CORRELATED RESPONSE IN LITTER SIZE COMPONENTS IN RABBITS SELECTED FOR LITTER SIZE VARIABILITY

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10 M.J. Argente[1*], E.W. Calle[2], M.L. García[1], A. Blasco[2]
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14 [1]*Departamento de Tecnología Agroalimentaria. Universidad Miguel Hernández de Elche,*
15
16 *Ctra de Beniel Km 3.2, 03312 Orihuela, Spain.*
17
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19
20
21 [2]*Institute for Animal Science and Technology. Universitat Politècnica de València, P.O. Box*
22
23 *22012. 46022 Valencia, Spain.*
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27 *Corresponding author: M.J. Argente. e-mail: mj.argente@umh.es
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32 Short title: Correlated Responses in litter size components
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16   **Summary**

17   A divergent selection experiment for litter size environmental variability has been carried out

18   in rabbits at the University Miguel Hernández of Elche in Spain over seven generations.

19   Environmental variability of litter size was estimated as phenotypic variance within female

20   after correcting for year-season and parity-lactation status. The aim of this study was to

21   analyse the correlated responses to selection in litter size components. Ovulation rate (OR)

22   and number of implanted embryos (IE) were measured by laparoscopy at 12 d of the second

23   gestation in females. At the end of the second gestation, litter size was measured as total

24   number of kits born at second parity (TB). Embryonic (ES), fetal (FS) and prenatal (PS)

25   survival were estimated as IE/OR, TB/IE and TB/OR, respectively. A total of 405

26   laparoscopies were performed. Data were analysed using Bayesian methodology. Correlated

27   response to selection for litter size environmental variability in litter size components was

28   estimated either as genetic trends from the estimated genetic means and as phenotypic

29   differences between lines. Ovulation rate was similar in both lines. However, after seven

30   generations of selection, the line selected for homogeneity in litter size showed more embryos

31   at implantation (1.09 embryos for genetic means and 1.23 embryos for phenotypic means, P =

32   1.00) and higher embryonic survival than the heterogeneous one (0.07 for genetic means and

33   0.08 for phenotypic means, P = 0.99). A higher uterine overcrowding of embryos in the

34   homogeneous line did not penalise fetal survival, and as a result, this line continued showing

35   a greater number of kits born at birth (1.01 kits for genetic means and 1.30 kits for phenotypic

36   means, P = 0.99, in the seventh generation of selection). In conclusion, a decrease in litter size

37   variability showed a favourable effect on embryonic survival leading to a higher litter size at

38   birth.

Introduction

Interest in the genetic determination of environmental variance is increasing, since the livestock industry is demanding a more homogeneous production (Mulder *et al.* 2008); for example, increasing uniformity in litters can help management and increase litter viability. On the other hand, a decrease in environmental variance will increase the heritability, being particularly interesting for increasing the response to selection in low heritability traits, such as litter size (Argente *et al.* 2010; Formoso-Rafferty *et al.* 2016). A direct divergent selection experiment for litter size environmental variance is currently being carried out in rabbits. The experiment has had success, showing a difference for litter size variability of 30% between the divergent lines (Blasco *et al.* 2017). Litter size environmental variance is related to litter size, but the sign of this relationship is controversial. In pigs' litter size and in rabbits' uterine capacity, Yang *et al.* (2011) found that, after the Box-Cox transformation, the relationship between mean and environmental variance changed from negative to positive. Hence, it will be interesting to learn how this selection process is affecting litter size, and also at which gestation moment the selection process is acting. The objective of this study is to analyse the correlated responses to selection for litter size environmental variability in litter size components.

Materials and Methods

Animals

A divergent selection experiment for litter size environmental variability has been carried out in rabbits during seven generations. Each divergent line had approximately 125 females and 25 males per generation. Selection was based on phenotypic variance of litter size within female

63   after correcting litter size for year-season and parity-lactation status (first parity, and lactating

64   or not at mating in other parities). As all litters have almost the same genetic determination

65   (Piles *et al.* 2006) and the same environmental permanent effects, after correcting for

66   systematic effects, the phenotypic variance intra-doe is a record of its residual variance (Ve).

67   The selection pressure on females was approximately 20% in each line. Males were chosen

68   within sire families in order to avoid an increase of inbreeding. All animals were kept on a

69   farm at the Miguel Hernández University of Elche (Spain). Rabbits were fed a standard

70   commercial diet (218 g acid detergent fibre and 174 g crude protein per kg of dry matter;

71   Cunilactal, Nutreco). Food and water were provided *ad libitum*. Females were kept in

72   individual cages under a constant photoperiod of 16 h continuous light: 8 h continuous

73   darkness and controlled ventilation. They were first mated at 18 wk of age and at 10 d after

74   parturition thereafter. Litters were not standardised. All experimental procedures involving

75   animals were approved by the Miguel Hernández University of Elche Research Ethics

76   Committee (Reference number DTA-MJA-001-11), in accordance with Council Directives

77   98/58/EC and 2010/63/EU.

