Differential response to dietary fat in large (LG/J) and small (SM/J) inbred mouse strains

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Cheverud, James M., L. Susan Pletscher, Ty T. Vaughn, and Bess Marshall. Differential response to dietary fat in large (LG/J) and small (SM/J) inbred mouse strains. Physiol. Genomics 1: 33–39, 1999.—The “large” (LG/J) and “small” (SM/J) inbred mouse strains differ for a wide variety of traits related to body size and obesity. Ninety-three LG/J and SM/J mice were divided into two treatment categories and fed a moderately high-fat diet (21% kcal fat) or a low-fat diet (12% kcal fat) from weaning to necropsy. Strain differences in obesity-related traits and differential response to dietary fat increases were analyzed using ANOVA. LG/J animals grow faster from 3 to 10 wk, have longer tails, and have heavier body weight, liver weight, and fat pad weight than SM/J animals. SM/J animals grow faster after 10 wk of age and have higher fasting glucose levels than LG/J animals. SM/J mice were more responsive to increased dietary fat than LG/J mice for growth after 10 wk, necropsy weight, liver weight, fat pad weights, and fasting glucose levels (in males). The growth from 3 to 10 wk had a much greater response in the LG/J strain, whereas tail length had no response. This pattern of dietary response is similar to that expected under the “thrifty” phenotype hypothesis. Genes affecting strain differences and the differential response of the strains to dietary fat can be successfully mapped in the intercross of the LG/J and SM/J strains. This intercross provides an excellent multigenic model for the genetic basis of complex traits and diseases related to body size and obesity.

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Body weight is of central importance in many aspects of mammalian morphology and physiology (23, 35, 40) and has long been considered as a paradigm character for studies of quantitative inheritance. Large body size, in particular obesity, is a risk factor for a wide variety of genetically complex diseases, such as heart disease, diabetes, and hypertension. In this study, we describe the characteristics of the “large” (LG/J) and “small” (SM/J) inbred mouse strains. These characteristics make populations derived from their intercross an excellent model for studying the polygenic inheritance of complex traits.

Much progress has been made in characterizing single-gene mutants leading to obesity in inbred mouse populations (24, 25). Recently, the molecular basis of the obese (ob; 57), diabetes (db; 7), fat (fat; 33), agouti yellow (Ay; 32), little (lit; 18) and tubby (tub; 25) mouse mutant phenotypes have been identified. In some cases, there has been a rapid application of these findings to understanding and treating human growth abnormali-
diet, including the SJL/J, I/STN, and SWR/J strains. West and colleagues (15, 42, 53) proceeded to investigate the dietgenesobesity relationship using two strains with very different responses to a high-fat diet, AKR/J and SWR/J. They found that adipocytes from AKR/J mice had greater insulin-stimulated glucose transport than SWR/J mice (15) and confirmed that the AKR/J strain has a stronger response to dietary fat than SWR/J and that this difference increases with the level of fat in the diet (53). The difference in response between the strains was on the order of 1.0 within-strain standard deviations (SD) on a raw scale (grams). They also found that the two strains differ in macronutrient selection and feeding rate, with the AKR/J strain consuming 30% more calories and a much higher percentage of calories from fat (69% vs. 28%) than the SWR/J strain (42). These findings suggest that obesity level of the AKR/J strain in response to a high-fat diet is based, in part, on hyperphagy and a preference for calories from fat over carbohydrates. Although West and colleagues (51, 52, 56) have mapped several genes affecting body weight and fat pad weight on a high-fat diet in the intercross of AKR/J and SWR/J, they did not specifically test for genes differentially responsive to dietary fat intake.

The strains used in the present study are the large (LG/J) and small (SM/J) inbred mouse lines. The extreme genetic variability between these strains for body size and fatness (26) make them and the crosses between them excellent rodent models for multigenic obesity. The LG/J strain originated from a strain selected for large body size at 60 days (19, 20). The SM/J strain was derived from a separate experiment in which selection was for small body size at 60 days (30). In each case, the original selected lines were systematically inbred and maintained by brother-sister mating to the present (2–6). The studies of Chai (2, 3) showed extreme body weight differences between the strains (24 g difference at 60 days).

