to clear pathogens, of three mice strains.
253 Throughout the experiment, C57BL/6 mice excreted the largest number of eggs, compared to mice
254 from the other strains. Similarly, estimates of EIC and fecundity at dissection confirmed that
255 C57BL/6 mice were the most susceptible to the infection, as previously reported (Behnke et al,
256 2006). The genetic factors controlling resistance to *H. bakeri* include the major histocompatibility
257 complex (MHC) H-2 loci with C57BL/6 mice categorised as susceptible and BALB/c and NIH mice as
258 resistant genotypes (Reynolds et al, 2012). During trickle infections, differences in worm burdens
259 are evident within 6 weeks of the first challenge (Behnke et al, 2006). However, following a single
260 challenge worm expulsion starts after week 10 post infections (Robinson et al, 1989), which would

261 be consistent with the similar worm numbers at 6 weeks post infection in all mice strains in our
262 experiment.

263

264 To estimate tolerance in the three strains of mice, body weight throughout the experiment and
265 carcass at dissections were taken. This detailed monitoring revealed that using carcass weight to
266 estimate tolerance may be the most appropriate indicator of animal performance. Parasitism
267 reduced carcass weight by an average of 5%, an effect that was not evident from body weight
268 monitoring. This was due to increases in internal organ weight in parasitized mice, namely the
269 small intestine, caecum, liver and spleen, which masked the penalties of parasitism on
270 performance. Body weight gain measurements alone showed that parasitism did not penalize
271 performance of NIH and C57BL/6 mice, whereas parasitized BALB/c mice appeared to grow faster
272 than their sham-infected counterparts. Our findings strongly suggest that the well established
273 negative impact of gastrointestinal nematode infections on animal performance, as measured by
274 change in body weight (e.g. Sykes 1997) may be underestimated.

275

276 The increase in the weight of the small intestine observed in parasitized mice is in agreement with
277 previous studies (Wong et al., 2007). This may be related to increased local inflammatory
278 responses (Cywiniska et al 2004), plasma extravasation and mucin production as a consequence of
279 parasitism (Wakelin, 1978). Furthermore, crypt hypertrophy and an increase in villi height has
280 been observed in mice infected with *H. polygyrus*; it has been hypothesised that this response is
281 adaptive to increase mucosal surface, to maintain nutrient absorption in the presence of the
282 nematodes (Wong et al., 2007). Spleen size was significantly increased in parasitized mice; spleen
283 enlargement has been observed during infections with filarial and gastrointestinal nematodes in
284 variety of hosts (John, 1994; Wong et al., 2007). This increase in size is likely the direct outcome of

285 splenic cell proliferation (Katona et al., 1983), which reflects host resistance. Although spleen size
286 was increased in all parasitized animals, the increase was greater in the resistant NIH mice, which
287 is in agreement with previous evidence (Ali and Behnke, 1985). *H. bakeri* infection also affected
288 liver weight in all strains. Hepatomegaly has been previously associated with nematode infection,
289 particularly during the visceral migration of the larvae in species such as *Toxocara canis* (Pecinali et
290 al., 2005) and in certain strains of mice during *H. bakeri* infection (Wong et al., 2007). It has been
291 shown that seven days post a *H. polygyrus* infection liver cytokines, including pro-inflammatory
292 cytokines, were up-regulated, in the absence of pathological and inflammatory response (Helmbly,
293 2009). This early up-regulation of pro-inflammatory cytokines, such as IFN- γ , may be responsible
294 for a liver inflammation at later stages of infection, which may result in hepatomegaly, as this was
295 observed in our study.

296

297 Our hypothesis was that strains more resistant to the *H. bakeri* infection are less tolerant
298 compared to less resistant strains. As a consequence of the detailed monitoring of host's
299 performance, it became apparent that the two resistant strains varied in their tolerance levels
300 (Table 3), with BALB/c more tolerant than NIH mice and thus the hypothesis is rejected. This
301 supports the view that disease resistance and tolerance are not always mutually exclusive, but
302 they may both be at intermediate levels if this promotes evolutionary fitness (Råberg, 2014). The
303 mechanistic basis of this relationship is still to be determined. The study has also clearly
304 characterised the variation in tolerance to *H. bakeri* of different strains of mice. Although it is
305 unclear at this stage what the underlying basis of this variation was, it ought to be considered to
306 inform on model choice for chronic nematode infection in human and animal hosts. BALB/c mice
307 do not appear to be a good model for livestock, as livestock do not tolerate well nematode
308 challenge, which is evident from the penalties on performance within weeks from the onset of an

309 infection (Coop et al, 1982). However, in humans, nematode parasitic gastroenteritis may be
310 asymptomatic and is often not manifested with changes in body weight or body weight gain
311 (<http://emedicine.medscape.com/article/224011-clinical>). Therefore, BALB/c mice may be a more
312 appropriate model for parasitic gastroenteritis in humans, whilst C57BL/6 mice may be the better
313 model for livestock.