78   *Traits*

79   Ovulation rate (OR), estimated as the number of corpora lutea in both ovaries, and the number

80   of implanted embryos (IE), estimated as the number of implantation sites, were measured by

81   using laparoscopy at d 12 of second gestation in females from 6th and 7th generations of

82   selection. The laparoscopy technique is described in detail by Argente *et al.* (2003). At the

83   end of the second gestation, litter size was measured as total number of kits born at second

84   parity (TB). Embryonic survival (ES) was estimated as IE/OR, fetal survival (FS) was

85   estimated as TB/IE, and prenatal survival (PS) was estimated as TB/OR.

86   Data from 405 laparoscopies and litter size at second parity were analysed. There were 2,082

87 records for litter size residual variance. The total number of animals in the pedigree was

88 2,775.

Statistical Analyses

90 Correlated response in litter size at second parity and its components was estimated as

91 differences between lines in 6th and 7th generation. The differences between lines were

92 analysed using a liner model with effects of line-generation, lactation status at mating

93 (lactating or non-lactating) and year-season.

94 Correlated response to selection was also estimated as the average of the genetic values in

95 each generation. Bivariate animal models were fitted in order to estimate the genetic

96 parameters and genetic responses. All analysis included selection trait, litter size residual

97 variance. The model for litter size residual variance included generation as fixed and genetic

98 value as random effect. For the rest of traits, the model considered fixed effects of lactation

99 status at mating (lactating or non-lactating at mating) and year-season, and random effect of

100 genetic value.

101 For the bivariate model, the traits were assumed to be conditionally normally distributed as

102 follows:

$$\begin{bmatrix} y_1 \\ y_2 \end{bmatrix} \mid b_1, b_2, a_1, a_2, R \sim N\left(X \begin{bmatrix} b_1 \\ b_2 \end{bmatrix} + Z \begin{bmatrix} a_1 \\ a_2 \end{bmatrix}, R \right)$$

103 Where b_1 and b_2 are random vectors including the effects of generation, lactation status at

104 mating and year-season, a_1 and a_2 are vectors of individual additive genetic effects, X, and Z

105 are known incidence matrices, and R is the residual (co)variance matrix. Between individuals,

106 only the additive random effects are assumed correlated. Between traits, the additive, and the

107 residual effects are assumed correlated. The residual (co)variance matrix can be written as R_0

108 $\otimes$ $\mathbf{I_n}$ with $\mathbf{R_0}$ being the 2×2 residual (co)variance matrix between the traits analysed and $\mathbf{I_n}$

109 an identity matrix of appropriate order. Bounded uniform priors were used to represent vague

110 previous knowledge of distributions of $\mathbf{b_1}$ and $\mathbf{b_2}$. Prior knowledge concerning additive effect

111 was represented by assuming that they were normally distributed, conditionally on the

112 associated (co)variance components, as follows:

$$\begin{bmatrix} a_1 \\ a_2 \end{bmatrix} \mid \mathbf{G} \sim \mathbf{N(0, G)}$$

113 Where $\mathbf{0}$ is a vector of zeros, and $\mathbf{G}$ is the genetic (co)variance matrix. The matrix $\mathbf{G}$ could be

114 written as $\mathbf{G_0} \otimes \mathbf{A}$, in which $\mathbf{G_0}$ is the 2×2 genetic and $\mathbf{A}$ is the known additive genetic

115 relationship matrix. Bounded uniform priors were used for the components of the

116 (co)variance matrices $\mathbf{R_0}$ and $\mathbf{G_0}$.

117 Bayesian analyses were performed, with bounded flat priors for all unknowns. Features of the

118 marginal posterior distributions were estimated using Gibbs sampling. For the differences

119 between lines, after some exploratory analyses, we used a chain of 60,000 samples, with a

120 burn-in period of 10,000, only one of every 10 samples saved for inferences. The Rabbit

121 program developed by the Institute for Animal Science and Technology (Valencia, Spain)

122 was used for these procedures. For the genetic analyses, we used a chain of 1,000,000

123 samples, and burn-in of 500,000; only one of every 100 samples saved for inferences. The

124 program TM developed by Legarra et al. (2008) was used for these procedures. Convergence

125 was tested using the Z criterion of Geweke (Sorensen and Gianola 2002).

126 **Results and Discussion**

127 *Genetic and phenotypic parameters*

128 For all the traits analysed, Monte Carlo SE were small. The Geweke test did not detect lack of

129 convergence in any case. Mean and median are similar for all the traits showing that, in all

130 cases, the marginal posterior distributions were symmetric, and therefore only median values

131 are given in the tables.