In a rodent model for multigenic obesity, body weight and fatness levels should be affected by many genes of nearly equal, relatively small effect, because this is considered to be the likely source of most genetic variation in human obesity (1), although some instances of obesity in humans may involve variation at only one or a few genes (34). A multigenic obesity model should have genetically well-characterized inbred parental strains and/or inbred derivatives from these strains to allow the use of powerful experimental breeding designs for gene mapping. The use of inbred strains or their crosses also allows replication of studies through recreation of the experimental mapping populations. The LG/J × SM/J intercross populations meet these criteria fully. Although other model systems have been successfully used for studying the genetics of obesity and dietary response, such as the AKR/J × SWR/J intercross (51, 52, 56), the BSB mice (48), and C57BL/6J × A/J crosses (44, 45, 49), it is likely that much new information can be gained from a new model.

The LG/J and SM/J inbred strains have been maintained by brother-sister mating for nearly 50 years, making them fully homozygous except for new mutations. In our own recent experiment, after correcting for sex differences, we found an ~20-g difference between strain body weights at 10 wk (26). We found that this difference is due to many loci of small but varying effect and their interactions (8, 10, 38). Eighteen potential quantitative trait loci (QTLs) for week 10 weight were identified in an earlier intercross experiment (10). Variation in this cross is due to more QTLs than any other mouse multigenic obesity model to date. The allele resulting in larger size tends to be dominant in this cross, although standardized measures of dominance for age-specific weight decline with age. We found considerable epistasis among genes affecting adult body weight (8, 38).

From previous studies (10, 26, 38; and J. M. Cheverud, T. T. Vaughn, L. S. Pletscher, A. Peripato, K. King-Ellison, E. Adams, and C. Erikson, unpublished observations), we know that the LG/J strain grows faster than the SM/J strain prior to 10 wk of age. At 10 wk, the LG/J strain has a longer tail, larger reproductive fat pad (J. M. Cheverud et al., unpublished observations), longer long bone lengths, and larger organ sizes (46) than the SM/J strain. These genetic differences between strains are substantial and have led to successful gene mapping experiments for the phenotypes in question (10, 46; and J. M. Cheverud et al., unpublished observations). Here we report the results of an experiment investigating the differential response of these strains to dietary fat. If increased dietary fat affects body size and composition differently in the two strains, then these differences have a genetic basis. The location and effects of such genes can then be mapped in further experiments.

**MATERIALS AND METHODS**

Mice from both the SM/J and LG/J strains were fed both low-fat (SM/J = 29 and LG/J = 25) and moderately high-fat (SM/J = 29 and LG/J = 10) diets after weaning at 3 wk. The low-fat diet was PicoLab Rodent Chow 20 (no. 5053) with 12% of its energy from fat, 23% from protein, and 65% from carbohydrate. This is the standard rodent diet used in our breeding facility. The high-fat diet is PicoLab Mouse Chow 20 (no. 5058) with 21% of its calories from fat, 22% from protein, and 57% from carbohydrate. This dietary difference is much smaller than that used in the studies of West and colleagues (42, 50–54, 56) but made use of easily available diets.

Animals were obtained by in-breeding LG/J females with LG/J males and SM/J females with SM/J males. Source animals were obtained from the Jackson Laboratories. All pups were weaned at 3 wk of age, at which time they were randomly placed on either the low- or high-fat dietary regime. Animals were weighed weekly to 10 wk, and periodically thereafter. Animals were killed and necropsied at 27 to 45 wk. Within the month prior to necropsy, all animals were tested for fasting glucose levels. We used Hemocue glucose analyzers to measure glucose levels in blood drawn from the SM/J and LG/J mice after fasting for 4 h. Animals ranged from 23 to 41 wk in age at the time of testing.

We measured growth in two periods, postweaning growth from 3 to 10 wk and later, adult growth from 10 wk to necropsy. To standardize for differences in age at necropsy, the body weight difference between necropsy and 10-wk...
weight was divided by the number of days between 10 wk and necropsy. Qualitatively similar results were obtained using adult growth without correction for age at necropsy. Ideally, all animals should be necropsied at the same age. By 10 wk, skeletal growth in mice is complete. Further growth consists of adding soft tissue mass. A series of measurements were collected at necropsy, including total body weight, tail length, heart, kidney, spleen, and liver weights and weights of the reproductive (parametrial in females and epididymal in males), kidney, mesenteric, and inguinal fat pads. Scores for all bilateral structures represent the sum of the two sides. The reproductive fat pad is well delineated in its own mesentery. The kidney fat pad consisted of the perirenal fat. This fat pad was located on the peritoneal faces of the kidney. The mesenteric fat pad was obtained by removing the gut between the stomach and rectum and separating the dorsal mesentery from the posterior body wall. The mesentery and its contents were then stripped from the gut and weighed.