314

315

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322

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324

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386 **Legends to Figures**

387

388 Figure 1. Backtransformed means of egg output (EO) of mice infected with 250 *Heligmosomoides*
389 *bakeri* infective larvae. Mice were one of three strains (n=10): C57BL/6, NIH, or BALB/c, which
390 have been characterised as susceptible or resistant to *H. bakeri* infection. Lower and upper error
391 bar values are backtransformed values of log-transformed mean minus or plus its standard error,
392 respectively.

393

394 Figure 2. Backtransformed means of colon egg counts (CEC) of mice infected with 250
395 *Heligmosomoides bakeri* infective larvae. Mice were one of three strains (n=10): C57BL/6, NIH, or
396 BALB/c, which have been characterised as susceptible or resistant to *H. bakeri* infection. Lower
397 and upper error bar values are backtransformed values of log-transformed mean minus or plus its
398 standard error, respectively.

399

400 Figure 3. Backtransformed means of adult male, adult female, and total worm burdens of mice
401 infected with 250 *Heligmosomoides bakeri* infective larvae. Mice were one of three strains (n=10):
402 C57BL/6, NIH, or BALB/c, which have been characterised as susceptible or resistant to *H.bakeri*
403 infection. Lower and upper error bar values are backtransformed values of log-transformed mean
404 minus or plus its standard error, respectively.