132 The features of the estimated marginal posterior distributions of heritabilities for the traits are

133 summarized in Table 1. Estimates of heritabilities were moderate for OR, IE and ES (0.33,

134 0.26, and 0.25, respectively), with a probability of 100% for OR, 97% for IE and 98% for ES

135 of being at least 0.10. The litter size at second parity had a low heritability (0.13 for TB),

136 being similar to the heritabilities of FS and PS (0.09 in both traits). Heritability was higher in

137 the traits that determinate the success of pregnancy at the early stages than in those are acting

138 at the end stages. The estimated heritabilities for OR, IE, ES, FS, PS and TB were within the

139 value range reported by other studies in rabbits (Blasco *et al.* 1993; Argente *et al.* 2000;

140 Garreau *et al.* 2004; Ibañez *et al.* 2006; Ziadi *et al.* 2013) and in pigs (Johnson *et al.* 1999;

141 Ruiz-Flores and Johnson, 2001; Rosendo *et al.* 2007).

142 The features of the estimated marginal posterior distributions of the genetic correlations are

143 shown in Table 2. In general, genetic correlations were estimated with large HPD$_{95\%}$ (Table

144 2). To obtain genetic parameters with greater precision, a larger set of data would be needed.

145 However, the nature of these kinds of experiments, which require techniques including

146 laparoscopy or slaughter, prevents the collection of large data sets. For this reason, we can

147 often only draw conclusions about the sign of these genetic correlations. In accordance with

148 that, the posterior medians of the genetic correlation between the selection criterion (Ve) with

149 IE, ES, PS and TB showed large HPD$_{95\%}$ (Table 2), but all them were negative with a high

150 probability (P was always higher than 90%, Table 2). Genetic correlations between Ve with

151 both OR and FS exhibited greater imprecision, as we can see in their large credibility

152 intervals. Their P does not allow to infer about their signs.

153   The features of the estimated marginal posterior distributions of the phenotypic correlations

154   are also summarized in Table 2. Generally, phenotypic correlations showed the same sign that

155   their genetics correlation, but with a higher accuracy, except for IE (see HPD$_{95\%}$, Table 2). All

156   traits exhibited a low negative phenotypic correlation with the selection criterion (Ve), with

157   the exception of OR, that had a positive phenotypic correlation although it was low. Selection

158   for environmental variance has been proposed under complex models (San Cristobal *et al.*

159   1998)*,* which robustness and effectiveness have been questioned (Sorensen, 2010). In this

160   regard, Yang *et al.* (2011) showed that small deviations from normality in the residuals can

161   substantially change the genetic parameters estimated, finding that the coefficient of

162   correlation between the trait and its variability changed the sign in the case of pigs litter size

163   after a Box-Cox transformation for normalizing the residuals. To avoid the possible

164   mathematical artefacts of complex models, we have performed a divergent selection

165   experiment in rabbits directly on environmental variance with success (Blasco *et al.* 2017).

166   This is the first time that environmental variance is treated as an observed trait, and it is

167   examined the consequences that this selection process had on litter size components. Our

168   results showed a negative correlation between litter size variability with number of implanted

169   embryos and with litter size. This is in agreement with Ibáñez-Escriche *et al.* (2008), who

170   reported a negative correlation between uterine capacity and its residual variability in rabbits, a

171   trait highly correlated with litter size (Argente *et al.* 2000).

172   *Correlated response to selection*

173   Table 3 shows phenotypic differences between the high and low lines for all traits in the sixth

174   and seventh generation of selection. Ovulation rate was similar in both lines in the last two

175   generations of selection. For the number of implanted embryos, the low line had 0.61 more

176   embryos at implantation (P=0.93) and a higher embryonic survival than the high line (0.04, P

177   = 0.92) in the sixth generation of selection. These differences were greater in the seventh

178   generation of selection (1.23 for number of implanted embryos, P=1.00; and 0.08 for

179   embryonic survival, P=0.99). In a Bayesian context, several confidence intervals can be easily

180   estimated. We can provide intervals [k, +∞), where k can be interpreted as a guaranteed value

181   with a determined probability (Blasco, 2005). The guaranteed value at 80% probability was

182   0.83 for number of implanted embryos and 0.05 for embryonic survival in the seventh

183   generation of selection; this means that the correlated response in these traits has been at least

184   0.83 and 0.05, respectively, with 80% probability. Fetal survival was also greater in the low

185   line than in the high line (0.06, P=0.95 in the sixth generation; 0.04, P=0.86 in the seventh

186   generation). Moreover, litter size at second parity was also consistently higher in the low line

187   than in the high line. In the seventh generation of selection, the difference in litter size

188   between the low and high lines was 1.30 kits (P=0.99), with a guaranteed value of 0.85 kits

189   with 80% probability.