The inguinal fat pad was defined as the subcutaneous fat in the perineal and inguinal regions. Fat extending around the proximal thigh was also included. All data except glucose level were transformed to the natural logarithmic scale to prevent spurious results due to scale. Glucose level was not transformed because its within-group distribution is normally distributed on a raw scale.

The data were analyzed using ANOVA and multivariate ANOVA (MANOVA) methods where appropriate (43). ANOVA was used for analyses of individual phenotypes, and MANOVA was used for groups of phenotypes, such as the various fat pad weights. These analyses include the factors of sex (male vs. female), diet (high fat vs. low fat), and strain (LG/J vs. SM/J) and their two- and three-way interactions. The major effects of interest are the strain differences, which are indicative of genetic effects on the phenotypes themselves, and the strain × diet interactions, which indicate differential response of the strains to added dietary fat.

The results are reported in terms of the number of within-group standard deviations represented by the contrast. This value is obtained by dividing the difference in means between factor categories by the square root of the residual variance. Reporting results on a standardized scale allows us to compare results for different phenotypes and for the same phenotypes in different studies.

**RESULTS**

Means and standard deviations of the raw phenotypic values organized by sex, strain, and diet are provided in Table 1. ANOVA results for growth, body size, and fasting glucose level are given in Table 2. Tail length is used in this analysis to represent skeletal size. The only two significant factors affecting tail length are sex (females were 0.59 SD shorter than males, \( P = 0.015 \)) and strain (LG/J were 4.96 SD longer than SM/J). Diet has no effect on tail length. None of the interactions, including strain × diet (\( P = 0.45 \)), have any effect on tail length. Tail length is not affected by diet in either strain.

Growth from 3 to 10 wk will be considered separately from growth from 10 wk to necropsy. In the earlier period, there are very strong, significant effects of sex (females were 1.09 SD units smaller than males; \( P = 2.22 \times 10^{-5} \)), diet (high-fat group was 1.74 SD faster than low-fat group; \( P = 2.97 \times 10^{-10} \)), strain (LG/J were growing faster than SM/J; \( P = 1.73 \times 10^{-11} \)), and the strain × diet interaction (LG/J were adding 2.05 SD more on a high-fat diet than the SM/J strain; \( P = 6.1 \times 10^{-5} \)). From 3 to 10 wk, the addition of dietary fat has little effect on the SM/J strain and a major effect on the LG/J strain.

Daily weight gain from 10 wk to necropsy shows a very different pattern of results. Again, the three main effects are all significant, but the relative rankings of the sexes and strains are reversed. Females grow 1.15 SD faster than males (\( P = 8.0 \times 10^{-6} \)), the high-fat diet leads to 2.25 SD faster growth than the low-fat diet (\( P = 2.2 \times 10^{-11} \)), and the SM/J animals grow faster than the LG/J animals (0.59 SD; \( P = 0.017 \)). The sex × diet (1.49 SD, \( P = 0.0028 \)) and strain × diet (1.29 SD, \( P = 0.0096 \)) interactions are both significant. Diet had a greater effect in females than in males and a greater effect in the SM/J strain than in the LG/J strain.

Necropsy weight showed significant differences for diet (high-fat diet animals were 1.15 SD larger than low-fat animals; \( P = 5.0 \times 10^{-6} \)) and strain (LG/J were 2.70 SD larger than SM/J; \( P = 2.1 \times 10^{-11} \)), but not for sex. Males and females were the same weight at necropsy, in strong contrast to results for 10-wk weight for which males are over 2.0 SD units larger than females (10, 26). The relative growth deficit of females prior to 10 wk is compensated for by growth enhancement after 10 wk. The only significant interaction term is the strain × diet interaction (high-fat diet had a 1.27