Figure 1

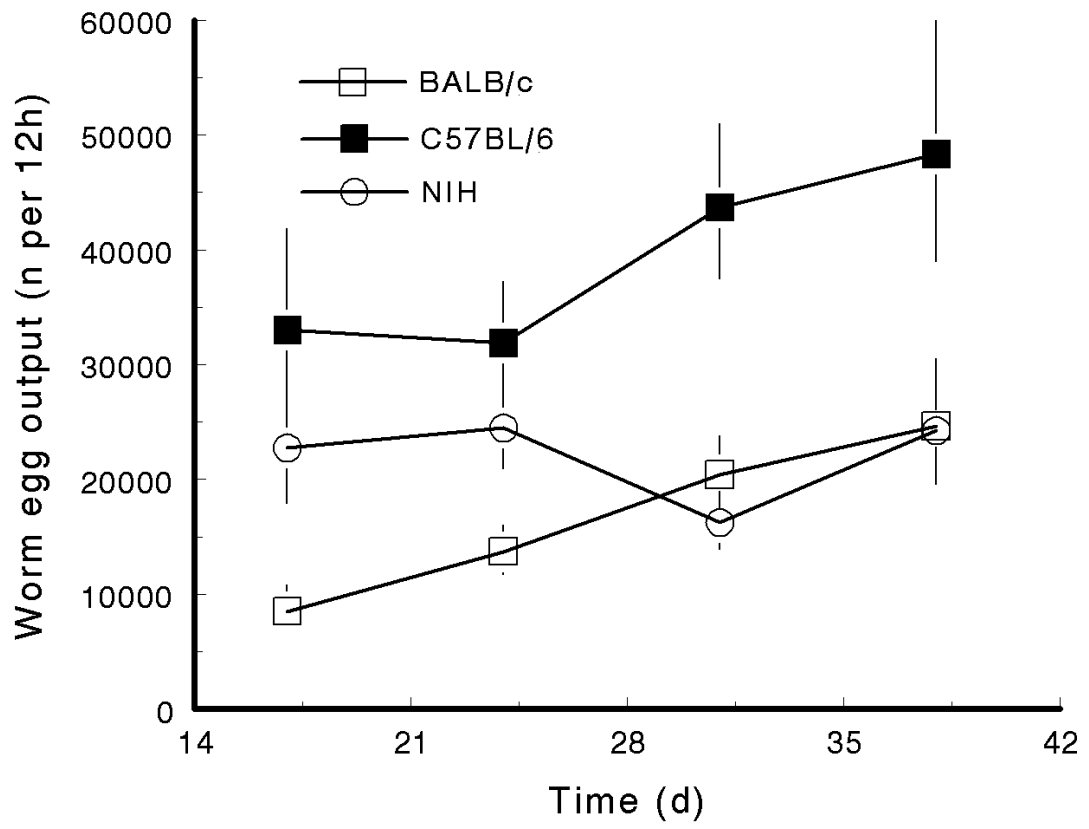


Figure 2

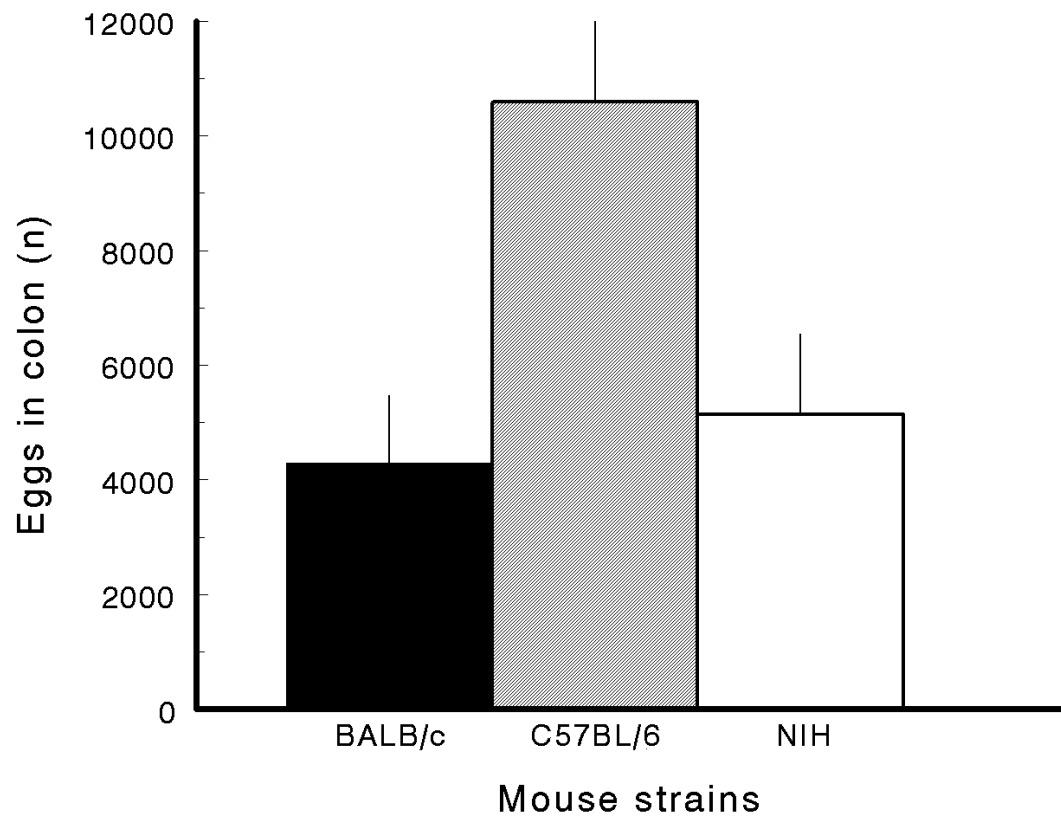


Figure 3

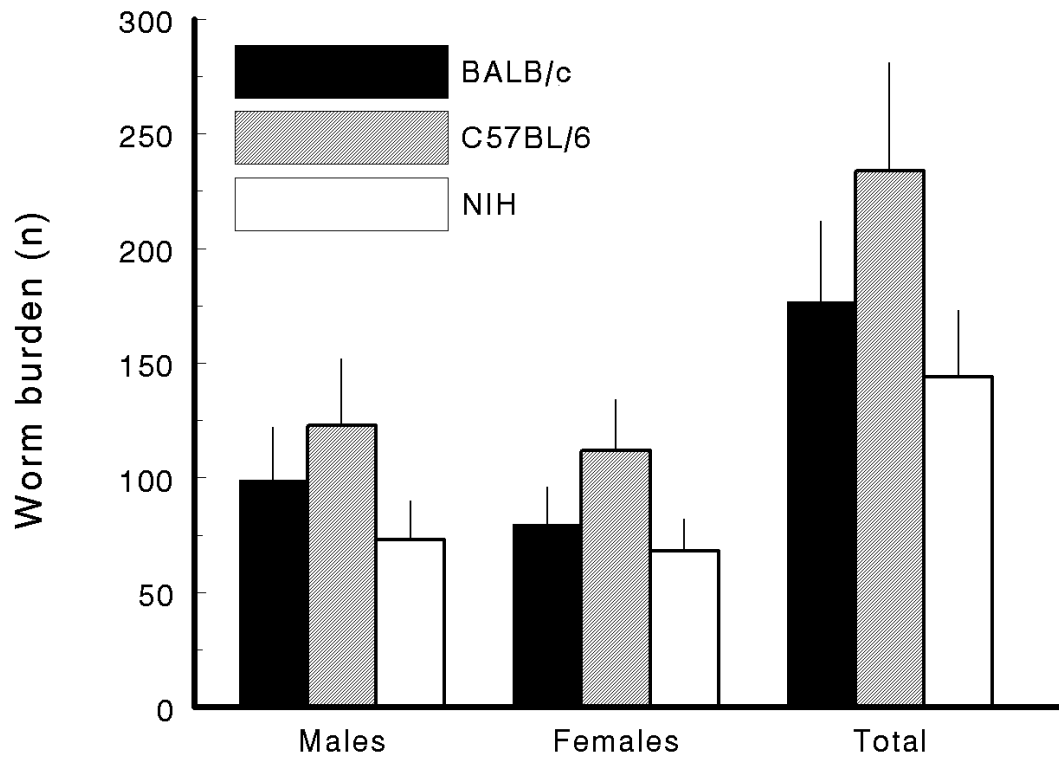


Table 1. Mean voluntary food intake (VFI, g/day) and average daily gain (ADG, g/day) of C57BL/6, NIH or BALB/c mice over 42 days after infection with 250 *Heligmosomoides bakeri* infective larvae in 0.2 ml water (Par) or sham-infected with 0.2 ml water (Sham).

Strain	Treatment	Period 1 ¹		Period 2 ¹	
		VFI	ADG	VFI	ADG
BALB/c	Par	4.18	0.271	4.52	0.152
	Sham	4.56	0.187	4.46	0.115
C57BL/6	Par	3.84	0.130	3.71	0.097
	Sham	4.01	0.169	3.69	0.117
NIH	Par	4.84	0.359	4.97	0.157
	Sham	5.31	0.365	4.80	0.151
	S.E.D. ²	0.095	0.036	0.114	0.021
Significance (P values) ³					
Strain		<0.001	<0.001	<0.001	0.009
Parasitism		<0.001	0.540	0.149	0.432
Strain × Parasitism		0.179	0.056	0.579	0.126

¹Period 1 relates to nematode establishment (day 0 – 16), whereas Period 2 relates to having a potent infection (day 1-42)

²Standard error of the differences between the means for the interaction term (n=10)

³The effect of the block was not significant and thus results are reported across the two blocks

Table 2. Final body weight, carcass, viscera and spleen weights (g) of C57BL/6, NIH or BALB/c mice, 42 days after infection with 250 *Heligmosomoides bakeri* infective larvae in 0.2 ml water (Par) or sham-infected with 0.2 ml water (Sham).