190   The Figure 1 and 2 show the evolution of the genetic trends for litter size at second parity and

191   its components in the high and low lines. Except for OR, the lines increased divergences in

192   the remaining traits when selection process advanced. We note that, in the last generation of

193   selection, the differences in genetic means between lines showed similar values to the

194   phenotypic differences in all analysed traits (0.11 ova in OR, 1.09 embryos in IE, 1.01 kits in

195   TB, 0.07 in ES, 0.03 in FS and 0.06 in PS). The correlated response to selection can be

196   estimated as phenotypic differences between lines and as genetic trends from the estimated

197   genetic means. All methods based in genetic trends (BLUP-REML or Bayesian methods) are

198   model-dependent and the genetic trends directly depend on the genetic parameters used

199   (Thompson, 1986; Sorensen and Johansson, 1992). The advantage of the simple difference

200   between high and low lines is that they are independent of any model; whether there are major

201   genes, dominance or other effects. We reported in this study that the phenotypic differences

202   are coincident with the estimates based in a genetic model. Therefore this would corroborate

203   the model used.

204   Homogeneity is an economically important trait in livestock production (Mulder *et al.* 2008).

205   In the case of litter size, a reduction in environmental variability can be related to better

206   adaptation of the animal to environmental changes, and in consequence, with an improvement

207   in welfare to the animal. After seven generations of selection, we report that selection for litter

208   size variability has a negative correlated response with litter size. Our results show that the

209   difference in litter size between lines was established at implantation. There is evidence that

210   maternal stress around the time of implantation increases the failure rate in blastocyst

211   implantation (Burkuš *et al.* 2015). We hypothesise that the line selected for heterogeneity in litter

212   size should be more sensitive to stress and diseases than the homogeneous line. In this regard,

213   Argente *et al.* (2014) found a lower immune response to pathogenic agents in females from the

214   heterogeneous line, showing greater sensitivity to diseases. This would be in agreement with a

215   larger number of embryonic losses around implantation in this line.

216   In conclusion, selection for litter size variability showed a negative correlated response in

217   embryonic survival, which continued at birth for litter size.

Acknowledgments

References

224 Argente, M.J., Santacreu, M.A., Climent, A., Blasco, A. (2000). Genetic correlations between

225 litter size and uterine capacity. In Proceeding of the 8th World Rabbit Congress. Valencia

226 (Spain), 4-7 July 2000, pp 333-338.

227 Argente, M.J., Blasco, A.; Ortega, J.A., Haley, C.S., Visscher, P.M. (2003) Analyses for the

228 presence of a major gene affecting uterine capacity in unilaterally ovariectomized rabbits.

229 *Genetics*, 163(3), 1061–1068.

230 Argente, M.J., Garcia, M.L., Muelas, R., Santacreu, M.A., Blasco, A. (2010). Preliminary

231 results in a divergent selection experiment on variance for litter size in rabbits. In

232 Proceedings of the 9th World Congress on Genetics Applied to Livestock Production.

233 Leipzig (Germany), 1-6 August 2010, Communication 0526.

234 Argente, M.J., García, M.L., Zbynovska, K., Petrusca, P., Capcarova, M., Blasco, A. (2014).

235 Effect of selection for residual variance of litter size on haematology parameters as

236 immunology indicators in rabbits. In Proceedings of 10th World Congress on Genetics

237 Applied to Livestock Production. Vancouver (Canada), 17-22 August 2014,

238 Communication 631.

239 Blasco, A., Santacreu, M.A., Thompson, R., Haley, C. (1993). Estimates of genetic

240 parameters for ovulation rate, prenatal survival and litter size in rabbits from an elliptical

241 selection experiment. *Livestock. Prod. Sci*. 34: 163-174.

242 Blasco A. (2005). The use of Bayesian statistics in meat quality analyses. *Meat Sci.* 69:15 -

243 122.

244 Blasco, A., Martínez-Álvarado, M., García, M.L., Ibáñez-Escriche, N., Argente, M.J. (2017).

245 Selection for genetic environmental sensitivity of litter size in rabbits. *Gen. Sel. Evol.*

246 Accepted to publication.

247 Burkuš, J., Kačmarová, M., Kubandová, J.: Kokošová, N., Fabianová, K.: Fabian, D., Koppel,

248 J., Čikoš Š. (2015). Stress exposure during the preimplantation period affects blastocyst

249 lineages and offspring development. *J. Reprod. Develop.* 61(4): 325-331.

250 Formoso-Rafferty, N., Cervantes, I., Ibáñez-Escriche, N., Gutiérrez, J.P. (2016). Modulación

251 de la heredabilidad del peso al nacimiento en ratones. In Proceeding of the XVIII

252 Reunión Nacional de Mejora Genética Animal. Valencia (Spain), 2-3 Junio 2016,

253 Communication 22.

254 Garreau, H., Piles, M., Larzul, C., Baselga, M., Rochambeau, H. (2004). Selection of maternal

255 lines: Last results and prospects. In Proceeding of 8th World Rabbit Congress. Puebla

256 (México), 7-10 September 2004, pp 14–25.