<table>
<thead>
<tr>
<th>Table 1. Sex-, diet-, and strain-specific data</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LF</td>
<td>HF</td>
</tr>
<tr>
<td>Early growth</td>
<td>22.18 (0.55)</td>
<td>24.31 (1.15)</td>
</tr>
<tr>
<td>Adult growth</td>
<td>0.055 (0.0077)</td>
<td>0.125 (0.0161)</td>
</tr>
<tr>
<td>Tail length</td>
<td>69.63 (1.26)</td>
<td>95.19 (2.63)</td>
</tr>
<tr>
<td>Necropsy weight</td>
<td>46.02 (1.51)</td>
<td>54.08 (3.15)</td>
</tr>
<tr>
<td>Liver weight</td>
<td>2.37 (0.13)</td>
<td>2.28 (0.27)</td>
</tr>
<tr>
<td>Glucose level</td>
<td>153 (6.88)</td>
<td>117 (13.17)</td>
</tr>
<tr>
<td>Reproductive fat pad</td>
<td>1.24 (0.29)</td>
<td>3.35 (0.30)</td>
</tr>
<tr>
<td>Kidney fat pad</td>
<td>1.50 (0.29)</td>
<td>5.62 (0.62)</td>
</tr>
<tr>
<td>Mesenteric fat pad</td>
<td>1.52 (0.10)</td>
<td>1.84 (0.20)</td>
</tr>
<tr>
<td>Inguinal fat pad</td>
<td>0.72 (0.17)</td>
<td>2.98 (0.42)</td>
</tr>
</tbody>
</table>

Values are means with SD in parentheses. All weights are given in g, except adult growth which is in g/day. Tail length is measured in millimeters, and glucose levels are in mg/dl. F, female; M, male; HF, high-fat diet; LF, low-fat diet.
The SM/J strain than on the LG/J strain. The reproduc-
itive, kidney, and mesenteric fat pads all show this si-
Table 2. ANOVA results for growth and obesity-related traits

<table>
<thead>
<tr>
<th>Source</th>
<th>Group</th>
<th>Early Growth</th>
<th>Adult Growth</th>
<th>Tail Length</th>
<th>Necropsy Weight</th>
<th>Liver Weight</th>
<th>Glucose Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sx</td>
<td>F</td>
<td>-1.09 2.2 × 10⁻⁵</td>
<td>1.15 8.0 × 10⁻⁶</td>
<td>-0.59 0.015</td>
<td>-0.08 0.725</td>
<td>-0.20 0.390</td>
<td>-0.87 0.00054</td>
</tr>
<tr>
<td>D</td>
<td>HF</td>
<td>1.74 3.0 × 10⁻¹⁰</td>
<td>2.25 2.2 × 10⁻¹¹</td>
<td>-0.19 0.433</td>
<td>1.15 5.0 × 10⁻⁵</td>
<td>0.26 0.277</td>
<td>0.37 0.12</td>
</tr>
<tr>
<td>St</td>
<td>L</td>
<td>4.37 1.7 × 10⁻¹⁰</td>
<td>-0.59 0.017</td>
<td>4.96 1.6 × 10⁻¹¹</td>
<td>2.70 2.1 × 10⁻¹¹</td>
<td>1.04 3.1 × 10⁻⁵</td>
<td>1.89 2.4 × 10⁻¹¹</td>
</tr>
<tr>
<td>D × Sx</td>
<td>F, HF</td>
<td>0.54 0.273</td>
<td>1.01 0.003</td>
<td>-0.49 0.302</td>
<td>0.92 0.056</td>
<td>-0.32 0.507</td>
<td>-0.15 0.75</td>
</tr>
<tr>
<td>St × Sx</td>
<td>F, L</td>
<td>0.51 0.293</td>
<td>0.09 0.854</td>
<td>0.25 0.593</td>
<td>-0.44 0.351</td>
<td>-0.75 0.116</td>
<td>0.36 0.45</td>
</tr>
<tr>
<td>St × D</td>
<td>L, HF</td>
<td>2.05 6.1 × 10⁻⁵</td>
<td>-1.29 0.009</td>
<td>0.36 0.45</td>
<td>-1.27 8.7 × 10⁻³</td>
<td>-0.98 0.040</td>
<td>-0.62 0.20</td>
</tr>
<tr>
<td>St × D × Sx</td>
<td>F, L, HF</td>
<td>0.96 0.324</td>
<td>0.56 0.567</td>
<td>0.38 0.69</td>
<td>0.40 0.672</td>
<td>1.29 0.178</td>
<td>2.25 0.022</td>
</tr>
</tbody>
</table>

Effect size is given relative to the within sex-strain-diet group standard deviation. Group column indicates the direction of difference. A positive value indicates a positive effect for the identified group, whereas a negative value indicates a positive effect of the contrasting group. F, female; HF, high-fat diet; and L, LG/J strain. Sx, sex; D, diet; St, strain.