Strain	Treatment	BW ¹	Carcass	Stomach	SI ²	LI ³	Caecum	Liver	Spleen
BALB/c	Par	29.1	21.5	0.34	2.83	0.35	0.68	1.50	0.138
	Sham	27.1	21.7	0.39	1.59	0.32	0.51	1.32	0.101
C57BL/6	Par	25.3	18.9	0.39	2.73	0.24	0.92	1.23	0.097
	Sham	25.4	20.8	0.32	1.45	0.21	0.59	1.11	0.067
NIH	Par	32.6	24.8	0.57	3.07	0.32	0.68	1.71	0.195
	Sham	32.3	26.2	0.48	1.93	0.29	0.63	1.58	0.113
	S.E.D. ⁴	0.90	0.68	0.093	0.121	0.040	0.073	0.075	0.006
Significance (P-values) ⁵									
Strain		<0.001	<0.001	0.022	<0.001	0.002	0.020	<0.001	<0.001
Parasitism		0.166	0.003	0.475	<0.001	0.258	<0.001	0.002	<0.001
Strain × Parasitism		0.214	0.168	0.503	0.679	0.966	0.030	0.792	<0.001

¹Final body weight at post mortems

²Small Intestine with content

³Large Intestine without content

⁴Standard error of the differences between the means for the interaction term (n=10)

⁵The effect of the block was not significant and thus results are reported across the two blocks.

Table 3. Pearson's correlations¹ between worm counts or the number of worm eggs in the colon contents (EIC), and average daily body weight gain (ADG), carcass and spleen weight in selected mice strains (n=10).

		BALB/c	C57BL/6	NIH
Worms	ADG	0.22	0.12	0.62*
	Carcass	0.37	-0.08	-0.48
	Spleen	-0.35	-0.62*	-0.49
EIC	ADG	0.30	-0.31	0.33
	Carcass	0.50	-0.06	-0.15
	Spleen	0.16	-0.36	-0.50

¹Superscripts denote significance of r at P<0.05 (*)