257 Ibáñez, N., Santacreu, M.A., Martínez, M., Climent, A., Blasco, A. (2006). Selection for

258 ovulation rate in rabbits. *Livest. Sci.* 101: 126-133.

259 Ibáñez-Escriche, N., Sorensen, D., Waagepetersen, R., Blasco, A. (2008). Selection for

260 environmental variation: a statistical analysis and power calculations to detect response.

261 *Genetics*. 180(4): 2209-2226.

262 Johnson, R. K., Nielsen, M.K., Casey, D.S. (1999). Responses in ovulation rate, embryonal

263 survival and litter traits in swine to 14 generations of selection to increase litter size. *J.*

264 *Anim. Sci.* 77:541–557

265 Legarra, A., Varona, L., López de Maturana, E. (2008). Program TM.

266 http://snp.toulouse.inra.fr/~alegarra/. Accessed September 17, 2016

267 Mulder, H.A., Bijma, P., Hill, W.G. (2008). Selection for uniformity in livestock by

268 exploiting genetic heterogeneity of residual variance. *Gen. Sel. Evol.* 40(1): 37-59.

269 Piles M., García M.L., Rafel O., Ramon J., Baselga M. (2006). Genetics of litter size in three

270 maternal lines of rabbits: Repeatability versus multiple-trait models. *J. Anim. Sci.*

271   84:2309–2315.

272   Rosendo, A., Druet, T., Gogue, J., Bidanel, J.P. (2007). Direct responses to six generations of

273   selection for ovulation rate or prenatal survival in Large White pigs. *J. Anim. Sci.* 85:356-

274   364.

275   Ruiz-Flores, A., Johnson, R.K. (2001). Direct and correlated responses to two-stage selection

276   for ovulation rate and number of fully formed pigs at birth in swine. *J. Anim. Sci.*

277   79:2286-2299

278   San Cristobal, M., Elsen, J.M., Bodin, L., Chevalet, C. (1998). Prediction of the response to a

279   selection for canalisation of a continuous trait in animal breeding. *Genet. Sel. Evol.* 30:

280   423-451.

281   Sorensen, D.A., Johansson, K. (1992). Estimation of direct and correlated responses to

282   selection using univariate animal models. *J. Anim. Sci.* 70: 2038-2044.

283   Sorensen, D. (2010). The Genetics of Environmental Variation. In Proceeding of 9th World

284   Congress *on* Genetics Applied to Livestock Production. Leipzig (Germany), 1-6 August

285   2010. paper 72.

286   Sorensen, D., Gianola, D. (2002). Likelihood, bayesian, and MCMC Methods in quantitative

287   genetics. Springer Science and Business Media

288   Thompson, R. (1986). Estimation of realized heritability in a selected population using mixed

289   model methods. *Gen. Sel. Evol.* 18:475-484.

290   Yang Y., Christensen, O.F., Sorensen, D. (2011). Analysis of a genetically structured variance

291   heterogeneity model using the box–cox transformation. *Genet. Res.* 93: 33–46.

292   Ziadi, C., Mocé, M.L., Laborda, P., Blasco, A., Santacreu, M.A. (2013). Genetic selection for

293   ovulation rate and litter size in rabbits: Estimation of genetic parameters and direct and

294   correlated responses. *J Anim Sci.* 91(7): 3113-3120.

295

296 Table 1. Features of the marginal posterior distributions of heritability for ovulation rate (OR),

297 number of implanted embryos (IE), total number of kits born at second parturition (TB),

298 embryonic survival (ES), fetal survival (FS) and prenatal survival (PS).

Trait	median	HPD$_{95\%}$	P$_{0.10}$	k$_{80\%}$
OR	0.33	0.15, 0.56	1.00	0.24
IE	0.26	0.08, 0.46	0.97	0.17
ES	0.25	0.09, 0.45	0.98	0.18
FS	0.09	0.01, 0.24	0.48	0.05
PS	0.09	0.02, 0.24	0.47	0.06
TB	0.13	0.02, 0.29	0.67	0.08

299 HPD$_{95\%}$: high posterior density interval at 95%. P$_{0.10}$: probability of the heritability being

300 higher than 0.10. k$_{80\%}$: limit for the interval [k, $+\infty$) having a probability of 80%.