The fat pads were analyzed with MANOVA because of their relatively high intercorrelations (within-group Pearson’s r ~ 0.7 to 0.8). Significant effects were found for all three main effects and for the strain × sex and strain × diet interactions (see Table 3). Females were heavier than males for all four fat pads, and those fed a high-fat diet had more fat than those fed a low-fat diet. The LG/J strain had more fat than the SM/J strain for the reproductive, kidney, and mesenteric fat pads, but not for the inguinal fat pad. The significant sex × strain interaction indicates that strain differences are much more pronounced in females than in males but this effect is restricted to the reproductive fat pad. Significant sex × diet interactions indicate that the effects of additional dietary fat have a much larger effect on the SM/J strain than on the LG/J strain. The reproduc-

Table 3. MANOVA results for fat pad weights

<table>
<thead>
<tr>
<th>Source</th>
<th>Group</th>
<th>Reproductive Fat Pad</th>
<th>Kidney Fat Pad</th>
<th>Mesenteric Fat Pad</th>
<th>Inguinal Fat Pad</th>
<th>Multivariate Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sx</td>
<td>F</td>
<td>1.22 1.8 × 10⁻⁶</td>
<td>0.67 5.9 × 10⁻³</td>
<td>0.80 1.2 × 10⁻³</td>
<td>0.79 1.3 × 10⁻³</td>
<td>2.1 × 10⁻⁵</td>
</tr>
<tr>
<td>D</td>
<td>HF</td>
<td>1.23 1.5 × 10⁻⁶</td>
<td>1.24 1.2 × 10⁻⁶</td>
<td>1.37 1.3 × 10⁻⁷</td>
<td>1.61 1.0 × 10⁻⁹</td>
<td>1.7 × 10⁻⁷</td>
</tr>
<tr>
<td>St</td>
<td>L</td>
<td>0.94 7.1 × 10⁻⁴</td>
<td>1.22 1.8 × 10⁻⁹</td>
<td>1.64 1.0 × 10⁻⁹</td>
<td>0.39 1.0 × 10⁻⁹</td>
<td>1.8 × 10⁻¹³</td>
</tr>
<tr>
<td>D × Sx</td>
<td>F, HF</td>
<td>0.72 0.14</td>
<td>0.40 0.40</td>
<td>0.68 0.16</td>
<td>0.52 0.28</td>
<td>0.58</td>
</tr>
<tr>
<td>St × Sx</td>
<td>F, L</td>
<td>1.22 0.01</td>
<td>-0.01 0.09</td>
<td>-0.67 0.16</td>
<td>0.39 0.42</td>
<td>1.1 × 10⁻⁷</td>
</tr>
<tr>
<td>St × D</td>
<td>L, HF</td>
<td>-1.05 0.03</td>
<td>-1.11 0.02</td>
<td>-1.02 0.03</td>
<td>-0.04 0.94</td>
<td>3.4 × 10⁻³</td>
</tr>
<tr>
<td>St × D × Sx</td>
<td>F, L, HF</td>
<td>-0.69 0.47</td>
<td>0.28 0.77</td>
<td>-0.26 0.79</td>
<td>-0.94 0.33</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Effect size is given relative to the within sex-strain-diet group standard deviation. Group column indicates the direction of difference. A positive value indicates a positive effect for the identified group, whereas a negative value indicates a positive effect of the contrasting group. F, female; HF, high-fat diet; and L, LG/J strain. Sx, sex; D, diet; St, strain.
The pre-10-wk period includes neural growth, skeletal growth, and consequent muscular growth. Growth in the post-10-wk period can be estimated by comparing the present necropsy data with that obtained from previous experiments (26). Adult growth involves a 25% increase in body weight, an 11% increase in kidney weight, a 4–5% increase in spleen and heart weights, no increase in liver weight, and an 85% increase in reproductive fat pad weight. Clearly, added fat is the primary source of additional body weight growth in the post-10-wk period.