301

302   Table 2. Features of the posterior distributions of genetic and phenotypic correlation.

	Genetic correlation				Phenotypic correlation			
Trait	Median	$HPD_{95\%}$	P	$k_{80\%}$	Median	$HPD_{95\%}$	P	$k_{80\%}$
Ve, OR	-0.08	-0.65, 0.49	0.61^{b}	0.17	0.15	0.07, 0.24	1.00^{a}	0.11
Ve, IE	-0.49	-0.97, 0.08	0.92^{b}	-0.20	-0.04	-0.12, 0.05	0.71^{b}	-0.02
Ve, ES	-0.43	-0.97, 0.11	0.91^{b}	-0.15	-0.08	-0.17, 0.01	0.97^{b}	-0.04
Ve, FS	-0.18	-0.99, 0.63	0.65^{b}	0.17	-0.27	-0.36, -0.19	1.00^{b}	-0.24
Ve, PS	-0.54	-0.99, 0.08	0.93^{b}	-0.21	-0.27	-0.35, -0.19	1.00^{b}	-0.24
Ve, TB	-0.45	-0.99, 0.16	0.90^{b}	-0.77	-0.19	-0.28, -0.11	1.00^{b}	-0.16

303    $HPD_{95\%}$: high posterior density interval at 95%. P: probability of the genetic correlation being

304   greater than 0 (superscript a) or less than 0 (superscript b).$k_{80\%}$: limit for the interval [a] $[k+1)$, [b]

305    $(-1, k]$, having a probability of 80%. Ve: residual variance of litter size. OR: ovulation rate.

306   IE: number of implanted embryos. ES: embryonic survival. FS: fetal survival. PS: prenatal

307   survival. TB: total number of kits born at second parturition.

308 Table 3. Correlated response. Features of the estimated marginal posterior distribution of the

309 differences between the high and low lines in the sixth (G6) and the seventh (G7) generation

310 of selection.

	G6				G7			
	D_{H-L}	$HPD_{95\%}$	P	$k_{80\%}$	D_{H-L}	$HPD_{95\%}$	P	$k_{80\%}$
OR, ova	-0.11	-0.70, 0.48	0.65	-	-0.02	-0.74, 0.61	0.52	-
IE, embryos	-0.61	-1.42, 0.17	0.93	-0.23	-1.23	-2.14, -0.31	1.00	-0.83
ES, embryos / ova	-0.04	-0.09, 0.02	0.92	-0.02	-0.08	-0.14, -0.02	0.99	-0.05
FS, kits / embryos	-0.06	-0.12, 0.01	0.95	-0.03	-0.04	-0.12, 0.03	0.86	-0.01
PS, kits / ova	-0.07	-0.14, -0.01	0.98	-0.04	-0.09	-0.16, -0.01	0.99	-0.06
TB, kits	-1.03	-1.93, -0.13	0.99	-0.64	-1.30	-2.36, -0.29	0.99	-0.85

311 D_{H-L}: median of the difference between the High and Low lines. $HPD_{95\%}$: highest posterior

312 density region at 95%. P: probability of the difference being >0 when D_{H-L} >0 and probability

313 of the difference being <0 when D_{H-L}<0. $k_{80\%}$: limit of the interval [k, +∞) when D_{H-L} >0 and

314 (-∞, k] when D_{H-L} <0 at 80% of probability. It is displayed in the table only when D_{H-L} and

315 $k_{80\%}$ have the same sign. OR: ovulation rate. IE: number of implanted embryos. ES:

316 embryonic survival. FS: fetal survival. PS: prenatal survival. TB: total number of kits born at

317 second parturition.

318

319   Figure 1. Correlated response to selection in the High and Low lines. 1. a) Genetic means per

320   generation for ovulation rate at second gestation. 1. b) Genetic means per generation for

321   number of implanted embryos at second gestation. 1. c) Genetic means per generation for

322   total number of kits born at second parturition.

323

324   Figure 2. Correlated response to selection in the High and Low lines**.** 2.a) Genetic means per

325   generation for embryo survival at second gestation. 2.b) Genetic means per generation for

326   fetal survival at second gestation. 2.c) Genetic means per generation for prenatal survival at

327   second gestation.

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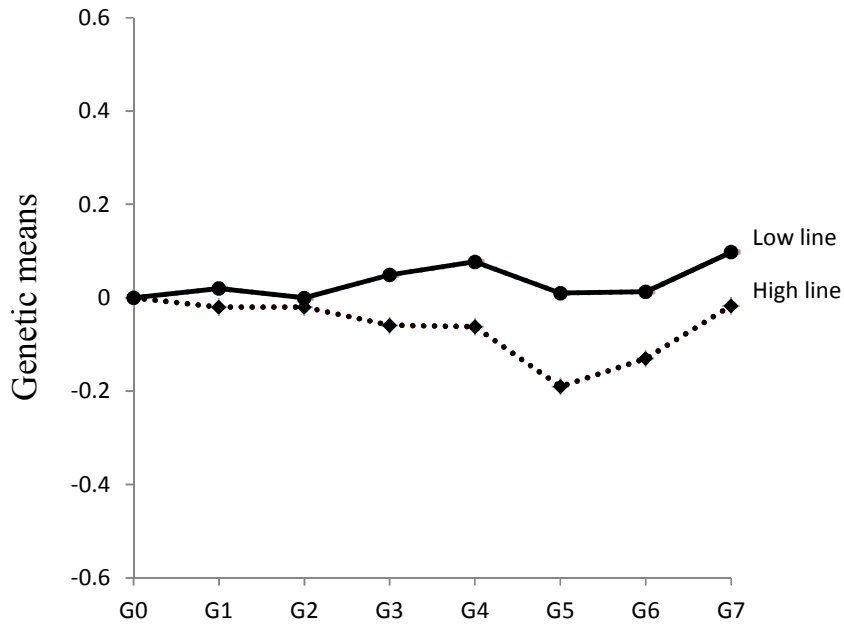
1. a) Correlated response to selection in ovulation rate

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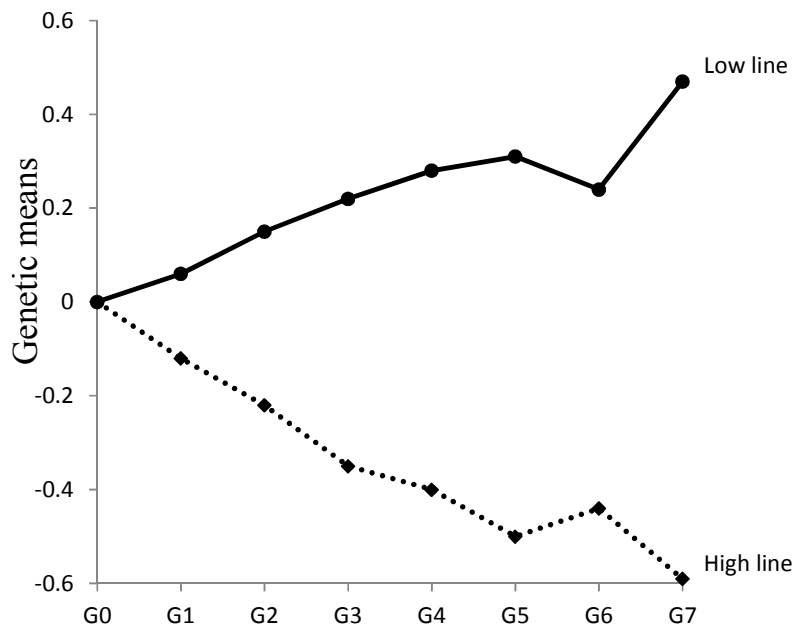
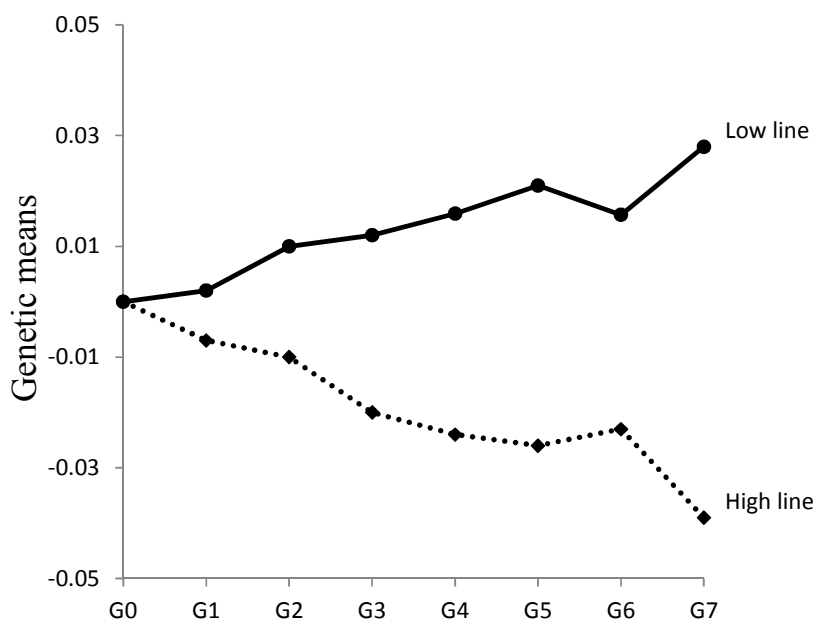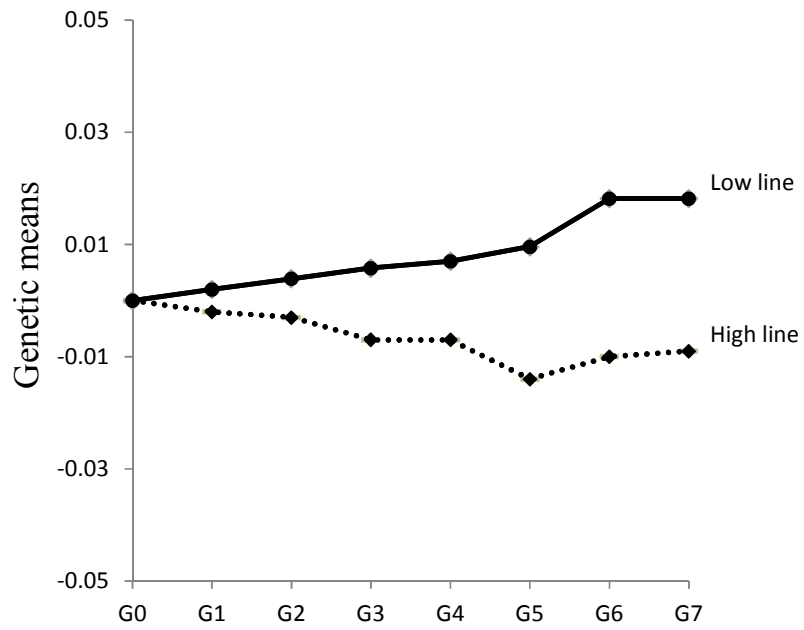1. b) Correlated response to selection in number of implanted embryos