Strains also differ dramatically in tail length (4.96 SD), necropsy weight (2.70 SD), liver weight (1.00 SD), and fat pad weights (~1.25 SD). In each case, the LG/J strain weighs more than the SM/J strain. However, strain differences in necropsy weight are small relative to differences in 10-wk weight. The LG/J strain is 6.45 SD larger than the SM/J strain at 10 wk and only 2.70 SD heavier than SM/J at necropsy. This reduction in difference is due to the faster growth of the SM/J strain in the adult period. Fasting glucose levels also differ between strains in a characteristic fashion, with the SM/J strain having 1.76 SD higher levels than the LG/J strain. Interstrain differences in all these phenotypes, postweaning and adult growth, organ weights, fat pad weights, and glucose levels make it possible to map genes for these traits in various experimental crosses of the LG/J and SM/J strains. Gene mapping studies of some of these phenotypes, such as postweaning growth, tail length, and reproductive fat pad weight, have already been completed or are presently ongoing (8–11, 27, 38; and J. M. Cheverud et al., unpublished observations). The present study indicates that the genetic basis of adult weight gain and glucose levels could also be addressed using crosses between these two strains. In future experiments, we should be able to map genes with an approximate effect size of ~0.25 SD, which would be the average effect of four to six genes.

Strain × diet interactions measure genetic variation between strains in their response to varying levels of dietary fat. These interactions were ubiquitous for body composition phenotypes and glucose levels. The LG/J strain responded much more dramatically to higher levels of dietary fat during the postweaning growth period, adding 2.05 SD more in weight than added by the SM/J strain. Perhaps the higher energy intake can be utilized for increased growth in the LG/J strain but not in the SM/J strain during this period. The effects of dietary fat differences on adult growth are reversed relative to those observed for the earlier period. Dietary fat has a much larger effect on adult growth in the SM/J strain than in the LG/J strain. This reversal of dietary effects over the life cycle indicates that genes promoting growth on a high-fat diet from 3 to 10 wk also reduce growth after 10 wk or that different sets of genes affect pre- and post-10-wk growth on a high-fat diet (10).
Other measured effects are of less direct importance for mapping genes in populations derived from the LG/J and SM/J strains. Males grew faster than females during the postweaning period but grew slower than females during the adult period. Female fat pads were larger than male fat pads and this was especially true in the LG/J strain. Males also have higher glucose levels than females.

Dietary effects are also as expected in that animals fed a relatively high-fat diet grow faster to a larger body weight with heavier fat pads and livers than animals fed a low-fat diet. Neither tail length nor glucose level exhibited a direct effect of diet. However, glucose level is different for SM/J males on low- and high-fat diets.

The contrast between LG/J and SM/J strains provides an excellent polygenic model for the genetics of body size, obesity, glucose level, and differential genetic response to dietary fat. As with complex diseases in human populations, differences between these strains are due to many genes of relatively small effect (10) and their epistatic interactions (8, 38). Furthermore, these strains are genetically variable in their response to dietary fat. The SM/J strain responds more strongly to increased levels of dietary fat than the LG/J strain for obesity-related characteristics. This makes populations formed from the cross of these strains a potent resource for mapping genes affecting the variable response to dietary environment.

We are presently developing a large series of recombinant inbred strains from the LG/J × SM/J F2 intercross. These strains will provide an efficient means for mapping quantitative trait loci affecting obesity-related phenotypes and responses to dietary fat (13). An advantage in using recombinant inbred strains for initial gene mapping purposes is that phenotypes measured at different times from different animals can be analyzed together; also, there is no need to genotype every individual, because animals within a strain are genotypically identical. Once a general map position is obtained from analysis of recombinant inbred strains, further fine-scale mapping can be pursued in an advanced intercross line (13, 14). We have maintained an advanced intercross line of more than 120 individuals each generation by random mating from the F2 generation. If necessary, replicate F2 populations can be generated again from the parental strains. The combination of these genetic mapping resources with strains showing variability in growth, obesity, and glucose levels, in addition to their differential response to a high-fat diet, makes the LG/J × SM/J cross an excellent model system for the polygenic basis of complex traits.

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REFERENCES