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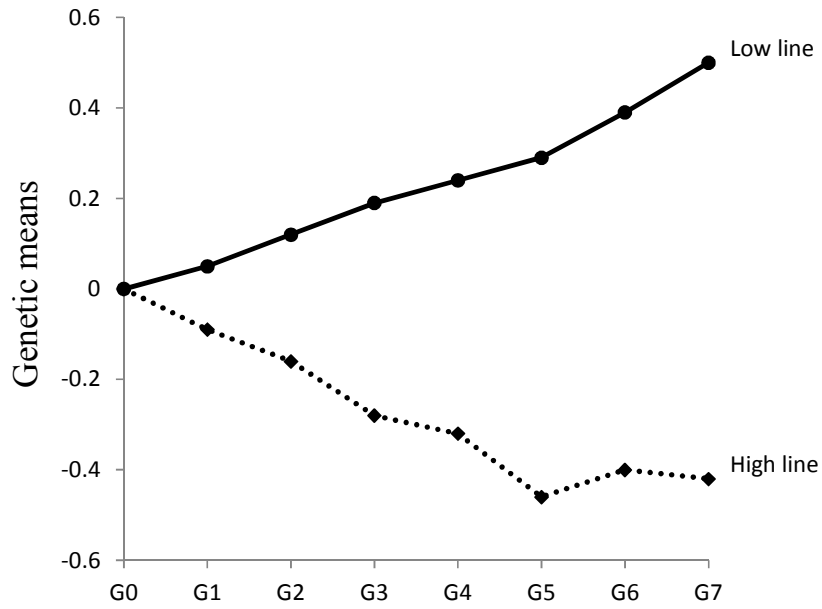
1. c) Correlated response to selection in litter size

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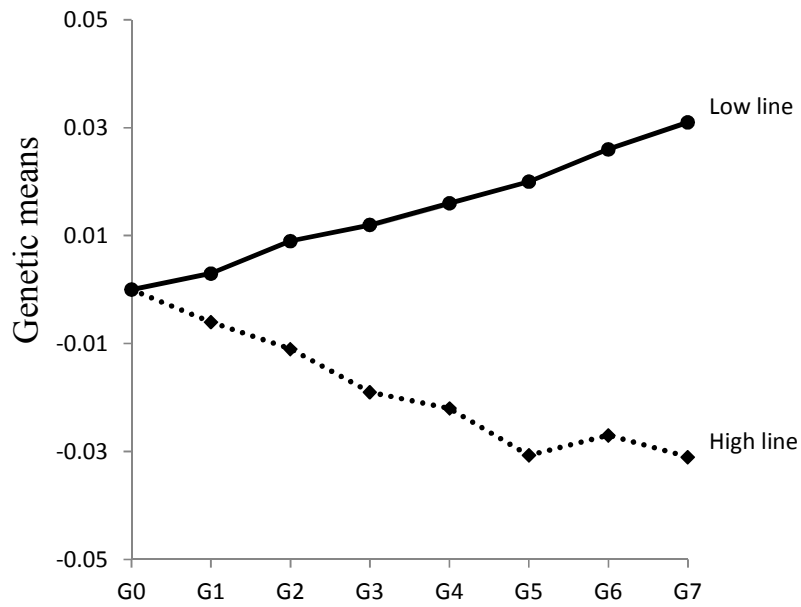41
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2. a) Correlated response to selection in embryonic survival

2. b) Correlated response to selection in
fetal survival

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2. c) Correlated response to selection in prenatal survival